EUROIMMUN Medizinische Labordiagnostika AG

Differentiated *Borrelia* diagnostics

All screening and confirmatory tests from one source

- Test systems for qualified two-step diagnostics according to the latest recommendations
- Comprehensive portfolio: ELISA, ChLIA, IIFT and immunoblots based on native and recombinant antigens
- NEW! EUROMicroblots – miniaturised immunoblots in microplate format
- Flexible automation solutions for all test systems

Lyme disease

Borrelia are the causative agent of Lyme disease, a bacterial infection that is transmitted through bites from ticks of the genus *Ixodes*. The most important human pathogenic *Borrelia* genospecies are collectively referred to as *Borrelia burgdorferi* sensu lato. The group includes *Borrelia afzelii*, *Borrelia burgdorferi* sensu stricto, *Borrelia garinii* and *Borrelia spielmanii*. An infection with *Borrelia* can manifest with dermatological, neurological or internal symptoms. The clinical expression of borreliosis is divided into three stages:

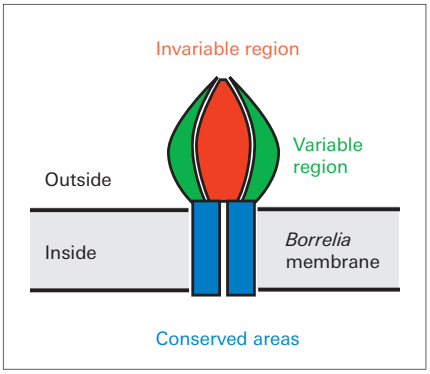
I) Localised early manifestation	II) Disseminated early manifestation	III) Late manifestation
Primary symptom is the characteristic **erythema migrans**, which occurs a few days to several weeks after the infection and spreads radially with central clearing. This is often accompanied by influenza-like symptoms, such as fever, shivering, headaches and vomiting. In rare cases, bulging nodular skin infiltrates develop, which consist predominantly of lymphocytes (lymphadenosis cutis benigna). IgM and later IgG antibodies are generally first detected during serological analysis. However, they may also be absent, especially in very short disease courses. This stage can be followed by spontaneous healing or develop into general borreliosis (see stages II and III).	Several weeks to months after the tick bite the second stage of the disease develops. It is characterised by **neurological, cardiac** (e.g. myocarditis) **and rheumatological** (e.g. arthritis) **manifestations**. The attack on the nervous system frequently appears as radiculitis (Bannwarth's syndrome), mono- or plexus neuritis with motor (mostly facial paralysis) and sensory disorders. Meningitis, myelitis, encephalitis and cerebral vasculitis occur less frequently. In this stage, antibodies against *Borrelia* antigens, primarily that of class IgG, can be detected in 70 to 90% of patients.	The characteristic manifestation of the late stage of the disease, months to years after the *Borrelia* infection, is a **chronic involvement of the joints, epidermis and CNS**. **Destructive arthritis** develops in many cases, predominantly in the large and mostly in the knee joints. A typical **acrodermatitis chronica atrophicans** is formed in the epidermis of the extremities. IgG antibodies can be detected in 90 to 100% of stage III patients, while IgM antibodies no longer play a role.

The diagnosis of Lyme disease is based on the patient anamnesis, clinical findings and the detection of antibodies against *Borrelia* antigens. Serology played a leading role in the discovery of Lyme disease and nowadays helps to achieve a diagnostic breakthrough in many cases. The prevalence of antibodies against *Borrelia* in Germany is around 20% in the case of forest workers, and below 5% for town dwellers. Following a tick bite, a serological baseline status should be determined and the patient be monitored for *Borrelia* antibodies in the ensuing weeks. For the diagnosis of neuroborreliosis, the determination of intrathecally synthesised antibodies is of decisive importance.

VlsE: The main antigen for *Borrelia* serology

VlsE (**v**ariable major protein-**l**ike **s**equence, **e**xpressed) is a **surface protein of *B. burgdorferi* sensu lato** which plays a key role in the survival strategy of *Borrelia*. After penetration into the host organism, *Borrelia* bacteria constantly change the VlsE localised on their surface and, in this way, try to escape recognition and elimination by the immune system. *Borrelia* do not express VlsE when cultivated, but only in vivo under immunological stress. The antigen can therefore only be produced using recombinant techniques.

