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PRODUCT INFORMATION

2009 / 2010

Institut Virion\Serion GmbH
Serion Immundiagnostica GmbH

SERION ELISA *classic*, SERION ELISA *antigen*, SERION Multianalyt™, SERION CFT, SERION Antigens, SERION Automation

SERION ELISA

SERION Multianalyt™

SERION CFT

SERION Antigens

SERION Automation

Institut Virion\Serion GmbH, Serion Immundiagnostica GmbH, Friedrich-Bergius-Ring 19, 97076 Würzburg, Germany

Dear customer,

Welcome to the Product Catalogue 2009 / 2010 of Institut Virion\Serion GmbH and Serion Immundiagnostica GmbH.

Thank you for your interest in our products.

In this catalogue you will find comprehensive information concerning the various technologies we employ for the serological diagnosis of infectious diseases and the full scope of our product range.

Following the presentation of our **SERION ELISA products** in the first part of the catalogue we introduce the new **SERION Multianalyt™ technology** for the simultaneous detection of multiple parameters while using a small sample volume. Extensive information regarding our reagents for **Complement Fixation Tests (CFT)** is detailed in part III. Many of the **Antigens** we use are also available as bulk raw material and these are listed in the fourth part. Last but not least, we present you the **Immunomat™** ***TWIN*****system** and the **Immuno***flow*; our solutions for modern laboratory automation.

Please visit our website www.virion-serion.de for more details on our products and the newest information on current developments. Please do not hesitate to contact us if you have any questions regarding our products and services.

We look forward to offering you support in your endeavours.

Best regards from Würzburg, Germany

Yours sincerely
Institut Virion\ Serion GmbH
Serion Immundiagnostica GmbH

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Content

Institut Virion\Serion GmbH
Serion Immundiagnostica GmbH

Progress by Experience and Innovation

1978 saw the founding of Institut Virion\Serion GmbH in the city of Würzburg in southern Germany. From the outset the company has specialised in the manufacture of *in vitro* diagnostic products for the infectious disease serology and has, due to continual growth, twice expanded into new premises over the past 30 years. This family run business with its roots in Würzburg has remained in the region and currently provides employment and career opportunities for more than 100 employees.

Our product range offers a selection of analysis methodologies to aid the diagnosis of viral, bacterial, fungal and parasitic diseases. The complement fixation test (CFT) range alone offers in excess of 50 antigens plus associated reagents and controls for the detection of pathogen specific antibodies. SERION ELISA *classic* products allow for the differentiation of antibody classes for disease state and immune status determinations.

All products manufactured by Institut Virion\Serion GmbH are in compliance with national and international quality assurance standards related to *in vitro* medical devices such as the European Directive (IVDD) 98/79/EC. The company operates under a quality management system based on the latest updated version of ISO 13485:2003.

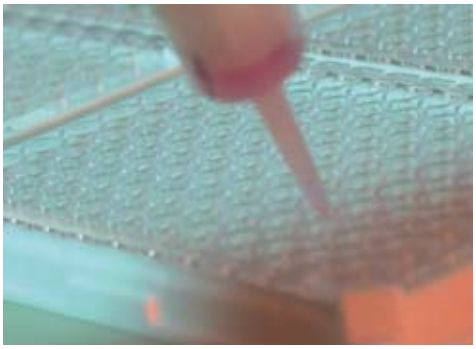
Customers in Germany are served by our sales team of product specialists while worldwide sales, which at present encompass over 80 countries, are coordinated through our subsidiary Serion Immunodiagnostica GmbH and an extensive network of local distributors. In order to provide an efficient service for our products in the Asiatic market we established a branch office in Beijing, China, in early 2003.

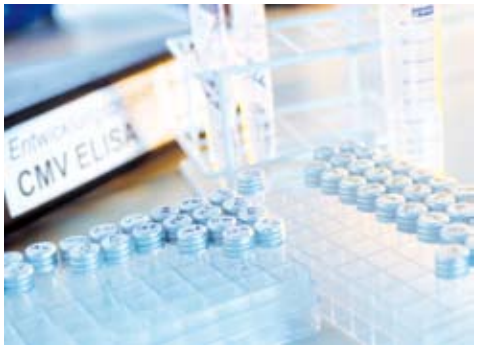
The company's commitment to innovation combined with a wealth of experience and the willingness to break new ground ensures that we are always going forward. One of our most recent product developments is the SERION Multianalyt™ technology. Based on the principles of flow cytometry, this technology allows for the simultaneous testing of multiple parameters while using very small sample quantities. This new methodology combines a diagnostic capability of the highest quality with time saving and cost effective solutions for the modern laboratory requirements. Parallel to this development we have introduced a new range of instruments. The **Immunomat™ *TWIN*system** is capable of automatically processing SERION ELISA *classic*, SERION ELISA *antigen* and SERION Multianalyt™ immunoassays. When used in combination with our new flow cytometer, **Immuno*flow***, this system fulfils the most stringent of modern laboratory automation requirements when utilising SERION Multianalyt™ for diagnostic analysis.

Due to the confidence of our customers and the continual engagement of all of employees Institut Virion\Serion GmbH and Serion Immundiagnostica GmbH, we have been able to sustain continual growth and we can look forward to a promising and successful future together.









SERION ELISA

Content

SERION ELISA from A to Z

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SERION ELISA *classic*

Test Principle

SERION ELISA *classic* tests are qualitative and quantitative immunoassays for the detection of human antibodies directed against specific antigens of bacteria, viruses, fungi and parasites in serum, plasma or, when indicated, cerebrospinal fluid, for the diagnosis of infectious diseases.

SERION ELISA *classic* test components

Diagnosis of infectious diseases

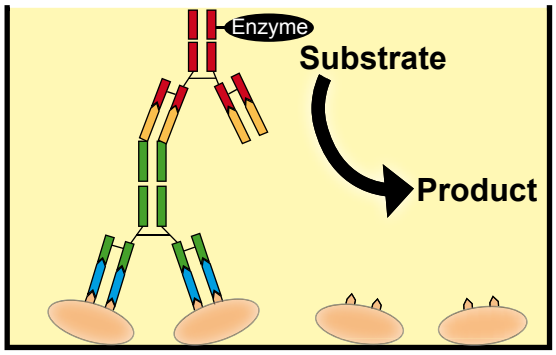
Serological investigations are important in the diagnosis of infectious diseases. The immune system produces antibodies as a vital component of the response to infection and the presence of foreign bodies or antigens. The detection of these antibodies is utilised in the diagnostic process.

Short insight into the humoral immune response

During the normal course of an infection the cells of the human immune system manufacture different types of antibodies which are classified as e. g. IgM, IgG or IgA and are responsible for different effector functions during the immune reaction. In the course of a primary infection, IgM antibodies are produced first. Since their presence wanes after a few weeks, IgM antibodies in human serum are a marker for an acute or fresh infection. Subsequently, IgG antibodies are produced, which often persist life-long. A significant increase in the IgG antibody level in human serum is a characteristic marker for a subsequent infection.
Antibodies of the IgA class are responsible for the defence against infectious pathogens in the mucosa of e. g. the respiratory tract.

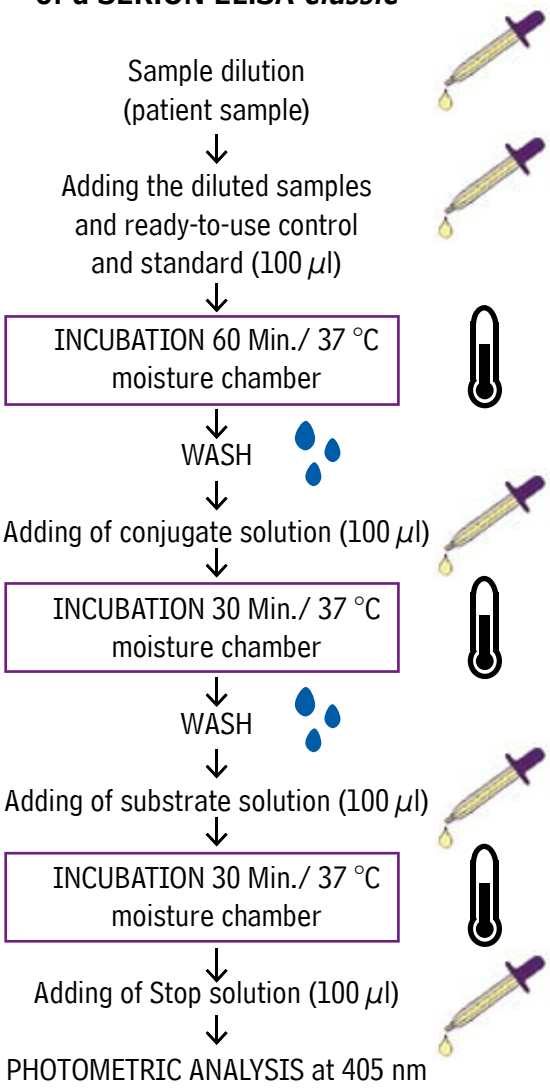
Principle of SERION ELISA *classic*

The ELISA (*Enzyme Linked Immunosorbent Assay*) is an immunoassay, which is particularily suited to the determination of antibodies in the field of infectious serology. The reaction is based on the specific interaction of antibodies with their corresponding antigen. Therefore, the test strips of the SERION ELISA *classic* microtitre plate are coated with specific antigens of the pathogen of interest. If antibodies in the patient´s serum sample are present, they bind to the fixed antigen. A secondary antibody, which has been conjugated with the enzyme alkaline phosphatase, detects the immune complex. The colourless substrate *p*-nitrophenolphosphate is then converted into the coloured product *p*-nitrophenol. The signal intensity of the reaction product is proportional to the concentration of the analyte in the sample and is measured photometrically.



Schematic design of a SERION ELISA *classic*

Schematic overview of a SERION ELISA *classic*



Advantages of SERION ELISA *classic* products

- High specificities and sensititivities by use of carefully selected antigens
- Strips of microtitre plates with individually breakable cavities
- Codes of pathogen and antibody class on the test strips to avoid mix-up
- Ready-to-use, coloured and barcoded reagents
- Consistent incubation periods for all SERION ELISAs (60 min, 30 min, 30 min)
- Combination of different tests in the frame of one plate possible
- Short incubation times unter defined conditions at 37 °C
- Standardised single-point calibration
- Compatibility with usual ELISA washer- and reader systems
- Application on Immunomat™, DYNEX DSX and comparable automates
- Fast and quantitative evaluation of measurement signals by use of the SERION *evaluate* software

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SERION ELISA *classic*

Adenovirus IgA / IgG

SERION ELISA *classic* Adenovirus IgA and IgG tests are quantitative and qualitative immunoassays for the detection of human antibodies, directed against all pathogenic human adenovirus serotypes, in serum or plasma. SERION ELISA *classic* Adenovirus IgA and IgG tests are recommended for detection of acute infections and for differential diagnosis of respiratory tract infections.

Pathogen

Adenoviruses belong to the family of *Adenoviridae* affecting a wide range of species (mammals, birds, reptiles and fish). Approximately 50 subtypes have been identified as human pathogens, with subtypes 1 to 8, 40 and 41, occuring most frequently. High prevalence of seropositivity, reaching over 50 %, reflects repeated infection with different subtypes in early childhood.

Disease

Adenoviruses may cause disease in a wide range of organs but particularly in the respiratory tract, gastrointestinal and urogenital tract and in the eye. Ocular infections (particularly keratoconjunctivitis) are often associated with hospital settings and nosocomial infections.

In adults infection with adenoviruses typically takes a mild or subclinical course and results in lifelong immunity to the infecting serotype so that, in the absence of immunosuppression, reinfection is rare.

Diagnosis

Direct antigen detection methods such as cell culture, electron microscopy and immunofluorescence are important aspects of adenovirus infection diagnosis. It should be recognised however that adenoviruses may behave like commensals and their presence is not always indicative of disease causation. Serological investigations are routinely employed for diagnosis of adenovirus infections and, while the CFT is a long established method, the ELISA methodology has the advantage of differentiating between immunoglobulin classes.

Validation of SERION ELISA *classic* Adenovirus

For the evaluation of the SERION ELISA *classic* Adenovirus IgG 170 serum samples, 156 serum pairs of persons with a respiratory infection as well as 61 serum samples from blood donors were analysed. The SERION ELISA *classic* Adenovirus IgA was validated by the analysis of 170 serum samples, 155 in process serum samples of a routine laboratory and 75 samples from blood donors. The complement fixation test (CFT) was used as a reference. Sera classified as borderline were not included in the calculation. Since the CFT does not detect IgA antibodies, the performance characteristics were calculated presuming that the humoral IgA antibody response sets on simultaneously with the production of complement binding antibodies.

SERION ELISA *classic*	Sensitivity	Specificity
Adenovirus IgA	80,0 % *	90,1 %
Adenovirus IgG	96,7 %	97,8 %

*Constraint information because comparison with CFT

The slightly lower sensitivity of the ELISA compared to the CFT is mainly due to serum samples which are evaluated as weakly positive by the CFT (one titer step above borderline titer). Such weak titers may be the result of post infections. The SERION ELISA *classic* Adenovirus assesses those samples in general as negative to get a clear separation between current acute and elder infections. The SERION ELISA *classic* Adenovirus IgG and IgA have been developed for Adenovirus diagnosis so as to exclude the high background seroprevalence.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Adenovirus IgA

Sample	Mean-Value OD	Intraassay CV (%) (n=20)	Mean-Value OD	Interassay CV (%) (n=10)
negative	0,292	8,6	0,354	9,2
weak positive	0,733	4,7	0,818	4,1
positive	1,119	2,3	1,198	5,2

SERION ELISA *classic* Adenovirus IgG

Sample	Mean-Value OD	Intraassay CV (%) (n=20)	Mean-Value OD	Interassay CV (%) (n=10)
negative	0,392	5,4	0,406	7,2
borderline	0,547	4,7	0,541	9,3
positive	1,188	4,8	1,209	8,3

Order Information

SERION ELISA *classic* Adenovirus IgA **Order Nr.: ESR 128 A**
SERION ELISA *classic* Adenovirus IgG **Order Nr.: ESR 128 G**
Reference serum Adenovirus IgA **Order Nr.: BR 128 A**
Reference serum Adenovirus IgG **Order Nr.: BR 128 G**

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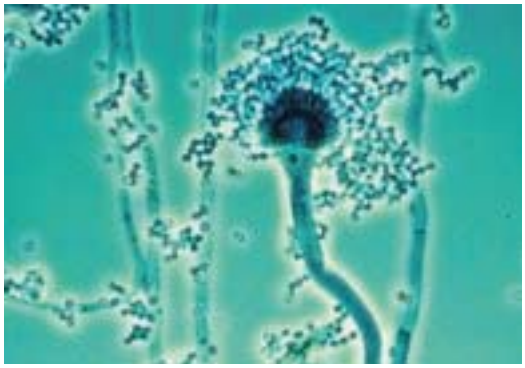
SERION ELISA *classic*

Aspergillus fumigatus IgA / IgG / IgM

SERION ELISA *classic* Aspergillus fumigatus IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *Aspergillus fumigatus*. The separate detection of individual immunoglobulin classes offers a more detailed view for the mycological monitoring of the risk patients´ immune response.



Micrograph of an *Aspergillus* conidiospore (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogens

The fungus *Aspergillus* belongs to the group of *ascomycetes*. These organisms develop branched mycelia and spread through conidiospores which are released from mycelia as extremely resistant lasting spores. 20 species of *Aspergillus* are opportunistic infectious agents affecting humans. The most important species is *Aspergillus fumigatus*.

Disease

Aspergillus fumigatus causes a range of allergic and invasive diseases in humans. Bronchopulmonal diseases belong to the most common manifestations of invasive aspergillosis. Patients with a persisting immune suppression after bone marrow transplantation or organ transplantation can develop a severe clinical picture of aspergillosis, e. g. an invasive aspergillosis of the lungs (IAL), which appears as an acute pneumonia, accompanied by high fever and increasing pulmonary infiltrates.

The fungal spores are transmitted through the air and inhaled by the lungs where due to their small size of about 3 μm they reach the lung alveoli. In the case of an invasive aspergillosis, fungal hyphae penetrate the bronchial mucosa and the surrounding lung parenchyma with the aid of released

proteases. The *Aspergillus* spores tend to penetrate the blood vessels and settle down in remote tissues after dissemination.

Diagnosis

For diagnosis of invasive aspergillosis indirect haemagglutination assays are widely used for the detection of Aspergillus specific antibodies, however, due to their low sensitivity they are not suitable as a screening assay.
ELISA techniques enable a differentiated analysis of the antibody response in the process of risk-patient monitoring by using immunoglobulin class-specific enzyme conjugates. For a further diagnosis of an invasive aspergillosis the lungs of a risk-patient should be examined for possible damage by biopsy.

Validation of SERION ELISA *classic* Aspergillus fumigatus

The SERION ELISA *classic* Aspergillus fumigatus IgA, IgG and IgM were validated by the analysis of serum samples from 86 risk patiens with a suspicion of an aspergillosis. The SERION ELISA *classic* Aspergillus fumigatus were compared to an indirect haemagglutination test (IHAT) of a competitor. An IHAT mainly detects IgM antibodies as well as IgG antibodies so that the results of SERION ELISA *classic* Aspergillus fumigatus IgM and SERION ELISA *classic* Aspergillus fumigatus IgG were combined during the validation process and compared to the IHAT results. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Aspergillus fumigatus IgG/M	89,7 %	95 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Aspergillus fumigatus IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
negative	0,052	4,1	0,033	11,8
negative	0,249	6,0	0,152	9,9
positive	0,901	8,3	1,199	5,9

SERION ELISA *classic* Aspergillus fumigatus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,054	7,6	0,042	19,9
positive	0,628	4,3	0,479	10,9
positive	2,284	3,1	0,596	7,2

SERION ELISA *classic* Aspergillus fumigatus IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,037	9,8	0,043	19,5
weak positive	0,725	4,5	0,288	11,2
positive	1,339	6,7	0,495	6,0

Order Information

SERION ELISA *classic* Aspergillus fumigatus IgA	**Order Nr.: ESR 132 A**
SERION ELISA *classic* Aspergillus fumigatus IgG	**Order Nr.: ESR 132 G**
SERION ELISA *classic* Aspergillus fumigatus IgM	**Order Nr.: ESR 132 M**
Reference serum Aspergillus fumigatus IgA	**Order Nr.: BR 132 A**
Reference serum Aspergillus fumigatus IgG	**Order Nr.: BR 132 G**
Reference serum Aspergillus fumigatus IgM	**Order Nr.: BR 132 M**

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SERION ELISA *classic*

Bacillus anthracis IgG

SERION ELISA *classic* Bacillus anthracis IgG test is a qualitative and quantitative immunoassay for the detection of human antibodies in serum or plasma directed against the protective antigen (PA) of *Bacillus anthracis*. The assay is recommended for vaccination control and for the determination of the current individual immune status to prevent hyper immune damage.

The SERION ELISA *classic* Bacillus *anthracis* IgG is especially interesting for the proof of protection of soldiers in conflict areas (source: US Department of Defense).

Pathogen

Splenic fever or Anthrax is an infectious disease, which is primarily found in animals. Especially in countries with warm climates, ungulates i.e. pigs, cattle, sheep, goats and horses are affected. Close contact with infected animals or exposure to infected animal products such as skin, meat or milk may transmit the pathogen to humans. The incubation period for the zoonosis is a few hours up to several days. This disease has become rare in industrial countries, however, endemic regions of South America, Africa and South East Asia still suffer from regular epidemics. In recent years, anthrax has been of increasing public interest due to its potential use in biological weapons.

The pathogen for splenic fever, *Bacillus anthracis,* is a gram positive, aerobic bacillus. Adverse conditions or increased temperatures lead to the production of stable spores, which can remain infectious for several years. Inhalation of significant numbers of spores (8.000 to 50.000) leads to infection. Due to a special protein shell, absorbed bacteria are able to escape defense mechanisms of the human immune system. They produce toxins that are assembled of the protective antigen (PA), the lethal (LF) and the edema factor (EF). These exotoxins are spread and damage small blood cells especially, so that they become permeable for red blood cells (erythrocytes). Inflammation and hemorrhage in form of hemorrhagic edema are the results.

Disease

Symptoms for splenic fever depend on the location of the entrance of the pathogen. Most subsequent forms are splenic fever of the skin. As in most cases, Anthrax spores are absorbed through small superficial skin injuries. After a short period of time, small red knots with a black center appear. Sanious vesicles develop quickly. As the disease progresses further vesicles develop and fuse to the so-called anthrax carbuncle (*Pustula maligna*).

Splenic fever of the lungs is far less common in humans. Breathing in spores causes the infection. The disease develops like severe pneumonia with highly infectious sanguineous sputum. Patients suffer from high fever, ague, cough and dyspnea. If not treated, splenic fever of the lungs is lethal in most cases.

A third form is splenic fever of the intestines, caused by consumption of contaminated produce from farm animals, e.g. raw meat or milk that was not boiled sufficiently. Severe hemorrhaeic inflammation of the intestines, sanguineous sputum and faeces are symptoms. This form of the disease is also lethal, if not treated.

All three types of splenic fever may develop sepsis, which rapidly causes death in most cases.

Diagnosis

Clinical picture and anamnesis lead to the diagnosis of splenic fever. Pathogen detection e.g. examination of bodily fluids or taking swabs confirm the diagnosis. Treatment with antibiotics must start as soon as possible. Avoiding contact with infected animals and their produce is the most effective form of prophylaxis. Immunization of certain risk groups e.g. soldiers, is possible with a PA containing vaccine, an extract from culture filtrate.

Validation of SERION ELISA *classic* Bacillus anthracis IgG

573 serum samples from blood donors and pregnant women as well as 48 serum samples from immunized blood donors were tested for the validation of SERION ELISA *classic* Bacillus anthracis IgG. The test was evaluated in comparison to immunization. Borderline results were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Bacillus anthracis IgG	> 99 %	99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Bacillus anthracis IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=20)
weak positive	0,591	1,8	0,584	3,9
positive	1,001	1,7	1,015	2,6
strong	1,938	2,0	1,865	2,6

Order Information

SERION ELISA *classic* Bacillus anthracis IgG **Order Nr.: ESR 140 G**

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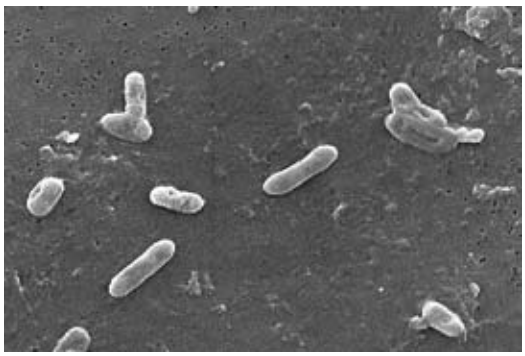
SERION ELISA *classic*

Bordetella pertussis IgA / IgG / IgM

SERION ELISA *classic* Bordetella pertussis IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *Bordetella pertussis*. The SERION ELISA *classic* Bordetella pertussis are recommended for differentiation of acute and recent infections as well as for epidemiological studies. The SERION ELISA *classic* Bordetella pertussis IgG is also recommended for vaccination control.



Electron micrograph of bacteria of genus *Bordetella* (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Bordetella pertussis is the pathogen responsible for whooping cough, a worldwide spread infectious disease that is transmitted from person to person by droplet infection. Particularily children up to four years old are affected and the mortality in infected infants is high. Although young people and adults usually do not get seriously ill, they are a risk as a source of infection for non protected and risk patients such as infants, old and ill people. Colonisation of the respiratory tract and establishment of infection are facilitated by the synergistic action of several virulence factors. A significant virulence factor is pertussis toxin (PT), which is synthesized and secreted exclusively by *Bordetella pertussis.*

Disease

Progression of typical whooping cough can be divided into three stages. After an incubation period of 1 to 2 weeks symptoms begin with the catarrhal phase (highly infectious), usually accompanied by a cough, rhinitis and conjunctivitis. Subsequently, the convulsive (paroxysmal) phase follows characterised by paroxysmal cough attacks combined with vomiting of viscid mucus, laryngospasm and bronchospasm, leading to a blue-cyanosed complexion in the child.

After four to six weeks attacks diminish and slowly subside (decrementi phase, up to 6 months).

Diagnosis

For diagnosis of an infection caused by *B. pertussis* the direct detection and isolation of the pathogen itself is the optimal method. The ELISA technique is the most commonly chosen method for *B. pertussis* specific antibody detection in serodiagnosis and complements direct antigen detection. In over 90 % of cases the IgG and IgA antibody responses are directed against the immunogens PT and FHA. Therefore, the SERION ELISA *classic* Bordetella pertussis IgG and IgA is based on antigen mixtures of PT and FHA. For the detection of IgM antibodies cellular bound lipopolysaccharid has outstanding diagnostic properties, whereas PT and FHA are not suitable. Therefore, a whole-cell antigen preparation of *B. pertussis* is used in the SERION ELISA *classic* Bordetella pertussis IgM.

Validation of SERION ELISA *classic* Bordetella pertussis

The SERION ELISA *classic* Bordetella pertussis IgG was validated by the analysis of 90 serum samples from blood donors, patients with suspected and with confirmed infection. The SERION ELISA *classic* Bordetella pertussis IgM and IgA were validated by analysis of 86 serum samples and 24 serum samples from patients with a current infection, respectively. The ELISA results were compared with the test results of a leading European manufacturer. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Bordetella pertussis IgA	> 99 %	> 99 %
Bordetella pertussis IgG	> 99 %	95,2%
Bordetella pertussis IgM	80,0 %	> 99 %

Precision

SERION ELISA *classic* Bordetella pertussis IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
borderline	0,605	1,7	0,625	5,3
positive	0,763	4,9	0,778	6,7
positive	0,914	2,5	0,949	7,0

SERION ELISA *classic* Bordetella pertussis IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,215	9,0	0,216	7,5
positive	0,529	3,9	0,482	9,2
positive	1,351	6,9	1,357	7,7

SERION ELISA *classic* Bordetella pertussis IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
positive	0,512	5,5	0,479	9,6
positive	0,551	4,6	0,516	14,2
positive	0,984	4,8	0,962	15,9

Order Information

SERION ELISA *classic* Bordetella pertussis IgA	**Order Nr.: ESR 120 A**
SERION ELISA *classic* Bordetella pertussis IgG	**Order Nr.: ESR 120 G**
SERION ELISA *classic* Bordetella pertussis IgM	**Order Nr.: ESR 120 M**
Reference serum Bordetella pertussis IgA	**Order Nr.: BR 120 A**
Reference serum Bordetella pertussis IgG	**Order Nr.: BR 120 G**
Reference serum Bordetella pertussis IgM	**Order Nr.: BR 120 M**

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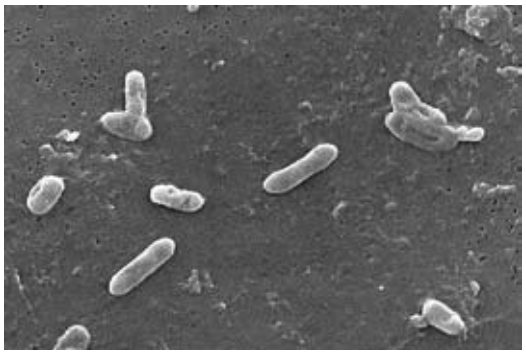
SERION ELISA *classic*

Bordetella pertussis Toxin IgG

SERION ELISA *classic* Bordetella pertussis Toxin IgG test is a quantitative and qualitative immunoassay for the detection of human antibodies in serum or plasma directed against *Bordetella pertussis* Toxin. The assay is recommended for vaccination control and for differential diagnosis of pneumonia in combination with the SERION ELISA *classic* Bordetella pertussis IgA, IgG and IgM.



Electron micrograph of bacteria of genus *Bordetella* (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Bordetella pertussis is the pathogen responsible for whooping cough, a worldwide spread infectious disease that is transmitted from person to person by droplet infection. Particularily children up to four years old are affected and the mortality in infected infants is high. Although young people and adults usually do not get seriously ill, they are a risk as a source of infection for non protected and risk patients such as infants, old and ill people. Colonisation of the respiratory tract and establishment of infection are facilitated by the synergistic action of several virulence factors. A significant virulence factor is pertussis toxin (PT), which is synthesized and secreted exclusively by *Bordetella pertussis.*

Disease

Combined Diphtheria-, Tetanus-, and Bordetella pertussis-vaccination has been recommended for children at the age of 6 and younger by the German vaccination committee "STIKO" (Robert-Koch-Institut, Berlin) since 1991. Acellular vaccines with significantly increased compatibility compared to whole-cell vaccines were licensed in 1995. The acellular vaccines currently available contain one, two, three or five *B. pertussis* components. All manufacturers use PT. The bi-, tri-, and multivalent vaccines contain amongst others FHA. Immunisation

is recommended for young people and adults with heart- and lung diseases, smokers, elderly people over 60 years of age, employees in child or nursing and other medical institutions.

Diagnosis

For the serological detection of *B. pertussis* specific antibodies the ELISA is the method of choice. IgM and IgG antibodies are detectable soon after vaccination. IgG antibodies are detectable in 90 % of cases after immunisation and may persist for several years or life long. The anti-*B. pertussis* toxin IgG titer is the most important marker for immunity. After vaccination IgA antibodies, which are an important diagnostic marker for acute infections, are produced in 20 to 40 % of cases only. IgA antibody response may be absent in infants younger than 6 months.

Validation of SERION ELISA *classic* B. pertussis Toxin IgG

For validation of SERION ELISA *classic* Bordetella pertussis Toxin IgG 92 serum samples from blood donors, children, patients with suspected infection and patients with a confirmed infection were analysed. The results were compared with the test results of a leading European manufacturer.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Bordetella pertussis Toxin IgG	97 %	> 99 %

Sera classified as borderline were not included in the calculation.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Bordetella pertussis Toxin IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV(%) (n=10)
negative	0,229	9,9	0,156	16,3
weak positive	0,846	8,5	0,954	13,1
positive	1,334	7,6	1,372	10,7

Order Information

SERION ELISA *classic* Bordetella pertussis Toxin IgG	**Order Nr.: ESR 1201 G**
SERION ELISA *classic* Bordetella pertussis IgA	**Order Nr.: ESR 120 A**
SERION ELISA *classic* Bordetella pertussis IgG	**Order Nr.: ESR 120 G**
SERION ELISA *classic* Bordetella pertussis IgM	**Order Nr.: ESR 120 M**
Reference serum Bordetella pertussis Toxin IgG	**Order Nr.: BR 1201 G**
Reference serum Bordetella pertussis IgA	**Order Nr.: BR 120 A**
Reference serum Bordetella pertussis IgG	**Order Nr.: BR 120 G**
Reference serum Bordetella pertussis IgM	**Order Nr.: BR 120 M**

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SERION ELISA *classic*

Borrelia burgdorferi IgG / IgM

SERION ELISA *classic* Borrelia burgdorferi IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum, plasma or cerebrospinal fluid directed against *Borrelia burgdorferi*. The detection of different immunoglobulin classes allows the differentiation between acute and previous infections as well as determination of disease status.

In Europe, *Borrelia burgdorferi* is transmitted to humans by infected ticks of the genus *Ixodes ricinus.*

Pathogen

Borrelia burgdorferi is the infectious agent which causes the disease syndrome known as Lyme-Borreliosis. *B. burgdorferi sensu stricto, B. garinii and B. afzelii* are the most important human pathogens of the genospecies *Borrelia burgdorferi sensu lato.* All three are distributed throughout Europe in all temperate climate zones. Reservoirs for the bacteria include a variety of small wild mammals, particularly mice. The bacteria, belonging to the taxonomic group of the spirochetes, are transmitted to human hosts by infected ticks (*Ixodes ricinus*, Europe; *Ixodes scapularis*, USA). The infection rate in adult ticks, nymphs and larvae with *Borrelia burgdorferi* ranges from 0 to 50 %, dependent upon geographical region and tick populations.

Disease

Lyme Disease is a multisystemic infection with many possible manifestations. Single or multiple organs may be involved. The time course of Lyme Disease can be divided into three separate stages. Stage I starts a few days up to several weeks after tick bite and subsequent infection with *Borrelia burgdorferi.* Patients suffer from non-specific symptoms such as fever, headache, muscle pain, joint pain, and exhaustion. Dermal manifestations with

Erythema migrans (EM) as a characteristic symptom of early disease are displayed by 30 to 60 % of infected persons. *Erythema migrans* is recognized as a specific clinical symptom which clearly demonstrates an early phase of Lyme borreliosis. Stage II occurs between a few weeks and several months post infection as a systemic disease. In addition to non-specific symptoms, in particular neurological disorders (Morbus Bannwarth), less frequently Lyme carditis and opthalmological disorders may be observed. Development of stage III symptoms may occur up to several years after the tick bite and are characterised by dermatological diseases (*Acrodermatitis chronicum athrophicans* (ACA), diseases of the joints (Lyme-Arthritis), and neurological diseases (chronical encephalomyelitis).

Diagnosis

Due to the complexity of the clinical picture and the generally unspecific symptoms, serological diagnosis is the appropriate method to ensure an optimal differential diagnosis. It is recommended to adopt a logical step-wise approach to serological diagnosis, using initially a sensitive screening test such as ELISA with subsequent confirmation of positive and borderline ELISA results by another specific test such as immunoblot. A European strain of the genospecies *Borrelia garinii* in addition to the strain PKo has been used as antigen for coating on microtiter wells, thus achieving a high diagnostic sensitivity. The genospecies we use contain the proteins OspC and VlsE, which are important for diagnosis in the early phase of Borreliosis and P100, which is important for the late phase. To increase the sensitivity, recombinant VlsE is also included. Specificity of the assay is optimized by supplementing the dilution buffer with a treponema phagedenis lysate, which absorbs potentially cross-reactive treponema antibodies.

Validation of SERION ELISA *classic* Borrelia burgdorferi

The SERION ELISA *classic* Borrelia burgdorferi IgG was evaluated by the analysis of 244 serum samples from blood donors, pregnant women and from patients with suspected borreliosis against two commercially avaliable ELISA of leading European manufacturers. The validation of the SERION ELISA *classic* Borrelia burgdorferi IgM was carried out by the analysis of 172 serum samples from blood donors and patients with suspected borreliosis compared to the commercially avaliable ELISA of a leading European manufacturer. Discrepant serum samples were further analysed by immunoblot. Sera classified as borderline were not included in the calculation.

SERION ELISA *classic*	Sensitivity	Specificity
Borrelia burgdorferi IgG	97,6 %	97,1 %
Borrelia burgdorferi IgM	97,3 %	> 99 %

SERION ELISA *classic* Borrelia burgdorferi IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,24	2,6	0,26	6,4
positive	0,56	6,4	0,76	10,3
positive	2,80	2,6	2,50	8,1

SERION ELISA *classic* Borrelia burgdorferi IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,19	5,0	0,19	7,7
positive	0,81	6,6	0,90	9,5
positive	3,75	4,5	3,84	5,8

Order Information

SERION ELISA *classic* Borrelia burgdorferi IgG **Order Nr.: ESR 121 G**
SERION ELISA *classic* Borrelia burgdorferi IgM **Order Nr.: ESR 121 M**
Reference serum Borrelia burgdorferi IgG **Order Nr.: BR 121 G**
Reference serum Borrelia burgdorferi IgM **Order Nr.: BR 121 M**

The SERION ELISA *classic* Borrelia burgdorferi IgG and IgM are evaluated for the **analysis of cerebrospinal fluid**.
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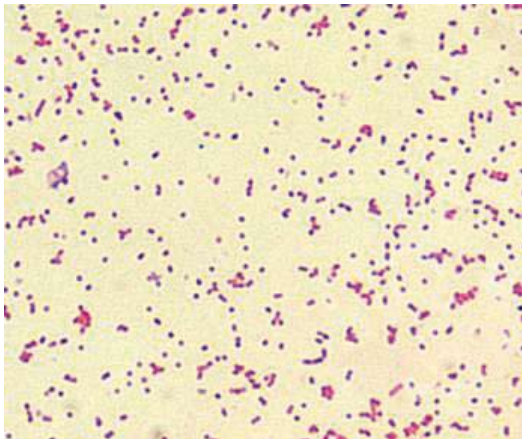
SERION ELISA *classic*

Brucella IgA / IgG / IgM

SERION ELISA *classic* Brucella IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum and plasma directed against *Brucella ssp.*. The evaluation of individual immunoglobulin classes can be used for the determination of pathogen contact and disease stage.



Micrograph of *Brucella ssp.* (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Brucella ssp. are gram-negative non-motile bacteria which live as intracellular parasites in a wide spectrum of host, particularily farm animals. Infections of humans are mainly caused by *Brucella melitensis* ("Malta fever"), *Brucella abortus* ("Morbus Bang"), *Brucella suis* and *Brucella canis*. The pathogen is transmitted by infected animals, their excretions and contaminated food.

Disease

The disease starts with moderate fever, which rises in the evenings during the acute stage of the disease, in which hepatomegaly and splenomegaly or swollen lymph nodes are characteristic. Undulating fever within afebrile intervals manifests often in *Brucella melitensis* and *Brucella suis* infections.

Spontaneous healing as well as transition into a chronic stage with a wide spectrum of symptoms is possible. Multiple organs or organ systems, bones or joints can be affected during the chronic stage. Histologically, characteristic granulomas are observed in infected tissues. Bacterial endocarditis might be fatal if it remains untreated.

During the late stage of brucellosis, neurologic and even psychiatric manifestations might occur.

Diagnosis

Due to the variable clinical picture of chronic brucellosis, accurate diagnosis is possible only by direct detection of the pathogen or detection of specific antibody response in serum or CSF. Direct pathogen detection in culture systems can be performed with punctate from blood, bone marrow, synovia or urine. In this regard the special demands on nutrients have to be taken into account. Generally direct pathogen detection is done by gram staining and agglutination with Brucella-specific hyperimmunoglobulin preparations. More rapid results are obtained with serological methods such as agglutination tests, Coombs-tests or Complement Fixation Tests (CFT). For differentiation of acute and chronic brucellosis, sensitive and specific ELISAs with separate detection of IgG, IgM and IgA antibodies is recommended.

Validation of SERION ELISA *classic* Brucella

For the validation of the SERION ELISA *classic* Brucella IgA, IgG and IgM 240 serum samples from blood donors and 27 samples from patients with a suspected brucellosis were analysed in comparison to another commercially available ELISA. Sera classified as borderline were not included in the calculation.

SERION ELISA *classic*	Sensitivity	Specificity
Brucella IgA	> 99 %	> 99 %
Brucella IgG	> 99 %	99,2%
Brucella IgM	91,3%	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Brucella IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,600	11,1	0,760	9,3
positive	1,790	7,5	2,270	7,6
positive	-	-	3,420	1,2

SERION ELISA *classic* Brucella IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,590	5,5	0,560	11,3
positive	1,240	7,2	1,350	13,3
positive	-	-	1,940	5,7

SERION ELISA *classic* Brucella IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,992	1,9	1,092	5,3
positive	1,781	2,6	1,842	3,4
positive	2,269	1,1	2,394	2,7

Order Information

SERION ELISA *classic* Brucella IgA	**Order Nr.: ESR 116 A**
SERION ELISA *classic* Brucella IgG	**Order Nr.: ESR 116 G**
SERION ELISA *classic* Brucella IgM	**Order Nr.: ESR 116 M**
Reference serum Brucella IgA	**Order Nr.: BR 116 A**
Reference serum Brucella IgG	**Order Nr.: BR 116 G**
Reference serum Brucella IgM	**Order Nr.: BR 116 M**

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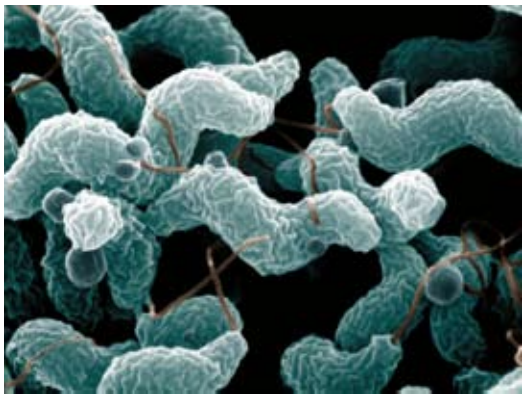
SERION ELISA *classic*

Campylobacter jejuni IgA / IgG / IgM

SERION ELISA *classic* Campylobacter jejuni IgA, IgG and IgM tests are qualitative and quantitative immunoassays for the detection of human antibodies in serum or plasma directed against *Campylobacter jejuni*. The assays are recommended for the differentiation of acute and past infections in cases of gastrointestinal diseases and reactive arthritis.



