

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k113439

B. Purpose for Submission:

New device

C. Measurand:

IgG antibodies to AMA-M2, M2-3E (BPO), Sp100, PML, gp210, LKM-1, LC-1, SLA/LP

D. Type of Test:

Manual and automated read-out, qualitative immunoblot assay

E. Applicant:

EUROIMMUN US Inc.

F. Proprietary and Established Names:

EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit

G. Regulatory Information:

1. Regulation section:

21CFR§866.5090 – Antimitochondrial antibody immunological test system
2 CFR§866.5660 – Multiple autoantibodies immunological test system

2. Classification:

Class II

3. Product code:

DBM - Antimitochondrial antibody, indirect immunofluorescent, antigen, control
NUM - Autoantibodies, nuclear body protein, Sp100
NRI - Autoantibodies, nuclear pore glycoprotein gp210
NIY - Autoantibodies, anti-soluble liver antigen (SLA), autoimmune hepatitis
NBS - Autoantibodies, LKM-1(liver/kidney microsome, type 1)

4. Panel:

Immunology (82)

H. Intended Use:

1. Intended use(s):

The EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit is an immune line-blot strip test intended for the qualitative detection of IgG class antibodies against 8 different antigens: AMA-M2, M2-3E (BPO), Sp100, PML, gp210, LKM-1, LC-1 and SLA/LP in human serum and plasma (EDTA, Li-heparin, Citrate).

Detection of these antibodies is used as an aid in the diagnosis of autoimmune liver diseases in conjunction with other laboratory and clinical findings.

2. Indication(s) for use:

Same as intended use

3. Special conditions for use statement(s):

For Prescription use only.

4. Special instrument requirements:

CanoScan LiDE Series flatbed scanner using ScanGear and EUROLiNE Scan softwares for automated read.

I. Device Description:

The EUROLiNE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit consists of antigen coated line blot strips, a positive control (100x concentrate), biotin-ExtrAvidin-alkaline phosphatase-labeled goat anti-human IgG conjugate (10X concentrate), sample buffer (ready-to-use), wash buffer (10X concentrate), Nitrobluetetrazoliumchloride/5-Bromo-4-chloro-3-indolylphosphate (NBT/BCIP) substrate solution (ready-to-use), incubation tray and test instruction.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) number(s):

EUROLiNE Profile Autoimmune Liver Disease Autoantibodies	Predicate device	510(k) number
Anti-AMA-M2/M2-3E (BPO)	Quanta Lite M2 EP (MIT3) ELISA	k052262
Anti-Sp100 and PML	Quanta Lite Sp100 ELISA	k050662
Anti-gp210	Quanta Lite gp210 ELISA	k040885
Anti-LKM-1 and LC-1	Quanta Lite LKM-1 ELISA	k000535
Anti-SLA/LP	Quanta Lite SLA ELISA	k021482

2. Comparison with predicate:

Similarities			
Item	Device		Predicate
Intended Use	Qualitative detection of IgG antibodies against 8 different antigens complete to aid in the diagnosis of autoimmune liver diseases.		Same (when combined)
Capture antigens	Sp100	Recombinant Sp100, expressed by cloning the corresponding human cDNA in <i>E.coli</i>	Same
	gp210	Recombinant gp210, expressed by cloning the corresponding	Same

Similarities			
Item	Device		Predicate
		human cDNA in <i>E.coli</i>	
	LKM-1	Recombinant cytochrome P450 IID6, expressed by cloning the corresponding human cDNA in insect cells using a baculovirus vector.	Same
	SLA/LP	Recombinant SLA/LP, expressed by cloning the corresponding human cDNA in <i>E.coli</i>	Same
Detection antibody	Goat anti-human IgG		Same
Sample dilution	1:101		Same