The VlsE protein is divided into several sections: conserved regions, which serve as transmembrane domains and anchor VlsE in the bacterial membrane, as well as variable and invariable regions. The variable regions of VlsE facing outwards are constantly changed by recombination, whereby the attacking immune system consistently encounters new, altered antigen epitopes. With living *Borrelia*, the invariable regions are covered by the variable regions and thus remain hidden from the immune system. When deceased *Borrelia* bacteria are processed by antigen-presenting cells, the complete VlsE protein is presented to the immune system and the host also forms **antibodies against the invariable and conserved regions of VlsE**. These antibodies are **highly suitable for *Borrelia* diagnostics because of the high level of conservation of their target antigens.** Using monospecific test systems, Lyme disease can be diagnosed in 85% of cases, regardless of the species, through the detection of antibodies against VlsE alone.

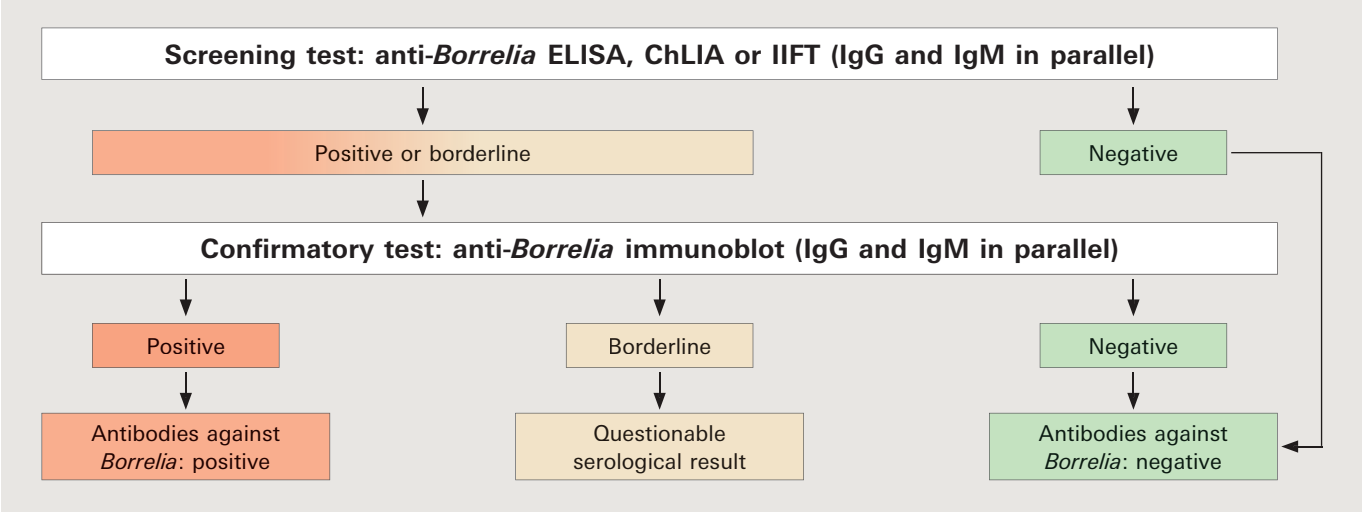


VlsE on *Borrelia* surface

Serological two-step strategy in infections with *Borrelia burgdorferi*

EUROIMMUN is one of the leading manufacturers of reagents for the diagnostics of infections with *B. burgdorferi* sensu lato. The product portfolio comprises all screening and confirmatory tests for the determination of antibodies against *Borrelia burgdorferi* which allow a qualified **two-step diagnostic procedure** as **recommended by the German Society for Hygiene and Microbiology, the Robert Koch Institute and the Centers for Disease Control and Prevention (USA)**.

In the first step, a preferably **sensitive screening test (ELISA, ChLIA or IIFT)** that also detects antibodies against the *Borrelia* major antigen VlsE is performed. During the early stage of borreliosis, the test result may still be negative. A second analysis should therefore be carried out after one to two weeks if borreliosis is indicated. In suspected cases of neuroborreliosis, *Borrelia*-specific antibodies are investigated simultaneously in CSF and serum.



If the screening test result is positive or borderline, it should be followed up by a **confirmatory test**. The **immunoblot** is the **method of choice** because it allows a reliable differentiation between antibodies against the individual specific and unspecific antigens. The reaction pattern of the different antigen bands is decisive for the diagnosis of borreliosis and the evaluation of the infection stage. Positive reactions of specific antigen bands in combination with significant clinical symptoms are considered to be an indication of an acute or past infection. If the immunoblot shows a negative result for IgG and IgM (after a positive or borderline screening test), an infection can generally be excluded. If the clinical suspicion of borreliosis persists, components of alternative *Borrelia* strains are used as test substrates in individual cases. Borderline immunoblot results combined with clinical symptoms should be followed up by further tests to monitor the disease course.