Electron micrograph of *Campylobacter jejuni* (Source: Agricultural Research Service, United States Department of Agriculture).

Pathogen

Campylobacter is a gram-negative bacterium consisting of 15 species, which have so far been described. In particular, *Campylobacter jejuni* (70 % of cases) and *Campylobacter coli* are associated with human diseases.
Campylobacter infections occur worldwide. The main reservoir are warm-blooded domestic and wild animals. Human Campylobacteriosis is primarily a foodborne infection. Insufficiently heated, contaminated poultry and poultry products (eggs excluded) are the main sources of infection.

Disease

Manifestations of *Campylobacter jejuni* infection are usually acute enteritis which is undistinguishable from enteritis due to other causes. 12 to 24 hours before enteritic symptoms, prodromal symptoms with fever (38 - 40 °C), headache, myalgia, anthralgia and weariness occur. Prevalent complaints are diarrhea, abdominal pain or cramps, fever, weariness. The disease generally lasts for one day to one week, sometimes longer. Normally infections are self limiting, but 5 to 10 % of untreated patients develop relapses. Guillain-Barré-Syndrome (GBS) or reactive arthritis are rare complications.

Diagnosis

Campylobacter jejuni infections are usually detected by pathogen isolations from stool and blood as well as serologically with Complement Fixation Tests (CFT). Diagnosis of *Campylobacter jejuni* infections has developed into an important routine diagnostic procedure in recent years. This results from the fact that they are the main reason for foodborne diarrhoea in industrial countries. While most *Campylobacter* infections resolve quickly, severe complications may occur. To analyse the etiology of reactive arthritis and GBS, reliable serological tests are required, since these diseases usually develop up to 3 weeks after *Campylobacter jejuni* infection. Stool culture testing is not suitable in such cases since at this stage isolation attempts are usually unsuccessful.

Validation of SERION ELISA *classic* Campylobacter jejuni

The SERION ELISA *classic* Campylobacter jejuni IgA, IgG and IgM were evaluated by the analysis of 78 serum samples from patients with either acute gastrointestinal infections, laboratory confirmed or suspected Guillain-Barré-Syndrome. The determined rather low specificity is explained with the general higher sensitivity of ELISA compared to CFT. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Campylobacter jejuni IgG/M	> 99 %	83,6 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Campylobacter jejuni IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
borderline	0,435	5,6	0,415	12,8
positive	0,576	6,6	0,522	4,3
positive	1,281	3,4	1,317	5,4

SERION ELISA *classic* Campylobacter jejuni IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV(%) (n=10)
borderline	0,526	7,2	0,493	6,6
positive	0,628	2,9	0,640	5,7
positive	1,219	2,3	1,225	4,9

SERION ELISA *classic* Campylobacter jejuni IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
borderline	0,166	2,9	0,154	8,8
positive	0,175	5,4	0,169	7,9
positive	1,086	4,2	1,194	4,8

Order Information

SERION ELISA *classic* Campylobacter jejuni IgA	**Order Nr.: ESR 139 A**
SERION ELISA *classic* Campylobacter jejuni IgG	**Order Nr.: ESR 139 G**
SERION ELISA *classic* Campylobacter jejuni IgM	**Order Nr.: ESR 139 M**
Reference serum Campylobacter jejuni IgA	**Order Nr.: BR 139 A**
Reference serum Campylobacter jejuni IgG	**Order Nr.: BR 139 G**
Reference serum Campylobacter jejuni IgM	**Order Nr.: BR 139 M**

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SERION ELISA *classic*

Candida albicans IgA / IgG / IgM

SERION ELISA *classic* Candida albicans IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *Candida albicans*. The assays are recommended for the monitoring of invasive and systemic mycosis and for diagnosis during the early stage of the infection.

Culure of *Candida albicans* on a SABHI Agarplate (Scource: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Candida albicans is a ubiquitous yeast responsible primarily for superficial infections, but may also cause more serious systemic diseases. *Candida* excrete multiple enzymes that enable the facultative pathogenic microorganism to penetrate blood vessels and mucosa barriers.

Disease

In general human *Candida ssp.* infection is passed on by smear contamination. Following infestation of the mucosa, invasive mycosis spreads out from the gastro-intestinal tract. The attachment of *Candida ssp.* to various mucosal surfaces is facilitated by adherence proteins and other structures of the outer cytomembrane.

Diagnosis

The diagnosis of candida infections on the basis of serological methods is not straight forward: On the one hand transient yeast colonisation may induce an antibody response, on the other hand systemic Candida mycosis at immunosuppressed patients may only lead to low antibody activities. Such situations make critical interpretation of serological findings necessary. In addition, systemic candida infections may not cause typical symptoms.
Currently no single technique in isolation allows for a diffilitive serological diagnosis of Candida. Surveillance of risk patients and therapy control requires the use of a variety of methods including serology and antigen detection.

Validation of SERION ELISA *classic* Candida albicans

For the evaluation of the SERION ELISA *classic* Candida albicans IgA, IgG and IgM 10 serum samples of blood donors, 15 serum samples from pregnant women and 64 serum samples from patients with suspected candidosis were analysed in comparison to three assays of competitors.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Candida albicans IgA	> 99 %	> 99 %
Candida albicans IgG	> 99 %	> 99 %

A serum was evaluated positive, respectively negative, in case the results were corresponding in three out of four tests. Sera classified as borderline were not included in the calculation.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Candida albicans IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,369	8,5	0,304	6,2
borderline	1,880	7,9	1,587	5,4

SERION ELISA *classic* Candida albicans IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,507	6,6	0,496	11,7
borderline	1,618	5,2	1,51	8,2

SERION ELISA *classic* Candida albicans IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,371	6,4	0,452	10,9
borderline	0,519	7,8	0,634	11,0
positive	1,358	7,5	1,567	8,9

Order Information

SERION ELISA *classic* Candida albicans IgA	**Order Nr.: ESR 117 A**
SERION ELISA *classic* Candida albicans IgG	**Order Nr.: ESR 117 G**
SERION ELISA *classic* Candida albicans IgM	**Order Nr.: ESR 117 M**
Reference serum Candida albicans IgA	**Order Nr.: BR 117 A**
Reference serum Candida albicans IgG	**Order Nr.: BR 117 G**
Reference serum Candida albicans IgM	**Order Nr.: BR 117 M**

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SERION ELISA *antigen*
Candida

SERION ELISA *antigen* Candida is a quantitative and qualitative immunoassay for the detection of Candida antigen in human serum. The assay is recommended for the detection of invasive and systemic candidosis.

Culure of *Candida albicans* on a SABHI Agarplate (Scource: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Candida albicans is a ubiquitous yeast responsible primarily for superficial infections, but may also cause more serious systemic diseases. *Candida* excrete multiple enzymes that enable the facultative pathogenic microorganism to penetrate blood vessels and mucosa barriers.

Disease

In general human *Candida ssp.* infection is passed on by smear contamination. Following infestation of the mucosa, invasive mycosis spreads out from the gastro-intestinal tract. The attachment of *Candida ssp.* to various mucosal surfaces is facilitated by adherence proteins and other structures of the outer cytomembrane.

Diagnosis

The diagnosis of candida infections on the basis of serological methods is not straight forward: On the one hand transient yeast colonisation may induce an antibody response, on the other hand systemic Candida mycosis at immunosuppressed patients may only lead to low antibody activities. Such situations make critical interpretation of serological findings necessary. In addition, systemic candida infections may not cause typical symptoms.
Currently no single technique in isolation allows for a diffilitive serological diagnosis of Candida. Surveillance of risk patients and therapy control requires the use of a variety of methods including serology and antigen detection.

Validation of SERION ELISA *antigen* Candida

The SERION ELISA *antigen* Candida was evaluated by the analysis of 245 serum samples from blood donors and from patients, who showed signs of candidosis during intensive care treatment. The results were compared to the results of a commercially avaliable assay of a leading European manufacturer. Sera classified as borderline were not included in the calculation.

SERION ELISA *antigen*	Sensitivity	Specificity
Candida	> 99,9 %	96 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *antigen* Candida

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
pos. / pos.	0,566	8,4	0,689	10,4
pos. / pos.	0,876	5,2	0,977	9,0
pos. / pos.	0,900	6,5	1,722	6,4
pos. / pos.	0,941	8,0	2,787	5,0

In another internal study, cross reactivity with the Candida species *Candida* (*Pichia*) *guillermondii*, *Candida glabrata*, *Candida* (*Issatchenkia*) *parapsilosis*, *Candida orientalis*, *Candida tropicalis* and *Candida dubliniensis* with the SERION ELISA *antigen* Candida were determined in order to guarantee a comprehensive Candida diagnostic.

Furthermore we tested the cross reactivity with hydroxyethylstarch which is used in plasma expanders for treatment of circulatory failure (hypovolaemic, häemorrhagic and septic shock). Due to a similiarity to mannan it is important to know if cross reactivity could occur. Using the SERION ELISA *antigen* Candida assay no cross reaction was measureable for hydroxyethylstarch.

Order Information

SERION ELISA *antigen* Candida	**Order Nr.: A 117**
SERION ELISA *classic* Candida albicans IgA	**Order Nr.: ESR 117 A**
SERION ELISA *classic* Candida albicans IgG	**Order Nr.: ESR 117 G**
SERION ELISA *classic* Candida albicans IgM	**Order Nr.: ESR 117 M**
Reference serum Candida albicans IgA	**Order Nr.: BR 117 A**
Reference serum Candida albicans IgG	**Order Nr.: BR 117 G**
Reference serum Candida albicans IgM	**Order Nr.: BR 117 M**

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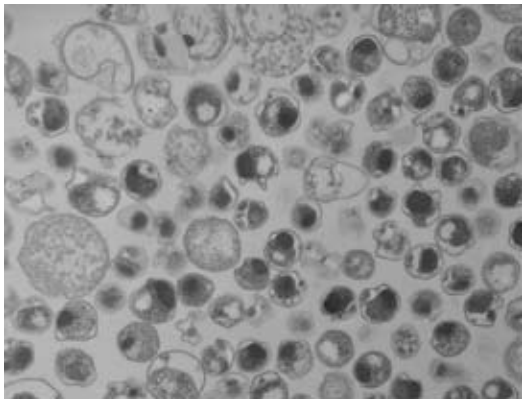
SERION ELISA *classic*

Chlamydia IgA / IgG

SERION ELISA *classic* Chlamydia IgA and IgG tests are quantitative and qualitative immunoassaayss for the detection of human antibodies in serum or plasma directed against genus specific antigens of *Chlamydia*. SERION ELISA *classic* Chlamydia IgA and IgG tests are recommended for the diagnosis of acute or recent infections.



Electron micrograph of elementary bodies and reticular bodies of *Chlamydia pneumoniae*.

Pathogen

The order Chlamydiales currently has one family, the *Chlamydiaceae*, containing two genera, Chlamydia and Chlamydophila. Three human pathogenic species, *Chlamydia trachomatis*, *Chlamydophila pneumoniae* and *Chlamydophila psittaci* belong to these genera. Nearly all birds and mammals can be infected with *C. psittaci*, whereas man is the primary host of *C. trachomatis.* Workers on poultry farms are at particulary high risk of *C. psittaci* infection which may cause a severe psittacosis disease. The different Chlamydia species are transmitted via different infections routes: *C. pneumoniae* via aerosol transmission, *C. trachomatis* via direct contact or smear infection, *C. psittaci* via inhalation of fecal droppings, feather dust or smear infection.
Chlamydia are coccoide, gram-negative bacterial pathogens which are metabolically deficient in their ability to synthesize ATP and thus have an obligate intracellular life cycle. During an infection with Chlamydia two characteristic cell forms occur: the highly infectious elementary bodies and the non-infectious intracellular reticular bodies which are able to propagate.

Disease

Infections with Chlamydia may be initially mild, but may lead to serious diseases later on if not treated. An infection with *C.*

trachomatis can be the cause of unspecific urethritis, cervicitis and conjunctivitis. Especially for younger men epididymitis and prostatitis and for women adnexitis, extrauterine pregnancy or sterility may result from repeated infection.
Infection of an infant during childbirth is a significat risk (60 - 70 %) in the case of an infected mother resulting in conjunctivitis or pneumonia in the new-born. A *C. trachomatis* infection may also lead to reactive arthritis.
Infection with *C. pneumoniae* is often asymptomatic or mil with symptoms such as hoarseness, dry cough and tiredness. However, the infection can also lead to longterm diseases and serious pneumonias. Latest seroepidemiological studies indicate a connection of a chronic *C. pneumoniae* infection with arteriosclerosis. The immunological reaction to the pathogen seems to enhance the risk for coronary heart disease and myocardial infarction. This hypothesis, however, still has to be confirmed by further investigations.

Diagnosis

Approximately two weeks after the first symptoms of a primary infection an increase of the IgA and IgM titers occurs, which peaks after five weeks and will have usually declined by the 10th week. As IgM and IgA antibodies peak, IgG production is initiated, peaking around week 12 and detectable for several years. On reinfection IgA and IgG antibodies reappear rapidly, whereas IgM antibodies are not evident.

Validation of SERION ELISA *classic* Chlamydia

The SERION ELISA *classic* Chlamydia IgA was evaluated in an internal study by the analysis of 42 serum samples of blood donors and patients with confirmed Chlamydia infektion. The immunofluorescence test (IFT, goldstandard) of a leading European manufacturer was used as as a reference. The validation of the SERION ELISA *classic* Chlamydia IgG was performed by the analysis of 86 serum samples in comparison to the assays of three competitors. Serum samples were evaluated positive if at least two of the three ELISA gave positive results. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Chlamydia IgA	> 99 %	> 99 %
Chlamydia IgG	88 %	89 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Chlamydia IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,446	8,1	0,388	12,0
positive	0,836	6,5	0,783	6,3
positive	1,314	4,9	1,485	9,7

SERION ELISA *classic* Chlamydia IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
borderline	0,324	5,0	0,333	7,5
positive	0,702	5,5	0,717	9,6
positive	1,445	5,1	1,528	5,8

Order Information

SERION ELISA *classic* Chlamydia IgA	**Order Nr.: ESR 137 A**
SERION ELISA *classic* Chlamydia IgG	**Order Nr.: ESR 137 G**
Reference serum Chlamydia IgA	**Order Nr.: BR 137 A**
Reference serum Chlamydia IgG	**Order Nr.: BR 137 G**

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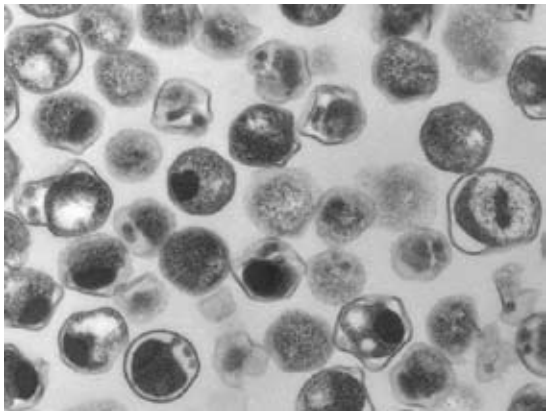
SERION ELISA *classic*

Chlamydia pneumoniae IgA / IgG

SERION ELISA *classic* Chlamydia pneumoniae IgA and IgG tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *Chlamydia pneumoniae*. SERION ELISA *classic* Chlamydia pneumoniae IgA and IgG tests are recommended for the diagnosis of acute or recent infections.



Electron micrograph of elementary bodies of *Chlamydia pneumoniae*.

Pathogen

Chlamydiae are gram-negative, obligat intracellular bacteria. Characteristically, the chlamydial cell wall lacks a peptidoglycan layer. Only the species *Chlamydia trachomatis*, *Chlamydia pneumoniae* (in recent years also referred to as *Chlamydophila pneumoniae*) and *Chlamydia psittaci* are relevant to human disease. Chlamydia can be transmitted via several routes: *Chlamydia pneumoniae* is an airborne pathogen spread by inhaled droplets, *Chlamydia trachomatis* is transmitted sexually or perinatally through contact or smear infection, and *Chlamydia psittaci* via inhalation of fecal droppings, feather dust or smear infection.

Disease

Infections with *C. pneumoniae* are often asymptomatic or mild. The spectrum of clinical symptoms comprises pharyngitis, sinusitis, bronchitis, pneumonia and myocarditis or endocarditis. Infection may occasionally lead to chronic disease resulting in immunopathological syndromes such as erythema nodosum, arthralgia, Guillain-Barré Syndrome (GBS), or myalgia. In addition, chronic infections with *C. pneumoniae* are implicated with the etiology of asthma, COPD, atherosclerosis and cardiovascular disease.

Diagnosis

Since an undetected and hence untreated *C. pneumoniae* infection may lead to chronic disease, it is crucially important to diagnose disease in a timely manner. Diagnosis of a *Chlamydia pneumoniae* infection is usually based on serological results by detection of specific serum antibodies. In the past, the microimmunofluorescence (MIF) test has been used as a reference method. It is, however, increasingly replaced by species-specific ELISA tests which allow for far better standardization.
Presumably, most people become infected with *C. pneumoniae* at least once in life. Seroprevalence rates rise rapidly in pre-school age and reaches >50% after adolescence. Later on in life, the prevalence of *C. pneumoniae* increases even further due to frequently re-occurring infections and due to its propensity to lead to chronic disease. Beyond 65 years of age, seroprevalence may reach 70 - 100%. Seroprevalence rates for IgA are barely lower (approximately 60 - 70%) than for IgG.

Validation of SERION ELISA *classic* Chlamydia pneumoniae

The SERION ELISA *classic* Chlamydia pneumoniae IgA and IgG were evaluated in an external study by the analysis of 70 serum samples of children and adult blood donors and 70 serum samples of patients with confirmed infection with *Chlamydia pneumoniae*. The in-house microimmunofluorescence test (MIF) of the cooperation partner was used as a reference. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Chlamydia pneumoniae IgA	89 %	99 %
Chlamydia pneumoniae IgG	81 %	> 99 %

Furthermore, test sensitivity was determined utilizing a set of 48 MIF-positive sera derived from patients with ARI (acute respiratory infections). As a result, 45 sera were identified as IgG- and/or IgA-positive giving 94 % sensitivity.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Chlamydia pneumoniae IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,461	4,2	0,494	6,3
positive	0,544	4,9	0,589	7,1
positive	1,543	3,7	1,608	4,9

SERION ELISA *classic* Chlamydia pneumoniae IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,282	2,3	0,270	6,3
weak positive	0,629	3,5	0,624	4,2
positive	2,061	1,5	2,082	2,6

Order Information

SERION ELISA *classic* Chlamydia pneumoniae IgA	**Order Nr.: ESR 1371 A**
SERION ELISA *classic* Chlamydia pneumoniae IgG	**Order Nr.: ESR 1371 G**
SERION ELISA *classic* Chlamydia trachomatis IgA	**Order Nr.: ESR 1372 A**
SERION ELISA *classic* Chlamydia trachomatis IgG	**Order Nr.: ESR 1372 G**
Reference serum Chlamydia pneumoniae IgA	**Order Nr.: BR 1371 A**
Reference serum Chlamydia pneumoniae IgG	**Order Nr.: BR 1371 G**
Reference serum Chlamydia trachomatis IgA	**Order Nr.: BR 1372 A**
Reference serum Chlamydia trachomatis IgG	**Order Nr.: BR 1372 G**

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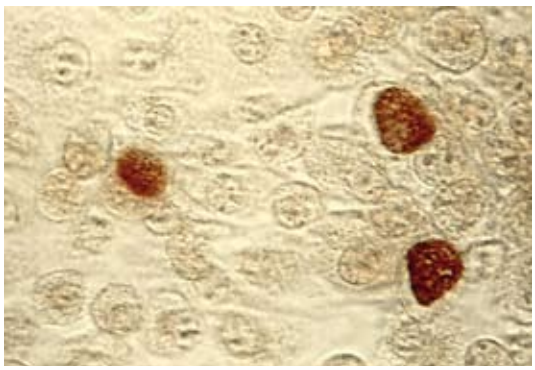
SERION ELISA *classic*

Chlamydia trachomatis IgA / IgG

SERION ELISA *classic* Chlamydia trachomatis IgA and IgG tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *Chlamydia trachomatis*. SERION ELISA *classic* Chlamydia trachomatis IgA and IgG tests are recommended for the diagnosis of acute or recent infections.



Electron micrograph of elementary bodies of *Chlamydia trachomatis* (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Chlamydia trachomatis is one of the most common sexually transmitted bacterial pathogens. Depending on the serovar, the pathogen may infect epithelial cells of the urogenital- and respiratory tract as well as the conjunctiva.

Disease

Chlamydia trachomatis infections may be asymptomatic in 70 % of female and in up to 50 % of males. Untreated, infections may result in serious damage and complications. The serovars A to C cause ceratoconjunctivits. Chronic infections during childhood can result in trachoma or blindness. Serovars D to K are pathogens of the urogenital tract, responsible for urethritis, proctitis and cervicitis. Salpinigits, endomitritis and perihepatitis are frequently the consequence of untreated cervicitis. Occasionally, tubal obstructions and ectopic pregnancy, which are one of the most common reasons for infertility in women, may result. Furthermore, the risk of a premature delivery for infected pregnant women is also increased.
In addition to urethritis and proctitis, epidiymitis and prostatitis, which may lead to infertility, are possible consequences for men.

Diagnose

Following an urogenital infection, the pathogen may migrate to the upper genital tract. This can cause difficulties in direct pathogen detection via cell-culture or PCR. In such cases, serological analysis is essential for the diagnosis of *Chlamydia trachomatis* infections. To date, the Microimmunofluorescence test (MIF) has been accepted as the reference method. More recently, standardised and automated ELISA tests are used in routine laboratories.
The SERION ELISA *classic* Chlamydia trachomatis tests are based on a specific domain of the major outer membrane protein (MOMP). The use of this antigen decreases the frequency of false-positive results and consequently increases the sensitivity of the antibody detection in comparison to Microimmunofluorescence tests and other ELISAs.

Validation of SERION ELISA *classic* Chlamydia trachomatis

The SERION ELISA *classic* Chlamydia trachomatis IgG was evaluated in a study by the analysis of 183 serum samples of adult blood donors and 140 serum samples of patients with suspected infection with *Chlamydia trachomatis*. The validation of SERION ELISA *classic* Chlamydia trachomatis IgA was performed by the analysis of 194 serum samples of blood donors and 106 patient samples. The ELISA tests of a leading European manufacturer were used as reference. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Chlamydia trachomatis IgA	92,6 %	98,6 %
Chlamydia trachomatis IgG	95,1 %	98,4 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples with a range of reactivities.

SERION ELISA *classic* Chlamydia trachomatis IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
borderline	0,314	2,3	0,352	6,3
positive	0,897	3,5	0,923	4,8
positive	1,659	4,7	1,875	5,2

SERION ELISA *classic* Chlamydia trachomatis IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,377	2,9	0,404	5,9
positive	0,650	2,2	0,612	9,1
positive	1,859	2,1	1,985	6,1

Order Information

SERION ELISA *classic* Chlamydia trachomatis IgA	**Order Nr.: ESR 1372 A**
SERION ELISA *classic* Chlamydia trachomatis IgG	**Order Nr.: ESR 1372 G**
SERION ELISA *classic* Chlamydia pneumoniae IgA	**Order Nr.: ESR 1371 A**
SERION ELISA *classic* Chlamydia pneumoniae IgG	**Order Nr.: ESR 1371 G**
Reference serum Chlamydia trachomatis IgA	**Order Nr.: BR 1372 A**
Reference serum Chlamydia trachomatis IgG	**Order Nr.: BR 1372 G**
Reference serum Chlamydia pneumoniae IgA	**Order Nr.: BR 1371 A**
Reference serum Chlamydia pneumoniae IgG	**Order Nr.: BR 1371 G**

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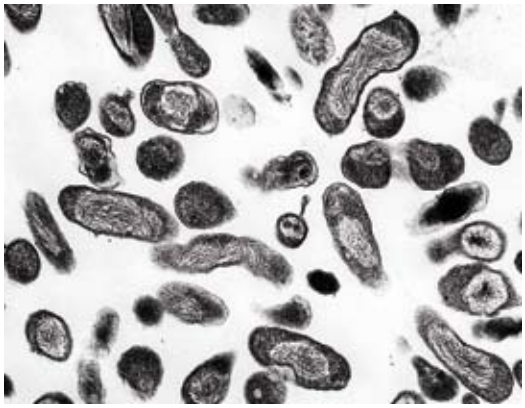
SERION ELISA *classic*

Coxiella burnetii IgA / IgG / IgM

SERION ELISA *classic* Coxiella burnetii tests are quantitative (Phase II IgG) and qualitative (Phase I IgG, IgA and Phase II IgM) immunoassays for the detection of human antibodies in serum or plasma directed against *Coxiella burnetii*. SERION ELISA *classic* Coxiella burnetii IgM is recommended for the detection of acute infections, while SERION ELISA *classic* Coxiella burnetii (Phase II) IgG supports the differential diagnosis of infections of the respiratory tract, especially atypical pneumonia. SERION ELISA *classic* Coxiella burnetii (Phase I) tests are recommended for the diagnosis of chronic Q-fever.



Electron micrograph of the Rickettsie *Coxiella burnetii* (Source: National Institutes of Health, United States Department of Health and Human Services).

Pathogen

Q-fever is a zoonosis with global distrbution. The pathogen responsable is the rickettsia *Coxiella burnetii*, a small, gram-negative, obligate intracellular bacterium. Bacteria multiply in the digestive system of ticks (*Dermacentor marginatus* in Germany) and in the trophoblasts of the placenta in the secondary host. Accordingly, tick faeces and the afterbirth of infected mammals (predominantly sheep) are highly infectious.

Disease

The incubation time is two to four weeks. The frequency of clinical evidence of infection is 30 to 50 %, the remaining beeing subclinical or with uncharacteristic general symptoms. Influenza-like symptoms are often evident. In about 50 % of cases an atypical, interstitial pneumonia develops. In some cases the acute progression can be complicated by meningoencephalitis, myoditis or pericarditis. If not treated the pathogen persists in a variety of organs, leading to chronic infection which often presents as an endocarditis and/or granulomatous hepatitis. About 65 % of chronic Q-fever cases are fatal.

Following primary infection specific IgM and IgG antibodies directed against the phase 2 antigen are detected after two weeks and two months, respectively. Anti-phase 2 IgM antibodies can be detected up to three months after infection, whereas IgG antibodies often persist over a period of about five years. In the lead up to chronic infection, IgG and IgA antibodies directed against the phase 1 antigen appear. These are of diagnostic value for Q-fever endocarditis.

Diagnosis

Due to the lack of characteristic clinical symptoms of acute and chronic Q fever infection, diagnosis is based on serological evidence. The use of ELISA is recommended by the WHO due to its high sensitivities and specificities and the possibility to perform a differential analysis of the antibody response.

Validation of SERION ELISA *classic* Coxiella burnetii

The SERION ELISA *classic* Coxiella burnetii (II) IgG was evaluated by the analysis of 414 serum samples from blood donors and pregnant women and 97 serum samples from patients with clinically and serologically (IFT) identified Q-Fever. For the validation of the SERION ELISA *classic* Coxiella burnetii (II) IgM 149 serum samples from blood donors and 114 serum samples from patients with suspected Q-Fever were analysed in comparison to the assay of a leading manufacturer.

Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Coxiella burnetii (II) IgG	93,4 %	98,5 %
Coxiella burnetii (II) IgM	94,4 %	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Coxiella burnetii (II) IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,661	5,7	0,669	15,0
positive	1,058	5,3	1,074	11,3
positive	2,353	3,7	2,231	4,0

SERION ELISA *classic* Coxiella burnetii (II) IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,218	5,1	0,221	10,4
weak positive	0,403	6,3	0,415	5,5
positive	0,808	4,6	0,900	11,5

Order Information

SERION ELISA *classic* Coxiella burnetii (II) IgG **Order Nr.: ESR 1312 G**
SERION ELISA *classic* Coxiella burnetii (II) IgM **Order Nr.: ESR 1312 M**
SERION ELISA *classic* Coxiella burnetii (I) IgA **Order Nr.: ESR 1311 A**
SERION ELISA *classic* Coxiella burnetii (I) IgG **Order Nr.: ESR 1311 G**
Reference serum Coxiella burnetii (II) IgG **Order Nr.: BR 1312 G**
Reference serum Coxiella burnetii (II) IgM **Order Nr.: BR 1312 M**

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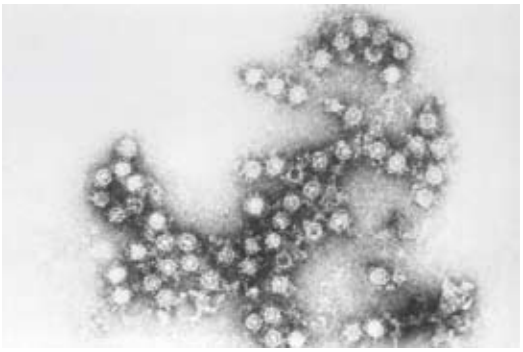
SERION ELISA *classic*

Coxsackievirus IgA / IgG / IgM

SERION ELISA *classic* Coxsackievirus IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Coxsackievirus. The separate detection of individual immunoglobulin classes offers a confirmation of contact with the pathogen and the determination of the disease state.



Electron micrograph of Coxsackievirus B4 Viriones (Source: United States Federal Government).

Pathogen

Coxsackieviruses A (23 serotypes) and B (6 serotypes) and Echoviruses (31 serotypes) belong to the family of *Picornaviridae*, genus Enterovirus. This virus group shares similar physical, chemical and biological properties and epidemiological patterns.
Enteroviruses are ubiquitous pathogens that are primarily transmitted by faecal-oral route and additionally by aerosol (droplet infection). The portal of entry of enteroviruses is the respiratory tract (especially the oropharynx) and the intestine, where they infect and multiply in the oropharyngeal and intestinal epithelium. From there, the viruses may be carried by the bloodstream to the cells of the reticulo-endothelial system and certain target tissues such as myocard, meninges and skin.

Disease

More than 90 % of enterovirus infections progress sublinically or result only in temporary mild complaints in the upper respiratory tract such as sore throat with or without rhinitis often accompanied by fever. In addition, adults may suffer from pharyngitis, tonsilitis and common cold symptoms. In particular Coxsackieviruses are responsible for the so called summer flu and febrile, catarrhal infections.

The following diseases may be caused by Coxsackieviruses: vesicular pharyngitis (herpangina), aseptic meningitis, meningoencephalitis, "hand-foot-and-mouth" disease, pleurodynia (Bornholm disease), carditis (myocarditis, pericarditis, myopericarditis, encephalomyo-carditis), maculopapular exanthema, hepatitis, acute haemorrhagic conjunctivitis and fetal damage. Vesicular exanthema and paralysis are rare complications.
In patients with congenital or induced immune deficiency, Coxsackieviruses may persist after infection leading to chronic diseases such as arthritis, infection of the CNS, chronic enteritis or relapsing pericarditis.

Diagnosis

Coxsackievirus infections can be confirmed by virus isolation and identification or serologically by detection of specific antibodies. PCR completes the classic methods. In serodiagnostics ELISA techniques have been established during recent years. Due to the large number of serotypes, assays showing a broad reactivity are favoured for diagnosis. While intact virus particles show high type specificity, broad reactivity is achieved by using heat denaturated virions as antigens. In the SERION ELISA *classic* Coxsackievirus, highly purified, heat-treated Coxsackieviruses types B1 and B5 are bound to the solid phase. These two serotypes are described as sufficiently cross-reactive to enable heterotypical diagnosis of Coxsackievirus infection.

Validation of SERION ELISA *classic* Coxsackievirus

The SERION ELISA *classic* Coxsackievirus was evaluated in an external study by the analysis of 72 serum samples from patients with suspected Enterovirus infection. Two commercially available Enterovirus ELISA were used as a reference. Due to the fact, that only two positive serum samples were available for the evaluation of SERION ELISA *classic* Coxsackievirus IgM, a statistical confimred determination of sensitivity was not possible.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Coxsackievirus IgA	88,9 %	> 99 %
Coxsackievirus IgG	> 99 %	> 99 %
Coxsackievirus IgM	-	> 99 %

Precision

SERION ELISA *classic* Coxsackievirus IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,317	1,1	0,294	12,5
negative	0,569	1,4	0,586	10,5
positive	0,813	1,1	0,880	9,7

SERION ELISA *classic* Coxsackievirus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,158	4,6	0,164	7,3
weak positive	1,041	2,6	1,142	8,9
positive	1,162	2,7	1,250	9,6

SERION ELISA *classic* Coxsackievirus IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,349	1,6	0,337	9,9
positive	0,729	2,5	0,762	8,6
positive	1,728	2,3	1,767	7,9

Order Information

SERION ELISA *classic* Coxsackievirus IgA	**Order Nr.: ESR 134 A**
SERION ELISA *classic* Coxsackievirus IgG	**Order Nr.: ESR 134 G**
SERION ELISA *classic* Coxsackievirus IgM	**Order Nr.: ESR 134 M**
Reference serum Coxsackievirus IgA	**Order Nr.: BR 134 A**
Reference serum Coxsackievirus IgG	**Order Nr.: BR 134 G**

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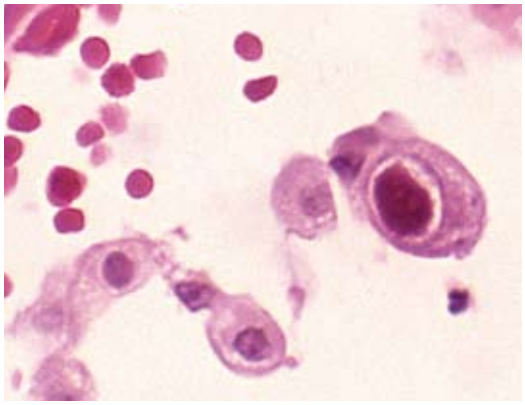
SERION ELISA *classic*

Cytomegalovirus IgG / IgM

SERION ELISA *classic* Cytomegalovirus IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum, plasma or cerebrospinal fluid directed against Cytomegalovirus. The SERION ELISA *classic* Cytomegalovirus IgM is recommended for the detection of acute infections and suitable for newborn screening on dried blood spots (DBS). Positive results should be further tested with conformatorial assays, e. g. avidity tests. The SERION ELISA *classic* Cytomegalovirus IgG is recommended for determining immune status.



Micrograph of a pneumocyte infected with Cytomegalovirus (Source: CDC, Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Cytomegalovirus (CMV) is a DNA virus and a member of the human Herpesvirus group. Primary infection may result from contact with saliva, genital secretions, urine and breast milk of infected persons, as well as transplacentally or iatrogenically (transfusions, transplantations). After primary infection a lifelong latent infection status ensues. The virus resides in lymphocytes where it may be reactivated under certain circumstances. The frequencies of infection in the developed and underdeveloped countries vary between 45 % and 50 % or over 90 %, respectively.

Disease

Primary infections are usually asymptomatic. Clinical manifestations vary considerably depending on age and immunocompetence ranging from localised infections to generalised disease. Significant clinical disease or death may follow infection of immuncompromised individuals. Reactivation in immunocompetent adults and concomitant secretion of the virus is usually asymptomatic. In immuncompromised patients reactivation of CMV infection

may result in clinically severe disease. CMV infection is the major cause of complications in iatrogenic immunsuppression after organ transplantation and in HIV-infected persons.
Primary as well as reactivated infections of pregnant women may result in foetopathy. The risk of fetal damage is higher in case of primary infections than during reactivations. If seroconversion occurs during pregnancy, virus transmission to the fetus occurs in 40 % of the cases. Up to 15 % of the affected infants suffering damage at birth. Late manifestations of disease can be observed in 10 to 15 % of infected children. CMV-infection is the most frequent congenital and postnatal infection.

Diagnosis

The diagnosis of a CMV infection is occured by clinical symptoms and medical examination. For serological diagnosis immunoglobulin specific ELISA are recommended.

Validation of SERION ELISA *classic* Cytomegalovirus

For the validation of SERION ELSA *classic* Cytomegalovirus IgG and IgM 331 serum samples from patients (pregnant women, patients undergoing transplantation, patients with HSV, VZV, HHV-6, EBV, Rubella Virus and Toxoplasma infections) were analysed in comparison to commercially available ELISA. Sera classified as borderline were not included in the calculation. Samples with slight to moderate haemolysis (n=25), lipaemic (n=15) and icteric sera (n=60) do not influence the test result.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Cytomegalovirus IgG	99,0 %	> 99 %
Cytomegalovirus IgM	> 99 %	92,0 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Cytomegalovirus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,548	5,70	0,477	10,30
positive	1,166	7,00	1,041	8,60
positive	2,644	4,80	2,276	6,70

SERION ELISA *classic* Cytomegalovirus IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,473	3,1	0,416	6,6
positive	1,346	2,3	1,098	14,2

Order Information

SERION ELISA *classic* Cytomegalovirus IgG — **Order Nr.: ESR 109 G**
SERION ELISA *classic* Cytomegalovirus IgM — **Order Nr.: ESR 109 M**
Avidity reagent Cytomegalovirus — **Order Nr.: B 109 AVID**
Reference serum Cytomegalovirus IgG — **Order Nr.: BR 109 G**
Reference serum Cytomegalovirus IgM — **Order Nr.: BR 109 M**
Reference serum Cytomegalovirus avidity — **Order Nr.: BR 109 AVID**

The SERION ELISA *classic* Cytomegalovirus IgG is evaluated for the **analysis of cerebrospinal fluid**.
The SERION ELISA *classic* Cytomegalovirus IgM is evaluated for **neonatal screening** on Dried Blood Spots
(For more information see SERION ELISA *classic* neonatal).

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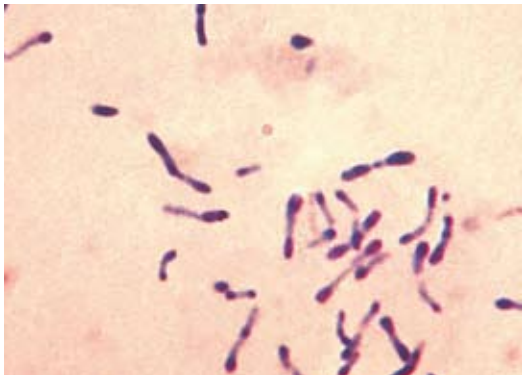
SERION ELISA *classic*
Diphtheria IgG

SERION ELISA *classic* Diphtheria IgG test is a quantitative immunoassay for the detection of human antibodies in serum or plasma directed against the diphtheria toxin. The SERION ELISA *classic* Diphtheria IgG is recommended for vaccination control and for the determination of the current individual immune status to prevent hyperimmune reactions.



Micrograph of *Corynebacterium diphtheriae* stained with methylenblue (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Diphtheria is caused by *Corynebacterium diphtheriae*, the toxin is responsible for pathogenicity.