Differences			
Item	Device		Predicate
Assay format	Qualitative, positive/negative		Semi-quantitative
Solid phase	Membrane test strips		Polystyrene microwells
Instrument	Manual visual readout		Spectrophotometer
Capture antigens	AMA-M2	Natively purified from bovine heart	Affinity purified recombinant M2 EP MIT3.
	M2-3E (BPO)	Recombinant fusion protein, produced in <i>E.coli</i>	
	PML	Recombinant PML, expressed by cloning the corresponding human cDNA in <i>E.coli</i>	Not included
	LC-1	Recombinant LC-1 expressed by cloning the corresponding human cDNA in insect cells using a baculovirus vector.	Not included
Sample type	Serum or plasma (EDTA, Li-heparin, Citrate)		Serum
Controls	One positive control, 100X concentrate		3 controls (high positive, low positive, negative)
Conjugate	biotin-ErxtAvidin-alkaline phosphatase, 10X concentrate		horseradish peroxidase
Substrate	NBT/BCIP		3,5',5',5' Tetramethylbenzidine
Interpretation of results	positive/negative compared to reaction control card		Units

K. Standard/Guidance Document Referenced (if applicable):

DIN EN 13640:2002: Stability testing of in vitro diagnostic reagents

L. Test Principle:

The principle of the EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit is that of an enzyme linked immunosorbent assay (ELISA), using a membrane as the solid phase instead of microtiter wells. Different purified antigens have been coated and applied in easy to read lines (bands) onto a membrane strip.

Autoantibodies in patient samples bind to the bands and are detected via a secondary antibody linked to an enzyme. The strips are evaluated visually by comparison of the band intensity with the reaction control card or scanned and then evaluated with EUROLineScan.

The control band on the strips contains (non-specific) anti-human IgG, which reacts with the sample IgG to show a color reaction if the incubation was performed correctly and so represents a function test on each single strip.

The positive control contains a mixture of the targeted antibodies which bind to the antigen coated on the blot strips. A strip incubated with the positive control shows a positive result. If either the control band or the strip incubated with the positive control is negative, test results are invalid and should be repeated.

The qualitative results are reported for each individual antibody separately as positive or negative. The intensity of the reaction is not reported but only as a means to distinguish between a positive and negative reaction and not as an indication of disease status. The interpretation of the test results does not include a combined score or diagnosis.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

Test results were evaluated by visual or automated reading of the test strips.

For visual evaluation, the reaction intensity of each antigen band on the test strip was compared to the two color bars on the reaction control card that correspond to the intensities just below (negative) and just above (positive) the cut-off.

For automated evaluation, the test strips are scanned using a flatbed scanner and evaluated with EUROLineScan with a cut-off of 11 grey scale units.

a. Precision/Reproducibility:

i. Visual evaluation.

Assay reproducibility was determined by testing 5 to 9 samples that cover the complete range of results (negative, positive and near to cut-off) for each antigen (see table below). The intra-assay reproducibility is based on 20 replicates tested in one day and the inter-assay reproducibility on 20 different runs, each run performed by the same reader on a different day. The lot-to-lot reproducibility was tested in 3 different runs using 3 different lots. The reproducibility data showed no positive sample was

found negative and vice versa.

The inter-reader reproducibility of 3 samples that cover the complete range of results (negative, positive and near to cut-off) for each antigen (see table below) was evaluated by 3 different technicians and under 3 different light conditions (sunlight, neon light and electric bulb light). No deviation was observed between the individual readings and from the light conditions.

Intra-assay reproducibility

Antigen band	Sample characterization	Sample Number	Visual evaluation result	
			% pos	% neg
AMA-M2	pos	2	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	2	0%	100%
M2-3E	pos	2	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	2	0%	100%
Sp100	pos	1	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	3	0%	100%
PML	pos	1	100%	0%
	pos (near to cut-off)	1	100%	0%
	neg	3	0%	100%
gp210	pos	1	100%	0%
	pos (near to cut-off)	1	100%	0%
	neg	3	0%	100%
LKM-1	pos	2	100%	0%
	neg (near to cut-off)	1	0%	100
	neg	2	0%	100%
LC-1	pos	1	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	3	0%	100%
SLA/LP	pos	1	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	3	0%	100%

Inter-assay reproducibility

Antigen band	Sample characterization	Sample Number	Visual evaluation result	
			% pos	% neg
AMA-M2	pos	2	100%	0%
	pos (near to cut-off)	3	100%	0%
	neg (near to cut-off)	1	40%	60%
	neg (near to cut-off)	1	55%	45%
	neg	2	0%	100%
M2-3E	pos	2	100%	0%
	pos (near to cut-off)	1	100%	0%
	neg (near to cut-off)	3	95%	5%
	neg (near to cut-off)	1	90%	10%
	neg	2	0%	100%