Possible result interpretation of the EUROIMMUN anti-*Borrelia* immunoblots:

Serological result		Final result
IgG	IgM	
Borderline or negative	**Borderline or negative**	No reliable detection of specific *Borrelia* antibodies. In the case of continued clinical suspicion, retest after one or two weeks (possibility of delayed antibody formation).
Borderline or negative	**Positive**	Detection of specific *Borrelia* antibodies indicates an early infection stage. Presence of chronic borreliosis unlikely. Possibility of a residual result with persisting IgM antibodies after successful therapy.
Positive (1 to 2 specific bands)	**Borderline or negative**	Detection of specific *Borrelia* antibodies indicates an early infection stage. Further tests for monitoring the disease course recommended to exclude residual antibodies from a past infection. The clinical symptoms should be taken into account!
Positive (1 to 2 specific bands)	**Positive**	Detection of specific *Borrelia* antibodies indicates an early infection stage. Also possibility of late manifestations, although atypical. Past infections with persisting IgM only occur in exceptional cases, particularly after therapy. Clinical symptoms and course of the disease are decisive. Serological monitoring of the disease course, if required.
Positive (> 2 specific bands)	**Borderline or negative**	Detection of specific *Borrelia* antibodies indicates chronic borreliosis (late clinical manifestation). An early infection stage is unlikely. A definitive differentiation between a florid infection and a residual result is not possible. Serological monitoring of the disease course, if required.
Positive (> 2 specific bands)	**Positive**	Detection of specific *Borrelia* antibodies indicates chronic borreliosis (late clinical manifestation). An early infection stage in secondary infections cannot be excluded. Residual antibodies after a recently cured borreliosis are possible (persisting IgM).

Note: Antibodies against several different variants of an antigen (e.g. VlsE, lipids) are considered as one band.

Screening test I: ELISA

Anti-Borrelia plus VlsE ELISA (IgG) and Anti-Borrelia ELISA (IgM)

- Native whole extracts from *Borrelia* strains *B. burgdorferi* sensu stricto, *B. afzelii* and *B. garinii*, incl. OspC (see bottom box)
- The Anti-Borrelia plus VlsE ELISA (IgG) also contains the recombinant *Borrelia* main antigen VlsE
- Excellent sensitivity due to broad antigen spectrum containing all diagnostically relevant proteins

Reference ranges: Levels of anti-*Borrelia burgdorferi* antibodies were measured in a panel of 500 healthy blood donors (University Clinic of Luebeck, Germany) using the EUROIMMUN ELISAs. With a cut-off value of 20 RU/ml, 5% (IgG) and 1.6% (IgM) of blood donors were anti-*Borrelia* positive, in agreement with the known infection rate in adults.

Prevalence: The prevalence of anti-*Borrelia* antibodies in the control panels (other infectious diseases: anti-CMV positive n = 18, anti-EBV positive n = 28, anti-*Toxoplasma* positive n = 7; rheumatic diseases: APF positive n = 10, RF (IgM) positive n = 10) corresponds to the data found in literature (Robert Koch Institute, Epidemiological Bulletin 14/98).

Panel	n	Anti-Borrelia plus VlsE ELISA (IgG)	Anti-Borrelia ELISA (IgM)
Other infectious diseases	53	13%	11%
Rheumatic diseases	20	15%	0%
Blood donors	500	5%	2%
Total	**573**	**6%**	**2%**

Clinical data: 364 sera from patients in different stages of clinically characterised borreliosis were analysed using the EUROIMMUN Anti-Borrelia plus VlsE ELISA (IgG) and the EUROIMMUN Anti-Borrelia ELISA (IgM). With parallel determination of IgG and IgM antibodies a sensitivity of 91 to 100% was achieved.