Disease

Diphtheria is a globally ubiquitous infectious disease, mainly transmitted by droplet infection and in rare cases by smear infection (skin diphtheria). The incubation time is usually two to five days, but may range up to eight days. Clinical symptoms of diphtheria in temperate zones mainly affect the respiratory tract. A primary infection can involve the tonsillar pharyngeal region or cause laryngeal, nasal or tracheobronchial primary infection sequentially. The most important complications are myocarditis and polyneuritis. In 5 to 25 % of cases the course of diphtheria is lethal due to respiratory obstruction or coronary failure.

In the Commonwealth of Independent States (CIS) regional epidemics have lead to an increase in diphtheria morbidity during the past 10 years, according to the WHO. As a consequence of extensive use of vaccination in western industrialized countries cases of this once common disease have declined considerably.

In recent years a reduction in vaccine uptake has resulted in lower immunity prevalence against diphtheria. Consequently, success of vaccination control as well as immunity status determination in order to avoid hyper immune reactions is becoming increasingly important for routine laboratories.
The STIKO (Ständige Impfkommission on the Robert-Koch-Institute in Berlin) recommends a combined vaccine for the active immunisation of babies. The first immunisation takes place upon the completion of the second month of life; afterwards two further immunisations are made in an interval of 4 to 8 weeks. Booster shots should be made between the 12th and 18th month of life and also in the 5th to 6th and 11th to 18th year of life. For Diphtheria a booster immunization is then necessary after ten years.

Diagnosis

For practical and economic reasons a passive hemagglutination test is used for the detection of diphtheria-antitoxin in human sera. It is specified in international units per milliliter (IU/ml). However, ELISA techniques have been increasingly utilized in recent years, because of increasing numbers of testings and their ability for automated processing. Adjusted to international reference sera, the specification of the SERION ELISA *classic* Diphtheria IgG is IU/ml.

Validation of SERION ELISA *classic* Diphtheria IgG

The SERION ELISA *classic* Diphtheria IgG was evaluated with commercially available reference sera (source: Serolife, Frauenfeld/Switzerland) against the indirect hemagglutination assay (IHA) as well as with tissue culture methods (TC). The activity was indicated in IU/ml. The sensitivity and specificity can not be calculated since the test does not differentiate between positive and negative results. However, the assay supports a continuous quantitative evaluation of antibody activity.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV(%) (n=10)
negative	0,322	3,60	--	--
weak positive	0,690	3,90	0,816	4,60
positive	1,048	3,90	1,344	7,00

Order Information

SERION ELISA *classic* Diphtheria IgG **Order Nr.: ESR 130 G**
Reference serum Diphtheria IgG **Order Nr.: BR 130 G**

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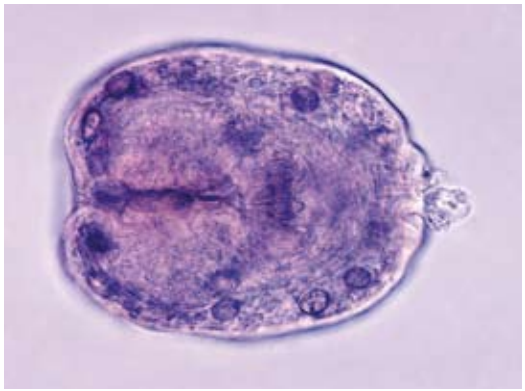
SERION ELISA *classic*
Echinococcus IgG

SERION ELISA *classic* Echinococcus IgG test is a quantitative and qualitative immunoassay for detection of human antibodies in serum or plasma directed against *Echinococcus granulosus* and *Echinococcus multilocularis*. The assay is used for the diagnosis of acute infections, serological follow up of therapy and epidemiological studies.



Micrograph of *Echinococcus granulosus* (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Echinococcosis is a zoonotic infection caused by developmental stages (larvae, hydatid, metacestodes) of two kinds of tapeworms *Echinococcus granulosus* and *Echinococcus multilocularis*. Infections with *E. granulosus* occur worldwide, while infections caused by *E. multilocularis* are restricted to the northern hemisphere. Sources of infection are final hosts i. e. dogs for *E. granulosus* and primarily foxes for *E. multilocularis* as well as food contaminated with parasite eggs.

Disease

After oral ingestion of parasite eggs by humans (as an intermediate host) and hematogenous distribution inside the host, the *E. granulosus* larvae (oncospheres) begin to vesiculate mainly in the liver (approx. 60 % of the patients), but also in the lungs (20 %) and in other organs (20 %). The parasites form spherical, unilocular, fluid-filled cysts which can achieve diameters between 1 to 15 cm. In contrast to cystic echinococcosis, *E. multilocularis* larvae are found almost exclusively (98 %) in the liver, but secondary lesions can spread metastatically to other organs (lungs, kidneys, CNS and others). The parasites grow infiltrative and tumor-like in the host tissue and, during weeks up to months, form a spongy „alveolar" system of connected cavities which are filled with small vesicles.

The diffuse borders are usually not well delimited from adjacent liver tissue. Cysts of *E. granulosus* cause pathological damage or dysfunction mainly by the gradual process of space-occupying repression or displacement of vital host tissue, vessels, or organs. Consequently, clinical pathology varies greatly, depending on the site and size of the cyst, e. g. epigastric and thoracic pain. For differential diagnosis tumors of different genesis (malign, benign) should be considered. Continuous tissue destruction caused by *E. multilocularis* leads to clinical manifestations of liver dysfunction after an incubation time of 5 up to 15 years. The nonspecific symptoms usually include epigastric pain (36 % of the patients) and obstructive jaundice
(27 %). In untreated patients lethality was found to be 94 to 100 %. Treatment significantly decreased mortality to 10 to 14 %.

Diagnosis

Diagnosis of echinococcosis relies on epidemiologic and clinical findings, on detection of cysts by radiology, ultrasonography and computer tomography, as well as on serologic techniques. With regard to *E. multilocularis*, most patients develop parasite-specific antibodies.
In infections caused by *E. granulosus* cyst integrity, vitality and size and the specific organ parasitized may affect the antibody response. Patients with liver infections by *E. granulosus* are more likely to be IgG antibody seropositive than patients with lung infections by *E. granulosus*. Consequently, seronegativity can not exclude echinococcosis.

Validation of SERION ELISA *classic* Echinococcus IgG

The SERION ELISA *classic* Echinococcus IgG was evaluated by analysis of 90 serum samples from blood donors and 34 serum samples from patients with suspected *Echinococcus* infection. The results were compared with the results of a commercially available ELISA, which, like the SERION ELISA *classic* Echinococcus IgG, is based on cyst fluid of *Echinococcus granulosus*. Sera classified as borderline were not included in the calcula-tion.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Echinococcus IgG	> 99 %	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Echinococcus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,34	5,3	0,38	4,2
positive	0,71	2,5	0,75	2,6
positive	1,40	1,9	1,44	3,2

Order Information

SERION ELISA *classic* Echinococcus IgG **Order Nr.: ESR 107 G**

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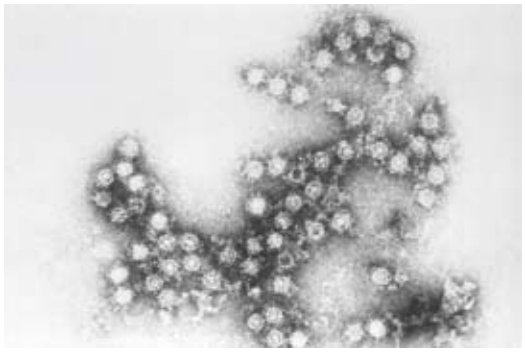
SERION ELISA *classic*

Echovirus IgA / IgG / IgM

SERION ELISA *classic* Echovirus IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Echovirus. The separate detection of individual immunoglobulin classes offers a confirmation of contact with the pathogen and the determination of the disease state.



Electron micrograph of Coxsackievirus B4 Viriones (Source: United States Federal Government).

Pathogen

Coxsackieviruses A (23 serotypes) and B (6 serotypes) and Echoviruses (31 serotypes) belong to the family of *Picornaviridae*, genus Enterovirus. This virus group shares similar physical, chemical and biological properties and epidemiological patterns.
Enteroviruses are ubiquitous pathogens that are primarily transmitted by faecal-oral route and additionally by aerosol (droplet infection). The portal of entry of enteroviruses is the respiratory tract (especially the oropharynx) and the intestine, where they infect and multiply in the oropharyngeal and intestinal epithelium. From there, the viruses may be carried by the bloodstream to the cells of the reticulo-endothelial system and certain target tissues such as myocard, meninges and skin.

Disease

More than 90 % of enterovirus infections progress sublinically or result only in temporary mild complaints in the upper respiratory tract such as sore throat with or without rhinitis often accompanied by fever. In addition, adults may suffer from pharyngitis, tonsilitis and common cold symptoms. In particular Coxsackieviruses are responsible for the so called summer flu and febrile, catarrhal infections.

The following diseases may be caused by Echoviruses: aseptic meningitis, encephalitis, ataxia, Guillain-Barré syndrome, exanthema, diarrhoea, hepatic disorders and fetal damage. Paralysis, epidemic myalgia, pericarditis and myocarditis rarely occur.
In patients with congenital or induced immune deficiency Echoviruses may persist after infection, leading to chronic diseases like enteritis, arthritis, affection of the CNS or chronic heart disease.

Diagnosis

Echovirus infections can be confirmed by virus isolation and identification or serologically by detection of specific antibodies. PCR completes the classic methods. In serodiagnostics ELISA techniques have been established during the recent years. Due to the large number of Echovirus serotypes, assays showing a broad Echovirus reactivity are favoured for diagnosis. While intact virus particles show high type specificity, broad reactivity is achieved by using heat denaturated virions as antigens. In the SERION ELISA *classic* Echovirus highly purified, heat-treated Echoviruses type 6 and 9 are bound to the solid phase. These two serotypes are described as sufficiently cross-reactive to enable heterotypical diagnosis of Echovirus infection

Validation of SERION ELISA *classic* Echovirus

The SERION ELISA *classic* Echovirus were evaluated in an external study by the analysis of 72 serum samples from patients with suspected Enterovirus infection. Two commercially available ELISA were used as a reference. Sera classified as borderline were not included in the calculation.

SERION ELISA *classic*	Sensitivity	Specificity
Echovirus IgA	88,9 %	> 99 %
Echovirus IgG	> 99 %	97,6 %
Echovirus IgM	> 99 %	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Echovirus IgA

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
borderline	0,320	9,5	0,336	8,9
positive	0,807	3,3	0,843	7,9
positive	0,999	4,3	1,068	4,5

SERION ELISA *classic* Echovirus IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
negative	0,200	3,4	0,234	5,4
weak positive	0,578	2,4	0,671	4,0
positive	0,848	1,9	0,893	4,4

SERION ELISA *classic* Echovirus IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
negative	0,166	5,7	0,166	5,7
weak positive	0,353	1,5	0,353	1,5
positive	0,684	2,2	0,684	2,2

Order Information

SERION ELISA *classic* Echovirus IgA	**Order Nr.: ESR 135 A**
SERION ELISA *classic* Echovirus IgG	**Order Nr.: ESR 135 G**
SERION ELISA *classic* Echovirus IgM	**Order Nr.: ESR 135 M**
Reference serum Echovirus IgA	**Order Nr.: BR 135 A**
Reference serum Echovirus IgG	**Order Nr.: BR 135 G**

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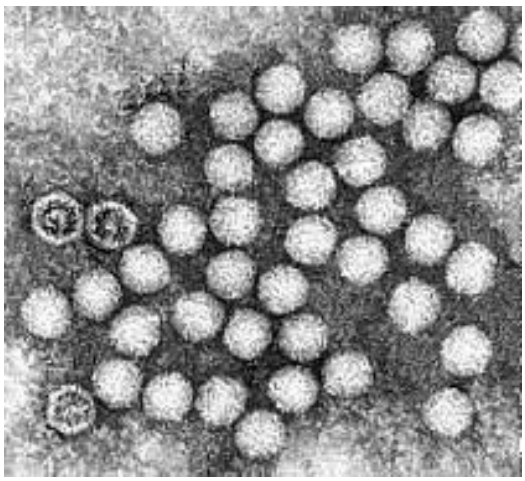
SERION ELISA *classic*

Enterovirus IgA / IgG / IgM

SERION ELISA *classic* Enterovirus IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Enterovirus. The separate detection of individual immunoglobulin classes offers a confirmation of contact with the pathogen and the determination of the disease state.



Electron micrograph of Enterovirus (Source: King Saud University).

Pathogen

Coxsackieviruses A (23 serotypes) and B (6 serotypes) and Echoviruses (31 serotypes) belong to the family of *Picornaviridae*, genus Enterovirus. This virus group shares similar physical, chemical and biological properties and epidemiological patterns.
Enteroviruses are ubiquitous pathogens that are primarily transmitted by faecal-oral route and additionally by aerosol (droplet infection). The portal of entry of enteroviruses is the respiratory tract (especially the oropharynx) and the intestine, where they infect and multiply in the oropharyngeal and intestinal epithelium. From there, the viruses may be carried by the bloodstream to the cells of the reticulo-endothelial system and certain target tissues such as myocard, meninges and skin.

Disease

More than 90 % of enterovirus infections progress sublinically or result only in temporary mild complaints in the upper respiratory tract such as sore throat with or without rhinitis often accompanied by fever. In addition, adults may suffer from pharyngitis, tonsilitis and common cold symptoms. In particular Coxsackieviruses are responsible for the so called summer flu and febrile, catarrhal infections.

The following diseases may be caused by Enteroviruses: abacterial meningitis, meningoencephalitis, herpangina, exanthema (Enteroviruses), pleurodynia, carditis (Coxsackie B), hemorrhagic conjunctivitis (Coxsackieviruses), encephalitis, ataxia, Guillain-Barré syndrome (Echoviruses). In patients with congenital or induced immune deficiency Enteroviruses may persist after infection, leading to chronic diseases like enteritis, arthritis, affection of the CNS or chronic heart disease.

Diagnosis

Enterovirus infections can be confirmed by virus isolation and identification or serologically by detection of specific antibodies. PCR supplements the classic methods. In serodiagnostics ELISA techniques have been established during the recent years. Due to the large number of serotypes, assays showing a broad reactivity are favoured for diagnosis. While intact virus particles show high type specificity, broad reactivity is achieved by using heat denaturated virions as antigens. In the SERION ELISA *classic* Enterovirus highly purified, heat-treated antigen preparations are used. Echovirus type 6 and Coxsackievirus type B5 are described as sufficiently cross-reactive to enable heterotypical diagnosis of Enterovirus infections

Validation of SERION ELISA *classic* Enterovirus

The SERION ELISA *classic* Enterovirus were evaluated by the analysis of 71 serum samples from patients with suspected Enterovirus infection and 103 serum samples from blood donors. Commercially available ELISA of a leading European manufacturer were used as a reference. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Enterovirus IgA	80,0 %	94,7 %
Enterovirus IgG	87,0 %	> 99 %
Enterovirus IgM	83,3 %	97,3 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Enterovirus IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,631	6,6	0,686	9,0
weak positive	0,731	5,6	0,773	4,5
positive	1,279	6,3	1,326	3,0

SERION ELISA *classic* Enterovirus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,434	3,4	0,490	4,4
negative	0,783	2,5	0,841	3,0
weak positive	0,982	2,7	1,026	5,8

SERION ELISA *classic* Enterovirus IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,316	1,9	0,309	4,5
weak positive	0,658	2,4	0,689	4,1
positive	0,745	3,3	0,756	2,8

Order Information

SERION ELISA *classic* Enterovirus IgA	**Order Nr.: ESR 133 A**
SERION ELISA *classic* Enterovirus IgG	**Order Nr.: ESR 133 G**
SERION ELISA *classic* Enterovirus IgM	**Order Nr.: ESR 133 M**
Reference serum Enterovirus IgA	**Order Nr.: BR 133 A**
Reference serum Enterovirus IgG	**Order Nr.: BR 133 G**

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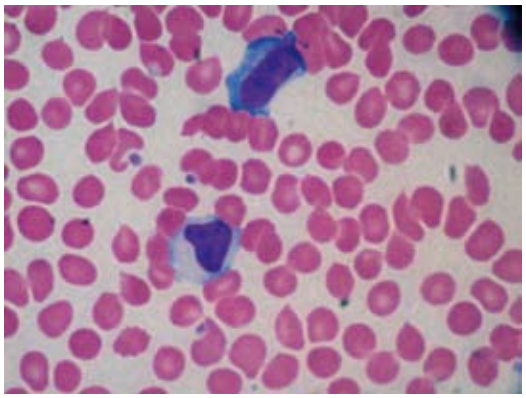
SERION ELISA *classic*

Epstein-Barr Virus IgG / IgM

SERION ELISA *classic* Epstein-Barr Virus EA IgG, VCA IgG, IgM and EBNA 1 IgG tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against components of the Epstein-Barr Virus. The SERION ELISA *classic* Epstein-Barr Virus EA IgG and VCA IgM are recommended for the detection of acute infections or reactivations. The SERION ELISA *classic* Epstein-Barr Virus VCA IgG determines primary and recent infections. The SERION ELISA *classic* EBNA1 IgG is recommended for the determination of past infections.



Micrograph of a blood smear with reactive lymphocytes.

Pathogen

The ubiquitous Epstein-Barr Virus (EBV) is a DNA virus and member of the Human Herpesvirus group. Seroprevalence in adults is high (90 - 95 %). In industrial countries primary infection is mainly restricted to teenagers or young adults. In contrast in non-developed countries, primary infection occurs typically much earlier in life. About 50 % of individuals infected in adulthood show clinical symptoms whereas clinical findings have been rarely observed in infections of younger children. Transmission takes place primarily via the saliva of infected individuals.

Disease

Primary infection, the cells of the salivary gland are infected first and the subsequent infection of B cells in the adjacent lymphoid tissue the virus spreads throughout the body. The disease resulting from primary infection is called infectious mononucleosis (IM) or glandular fever. In the later course of infection high fever, splenomegalia, lymphadenitis, thrombocytopenia and hepatitis may be observed. In some regions, the Epstein-Barr Virus is closely associated with nasopharyngeal carcinoma and Burkitt´s lymphoma.

Diagnosis

About two weeks after infection, anti-EA IgG, anti-VCA IgM and anti-VCA IgG-antibodies can be detected in the patient´s serum. Highest anti-VCA IgM antibody concentration is found about three weeks, highest anti-VCA IgG concentration about six weeks after onset of symptoms. Usually, this elevated level remains life-long. About three weeks after onset of symptoms the anti-EBNA 1 IgG antibody production starts. Anti-EBNA-1 IgG antibodies may be used to demonstrate previous infection. Following normal EBV infection the anti-EBNA-1 antibody concentration remains life-long at a high level. In most cases of reactivations, e. g. caused by immunosuppression, the anti-EA IgG antibody concentration increases sharply. Therefore high anti-EA-IgG titers are a reliable marker for reactivations.

Validation of SERION ELISA *classic* Epstein-Barr Virus

The SERION ELISA *classic* EBV EA IgG, VCA IgM, VCA IgG and EBNA-1 IgG were evaluated in comprehensive studies in comparision to assays of competitors and to the immunoblot based on recombinant antigens (Goldstandard).

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
EBV VCA IgG	98,1 %	98,5 %
EBV VCA IgM	97,4 %	97,3 %
EBV EA IgG	81,8 %	97,6 %
EBV EBNA 1 IgG	98,5 %	> 99 %

Precision

SERION ELISA *classic* VCA IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,554	2,2	0,644	7,1
positive	1,001	2,9	1,035	6,5
positive	2,034	2,4	2,067	3,2

SERION ELISA *classic* VCA IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
positive	1,582	5,1	1,703	6,4
positive	2,249	7,9	2,311	8,7

SERION ELISA *classic* EBNA 1 IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,887	3,2	0,927	4,4
positive	1,699	2,9	1,873	2,8
positive	2,434	2,1	2,616	2,2

SERION ELISA *classic* EA IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,420	4,2	0,396	11,5
positive	1,137	3,8	1,121	4,9
positive	1,368	8,0	1,252	8,2

Order Information

SERION ELISA *classic* EBV VCA IgG	**Order Nr.: ESR 1361 G**
SERION ELISA *classic* EBV VCA IgM	**Order Nr.: ESR 1361 M**
SERION ELISA *classic* EBV EBNA 1 IgG	**Order Nr.: ESR 1362 G**
SERION ELISA *classic* EBV EA IgG	**Order Nr.: ESR 1363 G**
Reference serum EBV VCA IgG	**Order Nr.: BR 1361 G**
Reference serum EBV VCA IgM	**Order Nr.: BR 1361 M**
Reference serum EBV EBNA 1 IgG	**Order Nr.: BR 1362 G**
Reference serum EBV EA IgG	**Order Nr.: BR 1363 G**

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SERION ELISA *classic*

Francisella tularensis IgG / IgM

SERION ELISA *classic* Francisella tularensis IgG and IgM tests are qualitative and quantitative immunoassays for the detection of human antibodies in serum or plasma directed against the lipopolysaccharide (LPS) of *Francisella tularensis*. The assays are recommended for the diagnosis of tularemia, to monitor the success of vaccination, to determine the immune status prior to immunisation to avoid vaccination injury as well as for epidemiological studies.

Feral hares as carrier of *Francisella tularensis*.

Pathogen

Tularemia is a zoonosis caused by the bacterium *Francisella tularensis* which can present in a variety of clinical manifestations. The condition in animals resembles that of plague and the disease often affects hares and wild rabbits, it is also called rabbit fever. *Francisella tularensis* (formerly also called *Pasteurella tularensis*) is a gram-negative, pleomorphic bacterium. The three clinically relevant forms of the four subspecies are difficult to differentiate serologically. However, two types can be distinguished epidemiologically, biochemically and genotypically: *Francisella tularensis biovar tularensis* (type A) is highly virulent. Untreated, the infection has a high mortality. *Francisella tularensis biovar holarctica* (type B) is much less virulent but can also cause severe illness.

Various small mammals, such as hares, rabbits, mice, rats and squirrels are natural reservoirs of *Francisella tularensis*. The pathogen has also been detected in soil samples and water courses and can survive there for prolonged periods depending on climatic conditions. Human infection may occur through direct skin and mucosal contact with infected animals or their excreta. Ectoparasites can also be considered as vectors. Consumption of infected and insufficiently cooked meat and inhalation of infectious dust are also potential routes of infection. Transmission from human to human has not been observed.

Disease

Tularemia occurs throughout the northern hemisphere between 30 and 71 degrees of latitude, especially in Scandinavia, Russia, Japan, China, USA and Canada. The rural population is often affected. In Germany, tularemia is regarded as a rare infectious disease.
The first symptoms of tularemia usually appear 2 to 5 days after the infection has occurred. However, depending on dose and route of infection and the virulence of the bacterial strain, the incubation period can vary between 1 and 21 days. Besides the classical general symptoms such as fever, malaise and joint and muscle pains, the clinical picture of tularemia can be very varied. Inhalation of the pathogen often leads to pulmonary manifestation (e.g. pneumonia) or to a septic, typhus-like illness. Infection through the digestive tract can lead to vomiting, abdominal pain and diarrhoea
When identified promptly, tularemia can be treated effectively with antibiotics. The failure of many organ systems and involvement of the central nervous system lead to death in 40 % of cases of infection with the type A bacteria if untreated. With treatment, the mortality is about 1 %. Infection with type B bacteria usually takes a mild course with low mortality.

Diagnosis

Detection through culture from peripheral blood, swabs and biopsy material is difficult and can take several weeks. Since it is a highly infectious pathogen, such diagnostic tests are reserved for special laboratories. For this reason, identification is usually indirect by immunological and molecular methods. Serological diagnosis can be made by means of ELISA through the detection of specific antibodies. The SERION ELISA *classic* Francisella tularensis IgG and IgM enables quantitative measurement of human IgG and IgM antibodies to the lipopolysaccharide (LPS) of *Francisella tularensis ssp. holarctica* (LVS strain) in serum or plasma.

Validation of SERION ELISA *classic* Francisella tularensis

To calculate the performance characteristics of SERION ELISA *classic* Francisella tularensis IgG and IgM 99 negative serum samples from blood donors and 101 positive serum samples from immunized individuals were examined. The assays were validated against the in-house test of the Medical Corps Academy of the Bundeswehr in Munich, Germany (national reference laboratory for tularemia). Sera classified as borderline were not included in the calculation.

SERION ELISA *classic*	Sensitivity	Specificity
Francisella tularensis IgG	> 99 %	96,9%
Francisella tularensis IgM	> 99 %	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Francisella tularensis IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=20)
weak positive	0,810	3,4	0,860	6,3
positive	1,153	2,1	1,239	8,4
positive	1,898	2,7	2,007	3,7

SERION ELISA *classic* Francisella tularensis IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=20)
weak positive	0,445	7,4	0,574	8,2
positive	0,604	5,9	0,607	9,2
positive	1,307	4,4	1,219	7,9

Order Information

SERION ELISA *classic* Francisella tularensis IgG **Order Nr.: ESR 142 G**
SERION ELISA *classic* Francisella tularensis IgM **Order Nr.: ESR 142 M**

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SERION ELISA *classic*

Hantavirus Puumala IgG / IgM

SERION ELISA *classic* Hantavirus Puumala IgG and IgM tests are qualitative and quantitative immunoassays for the detection of human antibodies in serum or plasma directed against the nucleocapsid protein of the Hantavirus serotype Puumala. The assays are recommended for the diagnosis of Hantavirus infections and epidemiological studies.

In Europe the Hantavirus serotype Puumala is transmitted by *Clethrionomys glareolus.*

Pathogen

Hantaviruses belong to the family *Bunyaviridae*. They occur throughout the world and there are several different serotypes. The Puumula virus is the main form in central and northern Europe. Rodents are the natural reservoir, particularly mice and rats. The viruses are transmitted to man in the excretions of infected animals, which are swirled up in dust and breathed in. People who spend a lot of time outdoors, such as hunters, foresters and soldiers, are thought to be at particular risk.

Disease

Hantaviruses of the serotype Puumala cause a mild form of haemorrhagic fever with renal syndrome, which is also known as epidemic nephropathy (EN). The incubation period is 10 to 20 days. The illness starts with general symptoms resembling flu, including headache, myalgia, chills and conjunctivitis. Additional clinical manifestations include abdominal and lumbar pain and transient impaired renal function, which may require dialysis treatment. The mortality of epidemic nephropathy is about 1 %. The clinical course of epidemic nephropathy is milder than that of haemorrhagic fever with renal syndrome, caused by viruses of the serotype Hantaan.

Diagnosis

Hantavirus infections are usually diagnosed from the clinical presentation, together with the results of serological assays. Laboratory confirmation of an infection is usually based on the detection of IgM and IgG antibodies to Hantaviruses of serotypes Puumala and Hantaan.

Validation of SERION ELISA *classic* Hantavirus Puumala

To calculate the performance characteristics of the SERION ELISA *classic* Hantavirus Puumala IgG, 131 negative and 85 positive serum samples were analysed in an external study. Analogously, 124 negative and 49 positive serum samples were used for the validation of the SERION ELISA *classic* Hantavirus Puumala IgM. The immunoassays were compared to the test of a leading European manufacturer. Borderline results were not included in the calculation of sensitivity and specificity.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Hantavirus Puumala IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=20)
weak positive	0,992	1,9	1,092	5,3
positive	1,781	2,6	1,842	3,4
positive	2,269	1,1	2,394	2,7

SERION ELISA *classic* Hantavirus Puumala IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=20)
weak positive	0,938	1,5	1,001	3,1
positive	1,610	1,2	1,683	2,7
positive	2,260	2,0	2,289	2,0

Order Information

SERION ELISA *classic* Hantavirus Puumala IgG **Order Nr.: ESR 145 G**
SERION ELISA *classic* Hantavirus Puumala IgM **Order Nr.: ESR 145 M**

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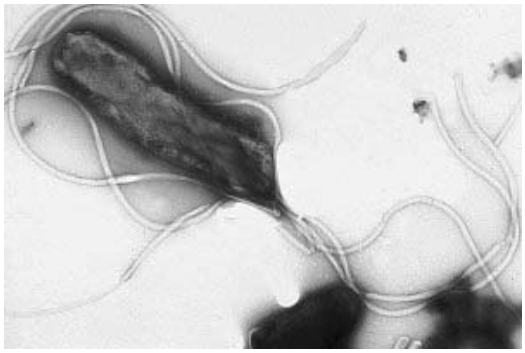
SERION ELISA *classic*

Helicobacter pylori IgA / IgG / IgM

SERION ELISA *classic* Helicobacter pylori IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *Helicobacter pylori*. The SERION ELISA *classic* Helicobacter pylori are recommended for the determination of exposure to *Helicobacter pylori* and disease stage.



Electron micrograph of *Helicobacter pylori* (Source: Yutaka Tsutsumi, Department of Pathology Fujita Health University School of Medicine).

Pathogen

Helicobacter pylori is a gram negative, motile, spiral bacterium. Associated infections have to be regarded in distinct relation to the age of the patients. In industrialized countries from North America to Central Europe, the prevalence per life-decade increases by 10 %. Total prevalence of the population in this area is about 40 %. In certain studies a causative relation between infection with *H. pylori* and gastric carcinoma have been tentatively established. Transmission routes have not been fully elucidated. Oral-oral and oral-faecal transmission are discussed.

Disease

Infections by *Helicobacter pylori* can be classified as acute or chronic infections. 80 to 90 % of gastritis cases are caused by *Helicobacter pylori*.
Diseases associated with *H. pylori* infections are *ulcus duodeni* (95 %), *ulcus ventriculi* (90 %) and the MALT (Mucosa Associated Lymphatic Tissue) lymphoma in 60 to 70 % of cases. Patients suffering from chronic *Helicobacter pylori* infection have a six times higher risk developing MALT-lymphoma compared to healthy individuals.

Diagnosis

Diagnosis of *H. pylori* infections may be devided in non-invasive and invasive techniques. Histology, urease rapid test (e.g. CLO test), microbiological techniques such as culture or molecular biologic tests (PCR) belong to the invasive methods. The C13-breath test and serological tests belong to the group of non-invasive methods. The detection of serum antibodies can be used for therapy control after eradication treatment. For the detection of significant titer movements, there has to be a time period of at least 6 months between eradication and serologic control. Particularily in the case of IgG antibodies, the possibility of persistence for several months or even years has to be taken into consideration. Consequently, serological control alone is limited and the non-invasive C13 breath-test is recommended in addition.

Validation of SERION ELISA *classic* Helicobacter pylori

146 serum samples from patients with suspected infection with *Helicobacter pylori* and from blood donors were used for the evaluation of the SERION ELISA *classic* Helicobacter pylori IgA and IgG. The samples were tested in comparison to a commercially available immunoblot. For the evaluation of the SERION ELISA *classic* Helicobacter pylori IgM 186 serum samples from patients with clinically manifested infections with *Helicobacter pylori* and from blood donors were tested in comparison to a commercially available ELISA of a leading European manu-facturer. Sera classified as borderline were not included in the calculation.

SERION ELISA *classic*	Sensitivity	Specificity
Helicobacter pylori IgA	84,3 %	> 99 %
Helicobacter pylori IgG	> 99 %	93,8%
Helicobacter pylori IgM	> 99 %	80,1 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Helicobacter pylori IgA

Sample	Mean value OD	Intraas-say CV (%) (n=20)	Mean value OD	Interas-say CV (%) (n=10)
weak positive	0,484	7,8	0,551	10,5
positive	1,152	4,9	1,300	8,7

SERION ELISA *classic* Helicobacter pylori IgG

Sample	Mean value OD	Intraas-say CV (%) (n=20)	Mean value OD	Interas-say CV (%) (n=10)
weak positive	0,760	10,1	0,753	10,9
positive	1,239	5,0	1,249	6,9
positive	1,558	7,4	1,639	4,9

SERION ELISA *classic* Helicobacter pylori IgM

Sample	Mean value OD	Intraas-say CV (%) (n=20)	Mean value OD	Interas-say CV (%) (n=10)
negative	0,154	7,0	0,161	15,2
positive	0,709	9,1	0,691	15,3
positive	1,872	6,1	1,628	7,2

Order Information

SERION ELISA *classic* Helicobacter pylori IgA	**Order Nr.: ESR 118 A**
SERION ELISA *classic* Helicobacter pylori IgG	**Order Nr.: ESR 118 G**
SERION ELISA *classic* Helicobacter pylori IgM	**Order Nr.: ESR 118 M**
Reference serum Helicobacter pylori IgA	**Order Nr.: BR 118 A**
Reference serum Helicobacter pylori IgG	**Order Nr.: BR 118 G**
Reference serum Helicobacter pylori IgM	**Order Nr.: BR 118 M**

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SERION ELISA *classic*

Herpes Simplex Virus 1/2 IgA / IgG / IgM

SERION ELISA *classic* Herpes Simplex Virus 1/2 IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum, plasma or cerebrospinal fluid directed against Herpes Simplex Virus (HSV). The SERION ELISA *classic* HSV IgM test is recommended for the detection of acute infections. The SERION ELISA *classic* HSV IgG test is used for the determination of the immune status and for the detection of antibodies in cerebrospinal fluid. The SERION ELISA *classic* HSV IgA test is recommended for the diagnosis of reactivations.

Lips with *Herpes labialis.*

Pathogen

Herpes Simplex Virus 1 and Herpes Simplex Virus 2 are human pathogen DNA viruses belonging to the family of *Herpesviridae*. Herpes viruses occur globally. In industrialized countries seroprevalence for Herpes virus infections amounts to 50 % in the second decade of life, in adults even up to 90 % for HSV Serotype 1 (HSV 1) and 10 to 15 % for HSV Serotype 2 (HSV 2).

Disease

Primary infection may result from direct contact with infected persons (saliva or urogenital secretion), transplacental transmission or iatrogenic through transfusions or transplantations. After primary infection local ganglions show lifelong virus persistence, enabling the reactivation of latent infections.
The transmission of Herpes genitalis during childbirth may progress subclinically. In most cases it leads to localized or disseminated sepsis-like diseases. The incubation period is 2 to 12 days. Contagiousness can persist as long as there are skin and mucosa efflorescences (about 3 weeks).

Primary HSV 1 infections process inapparently in 90 % of cases. The remainder show characteristic herpes vesiculation in areas of the lips, mouth or cornea and conjunctiva. These pustular eruptions can spread on eczematous skin with life-threatening effects. Further complications are encephalitis (70 % lethality) or meningo-encephalitis. 12 % of primary HSV 2 infections are apparent with sudden abortion, vulvovaginitis or penis scrotum efflorescences.

Diagnosis

Specific antibodies against HSV can be detected a few days after onset of the primary infection. SERION ELISA *classic* HSV 1+2 are based on a mixture of both purified whole-virus antigens of HSV 1 and HSV 2.

Validation of SERION ELISA *classic* HSV 1/2

The SERION ELISA *classic* HSV 1/2 IgG was validated in an internal study by the analysis of 111 positive and 51 negative serum samples in comparison to the assay of a leading European manufacturer. The evaluation of the SERION ELISA *classic* HSV 1/2 IgM was performed by the analysis of 50 serum samples in comparison to the test results of a leading European manufacturer. The SERION ELISA *classic* HSV 1/2 IgA was evaluated in an external study with 70 positive and 54 negative serum samples in comparison to the *in-house* test of a German university. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
HSV 1/2 IgA	94,3 %	92,6 %
HSV 1/2 IgG	> 99 %	> 99 %
HSV 1/2 IgM	98 %	98 %

Precision

SERION ELISA *classic* Herpes Simplex Virus 1/2 IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,537	6,2	0,542	9,0
positive	0,966	7,1	0,920	5,8
positive	2,435	3,2	1,684	9,7

SERION ELISA *classic* Herpes Simplex Virus 1/2 IgG

Sample	Mean value OD	Intraassay CV(%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,391	2,7	0,435	6,7
positive	1,138	2,2	1,179	3,5
positive	1,773	2,2	1,841	2,3

SERION ELISA *classic* Herpes Simplex Virus 1/2 IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,924	3,7	0,970	5,9
positive	1,178	2,8	1,146	6,0
positive	2,272	1,9	2,077	5,8

Order Information

SERION ELISA *classic* Herpes Simplex Virus 1/2 IgA **Order Nr.: ESR 105 A**
SERION ELISA *classic* Herpes Simplex Virus 1/2 IgG **Order Nr.: ESR 105 G**
SERION ELISA *classic* Herpes Simplex Virus 1/2 IgM **Order Nr.: ESR 105 M**
Reference serum Herpes Simplex Virus 1/2 IgA **Order Nr.: BR 105 A**
Reference serum Herpes Simplex Virus 1/2 IgG **Order Nr.: BR 105 G**
Reference serum Herpes Simplex Virus 1/2 IgM **Order Nr.: BR 105 M**

The SERION ELISA *classic* Herpes Simplex Virus 1/2 IgG is evaluated for the **analysis of cerebrospinal fluid**.

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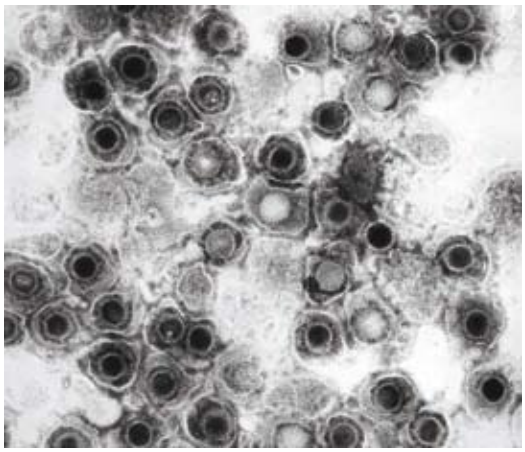
SERION ELISA *classic*

Herpes Simplex Virus 1 and 2 IgG / IgM

SERION ELISA *classic* Herpes Simplex Virus Type 1, respectively Type 2 IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Herpes Simplex Virus (HSV). SERION ELISA *classic* Herpes Simplex Virus IgM tests are recommended for the diagnosis of acute infections. SERION ELISA *classic* Herpes Simplex Virus IgG tests are used for the typification of the infection.



Electron micrograph of Herpes Simplex Viruses (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Herpes Simplex Virus 1 and Herpes Simplex Virus 2 are human pathogen DNA viruses belonging to the family of *Herpesviridae*. Herpes viruses are globally spread. In industrialized countries seroprevalence for Herpes virus infections amounts to 50 % in the second decade of life, in adults even up to 90 % for HSV Serotype 1 (HSV 1) and 10 to 15 % for HSV Serotype 2 (HSV 2).

Disease

Primary infection may result from direct contact with infected persons (saliva or urogenital secretion), transplacental trans-mission or iatrogenic through transfusions or transplantations. The incubation period is 2 to 12 days. Contagiousness can persist as long as there are skin and mucosa efflorescences (about 3 weeks). Primary HSV 1 infections process inapparently in 90 % of cases. The remainder show characteristic herpes vesiculation in areas of the lips, mouth or cornea and conjunctiva. These pustular eruptions can spread on eczematous skin with life-threatening effects. Further complications are encephalitis (70 % lethality) or meningoencephalitis. 12 % of primary HSV 2 infections are apparent with sudden abortion, vulvovaginitis or penis scrotum efflorescences.

Diagnosis

Although most Herpes genitalis infections are caused by HSV 2, up to 20 % can be due to HSV 1. Symptoms of primary infection are identical, the reactivation rate of HSV 1 genitalis is lower. The SERION ELISA *classic* HSV 1 and HSV 2 IgM provide an comprehensive and sensitive detection of primary infections, the assays being based on inactivated HSV 1 and HSV 2. In contrast, IgG antibodies directed against the virus specific glycoproteins gG1 and gG2 are generated two to three months after primary infection in most cases. The detection by use of SERION ELISA *classic* HSV 1 and HSV 2 IgG based upon specific glycoproteins allows the differentiation of the virus type specific immune response.