Antigen band	Sample characterization	Sample Number	Visual evaluation result	
			% pos	% neg
Sp100	pos	2	100%	0%
	pos (near to cut-off)	5	100%	0%
	neg	2	0%	100%
PML	pos	1	100%	0%
	pos (near to cut-off)	1	100%	0%
	neg (near to cut-off)	2	80%	20%
	neg (near to cut-off)	2	75%	25%
	neg	2	0%	100%
gp210	pos	2	100%	0%
	pos (near to cut-off)	1	100%	0%
	neg (near to cut-off)	1	45%	55%
	neg (near to cut-off)	1	40%	60%
	neg	2	0%	100%
LKM-1	pos	1	100%	0%
	pos (near to cut-off)	3	100%	0%
	neg (near to cut-off)	2	80%	20%
	neg	2	0%	100%
LC-1	pos	1	100%	0%
	pos (near to cut-off)	1	100%	0%
	neg (near to cut-off)	1	90%	10%
	neg (near to cut-off)	1	80%	20%
	neg (near to cut-off)	1	75%	25%
	neg	2	0%	100%
SLA/LP	pos	1	100%	0%
	pos (near to cut-off)	1	100%	0%
	neg (near to cut-off)	2	55%	45%
	neg (near to cut-off)	1	45%	55%
	neg (near to cut-off)	1	40%	60%
	neg	2	0%	100%

Inter-reader reproducibility:

Antigen band	Sample characterization	Sample Number	Visual evaluation result	
			% pos	% neg
AMA-M2	pos	2	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	2	0%	100%
M2-3E	pos	3	100%	0%
	neg	2	0%	100%
Sp100	pos	2	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	2	0%	100%
PML	pos	2	100%	0%
	neg	3	0%	100%
gp210	pos	2	100%	0%
	neg	3	0%	100%
LKM-1	pos	2	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	2	0%	100%

Antigen band	Sample characterization	Sample Number	Visual evaluation result	
			% pos	% neg
LC-1	pos	2	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	2	0%	100%
SLA/LP	pos	1	100%	0%
	neg (near to cut-off)	1	0%	100%
	neg	3	0%	100%

ii. Automated evaluation.

The reproducibility of the automatic evaluation was investigated by repeated scanning and analysis of test strips incubated with 16 different serum samples displaying signals for different antibodies near the cut off. The processed test strips were scanned using three different flatbed scanners, each scanner was used 10 times scanning the same strips and the results were evaluated by EUROLinScan. The scanner intensity values of the 30 analyses were used to calculate coefficients of variation (CV's). The results are shown in the tables below.

Samples near the cut-off (n = 3 x 10 = 30)

Sample	EUROLinScan Intensity values		
	Mean value	SD	% CV
AMA-M2	13	0.7	5.5
M2-3E	14	0.4	2.7
Sp100	12	0.4	3.1
PML	13	0.4	3.4
gp210	12	0.0	0.0
LKM-1	14	0.5	3.9
LC-1	12	0.2	1.5
SLA/LP	14	0.7	4.9

Positive samples (n = 3 x 10 = 30)

Sample	EUROLinScan Intensity values		
	Mean value	SD	% CV
AMA-M2	69	0.7	1.0
M2-3E	37	0.4	1.0
Sp100	47	0.6	1.3
PML	66	0.4	0.7
gp210	51	0.7	1.3
LKM-1	73	0.6	0.8
LC-1	not available		
SLA/LP	39	0.4	0.9

iii. Comparability of visual and automatic reading

The use of the EUROLinScan software compared to visual reading was investigated using a panel of serum sample preparations covering the whole range of antigens. The samples were tested in 20 different runs, each run on a different day using the same kit lot. Each run was performed by the same technician and evaluation was performed both

visually using the reaction control card and automatically using the EUROLinScan software with a cut-off of 11 grey scale units. The results are shown in the table below. Only a few results from sample preparations exactly at the cut-off gave discrepant results between visual and automatic reading.