Panel	n	Anti-Borrelia plus VlsE ELISA (IgG) Anti-Borrelia ELISA (IgM)		
		IgG	IgM	IgG/IgM
Erythema migrans	205	76%	68%	**91%**
Neuroborreliosis	80	90%	49%	**96%**
Borrelia arthritis	49	84%	43%	**94%**
Acrodermatitis chron. atrop.	14	93%	21%	**93%**
Facial paralysis	16	100%	50%	**100%**

Anti-Borrelia Select ELISA (IgG and IgM)

- Selection of highly specific, recombinant *Borrelia* antigens, including VlsE (IgG) and OspC advanced (IgM)
- Significantly reduced cross reactivity compared to whole-antigen tests (cut-off ≥ 20 RU/ml):

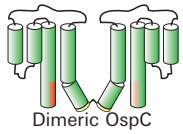
Panel	n	Anti-Borrelia plus VlsE ELISA (IgG)	Anti-Borrelia Select ELISA (IgG)	Anti-Borrelia ELISA (IgM)	Anti-Borrelia Select ELISA (IgM)
Anti-*Treponema pallidum* antibodies (highly positive sera)	92	65 (70.7%)	3 (3.3%)	26 (28.3%)	6 (6.5%)
Autoimmune diseases	27	6 (22.2%)	5 (18.5%)	7 (25.9%)	1 (3.7%)

Clinical data: 33 clinically characterised sera from patients in the early stage of Lyme disease (erythema migrans) were analysed using the Anti-Borrelia Select ELISA (IgG, IgM) and the Anti-Borrelia plus VlsE ELISA (IgG) and Anti-Borrelia ELISA IgM from EUROIMMUN. With parallel determination of IgG and IgM antibodies, the Anti-Borrelia Select ELISA (IgG, IgM) achieved the same sensitivity (91%) as the lysate-based tests.

Test system	IgG or IgM	IgG plus IgM
Anti-Borrelia Select ELISA (IgG)	21 (63.6%)	30 (91%)
Anti-Borrelia Select ELISA (IgM)	22 (66.7%)	
Anti-Borrelia plus VlsE ELISA (IgG)	27 (81.8%)	30 (91%)
Anti-Borrelia ELISA (IgM)	25 (75.8%)	

* cut-off, ≥ 20 RU/ml

In acute *Borrelia* infections, antibodies against native dimeric **OspC** (**o**uter **s**urface **p**rotein **C**) are the most important serological marker (sensitivity up to 90%). Since standardised production of the antigen is complicated, recombinant monomeric OspC is often used. For reliable identification of all *Borrelia* infections, high concentrations are used, which can lead to unspecific reactions. The **dimeric OspC advanced developed and patented** by EUROIMMUN provides a **higher specificity** than conventional recombinant OspC, at the same sensitivity as native OspC.


Dimeric OspC advanced

Screening test II: ChLIA

Anti-Borrelia ChLIA (IgG and IgM) for IDS-i10 and IDS-iSYS Multi-Discipline Automated System

- Chemiluminescence immunoassay (ChLIA) based on bead technology: recombinant *Borrelia* antigens, including VlsE (IgG) and dimeric OspC advanced (IgM) are immobilised on the surface of magnetic particles
- Exclusively automated processing using the random access devices IDS-i10 and IDS-iSYS Multi-Discipline Automated System

Diagnostic sensitivity and specificity: The performance of the EUROIMMUN Anti-Borrelia ChLIA (IgG and IgM) was determined using 134 samples from patients with suspected *Borrelia* infection and clinically and serologically precharacterised samples from a reference institute (panels 1 to 6). The sample panels were grouped based on clinical symptoms that provided information regarding the infection phase and on the therapy status. The test specificity was determined by analysing a reference panel of 81 samples comprising negative samples of the reference institute as well as samples from clinically inapparent children in whom *Borrelia* infection was unlikely but could not be entirely excluded given the natural infection rate (panel 7).

Panel	Total	EUROIMMUN Anti-Borrelia ChLIA (positive results)		
	n	IgG	IgM	IgG and/or IgM
1. Acute Lyme disease / erythema migrans	69	40.6%	73.9%	78.3%
2. Neuroborreliosis	3	100%	66.7%	100%
3. Lyme disease under / after therapy	37	54.1%	73.0%	91.9%
4. Residual antibodies or previous *Borrelia* infection	17	94.1%	17.6%	94.1%
5. Chronic Lyme disease	6	100%	33.3%	100%
6. Acrodermatitis chronica atrophicans Herxheimer	2	100%	50.0%	100%
7. Healthy donors without clinical indication of Lyme disease (reference panel)	81	0%	3.7%	3.7%

Correlation data: 171 or 271 samples from patients with suspected *Borrelia* infection (n = 197, European laboratory practice, daily laboratory routine; n = 34 samples from patients with clinically and serologically confirmed *Borrelia* infection, consecutive samples, European laboratory practice; n = 40 characterised quality assessment samples, Reference Institute for Bioanalytics RfB; Germany) were investigated using the Anti-Borrelia ChLIA (IgG or IgM) and the Anti-Borrelia Select ELISA (IgG or IgM) from EUROIMMUN.