Validation of SERION ELISA *classic* HSV 1 and HSV 2 IgG

The SERION ELISA *classic* HSV 1 IgG was evaluated by the analysis of 127 positive and 37 negative serum samples from blood donors. The ELISA of a leading European manufacturer was used as reference test. The evaluation of the SERION ELISA *classic* HSV 2 IgG was performed by the analysis of 193 serum samples in comparison to a FDA-approved reference test of a leading north American manufacturer. Sera classified as borderline were not included in the calculation.

SERION ELISA *classic*	Sensitivity	Specificity
Herpes Simplex Virus 1 IgG	> 99 %	> 99 %
Herpes Simplex Virus 2 IgG	> 99 %	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Herpes Simplex Virus 1 IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,278	3,4	0,290	4,4
positive	0,561	3,9	0,626	6,2
positive	1,228	2,6	1,391	4,9

SERION ELISA *classic* Herpes Simplex Virus 1 IgM

Sample	Mean Value OD	Intraassay VCV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,448	3,9	0,467	9,2
positive	0,940	3,0	0,918	10,5
positive	1,458	2,1	1,487	11,5

SERION ELISA *classic* Herpes Simplex Virus 2 IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,472	2,7	0,489	4,7
positive	1,131	2,7	1,082	5,6
positive	1,885	2,8	1,876	3,7

SERION ELISA *classic* Herpes Simplex Virus 2 IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,583	6,4	0,679	6,7
positive	1,081	4,8	1,170	6,4
positive	1,492	2,8	1,787	5,4

Order Information

SERION ELISA *classic* Herpes Simplex Virus 1 IgG	**Order Nr.: ESR 1051 G**
SERION ELISA *classic* Herpes Simplex Virus 1 IgM	**Order Nr.: ESR 1051 M**
SERION ELISA *classic* Herpes Simplex Virus 2 IgG	**Order Nr.: ESR 1052 G**
SERION ELISA *classic* Herpes Simplex Virus 2 IgM	**Order Nr.: ESR 1052 M**
Reference serum Herpes Simplex Virus 1 IgG	**Order Nr.: BR 1051 G**
Reference serum Herpes Simplex Virus 1 IgM	**Order Nr.: BR 1051 M**
Reference serum Herpes Simplex Virus 2 IgG	**Order Nr.: BR 1052 G**
Reference serum Herpes Simplex Virus 2 IgM	**Order Nr.: BR 1052 M**

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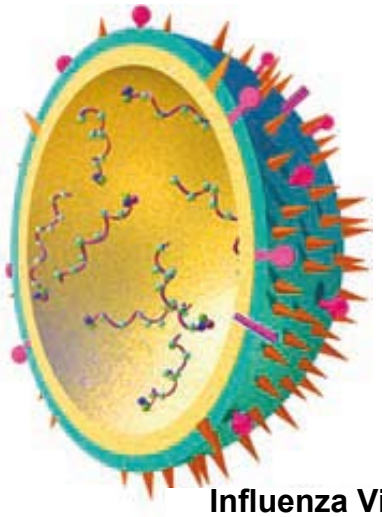
SERION ELISA *classic*

Influenza A Virus / Influenza B Virus IgA/IgG

SERION ELISA *classic* Influenza A Virus and Influenza B Virus IgA and IgG tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Influenza A and Influenza B Virus. The SERION ELISA *classic* are particularly recommended for the detection of acute infections. The determination of IgA antibody titers is a sensitive and specific complementation to IgG detection.



Influenza Virus
Credit: NIAID

Schematic drawing of Influenza Virus (Source: United States Federal Government).

Pathogen

Influenza (most commonly termed as "the flu") is caused by viruses which belong to the *Orthomyxoviridae* family. The main virus reservoirs are man and, in the case of Influenza A, a wide variety of other mammals and birds. Influenza B viruses almost exclusively infect humans. Influenza viruses are RNA viruses that carry pieces of segmented RNA and a surrounding lipid membrane coat with two specific glycoproteins, neuraminidase and hemagglutinin, protruding from the membrane.

Influenza viruses are characterised by genetic variability which is due to high mutation frequency and the ability to exchange genetic material with other influenzaviruses by virtue of their segmented genome. Point mutations introduce gradual changes of hemagglutinin and neuraminidase antigens (antigenic drift) resulting in the endemic occurrence of influenza. On the other hand, antigenic shift occurs following the coinfection of a host with two influenza viruses. This results in a reassortment of genetic material producing a new virus, the lack of immunity to which may result in devastating pandemics, such as in 1957 and 1968.

Disease

Influenza is an acute and highly contagious respiratory disease. Influenza viruses are transmitted through droplet infection and following a short incubation period of one to three days symptoms appear. The spectrum of symptoms is variable, ranging from asymptomatic infections to pneumonia, acute respiratory failure and death. A sudden onset of disease is very characteristic for influenza. Within a few hours, fever, cough, headache and muscle aches may develop.

Diagnosis

ELISA and CFT are serological tests for detection of type-specific antibodies against influenza A or B virus. ELISA allow to differentiate between different immunoglobulin classes. The SERION ELISA *classic* Influenza Virus were developed for Influenza Virus diagnostic in order to exclude the high-background prevalence of seropositivity.

Validation of SERION ELISA *classic* Influenza A and B Virus

The SERION ELISA *classic* Influenza A and Influenza B Virus were validated by the analysis of 101 serum samples from patients and 36 serum samples from blood donors in comparison to the complement fixation test (CFT). Since the CFT does not allow to differentiate between immunoglobulin classes, the test results were combined.

SERION ELISA *classic*	Sensitivity	Specificity
Influenza A Virus IgA / IgG	94 %	92 %
Influenza B Virus IgA / IgG	95 %	93 %

Precision

SERION ELISA *classic* Influenza A Virus IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,117	4,9	0,120	5,1
positive	1,008	3,0	0,948	3,7
positive	3,089	4,2	3,047	3,9

SERION ELISA *classic* Influenza A Virus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,160	9,2	0,159	7,2
weak positive	0,399	4,4	0,435	8,2
positive	1,219	3,9	1,451	4,3

SERION ELISA *classic* Influenza B Virus IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,694	4,1	0,711	4,7
positive	1,642	7,5	1,636	3,4
positive	2,173	2,7	2,273	6,6

SERION ELISA *classic* Influenza B Virus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,191	5,2	0,200	7,0
weak positive	0,633	4,8	0,653	5,5
positive	1,491	8,4	1,537	3,9

Order Information

SERION ELISA *classic* Influenza A Virus IgA	**Order Nr.: ESR 1231 A**
SERION ELISA *classic* Influenza A Virus IgG	**Order Nr.: ESR 1231 G**
SERION ELISA *classic* Influenza B Virus IgA	**Order Nr.: ESR 1232 A**
SERION ELISA *classic* Influenza B Virus IgG	**Order Nr.: ESR 1232 G**
Reference serum Influenza A Virus IgA	**Order Nr.: BR 1231 A**
Reference serum Influenza A Virus IgG	**Order Nr.: BR 1231 G**
Reference serum Influenza B Virus IgA	**Order Nr.: BR 1232 A**
Reference serum Influenza B Virus IgG	**Order Nr.: BR 1232 G**

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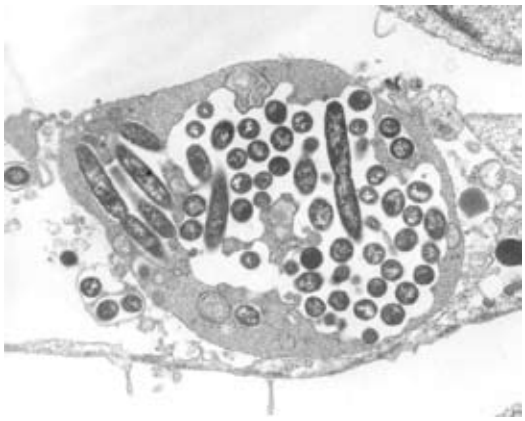
SERION ELISA *classic*

Legionella pneumophila 1-7 IgG / IgM

SERION ELISA *classic* Legionella pneumophila 1-7 IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *Legionella pneumophila* serotypes 1 to 7. The assays are recommended to complement the findings of direct detection methods and for differential diagnosis in case of atypical pneumonia.



Electron micrograph of *Legionella pneumophila* in a lung fibroblast (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Legionella belongs to the familiy of *legionellaceae*, genus *Legionella*. It is a gramnegative, aerobic, plemorphic non-spore forming bacillus which is motile by means of a single or multiple polar or subpolar flagella. The *legionellaceae* comprises more than 45 species, which are subdivided into various serovars. The most important human pathogen is the species *Legionella pneumophila* which comprises 14 serovars. Most Legionella associated pneumonias (80 - 85 %) are caused by serovars 1 to 6.

Disease

The classic legionellosis (Legionnaires´ disease) starts 2 to 10 days after infection with uncharacteristic prodromal symptoms such as general indisposition, headache, muscle aches and dry cough, chest pain, chill, temperature rise to 39 to over 40 °C. Occasionally gastrointestinal disturbances accompanied by diarrhoea and vomiting may be early onset symptoms. In 2 to 5 % of cases, severe pneumonia may result from the infection by *Legionella pneumophila* with lethality varying from 10 to 20 %. If not treated, lethality of immunosuppressed patients may increase up to 80 %.
The so called pontiac fever is a benign, non-pulmonal form of legionellosis characterized by a short incubation period

of one to two days and mild, influenza-like course of disease. The disease starts with headache, muscle- and chest pain, cough and fever. Despite severe discomfort, patients generally recover completely within five days.

Diagnosis

Direct pathogen detection in culture or in direct immunofluorescence assays (DFA) are of primary importance because fast diagnosis is often decisive for the patient. Sputum, tracheobronchial secretion and pleura punctates are ideal sample materials. However, the performance of the direct detection methods in culture or DFA is limited, since maximum sensitivities from 50 to 60 % are described for both techniques.
The SERION ELISA *classic* Legionella pneumophila 1-7 IgG and IgM are based on a mixture of the diagnostic relevant serovars 1 to 7.

Validation of SERION ELISA *classic* Legionella pneumophila

138 sera originated from different French cities, were provided by the National Reference Center for Legionella (Lyon, France). These sera were taken from 82 patients during the years 1998 and 1999. Selection and classification of sera was performed according to *Legionella pneumophila* antibody titers determined by IFT. These sera were tested in parallel with SERION ELISA *classic* Legionella pneumophila 1-7 IgG and IgM and in different in-house IFTs.

The determination of sensitivities and specificities of SERION ELISA *classic* Legionella pneumophila 1-7 was performed using the IFT as reference (gold standard).

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
L. pneumophila IgG / IgM	94,3 %	82,5 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Legionella pneumophila 1-7 IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,721	7,1	0,663	11,6
positive	0,833	9,1	0,829	10,2
positive	1,092	6,6	2,733	8,6

SERION ELISA *classic* Legionella pneumophila 1-7 IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
neg. /. pos.	0,301	9,8	0,690	16,7
positive	0,846	10,2	1,469	15,3
positive	1,092	8,8	3,390	1,9

Order Information

SERION ELISA *classic* Legionella pneumophila 1-7 IgG — **Order Nr.: ESR 106 G**
SERION ELISA *classic* Legionella pneumophila 1-7 IgM — **Order Nr.: ESR 106 M**
Reference serum Legionella pneumophila 1-7 IgG — **Order Nr.: BR 106 G**
Reference serum Legionella pneumophila 1-7 IgM — **Order Nr.: BR 106 M**

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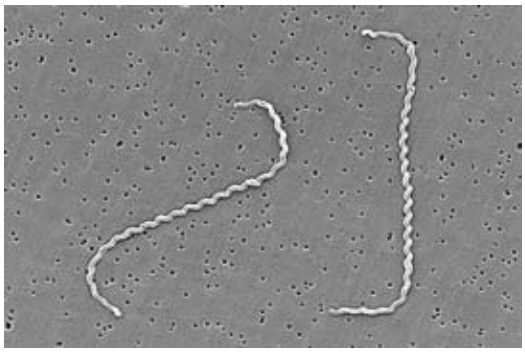
SERION ELISA *classic*

Leptospira IgG / IgM

SERION ELISA *classic* Leptospira IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Leptospira. The SERION ELISA *classic* Leptospira IgM test is recommended for the determination of acute leptospirosis, whereas the SERION ELISA *classic* Leptospira IgG test may be used in addition to the SERION ELISA *classic* Leptospira IgM test to provide a complete immunological picture.



Electron micrograph of *Leptospira interrogans* (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Leptospires are spiral-shaped, gram negative spirochetes with internal flagella. The genus is divided into two species: the pathogenic *Leptospira interrogans* and the free-living nonpathogenic *Leptospira biflexa*. *Leptospira interrogans* consists of around 200 different serovars based on the variability of surface antigens. Leptospires affect mammals (wild and domestic animals), reptiles and amphibians. They may be shed in the urine lifelong. Rats and other rodents are the primary reservoirs for human infection. The pathogen is transmitted by urine-contaminated soil or water, rat bites or animal tissue. In particular, occupational groups like agriculturists, plumbers, mine workers, fishermen and meat-industry workers are at increased risk to exposure.

Disease

Mucosa and skin lesions are the most likely sites of entry for leptospires. Bacteria mainly proliferate in the central nervous system, kidneys and liver. As a result, leptospirosis often is misdiagnosed as meningitis or hepatitis. The average incubation period is 7 to 14 days evidenced by sudden onset of fever, severe headache, muscle ache and nausea. The symptoms persist for approximately seven days.

Aproximately 5 to 15 % of clinically evident infections lead to multiorgan complications. 5 to 40 % of severe clinical cases are lethal. The most prevalent cause of death is kidney failure due to leptospirosis. Due to the immune environment of the convoluted tubules, leptospires within the of the kidneys may survive for long periods with consequent shedding in the urine.

Diagnosis

All patients with leptospirosis produce IgM antibodies directed against the pathogen. In contrast, less than 90 % of patients produce IgG antibodies. Microagglutination assays, ELISA and indirect fluorescence antibody tests (IFT) are most frequently used for serodiagnosis.

Validation of SERION ELISA *classic* Leptospira IgM

The SERION ELISA *classic* Leptospira IgM was evaluated by the analysis of 136 serum samples from patients with serologically proven leptospirosis, suspected leptospirosis, clinically or serologically detected infections with other pathogens as well as from healthy blood donors. The micro agglutination test (MAT) was used as a reference. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Leptospira IgM	97 %	96 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Leptospira IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,557	4,60	0,637	13,20
positive	1,536	3,80	1,752	7,60
positive	2,227	3,20	2,411	6,90

SERION ELISA *classic* Leptospira IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	1,299	7,50	1,376	12,10
positive	2,290	4,50	2,690	9,10
positive	2,784	6,80	2,747	12,40

Order Information

SERION ELISA *classic* Leptospira IgG — **Order Nr.: ESR 125 G**
SERION ELISA *classic* Leptospira IgM — **Order Nr.: ESR 125 M**
Reference serum Leptospira IgG — **Order Nr.: BR 125 G**
Reference serum Leptospira IgM — **Order Nr.: BR 125 M**

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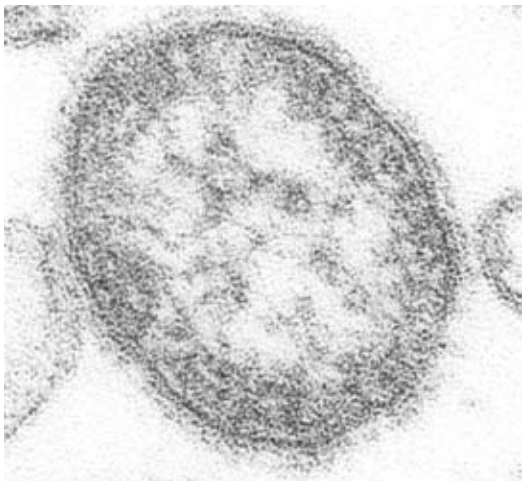
SERION ELISA *classic*

Measles Virus IgG / IgM

SERION ELISA *classic* Measles Virus IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum, plasma or cerebrospinal fluid directed against Measles Virus. The SERION ELISA *classic* Measles Virus IgM test is recommended for the determination of acute infections. The SERION ELISA *classic* Measles Virus IgG assay is recommended for determination of immunestatus and detection of intrathecal immunoglobulin synthesis.



Electron micrograph of a Measles Virus (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Measles Viruses occur worldwide and belong to the family of *paramyxoviridae*. According to estimations by WHO one million individuals die as a consequence of Measles Virus infections every year. Due to the highly infectious nature of the virus, "measles" is usually aquired in the childhood. The pathogen is transmitted by close contact with infected individuals primarily by droplet infection. The portal of entry for Measles Viruses is the upper respiratory tract.

Disease

After an incubation period of 10 to 12 days Koplik´s spots typically appear on oral mucosa in 60 to 70 % of cases. In the course of the prodromal period influenza-like symptoms may escalate until the typical measles exanthema arises with sharply increasing fever. The exanthema spreads from face over the trunk to the extremities. The clinical symptoms peak rapidly with a correspondingly rapid recovery. Complications are frequent consisting mainly of pneumonia and encephalitis. In developing countries poor nutrition combined with measles results in high levels of mortality. Once infected, lifelong immunity is generally acquired.

Vaccination is available in single as well as combined measles / parotitis or measles / parotitis / rubella vaccines. Live vaccines (attenuated virus strains) provide extensive immunity. Vaccination is recommended for infants older than 15 months.

Diagnosis

Direct virus detection in pharyngeal swabs, specific IgM antibody detection or seroconversion confirms Measles virus infection. PCR complements the classical methods. IgM antibody detection is possible after the second day of exanthema continuing about 4 to 6 weeks. IgG antibody titers persist lifelong. In countries aiming at eradication of Measles Virus, verification of each case of infection by laboratory methods is warranted to confirm clinical diagnosis. Furthermore, examinations for epidemic surveillance provide valuable information. SERION ELISA *classic* Measles Virus IgG permits detection of antibody activity measured in international units, therefore comparison of results obtained in different laboratories is possible and statements with regard to immune protection are possible.

Validation of SERION ELISA *classic* Measles Virus

For validation of the SERION ELISA *classic* Measles Virus IgG 69 serum samples with different antibody reactivities were analysed in an external study. 50 serum samples from healthy blood donors were additionally tested in house. A commercially available ELISA was used as a reference test. For validation of the SERION ELISA *classic* Measles Virus IgM 86 serum samples of patients with suspected acute measles infection were analysed in an external study. An indirect ELISA of a leading European manufacturer was used as reference test.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Measels Virus IgG	> 99 %	93,3 %
Measels Virus IgM	95,4 %	> 99 %

Borderline results were not included in the calculation of sensitivity and specificity.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Measles Virus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,296	4,4	0,353	9,3
positive	1,142	4,3	1,372	8,9
positive	2,087	2,3	2,425	9,1

SERION ELISA *classic* Measles Virus IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,631	2,2	0,635	5,7
positive	2,591	4,3	3,126	9,1
positive	2,810	3,1	3,522	10,4

Order Information

SERION ELISA *classic* Measles Virus IgG **Order Nr.: ESR 102 G**
SERION ELISA *classic* Measles Virus IgM **Order Nr.: ESR 102 M**
Reference serum Measles Virus IgG **Order Nr.: BR 102 G**
Reference serum Measles Virus IgM **Order Nr.: BR 102 M**

The SERION ELISA *classic* Measles Virus IgG is evaluated for the **analysis of cerebrospinal fluid**.

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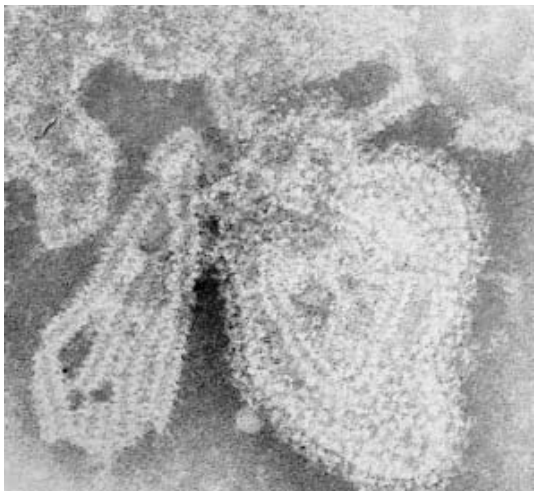
SERION ELISA *classic*

Mumps / Parotitis Virus IgG / IgM

SERION ELISA *classic* Mumps / Parotitis Virus IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum, plasma or cerebrospinal fluid directed against Parotitis Virus. The SERION ELISA *classic* Mumps /Parotitis Virus IgM is recommended for the determination of acute infections whereas the SERION ELISA *classic* Mumps /Parotitis Virus IgG is used for indication of immune status and for detection of intrathecal antibodies.



Micrograph of Mumps / Parotitis Virus (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Parotitis viruses belong to the family of *paramyxoviridae* and occur globally with humans being their only natural host. The pathogen is spread by droplet infection, virus entering the body through the upper respiratory tract. Parotitis viruses are less contagious (40 %) than Measles and Varicella-Zoster viruses. The highest prevalence is observed in industrial countries among children at the age of 5 to 9 years. By the age of 15 years, 90 % of children will have been infected. Since parotitis is less contagious than many other childhood infections, e. g. measles, a significant number of adults may also be affected.

Disease

The typical symptoms are one-sided or bilateral parotitis, obvious swellings develop after an incubation period of 18 to 21 days. The course of infection is clinically inapparent in about 30 % of cases, particularly in older patients. Infants develop typical symptoms only in 20 % of cases; preschoolers often exhibit symptoms of respiratory infections only. Childhood infections are mainly uncomplicated, but in adulthood a range of problems may occur.

25 % of infected postpubertal patients show organ manifestations such as orchitis or epididymitis, also pancreatitis, oophoritis, meningitis and meningoencephalitis may be observed. Late sequelae such as sterility as a consequence of testicular atrophy or deafness due to acoustic neuritis rarely occur.
Pregnant women are especially exposed to the risk of abortion but there is no risk of congenital malformation. Single as well as combined measles / parotitis or measles / parotitis / rubella vaccines are available. Live vaccines derived from attenuated virus strains provide durable immunity. Vaccination is recommended for children at the age of 15 months and older.

Diagnosis

In addition to the classical clinical symptoms of swellings, diagnosis of parotitis may be supported by serological methods especially when obvious symptoms are inapparent. Detection of antibodies in serum is possible with ELISA, CFT and HHT. Immunoglobuline specific ELISAs have been developed for routine diagnostics. Acute parotitis infection can be confirmed in an early stage of disease by detection of Parotits Virus specific IgM antibodies.

Validation of SERION ELISA *classic* Mumps / Parotitis Virus

The SERION ELISA *classic* Mumps / Parotitis Virus IgG was evaluated in an external study by the analysis of 100 serum samples from healthy adults and serum pairs of acute-phase and reconvalescent parotitis patients. Furthermore, 29 serum samples from patients with suspected acute parotitis infection, 101 serum samples from healthy adult blood donors, 84 serum samples from children and 13 serum samples from pregnant women were examined in an internal study. An indirect ELISA from a leading European manufacturer was used as a reference.
The validation of SERION ELISA *classic* Mumps / Parotis Virus IgM was carried out with 220 serum samples, thereof 45 serum samples from patients with suspected acute parotitis infection, 134 samples from healthy blood donors and 41 serum samples from pregnant women. Again, the indirect ELISA from a leading European manufacturer was used as a reference. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Mumps / Parotitis Virus IgG	> 99 %	95,1 %
Mumps / Parotitis Virus IgM	96,3 %	97,8 %

Precision

SERION ELISA *classic* Mumps / Parotitis Virus IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,383	5,1	0,492	7,2
positive	0,672	8,4	0,845	7,9
positive	0,967	4,4	1,182	5,5

SERION ELISA *classic* Mumps / Parotitis Virus IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,692	6,3	0,897	4,9
positive	0,856	4,1	1,123	6,6
positive	1,849	4,7	2,228	2,7

Order Information

SERION ELISA *classic* Mumps / Parotitis Virus IgG **Order Nr.: ESR 103 G**
SERION ELISA *classic* Mumps / Parotitis Virus IgM **Order Nr.: ESR 103 M**
Reference serum Mumps / Parotitis Virus IgG **Order Nr.: BR 103 G**
Reference serum Mumps / Parotitis Virus IgM **Order Nr.: BR 103 M**

The SERION ELISA *classic* Mumps / Parotitis Virus IgG is evaluated for the **analysis of cerebrospinal fluid**.

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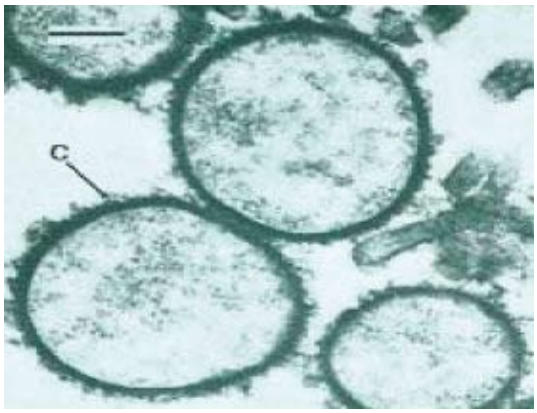
SERION ELISA *classic*

Mycoplasma pneumoniae IgA / IgG / IgM

SERION ELISA *classic* Mycoplasma pneumoniae IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies, directed against *Mycoplasma pneumoniae*, in serum or plasma. The use of these products to detect individual immunoglobulin classes provides information regarding exposure to the pathogen and disease state.



Electron micrograph of *Mycoplasma*.

Disease

Mycoplasma pneumoniae infections are responsible for a variety of respiratory syndromes which range from trivial to life-threatening, with primary atypical pneumonia, pharyngitis and tracheobronchitis being the most common clinical manifestations. The frequency of infection is illustrated by the fact that each year approximately 20 % of ambulatory cases of pneumonia in the USA are the result fo M. pneumoniae infection. Various clinical symptoms, particularly the presence of atypical pneumonia may complicate the identification of the causal agent when dealing with *M. pneumoniae* infections (e.g. RSV-, Influenza Virus-infections). *Mycoplasma pneumoniae* colonizes epithelia of the trachea, bronchia and bronchiolae leading, after an incubation time of 10 to 20 days, to non-specific symptoms such as headache and fever accompanied by a non-productive, dry cough. During the course of infection an interstitial pneumonia may develop. *M. pneumoniae* is responsible for some 15 to 20 % of ambulant obtained cases of pneumonia in older children and young adults. Super infections with *M. pneumoniae* after viral (e.g. measles) or bacterial infections (e.g. *Streptococcus pneumoniae*) are observed primarily in children. *Mycoplasma pneumoniae* infections in children younger than 5 years of age are often asymptomatic or associated with mild symptoms of the respiratory tract. Immunity following infection is not complete and consequently repeated infections, which can be protracted and more severe, are possible.

Diagnosis

The variety of clinical symptoms and possible causal agents requires that diagnosis not be limited to the clinical picture alone. Serological and direct detection methodologies must be employed to identify the pathogen responsible and so enable appropriate medical intervention strategies to be employed. The CFT has been used for many years in *M. pneumonia* diagnosis; however it suffers from low specificity due to the cross-reactive nature of the LPS on which it is based. ELISA tests use more specific antigen preparations and are able to differentiate between immunoglobulin classes so improving the diagnostic value of the results obtained.

Validation of SERION ELISA *classic* M. pneumoniae

For validation of SERION ELISA *classic* Mycoplasma pneumoniae IgG and IgM 11 serum samples from patients with clinically confirmed infection, 31 serum samples from patients with suspected mycoplasma infection, 58 serum samples from patients where mycoplasma infections could not be excluded and 59 serum samples from patients with improbable mycoplasma infection were analysed. The results were compared with the test results of ELISAs of two leading European manufacturers. Sera classified as borderline were not included in the calculation.

SERION ELISA *classic*	Sensitivity	Specificity
Mycoplasma pneumoniae IgA	76,9 %	96,1 %
Mycoplasma pneumoniae IgG	> 99 %	88,9 %
Mycoplasma pneumoniae IgM	96,4 %	92,9 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Mycoplasma pneumoniae IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,525	7,1	0,578	6,4
positive	1,155	8,6	1,295	7,1

SERION ELISA *classic* Mycoplasma pneumoniae IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,835	4,9	0,906	11,6
positive	1,269	4,7	1,470	6,9
positive	1,562	4,2	1,790	5,9

SERION ELISA *classic* Mycoplasma pneumoniae IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,375	7,7	0,434	12,8
positive	1,581	7,2	1,823	5,5
positive	1,702	7,9	1,943	8,3

Order Information

SERION ELISA *classic* Mycoplasma pneumoniae IgA	**Order Nr.: ESR 127 A**
SERION ELISA *classic* Mycoplasma pneumoniae IgG	**Order Nr.: ESR 127 G**
SERION ELISA *classic* Mycoplasma pneumoniae IgM	**Order Nr.: ESR 127 M**
Reference serum Mycoplasma pneumoniae IgA	**Order Nr.: BR 127 A**
Reference serum Mycoplasma pneumoniae IgG	**Order Nr.: BR 127 G**
Reference serum Mycoplasma pneumoniae IgM	**Order Nr.: BR 127 M**

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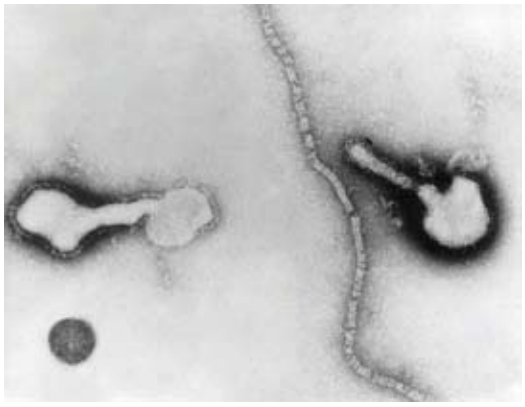
SERION ELISA *classic*

Parainfluenza Virus 1, 2, 3 IgA / IgG

SERION ELISA *classic* Parainfluenza Virus 1, 2, 3 IgA and IgG tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Parainfluenza Virus 1, 2 or 3. The SERION ELISA *classic* Parainfluenza Virus IgG tests are recommended for the individual determination of antibodies directed against Parainfluenza Virus types 1 to 3. The SERION ELISA *classic* Parainfluenza Virus IgA test is recommended for the detection of acute infection by a combined determination of antibodies against types 1 to 3.



Electron micrograph of Parainfluenza Virus (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Parainfluenza viruses belong to the family of *Paramyxoviridae*. Currently, Parainfluenza viruses can be divided into four types of which types 1 to 3 are most significant clinically.

Disease

Infections are transmitted by droplets, fomites or direct contact via mucous membranes of the eyes, mouth, or nose. Parainfluenza viruses cause mild to severe infections in the lower and upper respiratory system tract. Between 30 to 40 % of acute respiratory infections are caused by Parainfluenza viruses, which are of particular significance for infants. Seroprevalence may reach 90 % in young children by the age of 10 years.

Diagnose

Despite their ubiquitous nature and clinical relevance for infants, only a few standardized, commercial reagents for laboratory diagnostics are available for Parainfluenza Virus diagnosis. CFT and ELISA are established methods, whereby ELISA is to be preferred due to the ability to differentiate between

immunoglobulins. While the majority of patients infected with Parainfluenza virus develop IgG antibodies, IgM antibodies are detectable in approximately 50 % of cases. Analogous to other infectious diseases of the respiratory tract (e. g. Respiratory Syncytial Virus infections), the specific detection of IgA antibodies should be performed to allow a precise diagnosis in case of suspected acute infection.

Validation of SERION ELISA *classic* Parainfluenza Virus

The SERION ELISA *classic* Parainfluenza Virus tests were validated in an internal study. The CFT was used as a reference. As an example the results for SERION ELISA *classic* Parainfluenza Virus 2 IgG are presented. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Parainfluenza Virus 2 IgG	> 99 %	98,6 %

The SERION ELISA *classic* Parainfluenza Virus IgG and IgA were developed for Parainfluenza Virus diagnosis in order to exclude high background seropositivity.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Parainfluenza Virus 1, 2, 3 IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,172	6,9	0,152	8,1
positive	0,829	8,6	0,885	8,9
positive	1,179	6,8	1,178	7,5

SERION ELISA *classic* Parainfluenza Virus 1 IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,237	8,1	0,376	7,5
positive	0,734	6,1	0,825	12,7
positive	0,967	5,0	1,137	3,1

SERION ELISA *classic* Parainfluenza Virus 2 IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,225	4,8	0,222	8,5
positive	0,673	4,4	0,661	5,7
positive	1,301	2,3	1,346	4,1

SERION ELISA *classic* Parainfluenza Virus 3 IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
negative	0,140	4,3	0,124	5,5
positive	0,587	3,0	0,611	4,5
positive	0,941	2,3	1,014	5,9

Order Information

SERION ELISA *classic* Parainfluenza Virus 1, 2, 3 IgA **Order Nr.: ESR 126 A**
SERION ELISA *classic* Parainfluenza Virus 1 IgG **Order Nr.: ESR 1261 G**
SERION ELISA *classic* Parainfluenza Virus 2 IgG **Order Nr.: ESR 1262 G**
SERION ELISA *classic* Parainfluenza Virus 3 IgG **Order Nr.: ESR 1263 G**
Reference serum Parainfluenza Virus IgA **Order Nr.: BR 126 A**
Reference serum Parainfluenza Virus 1 IgG **Order Nr.: BR 1261 G**

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SERION ELISA *classic*

Parvovirus B19 IgG / IgM

SERION ELISA *classic* Parvovirus B19 IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Parvovirus B19 and are recommended for the differentiation of acute and past infections.

Pathogen

Parvovirus B19 is the most important pathogen for clinically relevant human infections with Parvoviruses. The virus replicates in dividing human erythroid cells.

Disease

Parvovirus B19 infections are mainly transmitted by droplet infection of nasopharyngal secretions to people in close contact with infected individuals. Infected children in preschools or schools may develop *erythema infectiosum* (fifth disease). After an incubation period of 13 to 17 days garland-shaped exanthemas spread from the face downwards. The rash, possibly accompanied by arthralgia in the small joints and lymphadenosis, may last for up to 3 weeks.
In industrialized countries 2 to 10 % of children younger than five years show evidence of infection and 40 to 60 % of individuals older than 20 years have antibodies against Parvovirus B19. In 5 % of pregnant women with primary infection, the virus is transmitted to the fetus, leading to complications. In the first and second trimesters the risk of hydrops fetalis and fetal abortion is highest.
In general neutralizing antibodies are produced during the course of infection, and lifelong immunity is acquired.

In individuals lacking neutralizing antibodies e. g. immunosuppressed patients and patients with chronic hemolytic anemia, infection may have severe clinical consequences. Chronic bone marrow aplasia or aplastic crisis accompanied by inhibition of erythrocyte differentiation (erythropoiesis inhibition) may be life-threatening.

Diagnosis

Serological testing for Parvovirus B19 is particularly indicated for those high risk patients with uncharacteristic clinical pictures, with suspected acute or recent infection (less than 60 days ago). This risk especially applies to pregnant women particularily working in institutions such as schools, hospitals and child-care. ELISAs are especially suited for the detection of Parvovirus B19 IgG and IgM antibodies due to their accurate immunoglobulin class specific analysis of the immune response.

Validation of SERION ELISA *classic* Parvovirus B19

The SERION ELISA *classic* Parvovirus B19 IgG was evaluated with more than 150 serum samples from healthy blood donors, pregnant women and quality control sera. The IgG antibody activity is measured in IU/ml based on the WHO-Standard International Standard for Anti-Parvovirus B19 plasma, human; NIBSC code 01/602.
More than 80 serum samples from patients with suspected acute Parvovirus B19 infection and from pregnant women were tested to determine sensitivity and specificity of the SERION ELISA *classic* Parvovirus B19 IgM. Commercially available ELISA of a competitor were used as a reference. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Parvovirus B19 IgG	> 99 %	98%
Parvovirus B19 IgM	91 %	97 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Parvovirus B19 IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,325	4,7	0,352	6,2
positive	1,160	2,7	1,232	4,6
positive	1,381	3,8	1,490	4,0

SERION ELISA *classic* Parvovirus B19 IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,665	8,8	0,831	12,1
positive	1,235	4,8	1,354	12,5
positive	2,191	3,9	2,284	11,6

Order Information

SERION ELISA *classic* Parvovirus B19 IgG **Order Nr.: ESR 122 G**
SERION ELISA *classic* Parvovirus B19 IgM **Order Nr.: ESR 122 M**
Reference serum Parvovirus B19 IgG **Order Nr.: BR 122 G**
Reference serum Parvovirus B19 IgM **Order Nr.: BR 122 M**

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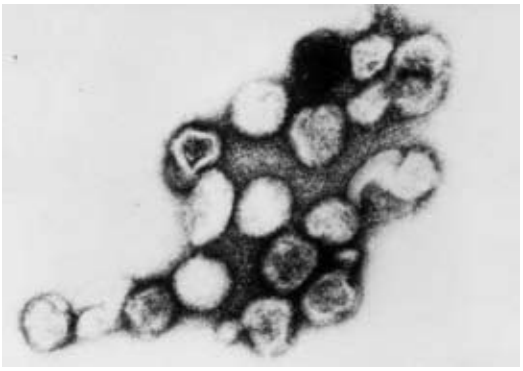
SERION ELISA *classic*

Rubella Virus IgG / IgM

SERION ELISA *classic* Rubella Virus IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum, plasma or cerebrospinal fluid directed against Rubella Virus. The SERION ELISA *classic* Rubella Virus IgM test is the initial assay for the detection of acute infections and also suitable for newborn screening on dried blood spots (DBS). Positive results should be further tested with conformatorial assays, e. g. avidity tests. The SERION ELISA *classic* Rubella Virus IgG is recommended for the determination of the immune status.



Electron micrograph of Rubella virus (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Rubella Virus is a human pathogen belonging to the Togavirus family of RNA viruses. It is transmitted by droplets and direct contact and the incubation period lies between 10 and 21 days.

Disease

The infection is accompanied in approximately 50 % of cases by an, initially, discrete rash in the form of pinpoint macular lesions which may later coalesce. Postnatal infection usually presents no problems with 25 to 30 % of cases being subclinical although complications such as myocarditis, neuritis, otitis, bronchitis and encephalitis may occur. A clinical diagnosis of Rubella infection should, in all cases, be supported by serological evidence as manifestations of rash and arthritis may be caused by other viral agents.

Rubella infection during pregnancy may lead to multisystem disease and severe damage in the fetus. Consequently the diagnosis of Rubella during gestation is of considerable importance.

Diagnosis

Serological investigations are carried out to determine Rubella immune status in addition to the diagnosis of Rubella infection and associated disease. Interpretation of results of serological tests can only be made in conjunction with a full clinical picture.The SERION ELISA *classic* Rubella Virus IgG test is valuable in determining immune status and as a confirmatory test when other test systems (such as haemagglution inhibition test) produce an equivocal or weak positive result from which immune status cannot reliably be determined.
A positive result in the SERION ELISA *classic* Rubella Virus IgM test is generally indicative of a primary infection. Due to the severe consequences for the fetus, pregnant patients testing positive for anti-Rubella IgM antibodies should also be tested for IgM using an ELISA test system utilising an alternative reaction principle. In doubtfull cases further diagnosis procedures should be adopted e. g. avidity tests.