Antigen	Sample Characterization	Visual evaluation result		EUROLinScan result		Grey scale units result	
		% pos	% neg	% pos	% neg	Mean	Range
AMA-M2	pos (near to cut-off)	100%	0%	100%	0%	15	13 – 18
	pos	100%	0%	100%	0%	68	60 - 76
	Neg	0%	100%	0%	100%	1	0 - 1
	neg	0%	100%	0%	100%	1	0 - 2
	pos	100%	0%	100%	0%	54	48 - 58
	pos (near to cut-off)	100%	0%	100%	0%	13	11 - 15
	pos (near to cut-off)	100%	0%	100%	0%	14	11 - 16
	neg (near to cut-off)	40%	60%	40%	60%	10	6 – 12
	neg (near to cut-off)	55%	45%	55%	45%	11	8 – 12
M2-3E	pos (near to cut-off)	100%	0%	100%	0%	18	14 - 23
	pos	100%	0%	100%	0%	47	38 - 57
	neg	0%	100%	0%	100%	2	2 - 3
	neg	0%	100%	0%	100%	3	2 - 4
	pos	100%	0%	100%	0%	40	32 - 45
	pos (near to cut-off)	95%	5%	95%	5%	13	10 - 15
	neg (near to cut-off)	95%	5%	95%	5%	12	10 - 15
	neg (near to cut-off)	90%	10%	90%	10%	12	10 - 15
	pos (near to cut-off)	95%	5%	95%	5%	13	10 – 15
Sp100	pos	100%	0%	100%	0%	45	38 - 49
	pos (near to cut-off)	100%	0%	100%	0%	14	11 - 17
	neg	0%	100%	0%	100%	0	0 - 1
	neg	0%	100%	0%	100%	0	0 - 1
	pos	100%	0%	100%	0%	86	75 - 96
	pos (near to cut-off)	100%	0%	100%	0%	14	11 - 17
	pos (near to cut-off)	100%	0%	100%	0%	14	11 - 17
	pos (near to cut-off)	100%	0%	100%	0%	14	11 - 18
	pos (near to cut-off)	100%	0%	100%	0%	14	11 - 19
PML	pos (near to cut-off)	100%	0%	100%	0%	16	12 - 20
	pos	100%	0%	100%	0%	68	62 - 78
	neg	0%	100%	0%	100%	1	1 - 2
	neg	0%	100%	0%	100%	1	0 - 2
	neg (near to cut-off)	75%	25%	75%	25%	12	8 - 14
	neg (near to cut-off)	75%	25%	75%	25%	12	10 - 14
	neg (near to cut-off)	80%	20%	80%	20%	12	7 - 14
	neg (near to cut-off)	80%	20%	80%	20%	11	10 – 13
gp210	pos (near to cut-off)	100%	0%	100%	0%	13	11 - 15
	pos	100%	0%	100%	0%	53	46 - 58
	neg	0%	100%	0%	100%	1	1 - 2
	neg	0%	100%	0%	100%	0	0 - 1
	pos	100%	0%	100%	0%	135	131 - 140
	neg (near to cut-off)	45%	55%	45%	55%	11	8 - 12
	neg (near to cut-off)	40%	60%	40%	60%	10	9 - 12
	neg (near to cut-off)	45%	55%	45%	55%	11	9 – 13
	neg (near to cut-off)	40%	60%	40%	60%	11	9 - 13