n = 171		Anti-Borrelia Select ELISA (IgG)			
		positive	borderl.	negative	total
Anti-Borrelia ChLIA (IgG)	positive	77	2	6	85
	borderl.	0	0	1	1
	negative	1	0	84	85
	total	78	2	91	171

- Negative agreement: 93.3%
- Positive agreement: 98.7%
- Mean concordance: 95.8%

n = 271		Anti-Borrelia Select ELISA (IgM)			
		positive	borderl.	negative	total
Anti-Borrelia ChLIA (IgM)	positive	110	7	13	130
	borderl.	4	4	8	16
	negative	5	3	117	125
	total	119	14	138	271

- Negative agreement: 90.0%
- Positive agreement: 95.7%
- Mean concordance: 92.7%

Evaluations without borderline samples

Screening test III: IIFT

EUROPLUS: Anti-Borrelia IIFT plus VlsE and OspC

- Increased serological detection rate by combination of bacterial smears (*B. afzelii* and *B. burgdorferi*), recombinant VlsE and purified OspC
- Simple and standardised manual processing (TITERPLANE technique) – fully automatable

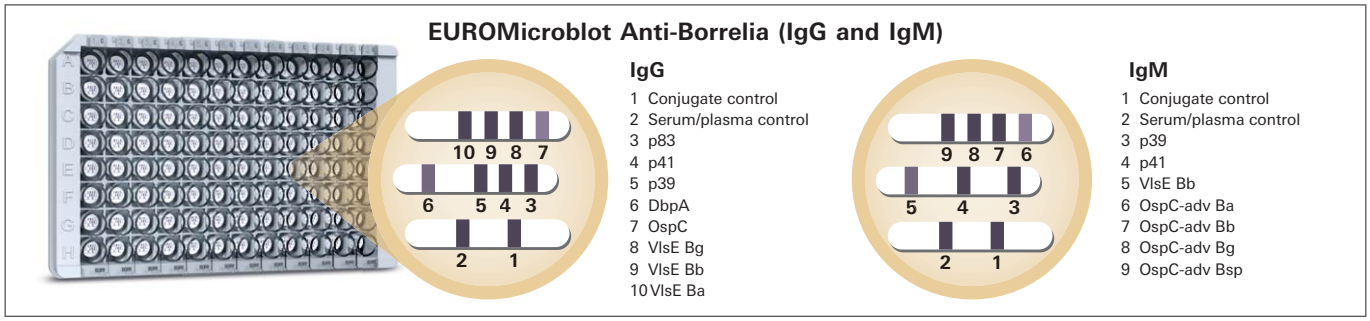
Clinical data: In a study, 577 Polish forest workers and 100 healthy blood donors were tested for antibodies against *Borrelia* antigens. For the substrate combination of *Borrelia afzelii* and *Borrelia burgdorferi* a sensitivity of 94% (IgG) and 77% (IgM), respectively, was found (reference: 137 (IgG) and 34 (IgM) sera with positive ELISA and Westernblot results). Using BIOCHIPs coated with VlsE or OspC these values can be increased to 98% and 91%, respectively. The single antigens showed a specificity of 100% (VlsE) and 98% (OspC) (reference: 234 (IgG) and 181 (IgM) sera with negative ELISA and Westernblot results).

Borrelia antigens	Sensitivity (prechar. panel)		Prevalence Blood donors	
	IgG n = 137	IgM n = 34	IgG n = 87	IgM n = 92
Borrelia afzelii	94%	77%	28%	3%
Borrelia burgdorferi	93%	71%	28%	3%
VlsE	89%	–	5%	–
OspC	–	85%	–	4%
B. afzelii + *B. burgdorferi*	94%	77%	28%	3%
B. afzelii + *B. burgd.* + VlsE	98%	–	29%	–
B. afzelii + *B. garinii* + OspC	–	91%	–	7%

For the automated processing and evaluation of the test systems, EUROIMMUN offers many flexible solutions for different throughputs, including the fully automated ELISA systems EUROIMMUN Analyzer I and I-2P and EUROLabWorkstation ELISA, the random access devices IDS-i10 and IDS-iSYS Multi-Discipline Automated System for ChLIA and the compact tabletop devices EUROBlotOne and EUROBlotMaster for EUROLINE test strips. In addition, our middleware EUROLabOffice 4.0 supports all laboratory processes, from request management to data archiving.