Validation of SERION ELISA *classic* Rubella Virus

The SERION ELISA *classic* Rubella Virus IgG was evaluated in an external study by the analysis of 427 serum samples from patients with suspicion of Rubella virus infection in comparison to various commercially available assays from competitors. The evaluation of SERION ELISA *classic* Rubella Virus IgM was performed by the analysis of 55 serum samples from patients with suspected infection as well as a serum panel from blood donors and pregnant women. A commercially available μ-capture ELISA of a competitor was used as a reference.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Rubella Virus IgG	99,1 %	98,9 %
Rubella Virus IgM	98,0 %	98,0 %

Sera classified as borderline were not included in the calculation.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Rubella Virus IgG

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,704	8,3	0,607	11,6
positive	1,352	6,6	1,291	10,4
positive	1,853	3,5	1,688	8,9

SERION ELISA *classic* Rubella Virus IgM

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,987	5,4	0,282	6,8
positive	1,456	5,3	1,106	6,4
positive	1,749	6,7	2,622	8,0

Order Information

SERION ELISA *classic* Rubella Virus IgG **Order Nr.: ESR 129 G**
SERION ELISA *classic* Rubella Virus IgM **Order Nr.: ESR 129 M**
Reference serum Rubella Virus IgG **Order Nr.: BR 129 G**
Reference serum Rubella Virus IgM **Order Nr.: BR 129 M**
Reference serum Rubella Virus Avidity **Order Nr.: BR 129 AVID**
Avidity reagent Rubella Virus **Order Nr.: B 129 AVID**

The SERION ELISA *classic* Rubella Virus IgG is evaluated for the **analysis of cerebrospinal fluid**.
The SERION ELISA *classic* Rubella Virus IgM is evaluated for **neonatal screening** on Dried Blood Spots
(For more information see SERION ELISA *classic* neonatal).

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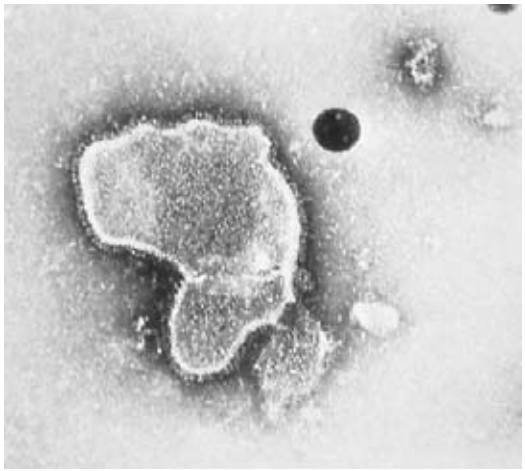
SERION ELISA *classic*

Respiratory Syncytial Virus IgA / IgG

SERION ELISA *classic* Respiratory Syncytial Virus (RSV) IgA and IgG tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against Respiratory Syncytial Virus. Determination of IgA antibodies is used as a sensitive and specific addition to IgG detection.



Electron micrograph of Respiratory Syncytial Virus (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

The Respiratory Syncytial Virus (RSV) is a negative strand RNA virus with pleomorphic structure. Originally the virus was isolated from chimpanzees, with its current name deriving from the production of syncytia in infected cell culture.

Disease

Respiratory Syncytial Virus (RSV) is a significant cause of disease especially in newborns and infants, varying from mild infections of the upper respiratory tract to life-threatening infections of the lower respiratory tract (bronchiolitis, pneumonitis). The course of disease in older children and adults is mild in contrast to older individuals who may be severely affected.

Infections are transmitted by contact with respiratory secretions. Epidemiological studies have indicated that the majority of children at the age of two years have been exposed to RSV.

Protective immunity as a result of infection is primarily mediated by antibodies against the viral glycoproteins G and F.

Diagnosis

Antigen and antibody detection methods are important in the diagnosis of RSV infections. ELISAs which allow the differentiation of immunoglobulin classes are of increasing importance for diagnosis during the first months of life. Detection of IgA antibodies is important due to the presence of maternal IgG antibodies in the serum of infants. Significant IgA titers are detectable in about 70 % of acute infections and IgA detection is more reliable in young patients between one and seven years of age than detection of RSV-specific IgM antibodies.

Validation of SERION ELISA *classic* RSV

The SERION ELISA *classic* Respiratory Syncytial Virus IgG and IgA were evaluated with 91 serum samples from blood donors, 12 paired serum samples from patients with clinically proven RSV infection and 69 sera of individuals with suspected RSV infection. Due to the fact that the CFT does not differentiate between immunoglobulin classes, the results of SERION ELISA *classic* Respiratory Syncytial Virus IgG and IgA were combined. Sera classified as borderline were not included in the calculation.
The SERION ELISA *classic* Respiratory Syncytial Virus IgG and IgA have been developed for RSV diagnosis so as to exclude the high background seroprevalence.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
RSV IgA / IgG	> 99 %	89 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Respiratory Syncytial Virus IgA

Probe	Mittlere Extinktion OD	Intraassay Vk (%) (n=20)	Mittlere Extinktion OD	Interassay Vk (%) (n=10)
schwach pos.	0,502	1,81	0,529	6,70
positiv	0,795	2,10	0,835	6,15
stark positiv	1,11	3,49	1,14	4,81

SERION ELISA *classic* Respiratory Syncytial Virus IgG

Probe	Mittlere Extinktion OD	Intraassay Vk (%) (n=20)	Mittlere Extinktion OD	Interassay Vk (%) (n=10)
schwach pos.	0,475	1,77	0,510	5,87
positiv	0,624	1,44	0,683	5,58
stark positiv	1,383	1,77	1,455	4,96

Order Information

SERION ELISA *classic* Respiratory Syncytial Virus IgA **Order Nr.: ESR 113 A**
SERION ELISA *classic* Respiratory Syncytial Virus IgG **Order Nr.: ESR 113 G**
Reference serum Respiratory Syncytial Virus IgA **Order Nr.: BR 113 A**
Reference serum Respiratory Syncytial Virus IgG **Order Nr.: BR 113 G**

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SERION ELISA *classic*

TBE Virus IgG / IgM

SERION ELISA *classic* TBE Virus IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum, plasma or cerebrospinal fluid directed against the TBE Virus. SERION ELISA *classic* TBE Virus IgM is recommended for determination of acute infections while SERION ELISA *classic* TBE Virus IgG is recommended for vaccination control.

In Europe, TBE Virus is transmitted to humans by infectious ticks of the genus I*xodes ricinus*.

Pathogen

The TBE Virus belongs to the group of Flaviviruses. There are two natural subtypes, the western subtype that is found in Europe and another subtype occurring in the Far East, Siberia and China. The TBE Virus is generally passed on to humans by infected tick bites. So far, cases of human-to-human transmission have not been reported.

Disease

60 to 70 % of TBE infections are clinically inapparent. After an incubation period of 2 to 28 days (depending on the location of the bite and the amount of viruses, it averages from 7 to 14 days). The first phase starts with an influenza-like clinical picture and a slight rise of temperature (rarely higher than 38 °C). This phase lasts for two to four days followed by an approximately 8-day interval when the patient may be symptom-free. 2/3 of the patients recover after this stage, while the remainder may proceed to the second phase of disease. Meningitis may occur accompanied by severe headache, stiffness of the neck, fever up to 40 °C, nausea and vomiting. Additionally meningoencephalitis with unconsciousness, restlessness, speech disorders or paralysis can occur. Symptoms such as paralysis, seizures or long-term headaches may last for several months, or even lifelong in severe cases. The disease is fatal in 1 to 2 % of the cases.

Natural infection provides lifelong immunity, while vaccination induced immunity requires regular booster shots.

Diagnosis

One week after the onset of symptoms, IgM concentrations rise. Towards the end of the symptom-free interval (or shortly after the onset of the second phase) the maximum level is reached. In the middle of the symptom-free interval IgG antibody production begins. IgM antibodies decrease to undetectable levels after about 10 months, while IgG antibodies reach a maximum concentration after 6 months and may remain elevated. Cross reactions may occur to Flaviviruses such as Dengue, Hepatitis C, Yellow Fever or Japan-B-Encephalitis.
A life-long immunity is usually the consequence of a natural infection by TBE virus. In contrast, only a limited immunity is generated by immunization. Therefore, vaccination has to be repeated in intervals of 10 years (www.tbe-info.com).

Validation of SERION ELISA *classic* TBE Virus

The SERION ELISA *classic* TBE IgG and IgM were evaluated by the analysis of 150 serum samples in comparison to the assay of a leading manufacturer. Sera classified as borderline were not included in the calculation.

Sensitivity and specificity

SERION ELISA *classic*	Sensitivity	Specificity
TBE Virus IgG	98,9 %	98,3 %
TBE Virus IgM	> 99 %	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* TBE Virus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
borderline	0,274	8,30	0,271	10,40
positive	0,765	8,00	0,693	13,40
positive	1,426	4,30	1,341	8,80

SERION ELISA *classic* FSME Virus IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
positive	0,764	5,4	0,69	11,6
positive	1,135	5,6	1,32	10,8

Order Information

SERION ELISA *classic* TBE Virus IgG — **Order Nr.: ESR 112 G**
SERION ELISA *classic* TBE Virus IgM — **Order Nr.: ESR 112 M**
Reference serum TBE Virus IgG — **Order Nr.: BR 112 G**
Reference serum TBE Virus IgM — **Order Nr.: BR 112 M**

The SERION ELISA *classic* TBE Virus IgG and IgM are evaluated for the **analysis of cerebrospinal fluid**.

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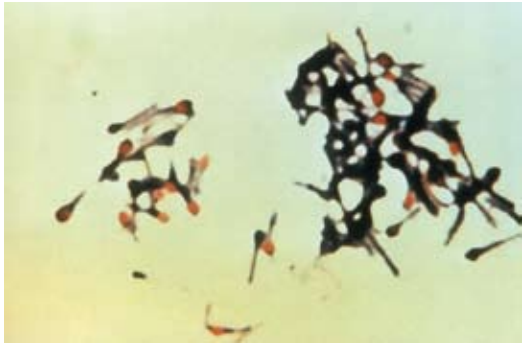
SERION ELISA *classic*

Tetanus IgG

SERION ELISA *classic* Tetanus IgG test is a quantitative immunoassay for the detection of human antibodies in serum or plasma directed against the Tetanus toxin. The SERION ELISA *classic* Tetanus IgG is recommended for vaccination control and for the determination of the current individual immune status to prevent hyperimmune reactions.



Micrograph of *Clostridium tetani* (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services).

Pathogen

Clostridium tetani is an ubiquitous obligate anaerobic bacteria, that lives in the intestines of many animals and, sometimes, humans without causing disease or inducing immunity. The extremely resistant spores reach the ground through faeces and are able to survive here for years. The pathogen enters the host by way of contaminated wounds. In the presence of nutrients and anaerobic conditions, spores will convert back to the vegetative form which then produce tetanospasmin, a very potent neurotoxin which causes an increase in neuromuscular stimulation.

Disease

After an incubation period of a few days up to several weeks (short incubation periods indicate a poor prognosis) the illness begins with nonspecific symptoms, primarily fatigue, followed, up to four days later, by characteristic cramps which spread craniofacial to caudal and may also affect the respiratory muscles. Sufferers are fully conscious during bouts of these extremely painful cramps which may be triggered by the slightest external stimuli. During the course of tetanospasmin poisoning the patient may suffer from renal, cardiac and circulatory failure, and a consumptive coagulopathy. Even with intensive care, over one third of patients die.

The safest prophylaxis against tetanus is an active immunization with an effective tetanus toxoid vaccine. The STIKO (Ständige Impfkommission on the Robert-Koch-Institute in Berlin) recommends a combined vaccine for the active immunisation of babies. The first immunisation takes place upon the completion of the second month of life; afterwards two further immunisations are made in an interval of 4 to 8 weeks. Booster shots should be made between the 12th and 18th month of life and also in the 5th to 6th and 11th to 18th year of life. For Tetanus, a booster immunization is then necessary after ten years. Side effects of immunization can occur after multiple vaccinations (repeated immunization or booster shots), varying from local and systemic allergic reactions to anaphylactic shock. Sporadic cases of death after tetanus vaccination have been described.

Diagnosis

To check for immune status serological detection of antitoxin IgG antibodies by ELISA techniques are used. Uncertain immune status possibly due to poor recollection or incomplete documentation, vaccination completions and immune depression are all indications for performing a confirmatory ELISA to determine antibody levels. Serologic techniques for the detection of tetanus immunity precisely determine the current antitoxin-antibody content. These are given in international units, and allow for practical vaccination recommendations.

Validation of SERION ELISA *classic* Tetanus IgG

The SERION ELISA *classic* Tetanus IgG was evaluated at the Central Institute of Medical Services of the German Federal Armed Forces in Koblenz in comparison to their in-house ELISA. The results are expressed in International Units per ml (IU/ml) to relate the duration of immune protection thereof. Accuracy of the test is not estimated by comparison of positive and negative results with the reference test, but by regression approach. The comparison of the SERION ELISA *classic* Tetanus IgG with an assay of a leading European manufacturer with 269 serum samples demonstrated excellent correlation within the measurement range of both tests.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

Sample	Mean Value OD	Intraassay CV (%) (n=20)	Mean Value OD	Interassay CV (%) (n=10)
weak positive	0,161	10,6	0,161	12,7
positive	1,085	7,3	1,143	7,3
positive	1,816	8,2	1,916	8,8

Order Information

SERION ELISA *classic* Tetanus IgG **Order Nr.: ESR 108 G**
Reference serum Tetanus IgG **Order Nr.: BR 108 G**

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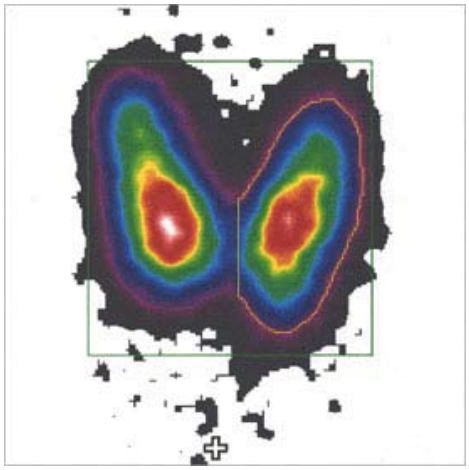
SERION ELISA *classic*

Thyroglobulin IgG

SERION ELISA *classic* Thyroperoxidase IgG test is a qualitative and quantitative immunoassay for the detection of human antibodies in serum or plasma directed against thyroperoxidase (TPO). The assay is recommended for the diagnsis of autoimmune thyroid diseases such as Hashimoto's thyroiditis or Graves' disease and for epidemiological investigations.



Clinical backround

The various symptoms of thyroid diseases such as goitre, thyroid pain, hyper- and hypothyroidism can be accompanied by autoimmune processes. The production of thyroid antibodies is a characteristic feature of Hashimoto's thyroiditis and Graves' disease, the most important autoimmune diseases of the thyroid gland. Such autoimmune disorders are the main causes of hypo- and hyperthyroidism. Thyroid antibodies are also often found in the serum of patients with other thyroid diseases such as myxoedema, granulomatous thyroiditis, nodular goitre and thyroid carcinoma. They occur in most cases of lymphatic thyroiditis in children and, but more rarely, in patients with pernicious anaemia or Sjögren's syndrome.

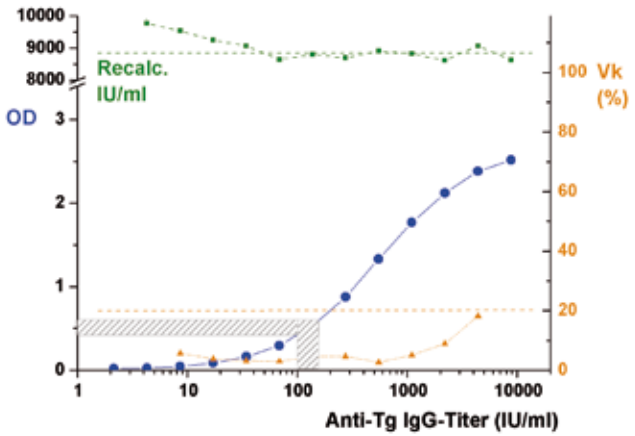
The thyroid antibodies are directed mainly against membrane or extracellular thyroid antigens. The most important autoantigens besides the TSH receptor are the water-soluble glycoprotein thyroglobulin (Tg) and thyroid peroxidase (TPO). The tyrosine residues of thyroglobulin are substrates for oxidative iodination by the enzyme thyroid peroxidase and so form the basis for the synthesis of the thyroid hormones, T3 and T4.

Diagnosis

Autoantibodies to thyroperoxidase are detected in nearly all patients with Hashimoto's thyroiditis and in the majority of patients with Graves' disease. Measurement of thyroid autoantibodies is thus an integral part of the diagnosis of thyroid disease.

Validation of SERION ELISA *classic* Thyroglobulin IgG

For the determination of the linearity range of SERION ELISA *classic* Thyroglobulin IgG the activities of serial dilutions of a high positive serum sample were assessed (blue curve) and multiplied with the respective dilution factor (green curve). Within the measurement range from 20 to 2000 IU/ml the coefficients of variation (CV) of the intraserial precision of the distinct dilutions were below 20 % (orange curve).



To calculate the performance characteristics of the SERION ELISA *classic* Thyroglobulin IgG 325 serum samples from blood donors and 75 serum samples from patients with suspected chronic thyroid disease were examined. The assay was calibrated using the NIBSC Anti-Thyroglobulin Serum International Reference Preparation (No. 65 / 093) and evaluated against the ELISA of a leading manufacturer.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Thyroglobulin IgG	98,6 %	> 99 %

Sera classified as borderline were not included into the calculation of sensitivity and specificity.

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=20)
weak positive	0,617	1,8	0,620	4,2
positive	0,697	2,3	0,709	2,4
positive	1,526	1,7	1,456	2,3

Order Information

SERION ELISA *classic* Thyroglobulin IgG **Order Nr.: ESR 144 G**
Reference serum Thyroglobulin IgG **Order Nr.: BR 144 G**

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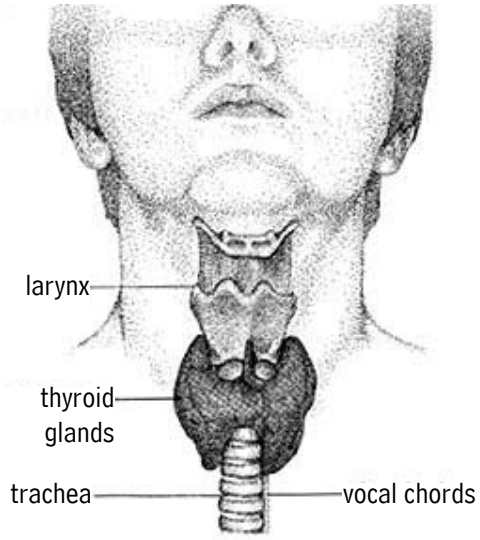
SERION ELISA *classic*

Thyroperoxidase IgG

SERION ELISA *classic* Thyroperoxidase IgG test is a qualitative and quantitative immunoassay for the detection of human antibodies in serum or plasma directed against thyroperoxidase (TPO). The assay is recommended for the diagnosis of autoimmune thyroid diseases such as Hashimoto's thyroiditis or Graves' disease and for epidemiological investigations.



Schematic drawing of the position of the thyroid gland.

Clinical backround

The various symptoms of thyroid diseases such as goitre, thyroid pain, hyper- and hypothyroidism can be accompanied by autoimmune processes. The production of thyroid antibodies is a characteristic feature of Hashimoto's thyroiditis and Graves' disease, the most important autoimmune diseases of the thyroid gland. Such autoimmune disorders are the main causes of hypo- and hyperthyroidism. Thyroid antibodies are also often found in the serum of patients with other thyroid diseases such as myxoedema, granulomatous thyroiditis, nodular goitre and thyroid carcinoma. They occur in most cases of lymphatic thyroiditis in children and, but more rarely, in patients with pernicious anaemia or Sjögren's syndrome.

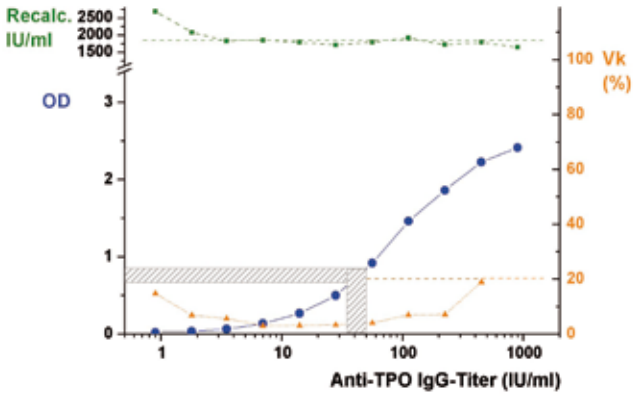
The thyroid antibodies are directed mainly against membrane or extracellular thyroid antigens. The most important autoantigens besides the TSH receptor are the water-soluble glycoprotein thyroglobulin (Tg) and thyroid peroxidase (TPO). The tyrosine residues of thyroglobulin are substrates for oxidative iodination by the enzyme thyroid peroxidase and so form the basis for the synthesis of the thyroid hormones, T3 and T4.

Diagnosis

Autoantibodies to thyroperoxidase are detected in nearly all patients with Hashimoto's thyroiditis and in the majority of patients with Graves' disease. Measurement of thyroid autoantibodies is thus an integral part of the diagnosis of thyroid disease.

Validation of SERION ELISA *classic* Thyroperoxidase IgG

For the determination of the linearity range of SERION ELISA *classic* Thyroperoxidase IgG the activities of serial dilutions of a high positive serum sample were assessed (blue curve) and multiplied with the respective dilution factor (green curve). Within the measurement range from 5 to 600 IU/ml the coefficients of variation (CV) of the intraserial precision of the distinct dilutions were below 20 % (orange curve).



To calculate the performance characteristics of the SERION ELISA *classic* Thyroperoxidase IgG 250 serum samples from blood donors and 150 serum samples from patients with suspected chronic thyroid disease were examined. The assay was calibrated using the NIBSC Research Standard Anti-Thyroid Microsome Serum (No. 66 / 387) and evaluated against the ELISA of a leading manufacturer. Sera classified as borderline were not included into the calculation of sensitivity and specificity.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Thyroperoxidase IgG	97,3 %	97,6 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=20)
weak positive	0,824	1,9	0,857	5,9
positive	1,714	3,2	1,740	3,4
positive	2,099	2,3	2,078	3,7

Order Information

SERION ELISA *classic* Thyroperoxidase IgG **Order Nr.: ESR 143 G**
Reference serum Thyroperoxidase IgG **Order Nr.: BR 143 G**

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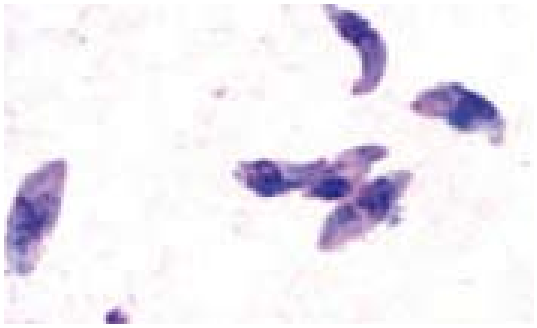
SERION ELISA *classic*

Toxoplasma gondii IgG / IgM

SERION ELISA *classic* Toxoplasma gondii IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against *Toxoplasma gondii*. The assays are recommended to determine the immune status and to differentiate acute from recent infections. The SERION ELISA *classic* Toxoplasma gondii IgG can be used as a screening test and, in combination with avidity reagent, for avidity determination. Additionally, the SERION ELISA *classic* Toxoplasma gondii IgM is suitable for screening of newborn using dried blood spots (DBS).



Micrograph of Giemsa-stained *Toxoplasma gondii* trachyzoites (Source: Centers for Disease Control and Prevention, US Department of Health and Human Services).

Pathogen

Toxoplasma gondii is an obligatory intracellular parasite with a worldwide distribution.

Disease

Following oral uptake of the parasite, e. g. with contaminated food, the organism penetrates the gut and enters the reticuloendothelial system. Due to this haematogenous dissemination, *Toxoplasma gondii* is able to infect many different organs and tissues within the host. The prevalence of infection with *Toxoplasma gondii* in the normal population is closely correlated with age. At age 50 years, nearly 50 % of the population is seropositive. The seroprevalence of antibodies to *Toxoplasma* increases with a frequency of 10 % per decade of life. Environmental and nutrition factors also play an important role and may significantly influence the seroprevalence. Approximately 50 % of infections with *Toxoplasma gondii* proceed subclinically. The remainder demonstrate only unspecific symptoms such as low fever, exhaustion, headache as well as muscle and joint pain- after an incubation period of one to three weeks.

A minority of patients suffer from high fever (up to 39 °C) and swelling of cervical lymph nodes. In 1 % of infected children and young adults complications such as myocarditis, meningitis or pneumonia are reported.
After recovery, *Toxoplasma gondii* persists in infected tissues by forming cysts which are resistant to attack by the immune system.

Diagnosis

ELISAs for the specific detection of IgG and IgM antibodies are recommended for serological diagnosis. Screening for *Toxoplasma* infections during pregnancy is of vital importance. The transmission of *Toxoplasma gondii* via the transplacental route has been observed in all stages of pregnancy, although the risk of a prenatal transmission as well as the outcome of infection depends on the stage of pregnancy. The risk of an infection of the unborn child via transplacental transmission is limited to seronegative women who acquire a primary infection during pregnancy. In Germany, an incidence of 2 to 7 infected newborns per 1000 viable births is reported. Since IgM antibodies against *Toxoplasma gondii* can persist for months or even years after infection, the detection of pathogen-specific IgM antibodies is no indication for an active infection by *Toxoplasma*.
The determination of avidity of anti-*Toxoplasma* IgG is important for differentiating between primary and past infection. The SERION ELISA *classic* Toxoplasma IgM is particularly suited for the screening of newborns using neonatal blood specimens dried on filter paper.

Validation of SERION ELISA *classic* Toxoplasma gondii

For validation of SERION ELISA *classic* Toxoplasma IgG 450 sera derived from patients and healthy persons were analyzed for evaluation in comparison with an indirect immunofluorescence assay. 76 serum samples were tested in comparison to a commercially available Toxoplasma IgM-μ-capture ELISA, for evaluation of sensitivity and specificity of the SERION ELISA *classic* Toxoplasma IgM. Borderline values were not taken into account.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Toxoplasma gondii IgG	98,2 %	> 99 %
Toxoplasma gondii IgM	> 99 %	97,2 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Toxoplasma gondii IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,559	8,3	0,535	14,4
positive	0,834	8,0	0,777	10,0
positive	1,653	5,6	1,500	12,8

SERION ELISA *classic* Toxoplasma gondii IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,302	5,1	0,202	9,9
positive	0,938	4,8	0,936	6,5
positive	1,146	5,3	1,142	5,8

Order Information

SERION ELISA *classic* Toxoplasma gondii IgG — **Order Nr.: ESR 110 G**
SERION ELISA *classic* Toxoplasma gondii IgM — **Order Nr.: ESR 110 M**
Reference serum Toxoplasma gondii IgG — **Order Nr.: BR 110 G**
Reference serum Toxoplasma gondii IgM — **Order Nr.: BR 110 M**
Reference serum Toxoplasma gondii avidity — **Order Nr.: BR 110 AVID**
Avidity reagent Toxoplasma gondii — **Order Nr.: B 110 AVID**

The SERION ELISA *classic* Toxoplasma gondii IgG is evaluated for the **analysis of cerebrospinal fluid**.
The SERION ELISA *classic* Toxoplasma gondii IgM is evaluated for **neonatal screening** on Dried Blood Spots
(For more information see SERION ELISA *classic* neonatal).
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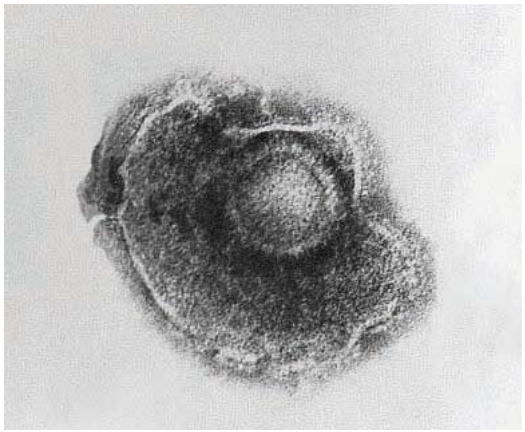
SERION ELISA *classic*

Varicella-Zoster Virus IgA / IgG / IgM

SERION ELISA *classic* Varicella-Zoster Virus IgA, IgG and IgM tests are quantitative and qualitative immunoassays for detection of human antibodies in serum, plasma or cerebrospinal fluid directed against Varicella-Zoster Virus. The SERION ELISA *classic* Varicella-Zoster Virus products are recommended for differentiation of acute infections from reactivations and for the determination of the immune status. The SERION ELISA *classic* Varicella-Zoster Virus IgG is validated for the detection of antibodies in cerebrospinal fluid.



Electron micrograph of a Varicella-Zoster Virus (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services)

Pathogen

The ubiquitous Varicella-Zoster Virus (VZV), as well as HSV, CMV and EBV, belong to the group of human Herpes viruses. The highly contagious viruses are transmitted by droplet- (contaminated aerosols) or smear-infection (vesicles with contaminated contents, or eschar).

Disease

A seasonal increase in infection rates during winter and spring is observed in temperate climate zones. Most pre-school children experience a primary infection, 95 % of adults are seropositive. Individuals are infectious 1 to 2 days before the onset of exanthema and for 7 days after the last efflorescence occurred. Following infection pathogens persist in spinal ganglia and may reactivate leading to Zoster. The incubation period is 2 to 3 weeks. After a short prodromal period with unspecific symptoms, the primary manifestation of a VZV infection, the clinical picture of varicella (chickenpox) appears. Polymorphic exanthemas with a strong itch leading to papulation, vesicles and eschar (so-called "starry sky") during the different development stages are typical for this children's disease. In general, the course of disease is benign.

Complications during primary infections are limited to individuals at-risk, e.g. immunocompromized patients, children younger than one year and elderly persons and pregnant women.
Bacterial super infections, varicella pneumonia and various CNS manifestations such as encephalitis, may present. Reactivation of persisting viruses can lead to the clinical picture of herpes zoster (shingles).

Diagnosis

Serological diagnosis of VZV infections is possible by the detection of specific IgA, IgG or IgM antibodies. Therefore, the ELISA is the method of choice in routine diagnostics, although FAMA is still the gold standard. The SERION ELISA *classic* Varicella-Zoster Virus IgG is based on glycoprotein antigens for detection of neutralizing antibodies. A good correlation with the FAMA was demonstrated. The antibody activity is measured in International Units based on the WHO standard "International Standard for Varicella Zoster Immunoglobulin". Therefore comparison of results from different laboratories is possible.

Validation of SERION ELISA *classic* Varicella-Zoster Virus

For validation of SERION ELISA *classic* VZV IgM more than 95 serum samples from unselected blood donors and 31 serum samples from patients with suspected VZV primary infection or reactivation were analysed in comparison to an ELISA from a leading European manufacturer. The SERION ELISA *classic* Varicella-Zoster Virus IgG was validated with 10 serum samples from immunized donors, 20 samples with a weak positive or borderline IgG-titer and 20 negative serum samples in comparison to another ELISA from a leading European manufacturer. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Varicella-Zoster Virus IgA	98 %	> 99 %
Varicella-Zoster Virus IgG	> 99 %	97,8 %
Varicella-Zoster Virus IgM	> 99 %	99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Varicella-Zoster Virus IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,432	5,9	0,486	9,4
positive	1,155	4,2	1,190	7,0
positive	2,298	4,4	2,374	6,9

SERION ELISA *classic* Varicella-Zoster Virus IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,718	6,4	0,789	6,4
positive	1,102	7,6	1,204	4,6
positive	2,675	3,9	3,070	4,2

SERION ELISA *classic* Varicella-Zoster Virus IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	1,035	3,3	1,090	5,3
positive	1,759	2,6	1,838	4,6
positive	2,943	1,5	3,113	2,4

Order Information

SERION ELISA *classic* Varicella-Zoster Virus IgA **Order Nr.: ESR 104 A**
SERION ELISA *classic* Varicella-Zoster Virus IgG **Order Nr.: ESR 104 G**
SERION ELISA *classic* Varicella-Zoster Virus IgM **Order Nr.: ESR 104 M**
Reference serum Varicella-Zoster Virus IgA **Order Nr.: BR 104 A**
Reference serum Varicella-Zoster Virus IgG **Order Nr.: BR 104 G**
Reference serum Varicella-Zoster Virus IgM **Order Nr.: BR 104 M**

The SERION ELISA *classic* Varicella-Zoster Virus IgG is evaluated for the **analysis of cerebrospinal fluid**.

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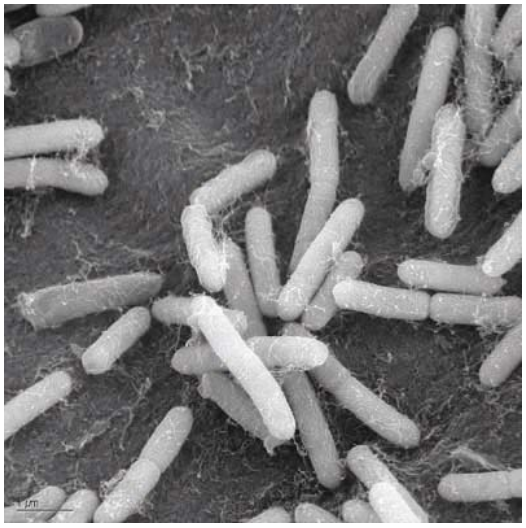
SERION ELISA *classic*

Yersinia IgA / IgG / IgM

SERION ELISA *classic* Yersinia IgA, IgG and IgM tests are quantitative and qualitative immunoassays for the detection of human antibodies in serum or plasma directed against plasmid encoded virulence markers of Yersinia. The SERION ELISA *classic* Yersinia are recommended for the differentiation of acute and recent infections in case of gastrointestinal diseases and reactive arthritis.



Electron micrograph of *Yersinia ssp.*

Pathogen

Yersinia are ubiquitous organisms but are primarily distributed in temperate and sub-tropical areas. They are found in the intestinal tracts and faeces of warm blooded wild and domesticated animals. Transmission to humans takes place primarily through contaminated foodstuffs. The virulence of the bacterium is dependent upon plasmid encoded proteins, referred to as YOPs (Yersinia Outer Proteins), which have been characterised and found to be important diagnostic markers.

Disease

Yersinia enterocolitica and *Yersinia pseudotuberculosis* are important human pathogens which are responsible for a range of intestinal syndromes e. g. enteritis, diarrhoeae, pseudoappendicitis and, in immune compromised patients, haemopathies and sepsis. The incubation period is only a few days. Post infection complications like reactive arthritis and erythema nodosum are common, mainly in individuals with the HLA-B27 antigen.

Diagnosis

The various antibody classes are important for the differential diagnosis of rheumatoid disease such as rheumatoid arthritis. In a normal uncomplicated infection caused by *Yersinia ssp.,* IgG titers may remain elevated for several years while the YOP specific IgA and IgM antibody activities decrease within a few months post infection. By contrast, in the case of post-infection complications the IgA titer remains elevated (possibly for years), often at a very high level, while the IgM titer drops off.

Validation of SERION ELISA *classic* Yersinia

The SERION ELISA *classic* Yersinia IgG and IgA were validated by the analysis of 50 serum samples from patients with suspected yersiniosis and 32 serum samples from healthy blood donors. The results were compared with those obtained from another commercially available Yersinia IgG and IgA ELISA. The SERION ELISA *classic* Yersinia IgM was evaluated with a serum panel derived from 22 patients suspected of having an acute *Yersinia* infection as well as with 150 serum samples from blood donors. The patients' sera were analysed in comparison to ELISA and Western Blot. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION ELISA *classic*	Sensitivity	Specificity
Yersinia IgA	97,4 %	96,3 %
Yersinia IgG	> 99 %	> 99 %
Yersinia IgM	> 99 %	90,0 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION ELISA *classic* Yersinia IgA

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,772	7,3	0,654	13,4
positive	1,921	5,5	1,486	9,2
positive	2,723	4,4	2,492	8,4

SERION ELISA *classic* Yersinia IgG

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,339	9,3	0,258	14,4
positive	1,378	5,6	1,131	11,0
positive	2,294	5,1	2,272	5,6

SERION ELISA *classic* Yersinia IgM

Sample	Mean value OD	Intraassay CV (%) (n=20)	Mean value OD	Interassay CV (%) (n=10)
weak positive	0,352	10,9	0,531	17,6
positive	1,053	9,5	0,834	15,2
positive	3,225	0,6	3,511	2,4

Order Information

SERION ELISA *classic* Yersinia IgA	**Order Nr.: ESR 138 A**
SERION ELISA *classic* Yersinia IgG	**Order Nr.: ESR 138 G**
SERION ELISA *classic* Yersinia IgM	**Order Nr.: ESR 138 M**
Reference serum Yersinia IgA	**Order Nr.: BR 138 A**
Reference serum Yersinia IgG	**Order Nr.: BR 138 G**
Reference serum Yersinia IgM	**Order Nr.: BR 138 M**

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SERION ELISA *classic*

Rf-Absorbent

SERION Rf-Absorbent is recommended for the removal of IgM rheumatoid factors from human serum and plasma samples prior to pathogen-specific IgM detection. The special Rf-Absorbent/CAg simultaneously binds rheumatoid factors and antibodies directed against membrane components of the host-cell used for pathogen cultivation. It is recommended for use with certain SERION ELISA *classic*.

Rheumatoid factors are predominantly anti-IgG directed autoantibodies of the IgM class that can be detected in serum samples of approximately 5 % of healthy individuals. Those IgM rheumatoid factors preferably bind to IgG immune complexes. Therefore, false positive results may appear in pathogen-specific IgM detection. In samples with a high concentration of pathogen-specific IgG antibodies, weakly binding pathogen-specific IgM antibodies may be displaced by stronger binding IgG antibodies. In those cases, IgM detection can show false negative results. Therefore, it is necessary to pretreat serum samples with rheumatoid factor-absorbens. Prior to pathogen-specific IgM detection, it precipitates up to 15 mg IgG / ml undiluted serum and thereby also IgG binding IgM rheumatoid factors. The special Rf-Absorbent/CAg simultaneously binds rheumatoid factors and antibodies directed against membrane components of the host-cell used for pathogen cultivation. It is recommended in combination with SERION ELISA *classic* Cytomegalovirus, Herpes Simplex Virus, Measles Virus, Mumps / Parotitis Virus, Rubella Virus, Toxoplasma gondii and Varicella-Zoster Virus IgM tests.

Order Information

Rf-Absorbent (4 ml for 20 determinations)	**Order Nr.: Z4**
Rf-Absorbent (20 ml for 100 determinations)	**Order Nr.: Z200**
Rf-Absorbent/CAg (4 ml for 20 determinations)	**Order Nr.: T4**
Rf-Absorbent/CAg (20 ml for 100 determinations)	**Order Nr.: T200**

Please visit our website www.virion-serion.com for more information on our SERION ELISA *classic* products.

SERION ELISA *classic*
Reference sera

Reference sera are control reagents for the antibody detection using immunoassays of the SERION ELISA *classic* product line. They are recommended as an aid to internal quality controls for the determination of validity, precision and constancy.