Antigen	Sample Characterization	Visual evaluation result		EUROLineScan result		Grey scale units result	
		% pos	% neg	% pos	% neg	Mean	Range
LKM-1	pos (near to cut-off)	100%	0%	100%	0%	13	12 - 16
	pos	100%	0%	100%	0%	71	63 - 79
	neg	0%	100%	0%	100%	1	0 - 2
	neg	0%	100%	0%	100%	1	0 - 1
	pos (near to cut-off)	100%	0%	95%	5%	14	10 - 17
	pos (near to cut-off)	100%	0%	100%	0%	13	12 - 16
	neg (near to cut-off)	80%	20%	80%	20%	11	10 - 14
	neg (near to cut-off)	80%	20%	80%	20%	12	10 - 14
LC-1	pos	100%	0%	100%	0%	52	36 - 59
	pos	100%	0%	100%	0%	98	89 - 104
	pos (near to cut-off)	100%	0%	100%	0%	12	11 - 16
	neg	0%	100%	0%	100%	1	0 - 2
	neg	0%	100%	0%	100%	0	0 - 2
	neg (near to cut-off)	55%	45%	40%	60%	11	8 - 17
	neg (near to cut-off)	90%	10%	90%	10%	12	10 - 16
	neg (near to cut-off)	75%	25%	75%	25%	12	10 - 14
	neg (near to cut-off)	80%	20%	80%	20%	12	10 - 14
SLA/LP	pos (near to cut-off)	100%	0%	100%	0%	16	13 - 18
	pos	100%	0%	100%	0%	41	36 - 45
	neg	0%	100%	0%	100%	1	0 - 1
	neg	0%	100%	0%	100%	0	0 - 1
	neg (near to cut-off)	55%	45%	55%	45%	11	8 - 12
	neg (near to cut-off)	40%	60%	40%	60%	11	8 - 14
	neg (near to cut-off)	45%	55%	45%	55%	11	10 - 14
	neg (near to cut-off)	55%	45%	55%	45%	11	8 - 14

b. *Linearity/assay reportable range:*

Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability: There are no reference standards for these analytes.

Kit Stability:

i. *Real-time and Accelerated stability*

The stability studies were performed in accordance with EN 13640 (Stability Testing of *In Vitro* Diagnostic Reagents) to demonstrate unopened kit shelf-life stability (from the date of manufacture when stored at recommended temperature 2-8°C) and opened kit shelf-life stability. The acceptance criteria are that results do not differ more than one result level [pos, pos (near the cutoff), neg (near the cutoff) and neg] from the reference run.

For real-time stability study, three lots of all kit components stored at recommended storage temperature 2-8°C were evaluated at different occasions with three samples per antigen band. Original sealed kits and opened kits were demonstrated to be stable for up to 18 and 12 months, respectively, when stored at 2-8°C.

For accelerated study, three lots of all kits components were stored for 7 days at 37°C and evaluated with 3 samples per antigen band. The same lots stored at 4°C were used as reference. Reagents were shown to be stable for 7 days at 37°C.

ii. *Transport stability*

To simulate transportation of kits from Europe to US, one lot of an example EuroLine test kit with equal composition and technology as EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit was stored for 7 days at 4°C and -20°C and evaluated with 4 different samples. Transportation has no significant influence on the results.

d. *Detection limit:*

Not applicable

e. *Analytical specificity:*

Cross-reactivity: Cross-reactivity was investigated using a panel of samples serologically positive for antibodies to granulocyte cytoplasm (n = 10), thyroid gland antigens (n=10), islet cell antigens (n=10), cardiolipin /anti-phospholipid syndrome (n=5) and the CDC ANA reference panel (n=12). Clinical samples from the following groups were also included: autoimmune hepatitis type 1 (n=84), primary sclerosing cholangitis (n=19), systemic lupus erythematosus (n=10), rheumatoid arthritis (n=50), celiac disease (n=7), non-alcoholic steatohepatitis (n=30) and viral hepatitis (HBV, HCV; n=39). Out of 286 total samples, 9 samples tested positive.

Interferences: Interference testing was performed for each antigen using at least 5 samples that cover the complete range of results (negative, positive and near to cut-off) for each antigen. Each sample was spiked with three different levels of endogenous interfering substances, namely hemoglobin, triglycerides and bilirubin. Evaluation of test results was performed visually and no significant interference was observed for concentrations up to 500 mg/dl for hemoglobin, 2000 mg/dl for triglycerides and 40 mg/dl for bilirubin.

f. *Assay cut-off:*

The cut-off is predefined by the visual evaluation. A sample is positive if the respective band is clearly visible. The cutoff for each antigen on the EUROLINE was set to the lowest limit of a clearly visible band. To achieve the uniform cut-off for each antigen, during the production several sample strips for each antigen are manufactured with the antigen used in different dilutions. These sample strips are then processed with positive and negative reference sera and the optimal dilution for each antigen is identified. Afterwards the strips are manufactured using each antigen in its optimal dilution.

To confirm the assay cut-off, 261 clinically characterized samples from PBC and AIH patients, as well as 171 control samples were tested. The results

showed that negative and positive results can clearly be discriminated by the assay.