Confirmatory test: Immunoblots

EUROMicroblot



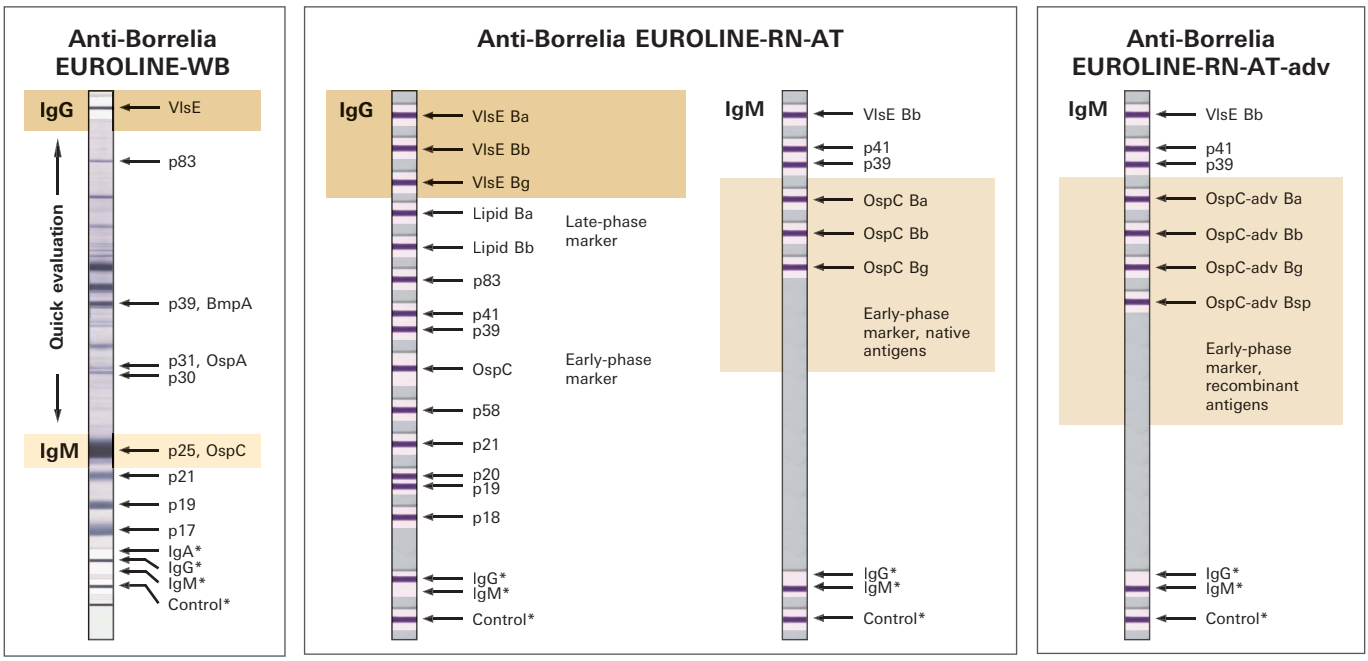
- Miniaturised immunoblots in 96-well microplate format – blot technology for high throughputs
- Parallel processing of screening and confirmatory tests in the same automated ELISA system
- Well-chosen combination of *Borrelia* antigens relevant for diagnostics: patented OspC advanced and VlsE of different genospecies, highly specific p39 (BmpA) and the late phase marker p83

62 and 58 certified quality assessment samples from two different reference laboratories were investigated using the EUROMicroblot Anti-Borrelia (IgG) and EUROMicroblot Anti-Borrelia (IgM), respectively. Compared to the specified target values of the QA institutes, positive agreement was 100 % (IgG, IgM) and negative agreement was 97.0 % (IgG) and 100 % (IgM).