Order Information for SERION ELISA *classic* Reference sera

Reference serum	Order Nr.
Adenovirus IgA	BR 128 A
Adenovirus IgG	BR 128 G
Aspergillus fumigatus IgA	BR 132 A
Aspergillus fumigatus IgG	BR 132 G
Aspergillus fumigatus IgM	BR 132 M
Bordetella pertussis IgA	BR 120 A
Bordetella pertussis IgG	BR 120 G
Bordetella pertussis IgM	BR 120 M
Bordetella pertussis Toxin IgG	BR 1201 G
Borrelia burgdorferi IgG	BR 121 G
Borrelia burgdorferi IgM	BR 121 M
Brucella IgA	BR 116 A
Brucella IgG	BR 116 G
Brucella IgM	BR 116 M
Campylobacter jejuni IgA	BR 139 A
Campylobacter jejuni IgG	BR 139 G
Campylobacter jejuni IgM	BR 139 M
Candida albicans IgA	BR 117 A
Candida albicans IgG	BR 117 G
Candida albicans IgM	BR 117 M
Chlamydia IgA	BR 137 A
Chlamydia IgG	BR 137 G
Chlamydia pneumoniae IgA	BR 1371 A
Chlamydia pneumoniae IgG	BR 1371 G
Chlamydia trachomatis IgA	BR 1372 A
Chlamydia trachomatis IgG	BR 1372 G
Coxiella burnetii (Phase 2) IgG	BR 1312 G
Coxiella burnetii (Phase 2) IgM	BR 1312 M
Coxsackievirus IgA	BR 134 A
Coxsackievirus IgG	BR 134 G

Reference serum	Order Nr.
Cytomegalovirus IgG	BR 109 G
Cytomegalovirus IgG Avidity	BR 109 AVID
Cytomegalovirus IgM	BR 109 M
Diphtheria IgG	BR 130 G
Echovirus IgA	BR 135 A
Echovirus IgG	BR 135 G
Enterovirus IgA	BR 133 A
Enterovirus IgG	BR 133 G
Epstein-Barr Virus / VCA IgG	BR 1361 G
Epstein-Barr Virus / VCA IgM	BR 1361 M
Epstein-Barr Virus / EBNA 1 IgG	BR 1362 G
Epstein-Barr Virus / EA IgG	BR 1363 G
Helicobacter pylori IgA	BR 118 A
Helicobacter pylori IgG	BR 118 G
Helicobacter pylori IgM	BR 118 M
Herpes Simplex Virus 1 IgG	BR 1051 G
Herpes Simplex Virus 1 IgM	BR 1051 M
Herpes Simplex Virus 2 IgG	BR 1052 G
Herpes Simplex Virus 2 IgM	BR 1052 M
Herpes Simplex Virus 1/2 IgA	BR 105 A
Herpes Simplex Virus 1/2 IgG	BR 105 G
Herpes Simplex Virus 1/2 IgM	BR 105 M
Influenza A Virus IgA	BR 1231 A
Influenza A Virus IgG	BR 1231 G
Influenza B Virus IgA	BR 1232 A
Influenza B Virus IgG	BR 1232 G
Leptospira IgG	BR 125 G
Leptospira IgM	BR 125 M
Measles Virus IgG	BR 102 G
Measles Virus IgM	BR 102 M

Reference serum	Order Nr.
Mumps / Parotitis Virus IgG	BR 103 G
Mumps / Parotitis Virus IgM	BR 103 M
Mycoplasma pneumoniae IgA	BR 127 A
Mycoplasma pneumoniae IgG	BR 127 G
Mycoplasma pneumoniae IgM	BR 127 M
Parainfluenza Virus 1 IgG	BR 1261 G
Parainfluenza Virus 1, 2, 3 IgA	BR 126 A
Parvovirus B19 IgG	BR 122 G
Parvovirus B19 IgM	BR 122 M
Respiratory Syncytial Virus IgA	BR 113 A
Rubella Virus IgG	BR 129 G
Rubella Virus IgG Avidity	BR 129 AVID
Rubella Virus IgM	BR 129 M
TBE Virus IgG	BR 112 G
TBE Virus IgM	BR 112 M
Tetanus IgG	BR 108 G
Thyroglobulin IgG	BR 144 G
Thyroperoxidase IgG	BR 143 G
Toxoplasma gondii IgG	BR 110 G
Toxoplasma gondii IgG Avidity	BR 110 AVID
Toxoplasma gondii IgM	BR 110 M
Varicella-Zoster Virus IgA	BR 104 A
Varicella-Zoster Virus IgG	BR 104 G
Varicella-Zoster Virus IgM	BR 104 M
Yersinia IgA	BR 138 A
Yersinia IgG	BR 138 G
Yersinia IgM	BR 138 M

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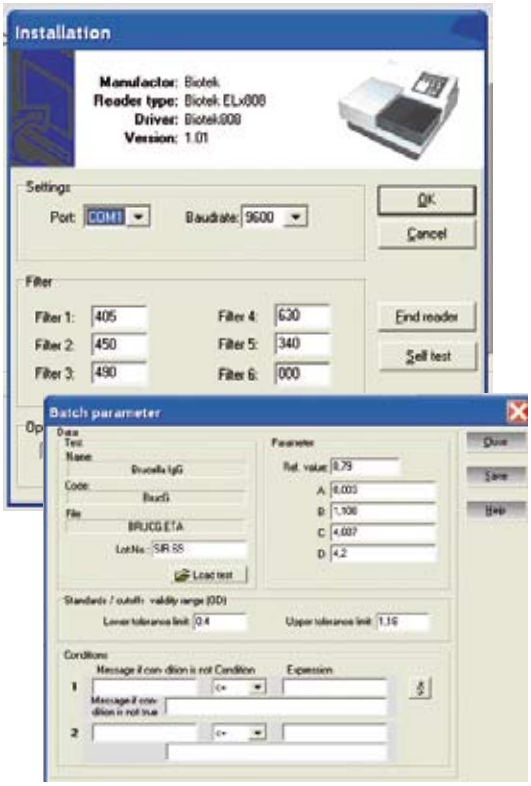
SERION
evaluate

The software SERION *evaluate* is recommended for the evaluation of photometrical measurement data derived from a range of commercially availabe photometers after processing of SERION ELISA *classic*, SERION ELISA *antigen* or comparable enzyme-linked immunosorbent assays based on the microtitre plate format.



SERION *evaluate*

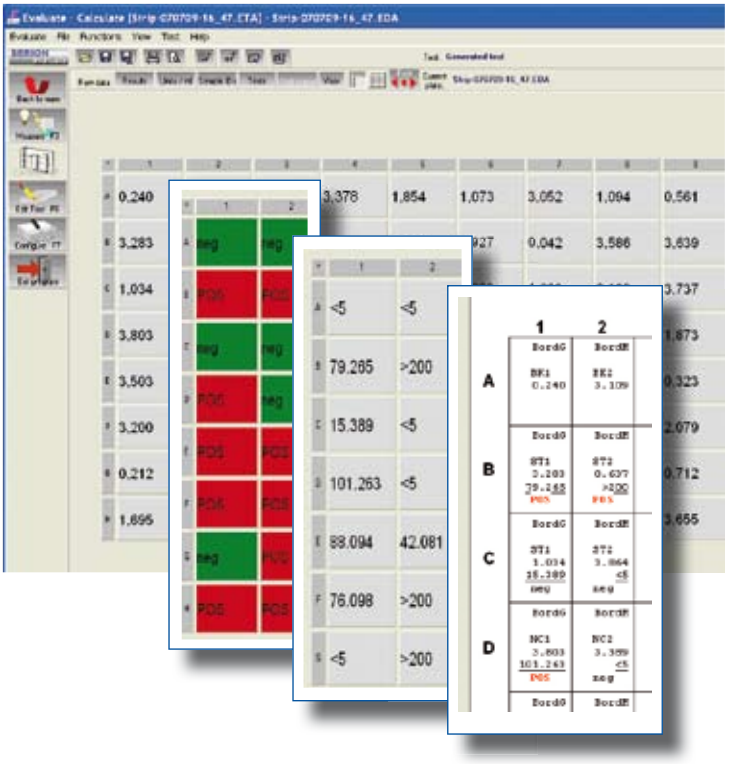
The SERION *evaluate* software facilitates the qualitative and quantitative analysis of optical measurement signals generated by ELISA tests and is recommended for use with a range of commercially available ELISA readers. The data analysis is processed according to pre-selected test patterns or manual test configurations. The analysis can be evaluated directly on the screen.

The program requirements are minimal and it can be run on any PC with an OS based on Windows 98 or later.

Analysis with SERION *evaluate*

After selection of the ELISA reader and installation of the corresponding driver, the optical filters and all test-specific parameters recommended for the analysis need to be adjusted. SERION ELISAs are pre-installed and can be conveniently chosen from an immunoassay menu. The user enters the relevant lot specific data, such as reference value of the standard and the four parameters for quantification from the quality control certificate in the software, and starts the analysis.

The positions of patient samples and controls are defined and saved in an assay protocol in order to transfer the measurement signals from the reader to the software and allocate them automatically to the positions on the microtitre plate. The optical signals as well as the qualitative and quantitative evaluation are clearly arranged and presented on separate result reports.



Quality assurance with SERION *evaluate*

Additionally, the validity of each test run is assessed by verification of the e. g. the standard reference value. By using the SERION *evaluate* software a standardised and valid evaluation of SERION ELISA immunoassays is guaranteed.

Advantages of SERION *evaluate*

- Compatibility with a range of different ELISA readers
- Flexible possibilities of user adjustments for evaluation of various enzyme-immunoassays
- Evaluation of qualitative, semi-quantitative and quantitative enzyme-immunoassays
- Free plate assignment with up to 24 measuring groups on one microtitre plate
- Processing of strip tests
- Complex representation of graphic and measuring data
- Extensive, integrated user administration with protocol function
- Flexible protection of the password with a multitude of functions
- Visor module for the representation of measuring results as color values for the quick evaluation of results

Order Information

SERION *evaluate* **Order Nr.: VT 013**

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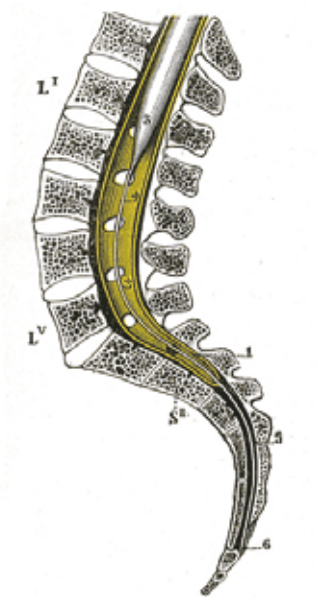
SERION ELISA *classic*

CSF diagnostics

Certain SERION ELISA *classic* have been evaluated for the determination of intrathecal antibodies and are recommended for the detection, as well as for the differentiation, of inflammatory processes within the central nervous system (CNS). A software tool supports the calculation of antibody indices according to a scheme of Prof. Hansotto Reiber (Reiber and Peter, 2001).



Location of spinal chord within the spinal column

Diagnostic Relevance

Determination and differentiation of inflammatory processes within the central nervous system (CNS) are the major objectives in CSF diagnostics. For acurate diagnosis it is important to determine whether the disease state is caused by infection or due to a chronic inflammatory process (e.g. Multiple Sclerosis).

Existing neurologic symptoms and the suspicion of infection of the CNS or a chronic inflammatory process make a diagnosis using cerebrospinal fluid based on the determination of intrathecal synthesized antibodies necessary. In the case of an acute infection of the CNS local antibodies are produced against the responsible pathogen. Since direct detection of the pathogen in the CSF is often not possible (e.g. in case of a Borrelia infection) or too time consuming, serological methods are primarily used for the differential diagnosis of an infection within the CNS. Chronic inflammatory processes of the CNS may result in the activation of a polyspecific immune response. In such cases specific antibodies against different viral pathogens may be detected although the related pathogens are not responsible for the disease. Analysis of the CSF alone is not sufficient for determination of intrathecal synthesized antibodies. Additional factors have to be taken into account.

The passage of large molecules and cells from the arterial blood across the blood/brain barrier and into the CSF is very limited due to the permeability properties of the vascular walls.

Amino acids, sugars and proteins, as a consequence of their particular molecular characteristics, have varying requirements for transfer across the barrier; however the permeability for proteins is primarily a function of their size. As a consequence, under normal conditions, the total protein concentration in the cerebrospinal fluid is approximately 1 % of that in the corresponding serum. If the blood/brain barrier is compromised, the levels of proteins in the CSF may be substantially elevated above the norm.

Antibodies found in the CSF may have their origin in the plasma, entering the CSF by diffusion, or be synthesized within the CSF itself. The determination of an intrathecal antibody synthesis is possible only by the simultaneous quantification of a range of proteins in the CSF as well as in the corresponding serum. Therefore, CSF / serum quotients and antibody indices (AI) are determined in accordance with a calculation scheme developed by Hansotto Reiber. This is done for quantitative SERION ELISA *classic* Borrelia burgdorferi IgG and IgM, SERION ELISA *classic* Cytomegalovirus IgG, SERION ELISA *classic* Herpes Simplex Virus 1/2 IgG, SERION ELISA *classic* Measles Virus IgG, SERION ELISA *classic* Mumps / Parotitis Virus IgG, SERION ELISA *classic* Rubella Virus IgG, SERION ELISA *classic* TBE Virus IgG and IgM as well as SERION ELISA *classic* Varicella-Zoster Virus IgG or, alternatively, by using the SERION Multianalyt™ CSF IgG in order to detect IgG antibodies directed against Measles Virus, Rubella Virus, Varicella-Zoster Virus and the Herpes Simplex Viruses 1 and 2 simultaneously. An evaluation software facilitates the calculation of antibody indices (AI) according to Reiber (see Reiber and Peter, 2001).

Validation of SERION ELISA *classic* for CSF diagnostics

The SERION ELISA *classic* and the SERION Multianalyt™ CSF IgG were evaluated for CSF diagnostics in comprehensive studies. As an example, the intra- and interserial precisions of calculated antibody indices in a selection of SERION ELISA *classic* tests are presented in the following table. The antibody indices were determined by the analysis of serum/CSF samples of different reactivities.

SERION ELISA *classic*	Antibody index (AI) Intraassay CV (%) (n=10)	Antibody index (AI) Interassay CV (%) (n=10)
Measles Virus IgG	12,7	14,8
Rubella Virus IgG	8,0	7,0
VZV IgG	8,8	6,3
HSV 1/2 IgG	7,8	7,8

Order Information

The following SERION ELISA *classic* are evaluated for the analysis of cerebrospinal fluid.

SERION ELISA *classic* Borrelia burgdorferi IgG **Order Nr.: ESR 121 G**
SERION ELISA *classic* Borrelia burgdorferi IgM **Order Nr.: ESR 121 M**
SERION ELISA *classic* Cytomegalovirus IgG **Order Nr.: ESR 109 G**
SERION ELISA *classic* Herpes Simplex Virus 1/2 IgG **Order Nr.: ESR 105 G**
SERION ELISA *classic* Measles Virus IgG **Order Nr.: ESR 102 G**
SERION ELISA *classic* Mumps / Parotitis Virus IgG **Order Nr.: ESR 103 G**
SERION ELISA *classic* Rubella Virus IgG **Order Nr.: ESR 129 G**
SERION ELISA *classic* TBE Virus IgG **Order Nr.: ESR 112 G**
SERION ELISA *classic* TBE Virus IgM **Order Nr.: ESR 112 M**
SERION ELISA *classic* Varicella-Zoster Virus IgG **Order Nr.: ESR 104 G**

or alternatively:

SERION Multianalyt™ CSF IgG **Order Nr.: MK 2360 G**

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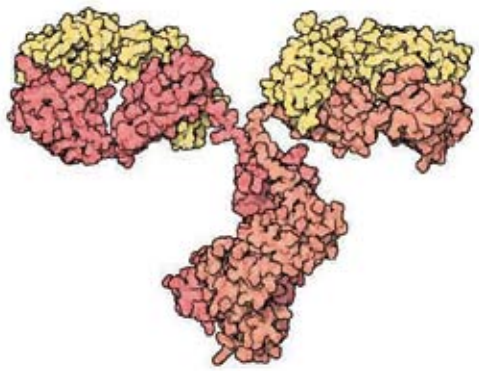
SERION ELISA *classic*

Avidity Reagents

The SERION ELISA *classic* Avidity Reagents are complementary components which, in combination with the corresponding SERION ELISA *classic*, enables the avidity of pathogen specific IgG antibodies to be determined. The SERION ELISA *classic* Avidity Reagents are recommended to aid the differentiation between acute primary infections and previous infections by Cytomegalovirus, Rubella Virus or *Toxoplasma gondii* particularly in serological investigation during pregnancy.



Schematic drawing of an IgG antibody
(Source: US Federal Government,
illustrated by David S. Goodsell)

Diagnostic Background

Avidity characterises the average affinity of specific polyclonal antibodies of an individual formed during the normal course of an infection. Avidity testing is based on the observation, that antibody affinities increase significantly as the immune response to pathogens progresses (affinity maturation). Therefore, highly avid IgG antibodies are an indicator of previous infection whereas IgG antibodies with low avidity are suggestive of a primary infection. Consequently, the determination of high antibody avidities in general excludes acute primary infections. Particularly during pregnancy, avidity testing of certain pathogen specific IgG antibodies is a valuable contribution in routine serology.

Primary infection of pregnant women caused by Cytomegalovirus, Rubella Virus or by *Toxoplasma gondii* are a a major cause of connatal damage. Determination of IgM antibodies should not be considered conclusive proof of a primary infection as pathogen-specific IgM antibodies may also arise from polyclonal stimulation, reinfection or reactivation. Determination of IgG antibody avidity provides therefore a valuable contribution towards the differentiation between acute primary and previous infections.

SERION avidity testing

SERION Avidity testing is performed using the appropriate SERION ELISA *classic* tests and based on the degradation of the interaction between antibodies and antigens. The SERION avidity reagents cause the dissociation of low affinity antibody-antigen complexes, whereas high affinity complexes are not affected.
The gold standard for avidity determination is the end-point titration method, which, due to the technical complexity involved is seldom used in routine laboratories. The simpler single-point method in which a quotient of OD-values is calculated of cavities with and without avidity reagent can lead to false avidity indices due to the variable antibody content of serum samples. As a consequence of the competition between high and low-affinity antibodies for the same binding sites on the coated microtiter plates, the concentration of antigen specific antibodies in the serum sample has a significant effect on the avidity indices obtained. Therefore, commercially available avidity tests frequently use the method of expressing the avidity index as a quotient of IgG antibody titers in order to compensate for the effect of variable antibody concentrations.
Determination of SERION avidity indices is performed on a special evaluation method based on measured signal intensities, but taking into account the pathogen specific antibody concentration in order to compensate for the influence of antibody content on the avidity index.
A comparison of the SERION evaluation technique with quantification methods of other manufacturers, which are based on quotients of measured antibody concentrations with and without avidity reagent, showed better intra- and interserial precision profiles with lower coefficients of variation with the SERION method. Furthermore, high lot-to-lot consistency is guaranteed.

Software SERION *avidity*

For calculation of SERION avidity indices and determination of high or low avidity, the free-of-charge Excel-based evaluation software tool SERION *avidity* is available on request.

Order Information

SERION ELISA *classic* Cytomegalovirus IgG	**Order Nr.: ESR 109 G**
SERION ELISA *classic* CMV avidity reagent	**Order Nr.: B 109 AVID**
Reference serum CMV avidity	**Order Nr.: BR 109 AVID**
SERION ELISA *classic* Rubella Virus	**Order Nr.: ESR 129 G**
SERION ELISA *classic* Rubella Virus avidity reagent	**Order Nr.: B 129 AVID**
Reference serum Rubella Virus avidity	**Order Nr.: BR 129 AVID**
SERION ELISA *classic* Toxoplasma gondii IgG	**Order Nr.: ESR 110 G**
SERION ELISA *classic* Toxoplasma gondii avidity reagent	**Order Nr.: B 110 AVID**
Reference serum Toxoplasma gondii avidity	**Order Nr.: BR 110 AVID**

Software SERION *avidity*

Normal **IgG determination in parallel** with avidity testing is possible.
Avidity testing is evaluated for manuel use as well as for processing on Immunomat™ and DYNEX DSX™.
The Excel-based **Software SERION *avidity*** is available on demand free of charge.

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SERION ELISA *classic*
neonatal

SERION ELISA *classic* Cytomegalovirus IgM, Rubella Virus IgM and Toxoplasma gondii IgM tests are qualitative and quantitative immunoassays, which are evaluated for the detection of human IgM antibodies directed against Cytomegalovirus, Rubella Virus and *Toxoplasma gondii* in neonatal blood samples. A newborn screening can be performed with the regular dried neonatal heel blood spots (DBS) on filter papers with a diameter of 1/8 inch (3.2 mm).

Diagnostic Relevance

Due to their size, maternal IgM antibodies are not normally able to cross the placenta into the foetal blood stream. Consequently, the detection of pathogen specific IgM in a newborn is highly indicative of an intrauterine infection with that pathogen. Screening for IgM antibodies directed against these three significant pathogens can be of considerable assistance in identifying asymptomatic infections in newborns, particularly in regions that do not offer prophylactic pre-partal examinations and where the sero-negativity rate in women is high.

Cytomegalovirus

Cytomegalovirus causes the most frequent congenital and postnatal infections. If seroconversion occurs during pregnancy, virus transmission to the fetus occurs in 40 % of the cases. Up to 15 % of the affected infants suffering damage at birth. Late manifestations of disease such as long-term neurological damage or deafness can be observed in 10 to 15 % of infected children.

Rubella Virus

During the first 8 to 11 weeks of pregnancy primary Rubella Virus infections lead to severe fetal malformations in 65 to 90 %. Infections between the 12th and 16th week of pregnancy cause malformations in approximately 10 %. There is only a minor risk of Rubella embryopathy after the 18th to 19th week of pregnancy.

Toxoplasma gondii

The transmission of *Toxoplasma gondii* via the transplacental route has been observed in all stages of pregnancy. In Germany, an incidence of 2 to 7 infected newborns per 1000 viable births is reported. Immediately after birth only 1 to 3 % of the infected newborns show clinical symptoms of toxoplasmosis. In contrast, up to 80 % of subclinically infected children suffer from late lesions and severe clinical manifestations.

Evaluation of SERION ELISA *classic* neonatal IgM

At the time of birth the content of IgM antibodies in newborn blood is significantly lower compared to adult samples. Therefore, a decrease of the borderline ranges of the SERION ELISA *classic* for neonatal diagnostics is necessary.

In addition to high sensitivity, immunoassays for neonatal diagnostics need high specificity, particularly with low borderline ranges. The high sensitivities in combination with high specificities of SERION ELISA *classic* tests allow the determination of threshold ranges for neonatal diagnostic as follows:

SERION ELISA *classic*	Treshold SERION ELISA neonatal (U/ml)	Treshold SERION ELISA *classic* (U/ml)
Cytomegalovirus IgM	2,5 - 3,8	10 - 15
Rubella Virus IgM	0,8 - 1,0	2,5 - 3,5
Toxoplasma gondii IgM	20 - 30	300 - 350

Specificity

The determination of the specificities of the SERION ELISA *classic* neonatal was assessed with DBS from more than 500 blood samples of anonymised newborns.

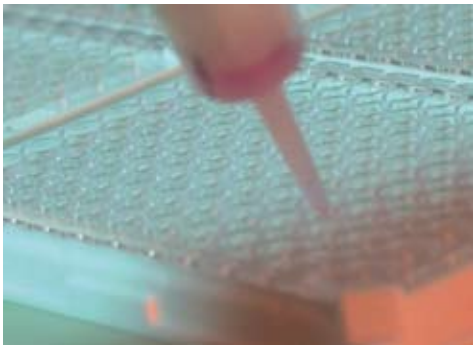
SERION ELISA *classic*	Specificity of SERION ELISA *classic* neonatal
Cytomegalovirus IgM	99,7 %
Rubella Virus IgM	99,5 %
Toxoplasma gondii IgM	99,8 %

Order Information

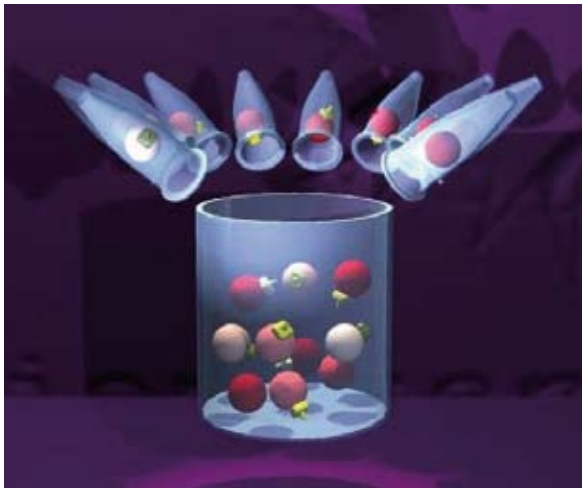
The following SERION ELISA *classic* are evaluated for neonatal screening on Dried Blood Spots (DBS).

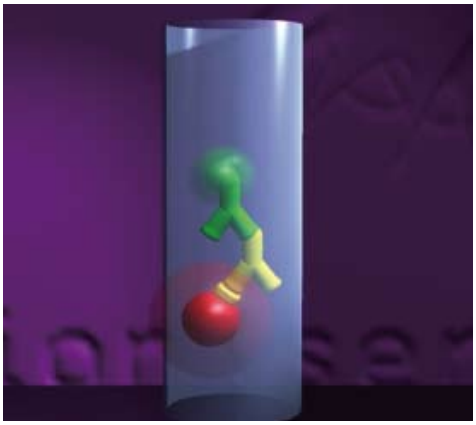
SERION ELISA *classic* Cytomegalovirus IgM **Order Nr.: ESR 109 M**
SERION ELISA *classic* Rubella Virus IgM **Order Nr.: ESR 129 M**
SERION ELISA *classic* Toxoplasma gondii IgM **Order Nr.: ESR 110 M**

Please visit our website www.virion-serion.com for more information on our SERION ELISA *classic* products.



SERION Multianalyt™





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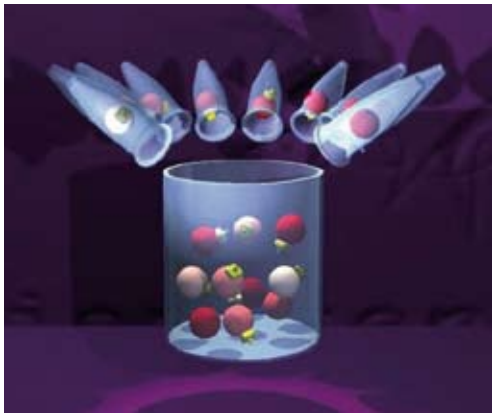
SERION Multianalyt™ Technology

Multiplex Analysis for Flow Cytometry

The SERION Multianalyt™ technology allows the simultaneous quantification of multiple parameters in a small sample volume using flow cytometry. The technique is based on polystyrene particles of varying size and fluorescence properties. Each particle population is coated with a specific capture molecule. Bound analytes are tagged with fluorescent detector reagents. The easy to handle and automatable technology allows the generation of innovative, time- and labor-saving solutions for many applications in modern research and diagnostics.



SERION Multianalyt™ Particle Plex

Technology

The SERION Multianalyt™ technology is based on 1 to 10 µm sized polystyrene particles which are used as the solid phase for immunoassays in the SERION Multianalyt™ product line. The beads are dyed with a fluorophore in ten different intensity steps. The use of the color coding in combination with the variable size of the particles leads to optically distinguishable bead populations. The differentiation of the particles in a flow cytometer allows the simultaneous performance of up to 40 different immunoreactions in one set up.

The covalent fixation of proteins, peptides or even nucleic acids is possible due to a surface modification on the polystyrene particles. Each particle population can be coated with a different capture molecule, for which purpose a simple and established coupling technology is available.

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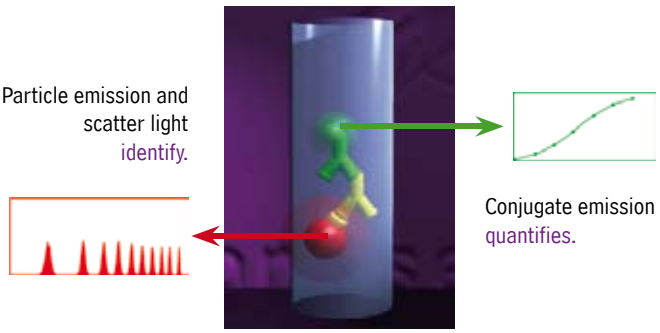
Assay Performance

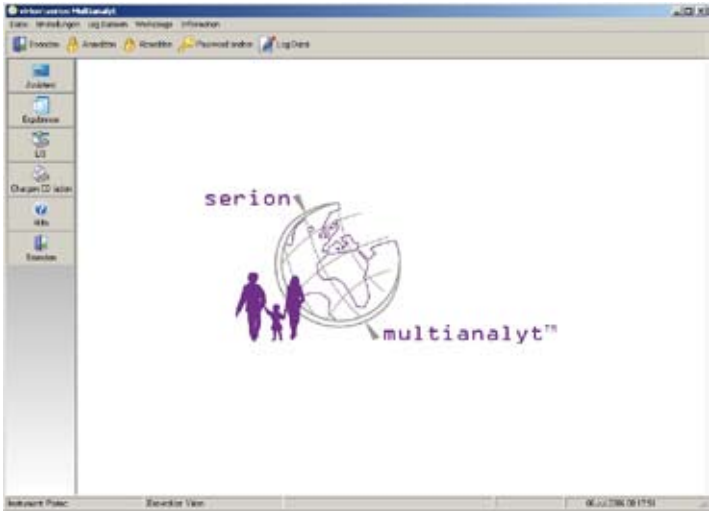
The analysis is performed in the cavities of a microtiter plate and starts with the addition of a prepared particle suspension to a diluted sample preparation. Subsequently, the analyte of interest bind to the solid phase. In a multiplex test performance various particle populations are mixed with the diluted sample. The higher the concentration of the analyte, the more molecules bind to the capture molecule coated on the surface of the particles. In a second step, a detector molecule, usually an antibody with a high specific affinity to the analyte, is added to the reaction mixture. The detector is labelled with another fluorescent dye. The use of fluorophores with high quantum efficiency, such as Phycoerythrin, guarantees a high sensitivity in the immunoreaction. Thereby, analysis of solutions with low analyte concentration as well as highly diluted samples can be performed. The use of a multiplexing test system requires very low sample quantities.



Design of a SERION Multianalyt™ immunoassay: Analytes, here an immunoglobuline, bind to the coated particle surface and are tagged by a detector molecule

Analysis

In a flow cytometer particles are separated and precisely gated through the focus of the laser-based detection system. The identification of the particles is performed by the scattering of light and by fluorescence intensity. Each particle is analysed individually. The analysis of more than a hundred particles per population assures the results statistically and guarantees the high reproducibility of the data. The fluorescence intensity of the bound detector molecule is proportional to the concentration of the analyte in the sample. Flow cytometers are able to analyse thousands of particles per second. Consequently, the measurement of a sample is performed in a few seconds.



Evaluation

The SERION Multianalyt™ technology is suited for use with different, commercially available flow cytometers. The measured signal intensities of a multiplex immunoreaction can be conveniently evaluated with the software SERION easy*PLEX*, independent from the flow cytometer used.

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User: Virion **Institute** Musterinstitut **Address:**
Date/Time: 24.08.2009 16:56:19
Run: 2009_08_24-16_52-MCZBK **SW Version:** 1.0.3.4
Instrument: FC500_Virion **Type:** FC500 Lin **SN:** xxx
FCS Directory: C:\090326-QK Borrelia IgG-MCZ.BK.tdf_20090326_111050

Lot / Plex		Total	Analyte 1			Analyte 2			Analyte 3			Analyte 4			Analyte 5			Analyte 6			Analyte 7			Analyte 8		
MCZ.BK	Borrelia total IgG		VlsE			OspC			p100			DbpA-PBr			DbpA-PKo			p58			p41i			Lysate		
	Points	Rating	U/ml	Eval.	P	U/ml	Eval.	P	U/ml	Eval.	P	U/ml	Eval.	P	U/ml	Eval.	P	U/ml	Eval.	P	U/ml	Eval.	P	U/ml	Eval.	P
T65	3	borderline	9,31	-	0	3,24	-	0	-11111,11	-	0	99999,99	+	3	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0
H18	11	positive	67,50	+	4	3,45	-	0	64,83	+	4	-11111,11	-	0	451,17	+	3	-11111,11	-	0	5,15	-	0	5,24	-	0
K02	11	positive	99999,99	+	4	99999,99	+	4	-11111,11	-	0	-11111,11	-	0	147,01	+	3	-11111,11	-	0	-11111,11	-	0	6,86	-	0
K02 1:800	11	positive	200,54	+	4	81,62	+	4	-11111,11	-	0	-11111,11	-	0	28,48	+	3	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0
K02 1:3200	0	negative	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0	-11111,11	-	0
T55 1:50	21	positive	45,17	+	4	12,85	?	2	40,91	+	4	99999,99	+	3	12,48	?	2	8,65	-	0	54,64	+	4	23,30	+	2
T55	7	positive	11,09	?	2	3,69	-	0	9,17	-	0	100,91	+	3	-11111,11	-	0	-11111,11	-	0	10,04	?	2	5,22	-	0

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SERION Multianalyt™

Bacillus anthracis (PA + LF) IgG

SERION Multianalyt™ Bacillus anthracis IgG test is a quantitative fluorescence immunoassay based on the principle of flow cytometry for the detection of human antibodies in serum or plasma directed against the Protective Antigen (PA) and the Lethal Factor (LF) of *Bacillus anthracis*. The assay is recommended for vaccination control and for the determination of the current individual immune status to prevent hyper immune damage.

SERION Multianalyt™ Bacillus anthracis IgG test is especially interesting for the proof of protection of soldiers in conflict areas (source: US Department of Defense)

Pathogen

Splenic fever or Anthrax is an infectious disease, which is primarily found in animals. Especially in countries with warm climates, ungulates i.e. pigs, cattle, sheep, goats and horses are affected. Close contact with infected animals or exposure to infected animal products such as skin, meat or milk may transmit the pathogen to humans. The incubation period for the zoonosis is a few hours up to several days. This disease has become rare in industrial countries, however, endemic regions of South America, Africa and South East Asia still suffer from regular epidemics. In recent years, anthrax has been of increasing public interest due to its potential use in biological weapons.

The pathogen for splenic fever, *Bacillus anthracis,* is a gram positive, aerobic bacillus. Adverse conditions or increased temperatures lead to the production of stable spores, which can remain infectious for several years. Inhalation of significant numbers of spores (8.000 to 50.000) leads to infection. Due to a special protein shell, absorbed bacteria are able to escape defense mechanisms of the human immune system. They produce toxins that are assembled of the protective antigen (PA), the lethal (LF) and the edema factor (EF). These exotoxins are spread and damage small blood cells especially, so that they become permeable for red blood cells (erythrocytes). Inflammation and hemorrhage in form of hemorrhagic edema are the results.

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Disease

Symptoms for splenic fever depend on the location of the entrance of the pathogen. Most subsequent forms are splenic fever of the skin. As in most cases, Anthrax spores are absorbed through small superficial skin injuries. After a short period of time, small red knots with a black center appear. Sanious vesicles develop quickly. As the disease progresses further vesicles develop and fuse to the so-called anthrax carbuncle (*Pustula maligna*).
Splenic fever of the lungs is far less common in humans. Breathing in spores causes the infection. The disease develops like severe pneumonia with highly infectious sanguineous sputum. Patients suffer from high fever, ague, cough and dyspnea. If not treated, splenic fever of the lungs is lethal in most cases.
A third form is splenic fever of the intestines, caused by consumption of contaminated produce from farm animals, e.g. raw meat or milk that was not boiled sufficiently. Severe hemorrhagic inflammation of the intestines, sanguineous sputum and faeces are symptoms. This form of the disease is also lethal, if not treated.
All three types of splenic fever may develop sepsis, which rapidly causes death in most cases.

Diagnosis

Clinical picture and anamnesis lead to the diagnosis of splenic fever. Pathogen detection e.g. examination of bodily fluids or taking swabs confirm the diagnosis. Treatment with antibiotics must start as soon as possible. Avoiding contact with infected animals and their produce is the most effective form of prophylaxis. Immunization of certain risk groups e.g. soldiers, is possible with a PA containing vaccine, an extract from culture filtrate.

Validation of SERION Multianalyt™ Bacillus anthracis IgG

The SERION Multianalyt™ Bacillus anthracis IgG was evaluated by the analysis of 100 negative serum samples from blood donors and 114 serum samples from immunized individuals. The test was evaluated against the status of immunization. Borderline results were not included in the calculation.

SERION Multianalyt™	Sensitivity	Specificity
Bacillus anthracis PA IgG	> 99 %	> 99 %
Bacillus anthracis LF IgG	98,0 %	96,5 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION Multianalyt™ Bacillus anthracis PA IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
negative	22,0	5,3	18,9	12,9
positive	240,8	3,1	240,8	3,1
positive	1000,8	2,7	1004,4	3,8
positive	2132,5	2,6	2120,2	3,7

SERION Multianalyt™ Bacillus anthracis LF IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
negative	11,9	3,7	11,6	2,7
positive	140,4	4,5	139,3	6,3
positive	387,1	4,3	382,2	4,2
positive	550,3	2,5	561,1	4,9

Order Information

SERION Multianalyt™ Bacillus anthracis IgG **Order Nr.: MK 2420 G**

The SERION Multianalyt™ Bacillus anthracis IgG can be individually combined with particles of SERION Multianalyt™ Brucella IgG, SERION Multianalyt™ Francisella tularensis IgG as well as SERION Multianalyt™ Hantavirus Puumala IgG.

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SERION Multianalyt™

Bordetella pertussis IgA + IgG

SERION Multianalyt™ Bordetella pertussis IgA + IgG test is a quantitative fluorescence immunoassay based on the principle of flow cytometry for the simultaneous detection of human IgA and IgG antibodies in serum or plasma directed against the Pertussis Toxin (PT) and the Filamentous Hemagglutinin (FHA) of *Bordetella pertussis*. The assay is recommended for the detection of acute and recent infections, for differential diagnosis of atypical pneumonias, for differential diagnosis of *B. pertussis* and *B. parapertussis* infections as well as for vaccination control.

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Pathogen

Bordetella pertussis is the pathogen responsible for whooping cough, a worldwide spread infectious disease that is transmitted from person to person by droplet infection. Particularily children up to four years old are affected and the mortality in infected infants is high. Although young people and adults usually do not get seriously ill, they are a risk as a source of infection for non protected and risk patients such as infants, old and ill people. Colonisation of the respiratory tract and establishment of infection are facilitated by the synergistic action of several virulence factors. A significant virulence factor is pertussis toxin (PT), which is synthesized and secreted exclusively by *Bordetella pertussis.*

Disease

Progression of typical whooping cough can be divided into three stages. After an incubation period of 1 to 2 weeks symptoms begin with the catarrhal phase (highly infectious), usually accompanied by a cough, rhinitis and conjunctivitis. Subsequently, the convulsive (paroxysmal) phase follows characterised by paroxysmal cough attacks combined with vomiting of viscid mucus, laryngospasm and bronchospasm, leading to a blue-cyanosed complexion in the child. After four to six weeks attacks diminish and slowly subside (decrementi phase, up to 6 months).

Diagnosis

For diagnosis of an infection caused by *B. pertussis* the direct detection and isolation of the pathogen itself is the optimal method. The ELISA technique is the most commonly chosen method for *B. pertussis* specific antibody detection in serodiagnosis and complements direct antigen detection. In over 90 % of cases the IgG and IgA antibody responses are directed against the immunogens PT and FHA. Therefore, the SERION Multianalyt™ Bordetella pertussis IgA+IgG allows the simultaneous quantification of IgA and IgG antibodies directed against PT and FHA. The antibody activity is adjusted to the International Standard for Pertussis Antiserum (06/140) of the WHO and given in IU/ml.