2. Comparison studies:

a. *Method comparison with predicate device:*

A total of 295 clinically characterized samples (99 from patients with autoimmune hepatitis, 89 from patients with primary biliary cirrhosis, 15 from patients with AIH/PBC overlap syndrome, 42 from patients with viral hepatitis, and 50 from patients with rheumatoid arthritis (RA)) were evaluated and results were compared to the results for the predicate devices. In addition, 6 to 29 artificial samples with antibody concentrations close to the cut-off were created for each antigen by mixing positive samples with negative sample as diluent of the same matrix. The results and the positive and negative agreement between the device and the predicates are shown below. Borderline results (from the predicate) were not included in the agreement calculations.

		Predicate ELISA			Positive agreement*	
		positive	borderline	negative	Negative agreement*	
					% (95% C.I.)*	
EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit	n = 281	M2 EP (MIT3)				
	AMA-M2 and/or M2-3E	positive	97	0	2	Pos: 95.1 % (88.9 – 98.4 %)
		negative	5	4	173	Neg: 98.9 % (95.9 – 99.9 %)
	n = 293	Sp100				
	Sp100	positive	34	1	2	Pos: 94.4 % (81.3 – 99.3 %)
		negative	2	2	252	Neg: 99.2 % (97.2 – 99.9 %)
	n = 296	gp210				
	gp210	positive	33	2	30***	Pos: 100 % (89.4 – 100 %)
		negative	0	0	231	Neg: 88.5 % (84.0 – 92.1 %)
	n = 325	LKM-1				
LKM-1	positive	50	0	3	Pos: 92.6 % (82.1 – 97.9 %)	
	negative	4	1	267	Neg: 98.9 % (96.8 – 99.8 %)	
n = 298	SLA					
SLA/LP	positive	30	0	1	Pos: 100 % (88.4 – 100 %)	
	negative	0	1	266	Neg: 99.6 % (97.9 – 100.0 %)	

* Calculations do not include borderline samples; ** 20 PBC, 1 artificial; *** 16 PBC, 7 AIH, 6 AIH/PBC, 1 RA.

b. *Matrix comparison:*

Comparisons between serum and each of EDTA, heparin, and citrated plasma were performed using 8-11 sample pairs selected to cover the complete range of results (negative, positive and close to cut-off) for each antigen. The results found no positive sample was found negative and vice versa.

1. Clinical studies:

a. *Clinical Sensitivity:*

A total of 734 clinically characterized samples obtained from different study sites were analyzed by the EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit. The sites providing the indicated panel of samples are as follow:

Panels of clinical samples	Sites
AIH	Prof. Lohse, University Clinic Eppendorf, Hamburg, Germany
	Mr. Gordon Dimmock, EUROIMMUN UK Ltd.
	Prof. D. Bogdanos, Institute of Liver Studies, School of Medicine, King's College Hospital, London, UK
PBC	Prof. Lohse, University Clinic Eppendorf, Hamburg, Germany
	Mr. Gordon Dimmock, EUROIMMUN UK Ltd.
	Prof. Fritzler, Department of Medicine, Faculty of Medicine, University of Calgary, Calgary, AB, Canada
Viral hepatitis	Prof. Lohse, University Clinic Eppendorf, Hamburg, Germany
Primary sclerosing cholangitis	Dr. Stöcker, Groß Grönau, Germany

The results of the clinical studies are shown in the following tables:

Sensitivity for Primary biliary liver cirrhosis (PBC)

Panel	n (men, women)	Mean age (age range)	EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit Positive (% positive) (95% C.I.)				
			AMA-M2	M2-3E	Sp100	PML	gp210
PBC	205 (20,185)	58 y (22-90 y)	175 (85.4 %) (79.8 – 89.9 %)	160 (78.0 %) (71.8 – 83.5 %)	54 (26.3 %) (20.5 – 32.9 %)	58 (28.3 %) (22.2 – 35.0 %)	68 (33.2 %) (26.8 – 40.1 %)

Sensitivity for Autoimmune hepatitis (AIH)