Test system		Anti-*Borrelia burgdorferi* sensu lato characterisation by RfB/CSCQ	
		positive	negative
EUROMicroblot Anti-Borrelia (IgG); n = 62	positive	28	1
	negative	0	33
EUROMicroblot Anti-Borrelia (IgM); n = 58	positive	6	0
	negative	0	52

RfB: Reference Institute for Bioanalytics; CSCQ: Swiss Centre for Quality Control

EUROLINE



Ba: *Borrelia afzelii*, Bb: *Borrelia burgdorferi*, Bg: *Borrelia garinii*, Bsp: *Borrelia spielmanii*, * Control bands of all incubation steps

Anti-Borrelia EUROLINE-WB (IgG and IgM)

- Westernblot and line blot in one: whole antigen extract from *B. afzelii* plus membrane chip with recombinant VlsE as early-phase marker, regardless of the species
- Combines the advantages of both test systems and enables identification of atypical reactions at a high sensitivity
- Presence of a positive VlsE (IgG) or p25/OspC antigen band (IgM) allows at-a-glance evaluation

Clinical data: A panel of 115 clinically defined patient samples was investigated using the EUROIMMUN Anti-Borrelia EUROLINE-WB (IgG, IgM). The following prevalences were detected (only positive results were taken into account):

Panel	n	EUROIMMUN Anti-Borrelia EUROLINE-WB (IgG, IgM)		
		IgG	IgM	IgG/IgM
Erythema migrans	47	51%	57%	83%
Neuroborreliosis	27	78%	33%	81%
Borrelia arthritis	33	94%	6%	94%
Acrodermatitis chronica atrophicans	8	100%	13%	100%

Anti-Borrelia EUROLINE-RN-AT (IgG and IgM)

- Exclusive combination of diagnostically relevant *Borrelia* antigens: Early-phase markers OspC and VlsE of different genospecies, highly specific p39 (BmpA), late-phase marker p83 as well as native, immunogenic lipids
- Increased specificity due to specifically manufactured immunoreactive designer antigens (p58, p21, p20, p19 and p18)

Borrelia antigens	EUROLINE-RN-AT, IgG (n = 617*)	
	Sensitivity	Specificity
VlsE *B. afzelii*	65.5%	98.6%
VlsE *B. burgdorferi*	88.5%	98.6%
VlsE *B. garinii*	67.6%	95.3%
Lipid *B. afzelii*	25.1%	100.0%
Lipid *B. burgdorferi*	25.1%	99.6%
p83	53.7%	95.3%
p39	61.3%	98.6%
OspC	48.7%	95.7%
p58	20.7%	97.5%
p21	8.9%	99.3%
p20	7.1%	100.0%
p19	9.1%	99.3%
p18	22.4%	99.3%

Clinical data: The specificities of the antigens used in the Anti-Borrelia EUROLINE-RN-AT (IgG and IgM) determined by ROC analysis ranged from 95.3% to 100% (IgG) and from 96.8% to 99.4% (IgM). The sensitivities vary greatly. In particular the main antigen VlsE from *B. burgdorferi* (IgG) and OspC from *B. afzelii* and *B. garinii* (IgM) have a very high sensitivity.

Borrelia antigens	EUROLINE-RN-AT, IgM (n = 644*)	
	Sensitivity	Specificity
VlsE *B. burgdorferi*	4.9%	99.4%
p39	15.9%	99.0%
OspC native *B. afzelii*	88.2%	99.0%
OspC native *B. burgdorferi*	77.1%	99.2%
OspC native *B. garinii*	84.1%	96.8%

*274/236 patients with active borreliosis, 198/204 patients with suspected borreliosis, 28/45 patients with other infections, 117/159 healthy blood donors

Anti-Borrelia EUROLINE-RN-AT-adv (IgM)

- Easy-to-read line blot with recombinant antigens, including OspC advanced of various pathogenic *Borrelia* genospecies and VlsE from *B. burgdorferi*
- High specificity due to patented OspC advanced

Clinical data: 276 clinically defined patient samples were investigated using the Anti-Borrelia EUROLINE-RN-AT-adv (IgM). The prevalences for native OspC and OspC advanced of different genospecies were as follows:

Panel	n	Prevalence of anti-OspC antibodies (IgM)					
		B. afzelii		*B. burgdorferi*		*B. garinii*	
		adv	native	adv	native	adv	native
Active borreliosis	150	65%	61%	69%	54%	66%	64%
Past *Borrelia* infection (persisting IgM)	16	13%	13%	13%	13%	13%	19%
Acute EBV infection	10	0%	0%	0%	0%	0%	0%
Pregnant women	50	2%	2%	2%	2%	2%	2%
Blood donors	50	4%	4%	6%	4%	4%	2%

Neuroborreliosis diagnostics

EUROIMMUN CSF ELISA

- High clinical sensitivity (> 95 % in patients with clinically confirmed neuroborreliosis) and specificity (> 95 % in patients with other neurological diseases)
- Excellent correlation with results from quality assessment schemes (INSTAND e.V.)
- Very good reproducibility of results over the entire measurement range
- 4-point standard curve for highest accuracy; extended measurement range owing to optionally usable, additional calibrators (included in the test kit)
- Standardised dilution and incubation scheme allows efficient standardised automation
- Automated calculation of results (evaluation software EUROLabCSF)
- CSF / serum control pairs available