Validation of SERION Multianalyt™ Bordetella pertussis

The SERION Multianalyt™ Bordetella pertussis IgA + IgG was evaluated in an internal study by the analysis of 140 serum samples from blood donors in comparison to the test results of the immunoblot of a leading European manufacturer. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION Multianalyt™ Bordetella pertussis	Sensitivity	Specificity
Pertussis Toxin IgA	> 99 %	> 99 %
Pertussis Toxin IgG	> 99 %	> 99 %
Filamentous Hemagglutinin IgA	> 99 %	98,9 %
Filamentous Hemagglutinin IgG	98,7 %	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

Precision

SERION Multianalyt™ Bordetella pertussis PT IgA

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	28,8	4,3	29,3	10,7
Serum 2	42,8	4,0	47,3	9,3
Serum 3	154,5	2,7	167,6	9,0
Serum 4	328,4	2,0	380,3	9,9

SERION Multianalyt™ Bordetella pertussis PT IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	103,6	3,1	113,9	8,2
Serum 2	548,3	3,3	618,6	8,4
Serum 3	1226,9	1,6	1318,4	7,0
Serum 4	1828,6	2,2	1964,2	8,7

SERION Multianalyt™ Bordetella pertussis FHA IgA

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	109,8	4,2	119,7	9,8
Serum 2	271,5	4,6	250,7	8,8
Serum 3	313,7	3,9	309,8	6,8
Serum 4	993,8	3,6	989,8	7,1

SERION Multianalyt™ Bordetella pertussis FHA IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	175,9	4,1	184,8	10,4
Serum 2	415,3	3,4	383,9	9,2
Serum 3	654,0	4,0	637,5	7,7
Serum 4	2183,2	2,5	2099,4	7,5

Order Information

SERION Multianalyt™ Bordetella pertussis IgA + IgG **Order Nr.: MK 2120 G**

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Borrelia burgdorferi IgG / IgM

SERION Multianalyt™ Borrelia burgdorferi IgG and IgM tests are quantitative fluorescence immunoassays based on the principle of flow cytometry for the detection of human antibodies in serum, plasma or cerebrospinal fluid directed against various antigens of *Borrelia burgdorferi*. The differential analysis of the humoral immune response against different antigens allows the determination of pathogen contact and disease status.

In Europe, *Borrelia burgdorferi* is transmitted to humans by infected ticks of the genus *Ixodes ricinus.*

Pathogen

Borrelia burgdorferi is the infectious agent which causes the disease syndrome known as Lyme-Borreliosis. *B. burgdorferi sensu stricto, B. garinii and B. afzelii* are the most important human pathogens of the genospecies *Borrelia burgdorferi sensu lato.* All three are distributed throughout Europe in all temperate climate zones. Reservoirs for the bacteria include a variety of small wild mammals, particularly mice. The bacteria, belonging to the taxonomic group of the spirochetes, are transmitted to human hosts by infected ticks (*Ixodes ricinus*, Europe; *Ixodes scapularis*, USA). The infection rate in adult ticks, nymphs and larvae with *Borrelia burgdorferi* ranges from 0 to 50 %, dependent upon geographical region and tick populations.

Disease

Lyme Disease is a multisystemic infection with many possible manifestations. Single or multiple organs may be involved. The time course of Lyme Disease can be divided into three separate stages. Stage I starts a few days up to several weeks after tick bite and subsequent infection with *Borrelia burgdorferi.* Patients suffer from non-specific symptoms such as fever, headache, muscle pain, joint pain, and exhaustion. Dermal manifestations with *Erythema migrans* (EM) as a characteristic symptom of early

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disease are displayed by 30 to 60 % of infected persons. *Erythema migrans* is recognised as a specific clinical symptom which clearly demonstrates an early phase of Lyme borreliosis. Stage II occurs between a few weeks and several months post infection as a systemic disease. In addition to non-specific symptoms, in particular neurological disorders (Morbus Bannwarth), less frequently Lyme carditis and opthalmological disorders may be observed. Development of stage III symptoms may occur up to several years after the tick bite and are characterised by dermatological diseases (*Acrodermatitis chronicum athrophicans* (ACA), diseases of the joints (Lyme-Arthritis), and neurological diseases (chronical encephalomyelitis).

Diagnosis

Due to the complexity of the clinical picture and the generally unspecific symptoms, serological diagnosis is the appropriate method to ensure an optimal differential diagnosis. It is recommended to adopt a logical step-wise approach to serological diagnosis, using initially a sensitive screening test such as ELISA with subsequent confirmation of positive and borderline ELISA results by another specific test such as immunoblot or SERION Multianalyt™ Borrelia burgdorferi.
The SERION Multianalyt™ Borrelia burgdorferi provides **quantitative antibody activities** directed against antigens of the genospecies *Borrelia afzelii, Borrelia garinii* und *Borrelia burgdorferi sensu stricto*. Different particle populations were coated with the following antigens: **VlsE** of *B. garinii* PBi, **p100** of *B. garinii* PBi, **OspC** of *B. afzelii* PKo, **DbpA** of *B. garinii* PBr, **DbpA** of *B. afzelii* PKo, **p58** of *B. garinii* PBi, **p41i** of *B. burgdorferi sensu stricto* GeHo and **lysate** of *B. afzelii* PKo. The interpretation of mean fluorescence intensities (MFI) is performed by the SERION Multianalyt™ easy*PLEX* Software in accordance with a scheme published by Wilske and Fingerle (Goettner *et al*., Clin. Microbiol. 2005, 43, 3602-9).

Validation of SERION Multianalyt™ Borrelia burgdorferi

The SERION Multianalyt™ Borrelia burgdorferi IgG test was evaluated in an external prospective study by the analysis of 490 serum samples from clinical routine. The results were compared to those obtained with an immunoblot of a leading European manufacturer. The SERION Multianalyt™ Borrelia burgdorferi IgM test was evaluated in an external study by the analysis of 50 serum samples in comparison to immunoblots and ELISA of three European manufacturers.

SERION Multianalyt™	Sensitivity	Specificity
Borrelia burgdorferi IgG	95,2 %	90,0 %
Borrelia burgdorferi IgM	> 99 %	97,5 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities. As an example two precision profiles are presented.

SERION Multianalyt™ Borrelia burgdorferi (VlsE) IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	132,9	4,5 %	131,5	5,1 %
Serum 2	659,5	2,0 %	643,8	4,1 %
Serum 3	1434,7	1,7 %	1418,5	5,1 %

SERION Multianalyt™ Borrelia burgdorferi (OspC) IgM

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	85,3	5,9 %	75,7	2,1 %
Serum 2	461,2	4,4 %	440,7	2,1 %
Serum 3	910,9	3,6 %	923,3	2,7 %

Order Information

SERION Multianalyt™ Borrelia burgdorferi IgG **Order Nr.: MK 2140 G**
SERION Multianalyt™ Borrelia burgdorferi IgM **Order Nr.: MK 2160 M**
The SERION Multianalyt™ Borrelia burgdorferi IgG und IgM are evaluated for the **analysis of cerebrospinal fluid**.

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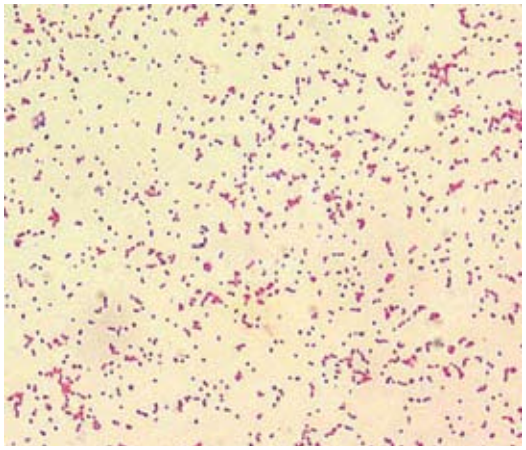
Brucella IgG

SERION Multianalyt™ Brucella IgG test is a quantitative fluorescence immunoassay based on the principle of flow cytometry for the detection of human antibodies in serum or plasma directed against *Brucella ssp.* The test is recommended for determination of pathogen contact and for the diagnosis of brucellosis.



Micrograph of *Brucella ssp.* (Source: Centers for Disease Control and Prevention, United States Department of Health and Human Services)

Pathogen

Brucella ssp. are gram-negative non-motile bacteria which live as intracellular parasites in a wide spectrum of host, particularily farm animals. Infections of humans are mainly caused by *Brucella melitensis* ("Malta fever"), *Brucella abortus* ("Morbus Bang"), *Brucella suis* and *Brucella canis*. The pathogen is transmitted by infected animals, their excretions and contaminated food.

Disease

The disease starts with moderate fever, which rises in the evenings during the acute stage of the disease, in which hepatomegaly and splenomegaly or swollen lymph nodes are characteristic. Undulating fever within afebrile intervals manifests often in *Brucella melitensis* and *Brucella suis* infections.

Spontaneous healing as well as transition into a chronic stage with a wide spectrum of symptoms is possible. Multiple organs or organ systems, bones or joints can be affected during the chronic stage. Histologically, characteristic granulomas are observed in infected tissues. Bacterial endocarditis might be fatal if it remains untreated.

During the late stage of brucellosis, neurologic and even psychiatric manifestations might occur.

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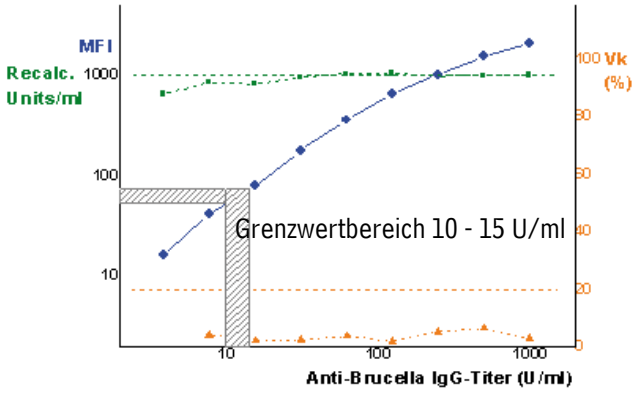
Diagnosis

Due to the variable clinical picture of chronic brucellosis, accurate diagnosis is possible only by direct detection of the pathogen or detection of specific antibody response in serum or CSF. Direct pathogen detection in culture systems can be performed with punctate from blood, bone marrow, synovia or urine. In this regard the special demands on nutrients have to be taken into account. Generally direct pathogen detection is done by gram staining and agglutination with Brucella-specific hyperimmunoglobulin preparations. More rapid results are obtained with serological methods such as agglutination tests, Coombs-tests or Complement Fixation Tests (CFT). For differentiation of acute and chronic brucellosis, sensitive and specific ELISAs with separate detection of IgG, IgM and IgA antibodies is recommended.

Validation of SERION Multianalyt™ Brucella IgG



For the determination of the linearity range of SERION Multianalyt™ Brucella IgG the activities of serial dilutions of a high positive serum sample were assessed (blue curve) and multiplied with the respective dilution factor (green curve). Within the measurement range from 5 to 700 U/ml the coefficients of variation (CV) of the intraserial precision of the distinct dilutions were below 20 % (orange curve).

Sensitivity and Specificity

For the validation of the SERION Multianalyt™ Brucella IgG 200 serum samples from blood donors, 200 serum samples from pregnant women and 8 serum samples from patients with a suspected brucellosis were analysed and compared to the results obtained with the SERION ELISA *classic* Brucella IgG as a reference. Sera classified as borderline were not included in the calculation.

SERION Multianalyt™	Sensitivity	Specificity
Brucella IgG	> 99 %	98,2 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION Multianalyt™ Brucella IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
negative	13,9	2,8	12,7	8,0
borderline	104,6	2,3	98,5	6,6
positive	591,7	1,6	564,0	3,4
positive	1183,0	3,2	1150,0	2,5

Order Information

SERION Multianalyt™ Brucella IgG **Order Nr.: MK 2480 G**

The SERION Multianalyt™ Brucella IgG can be individually combined with particles of SERION Multianalyt™ Bacillus anthracis IgG, SERION Multianalyt™ Francisella tularensis IgG as well as SERION Multianalyt™ Hantavirus Puumala IgG.

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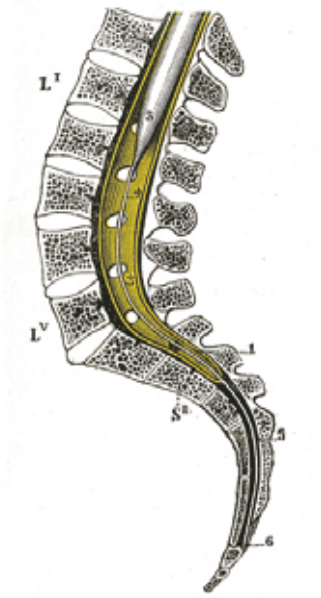
CSF IgG

The SERION Multianalyt™ CSF IgG test is a quantitative fluorescence immunoassay based on flow cytometry for the detection of intrathecal synthesized antibodies directed against Measles Virus, Rubella Virus, Varicella-Zoster Virus and Herpes Simplex Viruses 1 and 2 in human serum, plasma and cerebrospinal fluid (CSF). The assay is recommended for the determination and differentiation of inflammatory processes in the central nervous system (CNS).



Location of spinal chord within the spinal column

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Diagnostic Relevance

Analysis of cerebrospinal fluid (CSF) enables the detection and differentiation of inflammatory processes within the central nervous system (CNS). For accurate diagnosis it is important to determine whether the disease state is caused by infection or due to a chronic inflammatory process (e.g. Multiple Sclerosis).

Existing neurologic symptoms and the suspicion of infection of the CNS or a chronic inflammatory process make a diagnosis using cerebrospinal fluid based on the determination of intrathecal synthesized antibodies necessary. In the case of an acute infection of the CNS local antibodies are produced against the responsible pathogen. Since direct detection of the pathogen in the CSF is often not possible (e. g. in case of a Borrelia infection) or too time consuming, serological methods are primarily used for the differential diagnosis of an infection within the CNS. Chronic inflammatory processes of the CNS may result in the activation of a polyspecific immune response. In such cases specific antibodies against different viral pathogens may be detected although the related pathogens are not responsible for the disease. Analysis of the CSF alone is not sufficient for determination of intrathecal synthesized antibodies. Additional factors have to be taken into account.

The passage of large molecules and cells from the arterial blood across the blood/brain barrier and into the CSF is very limited due to the permeability properties of the vascular walls. Amino acids, sugars and proteins, as a consequence of their particular molecular characteristics, have varying requirements for transfer across the barrier; however the permeability for proteins is primarily a function of their size. As a consequence, under normal conditions, the total protein concentration in the cerebrospinal fluid is approximately 1 % of that in the corresponding serum. If the blood/brain barrier is compromised, the levels of proteins in the CSF may be substantially elevated above the norm.

Antibodies found in the CSF may have their origin in the plasma, entering the CSF by diffusion, or be synthesized within the CSF itself. The determination of an intrathecal antibody synthesis is possible only by the simultaneous quantification of a range of proteins in the CSF as well as in the corresponding serum. Therefore, CSF / serum quotients and antibody indices (AI) are determined in accordance with a calculation scheme developed by Hansotto Reiber. This is done by quantitative ELISAs or, alternatively, by using the SERION Multianalyt™ CSF IgG in order to detect IgG antibodies directed against Measles Virus, Rubella Virus, Varicella-Zoster Virus and the Herpes Simplex Viruses 1 and 2 simultaneously. An evaluation software facilitates the calculation of antibody indices (AI) according to Reiber (see Reiber and Peter, 2001).

Validation of SERION Multianalyt™ CSF IgG

The diagnostic efficiency of the SERION Multianalyt™ CSF IgG was determined for each immunoassay component individually by the analysis of 90 serum/CSF pairs. The ELISA of a leading European manufacturer were used as a reference.

Pathogen	Proportion of concordent results	Proportion of disparate results
Measles Virus	86 / 95 (91 %)	9 / 95 (9 %)
Rubella Virus	86 / 94 (91 %)	8 / 94 (9 %)
VZV	81 / 89 (91 %)	8 / 89 (9 %)
HSV 1/2	82 / 90 (91 %)	8 / 90 (9 %)

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION Multianalyt™ CSF IgG (serum sample)

Parameter	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Measles Virus	316,1	9,7	309,1	6,1
Rubella Virus	661,9	9,1	661,5	6,6
VZV	477,4	10,6	470,6	7,0
HSV 1/2	416,5	8,2	406,7	6,6

SERION Multianalyt™ CSF IgG (CSF sample)

Parameter	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Measles Virus	174,5	11,4	159,0	3,8
Rubella Virus	338,9	10,9	368,8	2,8
VZV	124,2	12,1	131,2	3,5
HSV 1/2	114,6	11,2	118,7	3,5

The determination of multiple parameters in a very small sample volume is time- and labor-saving and supports the diagnosis significantly better than the elaborate determination of each individual antibody specificity in separate immunoassays.

Order Information

SERION Multianalyt™ CSF IgG **Order Nr.: MK 2360 G**

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SERION Multianalyt™

Diphtheria / Tetanus / Pertussis toxin IgG

SERION Multianalyt™ Diphtheria / Tetanus / Pertussis toxin IgG test is a quantitative fluorescence immunoassay based on the principle of flow cytometry for the simultaneous detection of human IgG antibodies in serum or plasma directed against the Diphtheria, Tetanus and Pertussis toxins. The assay is recommended for vaccination control and to determine the immune status prior to immunisation to avoid vaccination injury.

Clinical background

The safest prophylaxis against infectious diseases is active immunisation. Nowadays inoculations are administered as combined vaccines, which primarily contain components of the pathogens causing Tetanus, Diphtheria and Pertussis. Control of immune status is especially indicated when immunity is questionable, when there is no recollection of prior vaccination, when documentation is incomplete, vaccine complications have occurred or when the patient suffers from immune deficiency.

Immune protection induced by vaccination wanes with time constantly. Therefore repeated immunisation with combined vaccines is recommended every 10 years in order to keep the individual´s immunity at high levels. Side effects can occur after multiple vaccinations (repeated immunization or booster shots), varying from local and systemic allergic reactions to anaphylactic shock. Determination of the immune status prior to immunisation to avoid vaccination injury is therefore highly recommended.

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Diagnosis

The SERION Multianalyt™ Diphtheria / Tetanus / Pertussis toxin IgG allows the quantitative determination of IgG antibody activity directed against the Diphtheria, Tetanus and Pertussis toxins simultaneously. The quantification of IgG antibody titers against Tetanus and Diphtheria toxins is adjusted to International Units/ml in order to allow practical vaccination recommendations. The activity against the Pertussis toxin is adjusted to the International Standard for Pertussis Antiserum (06/140) of the WHO and given in IU/ml.

Validation of SERION Multianalyt™ DTPt IgG

The SERION Multianalyt™ Diphtheria / Tetanus / Pertussis toxin IgG test was evaluated in an internal study by the analysis of 53 serum samples: 21 serum samples from blood donors, 10 serum samples with defined antibody activity against Pertussis toxin, 8 Pertussis toxin serial samples from the Berlin Reference Laboratory and 14 tetanus sera from the National External Quality Assessment Service (INSTAND). The SERION ELISA *classic* Diphtheria, Tetanus und Pertussis toxin IgG were used as a reference. A very good correlation of the assays was determined.

SERION Multianalyt™	Correlation to ELISA
Diphtheria toxin IgG	r = 0,994
Tetanus toxin IgG	r = 0,973
Pertussis toxin IgG	r = 0,991

The SERION Multianalyt™ Diphtheria and Tetanus toxin IgG components of the test allow a quantitative determination of serum activities. They are not recommended for differentiation between positive and negative results. Therefore, sensitivity and specificity could not be calculated. The SERION Multianalyt™ Pertussis toxin IgG component showed sensitivity and specificity values of > 99 % with the serum panel mentioned above.

Sensitivity and Specificity

SERION Multianalyt™	Sensitivity	Specificity
Pertussis toxin IgG	> 99 %	> 99 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION Multianalyt™ Diphtheria toxin IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	9,8	12,8	10,3	14,6
Serum 2	245,2	7,7	231,5	8,3
Serum 3	768,4	8,1	826,6	9,7
Serum 4	1748,6	4,3	1710,6	7,0

SERION Multianalyt™ Tetanus toxin IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	177,7	7,6	176,7	8,7
Serum 2	363,5	4,6	379,3	6,9
Serum 3	503,7	7,1	497,8	7,8
Serum 4	693,5	5,1	753,7	6,5

SERION Multianalyt™ Pertussis toxin IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	65,1	6,8	84,6	12,3
Serum 2	471,6	5,2	527,3	6,7
Serum 3	559,5	5,0	585,6	6,1
Serum 4	1092,2	6,4	1116,1	7,0

Order Information

SERION Multianalyt™ DTPt IgG **Order Nr.: MK 2020 G**

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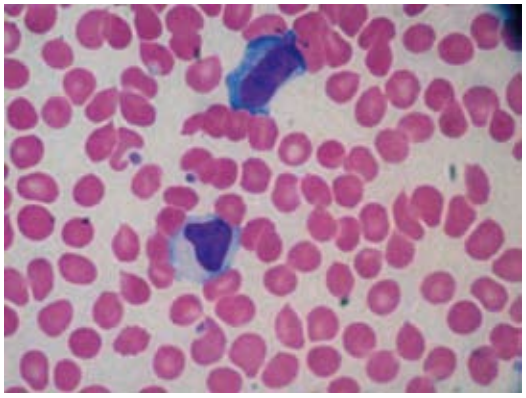
SERION Multianalyt™

Epstein-Barr Virus IgG / IgM

SERION Multianalyt™ Epstein-Barr Virus IgG and IgM tests are quantitative fluorescence immunoassays based on the principle of flow cytometry for the simultaneous detection of human antibodies in serum or plasma directed against various components of the Epstein-Barr Virus. SERION Multianalyt™ Epstein-Barr Virus IgG allows the quantification of antibodies directed against the virus capsid antigens VCA-p18 and VCA-p23, the nuclear antigen EBNA-1 (p72), and the early antigens EA-p54 and EA-p138. SERION Multianalyt™ Epstein-Barr Virus IgM allows the determination of antibodies against VCA-p18. The tests are recommended for the diagnosis of acute, recent and past infections.



Micrograph of a blood smear with reactive lymphocytes.

Pathogen

The ubiquitous Epstein-Barr Virus (EBV) is a DNA virus and member of the Human Herpesvirus group. Seroprevalence in adults is high (90 - 95 %). In industrial countries primary infection is mainly restricted to teenagers or young adults. In contrast in non-developed countries, primary infection occurs typically much earlier in life. About 50 % of individuals infected in adulthood show clinical symptoms whereas clinical findings have been rarely observed in infections of younger children. Transmission takes place primarily via the saliva of infected individuals.

Disease

In primary infection, the cells of the salivary gland are infected first and, following the subsequent infection of B cells in the adjacent lymphoid tissue, the virus spreads throughout the body. The disease resulting from primary infection is called infectious mononucleosis. In the later course of infection high fever, splenomegalia, lymphadenitis, thrombocytopenia and hepatitis may be observed. In some regions, EBV

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is closely associated with nasopharyngeal carcinoma and Burkitt´s lymphoma.

Diagnosis

About two weeks after infection, anti-EA IgG, anti-VCA IgM and anti-VCA IgG antibodies can be detected in the patient´s serum. Highest Peak of anti-VCA IgM antibody concentration is found about three weeks, highest anti-VCA IgG concentration about six weeks after onset of symptoms. Usually, this elevated level remains life-long. About three weeks after onset of symptoms the anti-EBNA-1 IgG antibody production starts. Anti-EBNA-1 IgG antibodies may be used to demonstrate previous infection. Following normal EBV infection the anti-EBNA-1 antibody concentration remains life-long at a high level. In most cases of reactivations, e. g. caused by immunosuppression, the anti-EA IgG antibody concentration increases sharply. Therefore high anti-EA IgG titers are a reliable marker for reactivations.

Validation of SERION Multianalyt™ Epstein-Barr Virus

The SERION Multianalyt™ Epstein-Barr Virus IgG test was evaluated with a panel consisting of 15 negative serum samples, 13 serum samples from patients with recent infection as well as with 118 serum samples from blood donors and pregnant women with past infection. The test results were compared with the results of an immunoblot based on recombinant antigens from a leading European manufacturer (Goldstandard) and are presented below.

Serum status	Proportion of concordent results	Proportion of disparate results
Negative	15 / 15	0 / 15
Recent Infection	13 / 13	0 / 13
Past Infection	118 / 118	0 / 118
Reactivation	17 / 18	1 / 18

For validation of the SERION Multianalyt™ Epstein-Barr Virus IgM test 20 negative serum samples and 61 serum samples from patients with acute infection were assessed. The results were compared with the results of an immunoblot based on recombinant antigens from a leading European manufacturer (Goldstandard) and are presented below.

Serum status	Proportion of concordent results	Proportion of disparate results
Negative	20 / 20	0 / 20
Acute Infection	61 / 61	0 / 61

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION Multianalyt™ Epstein-Barr Virus VCA-p23 IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	25,7	2,0%	24,5	5,9%
Serum 2	386,1	3,3%	385,5	7,2%
Serum 3	715,7	3,8%	701,0	5,2%

SERION Multianalyt™ Epstein-Barr Virus EBNA-1 IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	207,3	4,0%	208,7	6,8%
Serum 2	412,1	3,6%	402,0	6,6%
Serum 3	2127,6	2,6%	2285,8	2,7%

SERION Multianalyt™ Epstein-Barr Virus VCA-p18 IgM

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
Serum 1	68,4	4,2	65,9	6,3
Serum 2	711,0	5,2	624,6	3,9
Serum 3	1247,0	2,4	1181,3	2,9

Order Information

SERION Multianalyt™ Epstein-Barr Virus IgG **Order Nr.: MK 2080 G**
SERION Multianalyt™ Epstein-Barr Virus IgM **Order Nr.: MK 2100 M**

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SERION Multianalyt™
Francisella tularensis IgG

SERION Multianalyt™ Francisella tularensis IgG test is a quantitative fluorescence immunoassay based on the principle of flow cytometry for the detection of human antibodies in serum or plasma directed against the lipopolysaccharide (LPS) of *Francisella tularensis*. The assay is recommended for the diagnosis of tularemia, to monitor the success of vaccination, to determine the immune status prior to immunisation to avoid vaccination injury as well as for epidemiological studies.

Feral hares as carrier of *Francisella tularensis*

Pathogen

Tularemia is a zoonosis caused by the bacterium *Francisella tularensis* which can present in a variety of clinical manifestations. The condition in animals resembles that of plague and the disease often affects hares and wild rabbits, it is also called rabbit fever. *Francisella tularensis* (formerly also called *Pasteurella tularensis*) is a gram-negative, pleomorphic bacterium. The three clinically relevant forms of the four subspecies are difficult to differentiate serologically. However, two types can be distinguished epidemiologically, biochemically and genotypically: *Francisella tularensis biovar tularensis* (type A) is highly virulent. Untreated, the infection has a high mortality. *Francisella tularensis biovar holarctica* (type B) is much less virulent but can also cause severe illness.

Various small mammals, such as hares, rabbits, mice, rats and squirrels are natural reservoirs of *Francisella tularensis*. The pathogen has also been detected in soil samples and water courses and can survive there for prolonged periods depending on climatic conditions. Human infection may occur through direct skin and mucosal contact with infected animals or their excreta. Ectoparasites can also be considered as vectors. Consumption of infected and insufficiently cooked meat and inhalation of infectious dust are also potential

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routes of infection. Transmission from human to human has not been observed.

Disease

Tularemia occurs throughout the northern hemisphere between 30 and 71 degrees of latitude, especially in Scandinavia, Russia, Japan, China, USA and Canada. The rural population is often affected. In Germany, tularemia is regarded as a rare infectious disease. The first symptoms of tularemia usually appear 2 to 5 days after the infection has occurred. However, depending on dose and route of infection and the virulence of the bacterial strain, the incubation period can vary between 1 and 21 days. Besides the classical general symptoms such as fever, malaise and joint and muscle pains, the clinical picture of tularemia can be very varied. Inhalation of the pathogen often leads to pulmonary manifestation (e.g. pneumonia) or to a septic, typhus-like illness. Infection through the digestive tract can lead to vomiting, abdominal pain and diarrhoea. When identified promptly, tularemia can be treated effectively with antibiotics. The failure of many organ systems and involvement of the central nervous system lead to death in 40 % of cases of infection with the type A bacteria if untreated. With treatment, the mortality is about 1 %. Infection with type B bacteria usually takes a mild course with low mortality.

Diagnosis

Detection through culture from peripheral blood, swabs and biopsy material is difficult and can take several weeks. Since it is a highly infectious pathogen, such diagnostic tests are reserved for special laboratories. For this reason, identification is usually indirect by immunological and molecular methods. Serological diagnosis can be performed by the detection of specific antibodies. The SERION Multianalyt™ Francisella tularensis IgG test enables quantitative measurement of human IgG antibodies directed against the lipopolysaccharide (LPS) of *Francisella tularensis ssp. holarctica* (LVS strain) in serum or plasma.

Validation of SERION Multianalyt™ Francisella tularensis IgG

The SERION Multianalyt™ Francisella tularensis IgG test was evaluated in a comprehensive study by the analysis of 299 serum samples from blood donors, 200 serum samples from pregnant women and 101 serum samples from patients with clinically and laboratory confirmed tularemia. The results were compared to those obtained with SERION ELISA *classic* Francisella tularensis IgG as a reference. Sera classified as borderline were not included in the calculation.

Sensitivity and Specificity

SERION Multianalyt™	Sensitivity	Specificity
Francisella tularensis IgG	> 99 %	98,0 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION Multianalyt™ Francisella tularensis IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
borderline	137,5	4,3	144,5	4,8
positive	282,6	1,3	292,7	3,3
positive	767,8	7,8	957,8	3,7
positive	1539,4	5,5	1693,8	3,3

Order Information

SERION Multianalyt™ Francisella tularensis IgG **Order Nr.: MK 2440 G**

The SERION Multianalyt™ Francisella tularensis IgG can be individually combined with particles of SERION Multianalyt™ Bacillus anthracis IgG, SERION Multianalyt™ Brucella IgG as well as SERION Multianalyt™ Hantavirus Puumala IgG.

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Hantavirus Puumala IgG

SERION Multianalyt™ Hantavirus Puumala IgG test is a quantitative fluorescence immunoassay based on the principle of flow cytometry for the detection of human antibodies in serum or plasma directed against the nucleocapsid protein of Hantavirus serotype Puumala. The assay is recommended for the diagnosis of Hantavirus infections and epidemiological studies.

In Europe the Hantavirus serotype Puumala is transmitted by *Clethrionomys glareolus*.

Pathogen

Hantaviruses belong to the family *Bunyaviridae*. They occur throughout the world and there are several different serotypes. The Puumula virus is the main form in central and northern Europe. Rodents are the natural reservoir, particularly mice and rats. The viruses are transmitted to man in the excretions of infected animals, which are swirled up in dust and breathed in. People who spend a lot of time outdoors, such as hunters, foresters and soldiers, are thought to be at particular risk.

Disease

Hantaviruses of the serotype Puumala cause a mild form of haemorrhagic fever with renal syndrome, which is also known as epidemic nephropathy (EN). The incubation period is 10 to 20 days. The illness starts with general symptoms resembling flu, including headache, myalgia, chills and conjunctivitis. Additional clinical manifestations include abdominal and lumbar pain and transient impaired renal function, which may require dialysis treatment. The mortality of epidemic nephropathy is about 1 %. The clinical course of epidemic nephropathy is milder than that of haemorrhagic fever with renal syndrome, caused by viruses of the serotype Hantaan.

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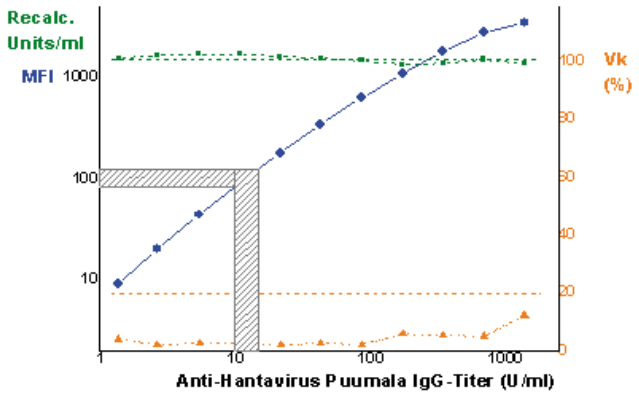
Diagnosis

Hantavirus infections are usually diagnosed from the clinical presentation, together with the results of serological assays. Laboratory confirmation of an infection is usually based on the detection of IgM and IgG antibodies to Hantaviruses of serotypes Puumala and Hantaan.

Validation of SERION Multianalyt™ Hantavirus Puumala IgG



For the determination of the linearity range of SERION Multianalyt™ Hantavirus Puumala IgG the activities of serial dilutions of a high positive serum sample were assessed (blue curve) and multiplied with the respective dilution factor (green curve). Within the measurement range from 4 to 1400 U/ml the coefficients of variation (CV) of the intraserial precision of the distinct dilutions were below 20 % (orange curve).

To calculate the performance characteristics of the SERION Multianalyt™ Hantavirus Puumala IgG, 201 serum samples from blood donors, 200 serum samples from pregnant women and 39 serum samples from patients with confirmed Hantavirus infection were assessed. The results were compared to the test results of a leading European manufacturer. Borderline results were not included in the calculation of sensitivity and specificity.

Sensitivity and Specificity

SERION Multianalyt™	Sensitivity	Specificity
Hantavirus Puumala IgG	> 99 %	98,5 %

Precision

The intra- and interserial precisions were determined by the analysis of serum samples of different reactivities.

SERION Multianalyt™ Hantavirus Puumala IgG

Sample	Signal Intensity (MFI)	Intraassay CV (%) (n=20)	Signal Intensity (MFI)	Interassay CV (%) (n=10)
borderline	95,2	2,3	98,3	6,2
positive	496,4	1,3	532,1	5,5
positive	719,9	2,1	803,3	4,1
positive	1316,6	2,1	1371,6	3,9

Order Information

SERION Multianalyt™ Hantavirus Puumala IgG **Order Nr.: MK 2460 G**

The SERION Multianalyt™ Hantavirus Puumala IgG can be individually combined with particles of SERION Multianalyt™ Bacillus anthracis IgG, SERION Multianalyt™ Brucella IgG as well as SERION Multianalyt™ Francisella tularensis IgG.

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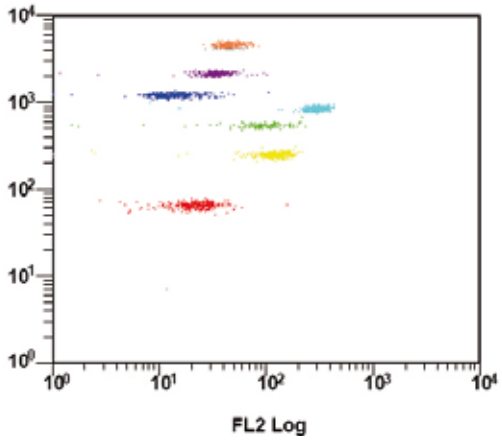
Setup

The SERION Multianalyt™ Setup is recommended for the calibration of flow cytometers for use with SERION Multianalyt™ immunoassays. Different particle suspensions allow the adjustment of the instrument parameters, such as voltages of photomultipliers and compensation. The identified optimal settings are saved in the form of a measurement protocol for standardised use with SERION Multianalyt™ immunoassays. The daily verification of the instrument settings is performed using the SERION Multianalyt™ Flow*Control*.



Different particle populations of the SERION Multianalyt™ Setup facilitate the calibration of flow cytometers for use with SERION Multianalyt™ immunoassays

Technology

The SERION Multianalyt™ technology is based on 1 to 10 μm sized polystyrene particles which are, additionally, dyed with a fluorophore in ten different intensity steps. The use of the color coding in combination with the variable size of the particles leads to optically distinguishable bead populations, which are used as the solid phase for immunoassays of the SERION Multianalyt™ product line.

Setup of Flow Cytometers

The calibration of flow cytometers with the aid of the SERION Multianalyt™ Setup is necessary in order to guarantee correct results when using SERION Multianalyt™ immunoassays. Therefore, the SERION Multianalyt™ Setup contains particles with defined sizes and fluorescence properties, which are assessed by various detectors of the instrument and which allow the optimal adjustment of the flow cytometer settings.

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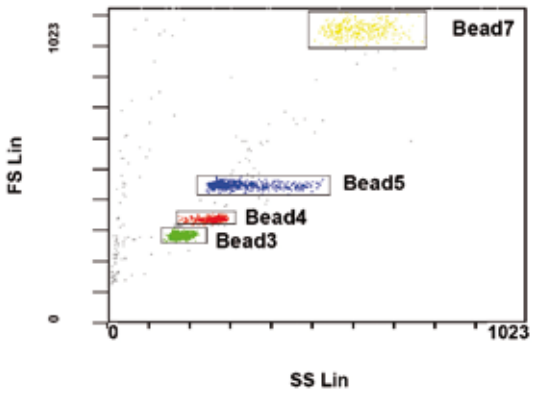
Adjusting the Scatter Voltages

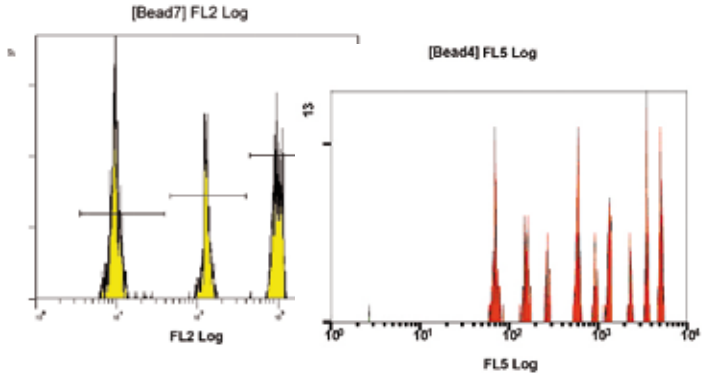
The size of the particles is measured utilising the forward (FS) and sideward (SS) scattering of light. After correctly calibrating the scatter settings in the instrument the different sized particles in the SERION Multianalyt™ Setup are optimally separated from one another as shown in the histogram.



After calibration of the flow cytometer the particles of the SERION Multianalyt™ Setup having different sizes are separated optimally from each other

Adjusting the Photomultipliers

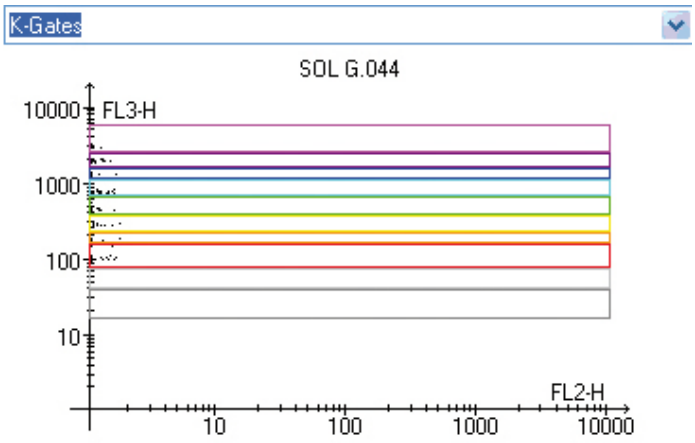
The fluorescence properties of particles and detector molecules used in SERION Multianalyt™ immunoassays are separated by the optical filters in flow cytometers and analysed by different photomultipliers (PMT). After adjustment of the instrument the particles of the SERION Multianalyt™ Setup having different fluorescence wavelengths and signal intensities are optimally separated. Subsequently, the SERION Multianalyt™ Setup facilitates adjustment of the compensation.



After calibration of the flow cytometer the particles of the SERION Multianalyt™ Setup with different bead fluorescence intensities (red) and detector molecule intensities (yellow) are optimally separated from each other

Measurement Protocoll Setting

The instrument settings are saved in the from of a standardised measurement protocol for use with SERION Multianalyt™ immunoassays. After parameterisation of the software SERION easy*PLEX* the optical measurement signals generated with SERION Multianalyt™ immunoassays are interpretated according to the test specifications to guarantee maximal user convenience.