Panel	n (men, women)	Mean age (age range)	EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit Positive (% positive) (95% C.I.)		
			LKM-1	LC-1	SLA/LP
AIH	163 (20, 59, 84 unknown)	38 y (1-86 y, 84 unknown)	20 (12.3 %) (7.7 – 18.3 %)	15 (9.2 %) (5.2 – 14.7 %)	15 (9.2 %) (5.2 – 14.7 %)
Type 1	142 (16, 42, 84 unknown)	48 y (20-86 y, 84 unknown)	2 (1.4 %) (0.2 – 5.0 %)	1 (0.7 %) (0.0 – 3.9 %)	15 (10.6 %) (6.0 – 16.8 %)
Type 2	21 (4, 17)	12 y (1-45 y)	18 (85.7 %) (63.7 – 97.0 %)	14 (66.7 %) (43.0 – 85.4 %)	0 (0.0 %) (0.0 – 16.1 %)

b. Clinical specificity:

Specificity for PBC

Panel	n (men, women)	Mean age (age range)	EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit Negative (% negative) (95% C.I.)				
			AMA-M2	M2-3E	Sp100	PML	gp210
AIH	163 (20, 59,	38 y (1-86 y,	162 (99.4 %)	162 (99.4 %)	162 (99.4 %)	163 (100 %)	154 (94.5 %)

Panel	n (men, women)	Mean age (age range)	EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit Negative (% negative) (95% C.I.)				
			AMA-M2	M2-3E	Sp100	PML	gp210
	84 un- known)	84 un- known)					
Viral hepatitis	39 (16, 23)	48 y (25-84 y)	39 (100 %)	39 (100 %)	39 (100 %)	39 (100 %)	39 (100 %)
PBC	19 (12, 7)	48 y (21-73 y)	19 (100 %)	19 (100 %)	19 (100 %)	19 (100 %)	19 (100 %)
Further controls*	308 (140, 167,1 un- known)	18 y (0-83 y)	304 (98.7 %)	307 (99.7 %)	308 (100 %)	304 (98.7 %)	302 (98.1 %)
Total	529		524 (99.1 %) (97.8 – 99.7 %)	527 (99.6 %) (98.6 – 100 %)	528 (99.8 %) (99.0 – 100 %)	525 (99.2 %) (98.1 – 99.8 %)	514 (97.2 %) (95.4 – 98.4 %)

Specificity for AIH

Panel	n (men, women)	Mean age (age range)	EUROLINE Profile Autoimmune Liver Disease 8 Ag (IgG) Kit Negative (% negative) (95% C.I.)		
			LKM-1	LC-1	SLA/LP
PBC	205 (20, 185)	58 y (22-90 y)	204 (99.5 %)	205 (100 %)	199 (97.1 %)
Viral hepatitis	39 (16, 23)	48 y (25-84 y)	39 (100 %)	39 (100 %)	39 (100.0 %)
PSC	19 (12, 7)	48 y (21-73 y)	19 (100 %)	19 (100 %)	19 (100.0 %)
Further controls*	308 (140,167, 1 unkn.)	18 y (0-83 y)	308 (100 %)	306 (99.4%)	307 (99.7 %)
Total	571		570 (99.8 %) (99.0 – 100 %)	569 (99.6 %) (98.7 – 100 %)	564 (98.8 %) (97.5 – 99.5 %)

*from the following groups: systemic lupus erythematosus (n = 10), Sjögren's syndrome (n = 5), systemic sclerosis (n = 5), myositis (n = 4), rheumatoid arthritis (n = 50), diabetes (n = 9), celiac disease (n = 7), A1 antitrypsin deficiency (n = 30), Alagille syndrome (n = 29), biliary atresia (n = 35), giant cell hepatitis (n = 16), non-alcoholic steatohepatitis (n = 30), hemochromatosis (n = 17), progressive familial intrahepatic cholestasis (n = 31), Wilson's disease (n = 30)

- c. Other clinical supportive data (when a. and b. are not applicable):
Not applicable.
4. Clinical cut-off:
See Assay cut-off.
5. Expected values/Reference range:
The levels of analytes were analyzed in a panel of 150 healthy blood donors of mixed age and sex. None of these samples were found positive. It is

recommended that each laboratory determine its own normal range based on the population and equipment used.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.