Anti-Borrelia EUROLINE-RN-AT (IgG and IgM) and Anti-Borrelia EUROLINE-RN-AT-adv (IgM)

- Broad antigen spectrum
- High specificity (100 %) and sensitivity (> 97 %), determined using clinically characterised CSF / serum pairs
- Low sample volumes (250 µl) and defined dilution factor for CSF (1 : 4) – without complicated calculations
- Short incubation periods (test result after approx. 300 min)
- Automatic processing with the EUROBlotMaster or EUROBlotOne (adapted incubations for CSF / serum pairs)
- Computer-aided evaluation using EUROLineScan (available from EUROIMMUN)

CXCL13 ELISA: Antigen detection of the activity and therapy marker CXCL13

- First CE-marked test for CXCL13 detection
- Early-phase marker in acute neuroborreliosis: high concentrations of CXCL13 can frequently be measured already at the start of the illness, often even before antibodies against *Borrelia* are detectable
- Marker for therapy monitoring: With successful antibiotic treatment, the CXCL13 concentration in the CSF sinks rapidly
- Differentiation between acute and past neuroborreliosis: pathological ASI/CSQ_{rel}, together with
  - a low CXCL13 concentration in the CSF: acute neuroborreliosis is rather unlikely
  - a high CXCL13 concentration in the CSF: acute neuroborreliosis is very likely
- 6 calibrators and 2 controls included in the test

EUROIMMUN test systems for *Borrelia* diagnostics

	Product name	Substrate	Order number	CSF tests
Screening tests	Anti-Borrelia ELISA (IgM)	Whole antigen, SDS extract from Ba / Bb / Bg	EI 2132-9601 M	EI 2132-L M
	Anti-Borrelia plus VlsE ELISA (IgG)	Whole antigen, SDS extract from Ba / Bb / Bg plus recomb. VlsE Bb	EI 2132-9601-2 G	EI 2132-L G
	Anti-Borrelia Select ELISA (IgG, IgM)	Recomb. Antigen mixture, incl. VlsE (IgG) or OspC-adv (IgM)	EI 2132-9601-5 G, M	
	Lyme ELISA (IgG / IgM)	VlsE, OspC	EI 2132-24 O	
	Anti-Borrelia ChLIA (IgG, IgM) Control Set Anti-Borrelia ChLIA (IgG, IgM)	Recomb. antigens, incl. VlsE (IgG) or OspC-adv (IgM)	LI 2132-10010 G, M LR 2132-10010 G, M	
	EUROPLUS: Anti-Borrelia afzelii and burgdorferi IIFT plus VlsE and OspC (IgG / IgM)	Smears of Ba and Bb (USA), incl. EUROPLUS BIOCHIPs with VlsE and OspC	FI 2136-1 G/M	
Confirmatory tests	Anti-Borrelia EUROLINE-RN-AT (IgG)	p18, p19, p20, p21, p58, OspC, p39, p41, p83, lipid Ba / Bb, VlsE Ba / Bb / Bg	DN 2131 G	DN 2131 G
	Anti-Borrelia EUROLINE-RN-AT (IgM)	OspC Ba / Bb / Bg, p39, p41, VlsE Bb	DN 2131 M	DN 2131 M
	Anti-Borrelia EUROLINE-RN-AT-adv (IgM)	OspC-adv Ba / Bb / Bg / Bsp, p39, p41, VlsE Bb	DN 2131-2 M	DN 2131-2 M
	Anti-Borrelia EUROLINE-WB (IgG, IgM)	Whole antigen, SDS extract from Ba plus recomb. VlsE	DY 2131-1 G, M	
	EUROMicroblot Anti-Borrelia (IgG)	p39, p41, p83, DbpA, OspC, VlsE Ba / Bb / Bg	KN 2131-9601 G	
	EUROMicroblot Anti-Borrelia (IgM)	p39, p41, OspC-adv Ba / Bb / Bg / Bsp, VlsE Bb	KN 2131-9601 M	
	CXCL13 ELISA	Anti-CXCL13 antibodies		EQ 6811-L

Ba: *Borrelia afzelii*, Bb: *Borrelia burgdorferi*, Bg: *Borrelia garinii*, Bsp: *Borrelia spielmanii*

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