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SERION Multianalyt™ Setup **Order Nr.: MK 2000**

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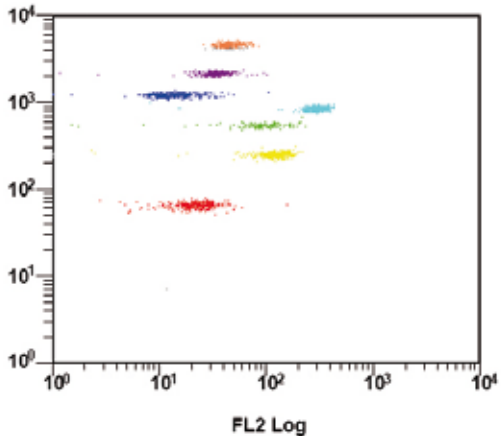
Flow*Control*

The SERION Multianalyt™ Flow*Control* is recommended for the daily control of the flow cytometer settings in order to guarantee correct test results when using SERION Multianalyt™ immunoassays. A suspension of fluorescent particles allows the verification of the instrument parameters, e. g. photomultiplier voltages and compensation, adjusted with the SERION Multianalyt™ Setup.



Different particle populations of the SERION Multianalyt™ Flow*Control* facilitate the verification of the flow cytometer calibration for use with SERION Multianalyt™ immunoassays

Setup of Flow Cytometers

The calibration of flow cytometers is necessary in order to guarantee correct test results when using SERION Multianalyt™ immunoassays. The SERION Multianalyt™ Setup contains different particle populations with defined sizes and fluorescence intensities. The parameters are assessed by different detectors of the flow cytometer, which was calibrated by usage of the SERION Multianalyt™ Setup.

Check of Flow Cytometer Settings

The SERION Multianalyt™ Flow*Control* is recommended for the daily control of the flow cytometer settings.

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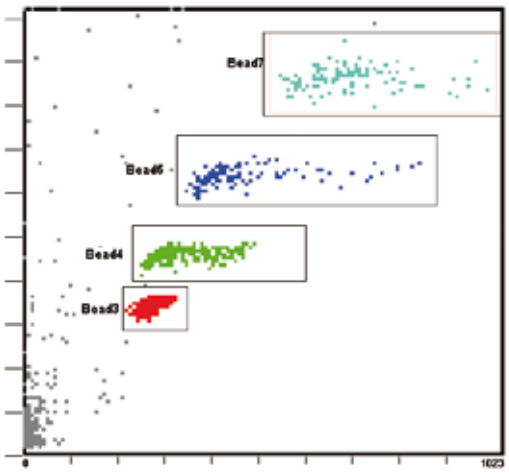
Verification of Scatter Voltages

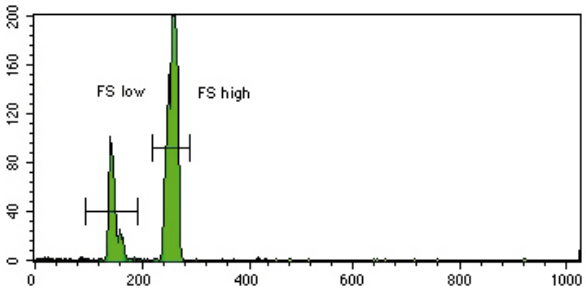
The size of the particles is measured utilising the forward (FS) and sideward (SS) scattering of light. After correctly calibrating the scatter settings in the instrument the different sized particles in the SERION Multianalyt™ Flow*Control* are optimally separated from one another as shown in the histogram.



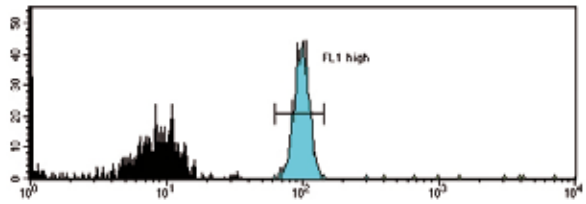
After calibration of the flow cytometer the particles of the SERION Multianalyt™ Flow*Control* having different sizes are separated from each other

Verification of the Photomultipliers

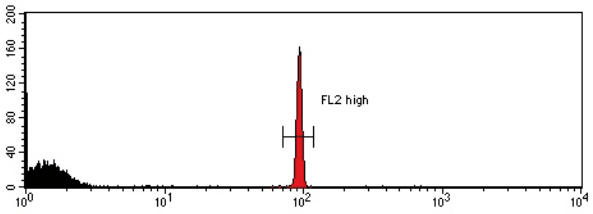
The fluorescence properties of particles and detector molecules used in SERION Multianalyt™ immunoassays are separated by the optical filters in flow cytometers and analysed by different photomultipliers (PMT). After calibration of the instrument the particles of the SERION Multianalyt™ Flow*Control* with different fluorescence signals are optimally separated.



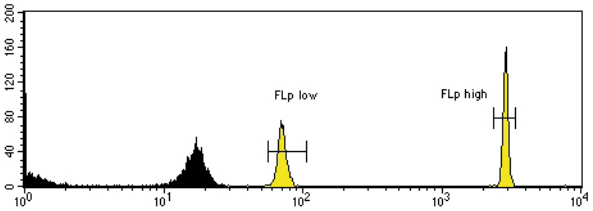
Histogram of forward scatter



Histogram of FL1



Histogram of FL2



Histogram of FLp (particle fluorescence)

After calibration of the flow cytometer the particles of the SERION Multianalyt™ Flow*Control* bearing different size and fluorescence properties are optimally separated from each other

Order Information

SERION Multianalyt™ Flow*Control* **Order Nr.: MA 3000**

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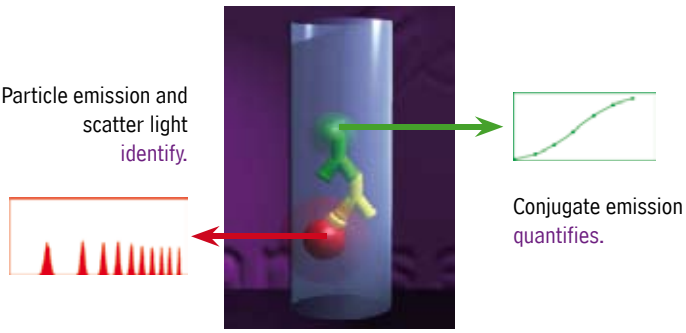
easy*PLEX*

The software SERION easy*PLEX* is recommended for the evaluation of measurements of flow cytometers after processing of SERION Multianalyt™ immunoassays.

The software SERION easy*PLEX* allows a fast evaluation of SERION Multianalyt™ immunoassays

Technology

After processing SERION Multianalyt™ immunoassays the particles, which are used as the solid phase for immunoassays of the SERION Multianalyt™ product line, are analysed in a flow cytometer. The particles are identified by their light scattering and fluorescence properties. Each particle is analysed individually. The fluorescence intensity of the bound detector molecule is proportional to the concentration of the analyte in the sample. Flow cytometers are able to analyse thousands of particles per second. Consequently, the measurement of a sample is performed in a few seconds.



Design of a SERION Multianalyt™ immunoassay: Analytes, here an immunoglobuline, bind to the coated particle surface and are tagged by a detector molecule

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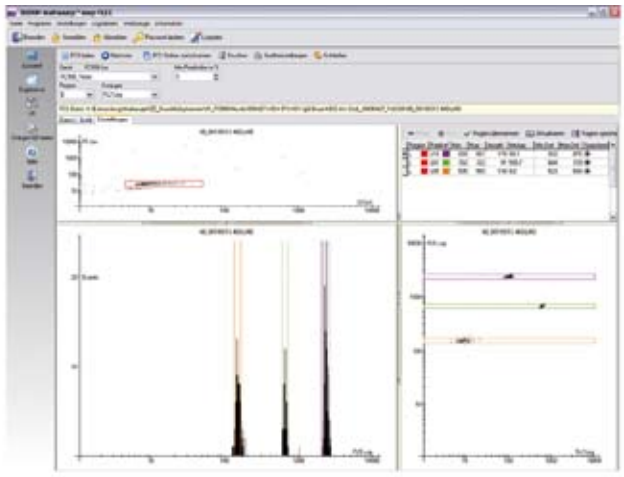
SERION easy*PLEX*

The SERION Multianalyt™ technology is suited for use with a range of commercially available flow cytometers.



The software SERION easy*PLEX* allows the discrimination of the different particle populations and a quantitative evaluation of SERION Multianalyt™ Immunoassays.

The measurement of more than a hundred particles per population leads consequently to large data volumes. The measured signal intensities of a multiplex immunoreaction can be conveniently evaluated with the software SERION easy*PLEX*, independent from the flow cytometer used. The signal intensities of each individual particle are assessed, evaluated according to the individual SERION Multianalyt™ immunoassay and presented in a clearly laid out result report.

Additionally, the validity of the test run is assessed by verification of the standard and control values as well as the number of particles analysed. By the use of the software SERION easy*PLEX* a standardised and valid evaluation of SERION Multianalyt™ immunoassays is guaranteed.

Of course, the software is accessible to the laboratory information system (LIS) in order to allow a convenient transfer of the collected data.

SampleID	Analyt	Ig	Plex	Bead	Signal	Dil.factor	Units	Unit	valid	Error	Result	Lot
5			DTPt IgG									MLX.AA
	Pertussis Toxin	IgG	SAMPLE	242	295,90		78,94	FDA-U/ml	☑		positive	
	Diphtherie	IgG	SAMPLE	180	152,70		0,24	IU/ml	☑		reliable protection	
	Tetanus	IgG	SAMPLE	350	119,70		0,53	IU/ml	☑		adequate protection, control in 2 years	
6			DTPt IgG									MLX.AA
	Pertussis Toxin	IgG	SAMPLE	239	3,30		-11111,11	FDA-U/ml	☑	1	negative	
	Diphtherie	IgG	SAMPLE	206	3,50		-11111,11	IU/ml	☑	1	no protection	
	Tetanus	IgG	SAMPLE	321	3,80		-11111,11	IU/ml	☑	1	no protection	
7			DTPt IgG									MLX.AA
	Pertussis Toxin	IgG	SAMPLE	241	326,70		88,13	FDA-U/ml	☑		positive	
	Diphtherie	IgG	SAMPLE	238	761,60		1,43	IU/ml	☑		long-term protection	
	Tetanus	IgG	SAMPLE	305	789,50		5,32	IU/ml	☑		long-term protection, control in 10 years	

Order Information

SERION easy*PLEX* **Order Nr.: VT 018**

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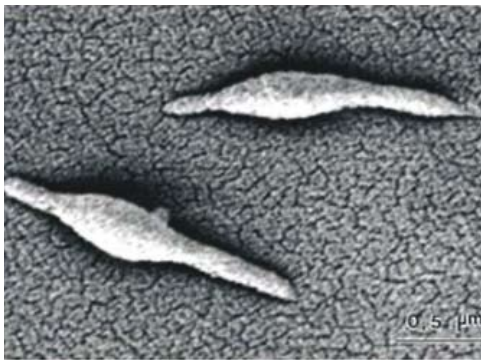
Complement Fixation Test (CFT)

The Complement Fixation Test (CFT) is a classical serological method for the detection of antibodies against pathogens of infectious diseases and has proved itself as a standard diagnostic method in many medical laboratories. With SERION CFT reagents, Institut Virion\Serion GmbH offers a great variety of antigens that are important in infectious serology of bacteria, viruses and parasites. The complement fixation test performance is a micromethod according to the KOLMER technique and to DIN 58 969 as well as to the WHO guidelines.



Complement

Complement is a system of functionally connected serum proteins, which are important components of the humoral immune system and are responsible for several biological functions involved in the process of infections. In the course of complement activation several proteins react in a distinct order similar to the cascade in blood coagulation. In the classical activation the complement cascade is initiating by complexes of antigens and IgG_1, IgG_2, IgG_3 und IgM antibodies, whereby the latter are the most efficient. In the so-called alternative activation pathway parts of microorganisms may activate complement without the participation of antibodies. The SERION Complement Fixation Tests make use of the classical complement activation pathway.

Test Principle

The first step in the SERION Complement Fixation Tests is the thermal inactivation of patient's serum samples to inactivate endogenous complement which may disturb the test calibration. Antigen is then added, leading to the formation of specific antibody-antigen complexes. Subsequent addition of complement will, in the presence of antibody-antigen complexes, lead to activation of the complement. An indicator system consisting of antibody coated erythrocytes (haemolytic system) is finally added to the system after a suitable time lapse for the complement fixation to complete. Lysis of the indicator system is dependent upon the presence or absence of immune complexes formed between the sample and specific antigen used. No lysis indicates the presence of immune complexes while lysis indicates non. Mild centrifugation of the system sediments any surviving erythrocytes, allowing the test to be evaluated visually. A button of red cells indicates a positive whereas a reddish clear solution is negative.

Diagnostics

Complement fixation tests can be used as screening tests for acute infections. The fact that one IgM molecule is capable of activating one C1-molecule of the complement complex whereas 168 IgG molecules are necessary to achieve the same effect, emphasises the significance of the test for the recognition of early infections. Positive CFT titres are often an indication for the presence of IgM antibodies or very high IgG antibody titres and are therefore an expression for an acute or recent infection, respectively. The CFT is especially helpful for acute respiratory infections: The, in general, strong IgG booster reaction is very well represented whereas residual titres of past infections are blanked out. The distinction between IgG and IgM antibodies is not possible. For determination of immune status the sensitivity of the method is, unfortunately, not sufficient. For more differentiated information about the immune status we recommend the use of the corresponding SERION ELISA *classic* for the separate detection of different immunoglobulin classes.

Advantages of SERION CFT products

- Large product portfolio for the indirect detection of various pathogens
- High specificities by use of carefully selected antigens and control antigens
- Early detection of acute primary infections and therapy sucesses
- Possibility to use SERION CFT as an economic, cost-effective screening assay
- Consistent complement and amboceptor concentration for all SERION CFT antigens
- Combination of different CFTs on one plate possible
- Normed CFT, therefore omission of pre-experiments in routine laboratories
- Long stabilities of antigens, control antigens, positive and negative control sera
- Use in human and veterinary diagnostics

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Order Information CFT - Reagents

Pathogen	Antigen 1,0 ml	Control Antigen 1,0 ml	Pos. Control Serum 0,1 ml	Neg. Control Serum 0,1 ml
Adenovirus	1121	2121	3121	4121
Brucella	1297	-	3297	4297
Campylobacter fetus / ssp.	1207	-	3207	4207
Campylobacter jejuni	1206	-	3206	4206
Chlamydia	1122	2122	3122	4122
Coxiella burnetii (Phase I)	1227	2227	3227	4227
Coxiella burnetii (Phase II)	1123	2123	3123	4123
Coxsackievirus A9	9060	9260	9061	9062
Coxsackievirus B1	1172	2179	3172	4172
Coxsackievirus B2	1173	2179	3173	4173
Coxsackievirus B3	1174	2179	3174	4174
Coxsackievirus B4	1175	2179	3175	4175
Coxsackievirus B5	1176	2179	3176	4176
Coxsackievirus B6	1177	2179	3177	4177
Coxsackievirus Pool (A9, B1 - B6)	1178	2178	3178	4178
Cytomegalovirus (CMV)	1130	2130	3130	4130
Echovirus Pool (4, 6, 9, 14, 24, 30)	1180	2180	3180	4180
Epstein-Barr Virus (EBV)	1132	2132	3132	4132
Herpes Simplex Virus (HSV) 1 / 2	1154	2154	3154	4154
Influenza A Virus	1112	2112	3112	4112
Influenza B Virus	1113	2113	3113	4113
Influenza A/B Virus Pool	1114	2114	3114	4114
Legionella pneumophila	1224	-	3224	4224
Leptospira biflexa	9120	-	3120	9072
Leptospira canicola	9090	-	9071	9072
Leptospira grippotyphosa	9070	-	9071	9072
Leptospira icterohaemorrhagiae	9080	-	9071	9072
Leptospira pomona	9100	-	9071	9072
Leptospira sejroe	9110	-	9071	9072
Listeria monocytogenes	1234	-	3234	4234

Order Information CFT - Reagents

Pathogen	Antigen 1,0 ml	Control Antigen 1,0 ml	Pos. Control Serum 0,1 ml	Neg. Control Serum 0,1 ml
Measles Virus	1190	2190	3190	4190
Mumps / Parotitis Virus	1125	2125	3125	4125
Mycoplasma pneumoniae	1111	-	3111	4111
Neisseria gonorrhoeae	1253	-	3253	4253
Parainfluenza Virus 1	1116	2116	3116	4116
Parainfluenza Virus 2	1117	2117	3117	4117
Parainfluenza Virus 3	1118	2118	3118	4118
Parainfluenza Virus Pool (1, 2, 3)	1115	2115	3115	4115
Picornavirus	1126	2126	3126	4126
Poliovirus	1127	2127	3127	4127
Respiratory Syncytial Virus (RSV)	1124	2124	3124	4124
TBE Virus	1192	2192	3192	4192
Rotavirus	1193	2193	3193	4193
Toxoplasma gondii	1331	2331	3331	4331
Varicella-Zoster Virus (VZV)	1191	2191	3191	4191
Yersinia enterocolitica O3	1203	-	3203	4203
Yersinia enterocolitica O9	1209	-	3209	4209
Yersinia pseudotuberculosis	1201	-	3201	4201

Order Information Supplementary CFT - Reagents

Product	Volume	Order Nr.
Haemolytic system, ready-to-use	50 ml	9000
Complement	1 ml	9001
Haemolytic amboceptor	2 ml	9002
CFT buffer	2 l	9009
50 % Sheep erythrocyte suspension in Alsever solution	50 ml	9004
1 % Sheep erythrocyte suspension, ready-to-use	50 ml	9008

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Antigens

In addition to being the foundation for immuno-assays, pathogen specific antigens have a wide range of applications in the fields of modern diagnostics and research. As always, the quality of the raw materials is a deciding factor in the success and performance of any application. Institut Virion\Serion, with more than 30 years experience in the cultivation and purification of infectious disease antigens, is a proven and dependable partner to the industry, supplying bulk antigens to customers around the world. Based on a comprehensive product portfolio antigens are offered for evaluation studies in aliquots à 250 µg. Larger amounts are available on request any time. Please contact us for more detailed product information.

Order Information

Antigen	Order Nr.
Adenovirus Type 2 Hexon	BA 128 VS
Aspergillus fumigatus	BA 132 VS
Brucella abortus	BA 116 VS
Borrelia afzelii	BA 121 VS
Borrelia garinii	BA 121 GVS
Campylobacter jejuni	BA 139 VS
Candida albicans	BA 117 VS
Chlamydia psittaci	BA 137 VS
Chlamydia pneumoniae EB (elementary bodies)	BA 1371 VSEB
Chlamydia pneumoniae RB (reticular bodies)	BA 1371 VSRB
Coxsackievirus B1	BA 134 B1VS
Coxsackievirus B5	BA 134 B5VS
Coxsackievirus B6	BA 134 B6VS
Cytomegalovirus	BA 109 VS
Echinococcus granulosus	BA 107 VS
Echovirus Type 6	BA 135 VS
Echovirus Type 9	BA 135-9 VS
Helicobacter pylori	BA 118 VS
Herpes Simplex Virus (HSV) Type 1	BA 1051 VS
Herpes Simplex Virus (HSV) Type 2	BA 1052 VS
Influenza A Virus	BA 1231 VS

Antigen	Order Nr.
Influenza B Virus	BA 1232 VS
Legionella pneumophila	BA 106 VS
Leptospira biflexa	BA 125 VS
Measles Virus	BA 102 VS
Measles Virus (High Specificity)	BA 102 VS-S
Mumps / Parotitis Virus	BA 103 VS
Mycoplasma pneumoniae	BA 127 VS
Parainfluenza Virus Type 1	BA 1261 VS
Parainfluenza Virus Type 2	BA 1262 VS
Parainfluenza Virus Type 3	BA 1263 VS
Respiratory Syncytial Virus (RSV)	BA 113 VS
Rotavirus	BA 1193 VS
Rubella Virus grade 1	BA 129 VS
Rubella Virus grade 2	BA 129 G2VS
TBE (Tick-Borne Encephalitis) Virus	BA 112 VS
Toxoplasma gondii	BA 110 VS
Varicella Zoster Virus (VZV)	BA 104 VS
Varicella Zoster Virus (VZV) Glycoprotein	BA 104 VSG
Yersinia enterocolitica O:3	BA 138 VS
Yersinia enterocolitica O:8	BA 138 08VS
Yersinia enterocolitica O:9	BA 138 09VS

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Automation

Content

Immunomat™ *TWIN*system

Fully automated SERION ELISA Analyser and SERION Multianalyt™ Processor

Immuno*flow*

SERION Multianalyt™ Analyser

The perfect combination for SERION Multianalyt™ technology: Immunomat™ *TWIN*system and Immuno*flow*

Immunomat™ *TWIN*system *BASE*plus *BASE*

The **Immunomat™** ***TWIN*system** is a 4-Plate automat and allows the processing of SERION ELISA *classic* and SERION Multianalyt™ immunoassays. The **Immunomat™** is consequently well suited for the application of two complementing technologies in *in-vitro* diagnostics.

2 ... in 1

Immunomat™ *TWIN*system

The **Immunomat™** ***TWIN*system** is a new benchtop automat with integrated pipetting system, plate transporter and ELISA reader. The system is equipped with an ELISA washer as well as a vacuum washing station for filter plates. Four plate positions and incubators with agitation function are integrated to guarantee an efficient workload of the instrument.

Immunomat™ *BASE*plus / *BASE*

The fully automated ELISA analyser **Immunomat™** ***BASE*plus** and **Immunomat™** ***BASE*** are able to process up to seven microtitre plates simultaneously. In contrast to **Immunomat™** ***TWIN*system**, a vacuum washer is not included. As a consequence, processing of SERION Multianalyt™ immunoassays is not possible. However, the **Immunomat™** ***BASE*plus** can be easily upgraded to **Immunomat™** ***TWIN*system**.

Fully automated ELISA Analyser

The **Immunomat™** attention to detail includes a barcode identification system for racks, reagents and microtitre plates and allows the processing of up to 16 different assays per plate. The easy access to buffers and reagents, level sensors for all fluid containers and software-controlled tip management system guarantee customer convenient handling.

Liquid Handling

SERION Multianalyt™ Processor

The **Immunomat™** ***TWIN*system** allows the automated processing of SERION Multianalyt™ immunoassays. The innovative technology based on the principle of flow cytometry allows the simultaneous analysis of multiple parameters in a small sample volume. SERION Multianalyt™ and SERION ELISA *classic* immunoassays are two complementing technologies for *in-vitro* diagnostics, which can be simultaneously processed with **Immunomat™** ***TWIN*system**. Samples of processed SERION Multianalyt™ immunoassays are subsequently analysed by a flow cytometer.

Barcoded SERION ELISA *classic* and
SERION Multianalyt™ kit components

Evaluation of Immunoassays

The **Immunomat™** is evaluated for antibody and antigen detection in serum, plasma and cerebrospinal fluid (CSF), if necessary, as well as for avidity determination with SERION ELISA *classic*, SERION ELISA *antigen* and SERION Multianalyt™ immunoassays.

Immunomat™ Software

The **Immunomat™** software allows the generation of assay protocolls, panel definitions and worklists for routine diagnostics. Connection to laboratory software systems is possible via bi-directional ASTM interface. Evaluation of SERION ELISA tests is carried out conveniently by using the **Immunomat™** software. For the analysis of SERION Multianalyt™ immunoassays an external software is available for our customers.

Comparison Immunomat™ *TWIN*system / *BASE*plus / *BASE*

Automat	Immunomat™ *BASE*	Immunomat™ *BASE*plus	Immunomat™ *TWIN*system
Fully automated SERION ELISA analyser	yes	yes	yes
Hardware for upgrade to Immunomat™ *TWIN*system pre-installed	no	yes	
Vacuum washer station	no	upgrade possible	yes
Multianalyt™ processor	no	upgrade possible	yes

Technical data of Immunomat™ *TWIN*system

Instrument	
W x D x H	114 cm x 156 cm x 100 cm
Weight	130 kg
Mains voltage	110 - 260 Universal a.c. Input
Temperatur of environment	5 - 40 °C
Max. number of plates	Up to 4 plates simultaneously
Barcode	Barcode identification of samples, reagents and microtitre plates
Barcodelaser	Scanner for racksystem
Max. number of samples	Max. 100 tubes (max. average 16 mm)
Reagents	SERION racks
Dilution positions	Up to 4 dilution plates
Max. number of tip racks	Up to 5 tip racks with 300 µl or 1100 µl disposable tips
Pipetting system	
Pipetting system	Liquid pipettor for disposable tips
Volumes min. / max.	For 300 µl tips 10 - 300 µl, for 1100 µl tips 301 - 1000 µl
Accuracy	< 15 % CV for 25 µl volumes; < 5 % CV for 100 µl volumes
Precision	< 5 % CV for 25 µl volumes; < 2,5 % CV for 100 µl volumes
Incubators	
Incubation capacity	4 independent chambers with agitation function
Incubation range	Between RT up to max. 50 °C with temperature control
Temperature	+/- 2 °C (determined in the plate with 100 µl Aqua)
Washer	
Capacity of buffers	Max. 4 positions
Dispense volume	200 - 2500 µl / well
Residual volume	< 2,5 µl in U-shaped bottom; < 4 µl in flat bottom
Fluid alarms	Automated warning in case of lack of reagents or filled waste bag.
Photometer	
Spectral range	400 - 700 nm
Dynamic range	-0,100 OD up to 3,00 OD
Accuracy	+/- 0,005 OD or 2,5 %
Reading time / 96 wells	< 15 sec.
Number of filters	Up to 8 filter positions

Highlights of Immunomat™ *TWIN*system

- *TWO in ONE*:
  Fully automated SERION ELISA test analyser and SERION Multianalyt™ test processor.
- Washer for 96-well ELISA MTPL,
  Vacuum washer for 96-well MTPL.
- Parallel processing of SERION ELISA and SERION Multianalyt™ immunoassays.
- Validated for antibody detection in serum, plasma or cerebrospinal fluid (CSF) with SERION ELISA *classic* and SERION Multianalyt™ immunoassays.
- Validated for avidity determination in serum, plasma or cerebrospinal fluid (CSF) with SERION ELISA *classic*.
- Validated for antigen detection with SERION ELISA *antigen*.
- Short loading times with reload function for patient samples, reagents and microtiter plates.
- Processing of up to 16 different assays per plate.
- Easy access to buffers and reagents.
- Level sensors for fluid containers with automated warning in case of lack of reagents or filled waste bag.
- Multishot dispenser function.
- Memory function for tip racks.
- Barcode identification of samples, reagents and microtitre plates.
- 2D hand barcode scanner for parameters of quality control certificates.
- Clot detection.
- Walk away funktion.
- Fast and quantitative evaluation of SERION ELISA *classic* tests.
- Bi-directional connection to laboratory software systems via ASTM interface.

Order Information

Immunomat™ *TWIN*system		**Order Nr.: VT 022**
Immunomat™ *BASE*plus	(Vacuum washer station upgradeable)	**Order Nr.: VT 021**
Immunomat™ *BASE*	(Vacuum washer station not upgradeable)	**Order Nr.: VT 020**

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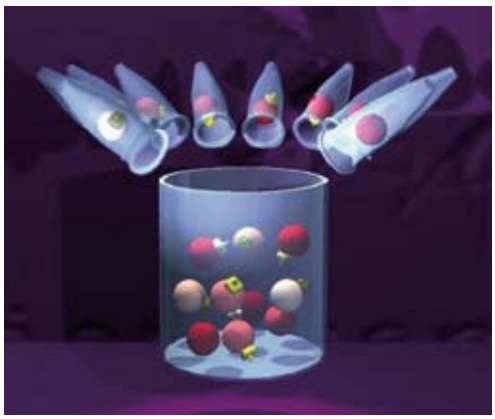
Immuno*flow*

The **Immuno*flow*** is a new, compact, portable, 5-parameter (FSC, SSC and three fluorescences) benchtop flow cytometer with an integrated microtitre plate loader for the analysis of processed SERION Multianalyt™ immunoassays. The integrated software, SERION easy*FLOW*, allows the quantitative evaluation of raw data generated by multiplexed immunoassays. Due to its small footprint, the **Immuno*flow*** can be placed conveniently even in smaller laboratories. Combination with the **Immunomat™ *TWIN*system** is the perfect solution for fully automated processing and analysis of SERION Multianalyt™ immunoassays.



SERION Multianalyt™ Particle Plex

Technology

The SERION Multianalyt™ technology is based on small polystyrene particles. The beads are dyed with a fluorophore in ten different intensity steps. The use of the color coding in combination with the variable size of the particles leads to optically distinguishable bead populations. The differentiation of the particles by **Immuno*flow*** allows the simultaneous performance of up to 40 different immunoreactions in one set up. Due to a surface modification, each particle population can be coated with a different capture molecule.

Immunoassay

The analysis is performed in the cavities of a microtitre plate and starts with the addition of a prepared particle suspension to a diluted sample preparation. Subsequently, the analytes of interest bind to the solid phase.

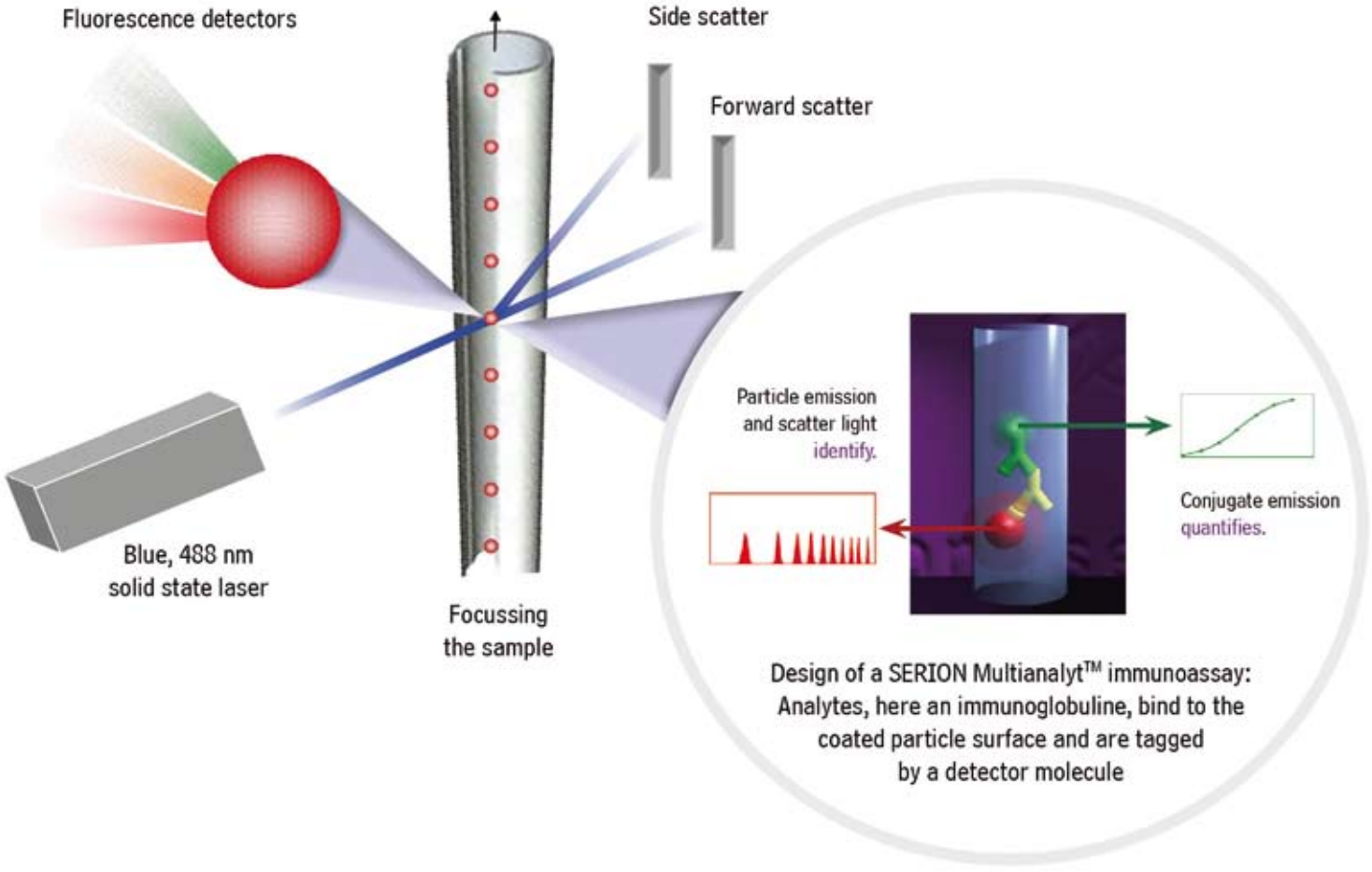
In a multiplex test performance, various particle populations are mixed with the diluted sample. The higher the concentration of the analyte, the more molecules bind to the capture molecule coated on the surface of the particles. In a second step, a detector molecule, usually an antibody with a high specific affinity to the analyte, is added to the reaction mixture. The detector is labelled with another fluorescent dye. The use of fluorophores with high quantum efficiency, such as Phycoerythrin, guarantees a high sensitivity in the immunoreaction. Thereby, analysis of solutions with low analyte concentration as well as highly diluted samples can be performed. The use of a multiplexing test system requires very low sample quantities. Automated processing of SERION Multianalyt™ immunoassays is evaluated on **Immunomat™ *TWIN*system**.

Analysis

The analysis of processed SERION Multianalyt™ immunoassays is performed on **Immuno*flow*** or comparable flow cytometers. Thereby, the particles are separated and precisely gated through the focus of the laser-based detection system. The identification of the particles is performed by their scattering of light and by their fluorescence properties. The fluorescence intensity of the bound detector molecule is proportional to the concentration of the analyte in the sample. Each particle is analysed individually. The analysis of more than a hundred particles per population assures the results statistically and guarantees the high reproducibility of the data.

Signal Processing

The optical bank of the **Immuno*flow*** is based on a blue 20 mW 488 nm solid state laser focussing the particle stream within the measuring cuvette. The emitted fluorescence is deflected via mirrors and optical filters on a range of detectors. The classification of the particles is performed by the analysis of the scattering of light in order to verify their size as well as their emitted fluorescence > 670 nm on FL3. The fluorescences of the detector molecules are measured on FL1 (Fluorescein) and FL2 (Phycoerythrin) to quantify the analyte of interest. The fluorescence intensity of the bound detector molecules are proportional to the concentration of the analyte in the sample.



Design of a SERION Multianalyt™ immunoassay: Analytes, here an immunoglobuline, bind to the coated particle surface and are tagged by a detector molecule

Data Evaluation

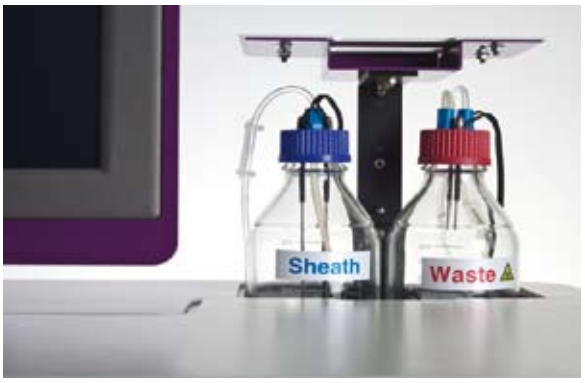
With **Immuno*flow***, raw data evaluation of multiplexed immunoassays is performed directly after each single sample analysis. The integrated software, SERION easy*FLOW*, allows the automated and quantitative evaluation of measured signal intensities according to the individual SERION Multianalyt™ immunoassays and presents the results in a clearly laid out report. Since flow cytometers are able to analyse thousands of particles per second, sample analysis is performed in a few seconds.

The software SERION easy*FLOW*
allows a fast evaluation of
SERION Multianalyt™ immunoassays

Additionally, the validity of the test run is assessed by verification of the standard and control values as well as the number of particles analysed. By the use of the **Immuno*flow*** a standardised and valid evaluation of SERION Multianalyt™ immunoassays is guaranteed.

The obtained data can be conveniently transferred into other data formats, e.g. Microsoft® Excel. Naturally, the software is accessible to the laboratory information system (LIS) in order to allow a convenient transfer of the collected data.

Easy Access to Buffers and Solutions



Level sensors in containers of sheeth fluid and waste guarantee the controlled and smooth running of the analysis. The easy access to fluid containers allows rapid filling or emptying, when necessary.

Technical Support

Institut Virion\Serion GmbH offers comprehensive service and technical support for all questions concerning **Immunomat™** and **Immuno*flow***. Our service guarentees the use of the SERION Multianalyt™ technology in routine laboratories.

Order Information

Immuno*flow* **Order Nr.: VT 200**

Please visit our website www.virion-serion.com for more information on our products.

Highlights of Immuno*flow*

- SERION Multianalyt™ Immunoassay Analyser

  Evaluated for antibody detection in serum, plasma and cerebrospinal fluid (CSF) using SERION Multianalyt™ immunoassays.

- W x D x H: 600 mm x 450 mm x 636 mm

- Stability and Precision

  The **Immuno*flow*** is immediately ready-to-use, when delivered. Time-consuming installations, laser adjustments or settings of the optical bank as for many other flow cytometers are not necessary.
  The stable 20 mW, blue 488 nm solid state laser is superior in power and durability to many other cooled lasers. Precision analysis of highest qualities are guaranteed.

- Detection of 5 optical Parameters: FSC, SSC, FL-1, FL-2, FL-3

- High Fluorescence Intensities ($<$ 100 MESF (FITC); $<$ 50 MESF (PE))

- Measuring Cuvette

  The **Immuno*flow*** contains a 200 μm x 350 μm quarz cuvette to focus the particle stream.

- Computer and Monitor

  Integrated All-in-One PC without fan, optimised for low energy consumption, Intel Celeron M 1.0 GHz Processor, 512 MB RAM, Compact Flash Slot, 2 x USB, 2 x RS-232, 1 x RS-232/422/485 (auto data flow control), Keyboard and Mouse, 10.4" SVGA TFT Monitor, Microsoft® Windows™ XP.

- Software

  The integrated software SERION easy*FLOW* can be used for the adjustment of the instrument parameters, such as voltages of photomultipliers and compensation. The software is recommended for the automated and quantitative evaluation of measured signal intensities directly after each single sample analysis in a clearly laid out result report. The obtained data can be conveniently transferred into other data formats, e.g. Microsoft® Excel. Naturally, the software is accessible to the laboratory information system (LIS) in order to allow a convenient transfer of the collected data.

- Easy to handle

- Universel 100 - 240 V / AC Input

  The **Immuno*flow*** works with a regular 100 - 240 V AC Input.
  Due to its small footprint, the **Immuno*flow*** can be placed conveniently even in smaller laboratories.

- Level sensors in fluid containers

  Level sensors in containers of sheeth fluid and waste guarantee the smooth running of the analysis.

- Easy access to buffers and waste containers

  The easy access to fluid containers allows rapid filling or emptying, when necessary.

- Technical Support

  Institut Virion\Serion GmbH offers comprehensive service and technical support for all questions concerning **Immunomat™** and **Immuno*flow***.

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Pipetting tips		
300 µl	(18 x 960 tips)	**Order Nr.: VT 111**
1100 µl	(10 x 960 tips)	**Order Nr.: VT 112**
Waste bags		
without label	(10 pieces per package)	**Order Nr.: VT 051**
with Biohazard label	(10 pieces per package)	**Order Nr.: VT 020-0102**
Plastic bottles		
white, with cap, 35 ml	(100 pieces per package)	**Order Nr.: VT 113**
yellow, with cap, 35 ml	(100 pieces per package)	**Order Nr.: VT 114**
white, with cap, 50 ml	(100 pieces per package)	**Order Nr.: VT 115**
Glas bottles		
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Incubation plate		**Order Nr.: VT 110**
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	(100 pieces à 20 x 5 pieces per package)	**Order Nr.: VT 121**

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