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Report

Quality of bacteriological infection serology in Germany: analysis of the 2016 proficiency testing trials

Zur Qualität bakteriologisch-infektionsserologischer Verfahren in Deutschland: Auswertung der infektionsserologischen Ringversuche 2016

Abstract

Serological testing that detects pathogen-specific antibodies and antigens remains the diagnostic gold standard in infection serology. Therefore, it is crucial to have standardized and accurate assays. Serological tests can also help to improve the quality of treatment and patient care. This paper summarizes and discusses the results of the proficiency testing trials for bacteriological infection serology that were conducted in Germany in 2016.

Keywords: external quality assurance, EQA, proficiency testing trials, bacteriological infection serology, Germany

Zusammenfassung

Serologische Tests zum Nachweis von erregerspezifischen Antikörpern und Antigenen sind nach wie vor ein diagnostischer Goldstandard in der Infektionsserologie. Daher sind standardisierte und genaue Testverfahren äußerst wichtig. Sie können auch dazu beitragen, die Qualität der Behandlung und Patientenversorgung zu verbessern. In der vorliegenden Arbeit werden die Ergebnisse der bakteriologischen Infektionsserologie in Ringversuchen für das Jahr 2016 in Deutschland zusammengefasst und diskutiert.

Schlüsselwörter: externe Qualitätssicherung, EQA, Ringversuche, bakteriologische Infektionsserologie, Deutschland

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Table 1: Study groups and the number of participants included in two proficiency testing trials in Germany, 2016

INSTAND Index No.	Study groups	5/2016 Participants (N)	11/2016 Participants (N)
310	Tetanus toxoid antibodies	133	126
311	*Treponema pallidum* antibodies	340	334
312	*Chlamydia trachomatis* antibodies	250	246
313	*Chlamydia trachomatis* antibodies – direct detection (ELISA/PCR)	14	13
314	*Chlamydia pneumonia* antibodies	219	223
315	Yersina antibodies	227	–
316	*Chlamydia trachomatis* antibodies – direct detection (IFT)	22	20
317	*Bordetella pertussis* antibodies	–	211
318	Diphtheria toxoid antibodies	123	118
319	*Campylobacter* antibodies	112	–
320	Procalcitonin	135	123
321	*Streptococcal* antibodies (ASL, aDNAse)	316	309
323	Rheumatoid factor	199	186
324	*Mycoplasma pneumonia* antibodies	–	257
325	*Coxiella burnetii* antibodies	–	89
331	Salmonella antibodies (Widal)	87	78
332	*Borrelia burgdorferi* antibodies	387	383
334	*Helicobacter pylori* antibodies	182	180

N=total number of participants with a diagnosis

1 Introduction

Serology is currently making a significant contribution to the etiology, prognosis and treatment success of many infectious diseases. It also serves as an efficient way to confirm past infections and determine an individual's vaccination/protection status. Therefore, serological testing that detects pathogen-specific antibodies and antigens plays an important diagnostic role in infectious serology [1]. The accuracy of the assays is essential since there are many test systems on the market and an insufficient amount of standardization [2]. External quality assurance (EQA) is a well-established method that enables interlaboratory comparisons by way of proficiency testing trials in order to assess the quality of results by an external agency [3]. In Germany, EQA is conducted by the Society for Promoting Quality Assurance in Medical Laboratories e.V. (INSTAND e.V., Düsseldorf) on behalf of the German Medical Association and in collaboration with other partners (i.e. German Society for Hygiene and Microbiology, DGHM) [1]. EQA forms the basis for the development of strategies to improve diagnostic processes and for the continuous improvement of analytical results [1]. It can also help to improve the quality of treatment and patient care [4]. This paper summarizes and discusses the results of the infectious serology as part of proficiency testing trials conducted in 2016. The findings can help to improve the diagnosis of individual constellations and to optimize the test systems used. This paper deals with a standardized form.

2 Methods

2.1 Participants

In 2016, 12,506 laboratories participated in two proficiency testing trials. 10,674 participants were from Germany and 1,340 were from other European countries. One trial was carried out in May and the other in November 2016 (Table 1).

2.2 Sample collection and EQA progress

The control samples (31, 32, 61 and 62) for each study group (310–334) originated from the whole blood of healthy donors or from blood donors with a positive history of infection, and were prepared according to standard operating procedures [5]. Samples 31 and 32 were sent to participating laboratories in May 2016, while samples 61 and 62 were sent in November 2016 [5]. The control samples of *Yersinia*, *Bordetella pertussis*, *Campylobacter*, *Mycoplasma pneumonia* and *Coxiella burnetii* were only analyzed once that year [6], [7].

Participants performed serological analyses on samples from each study group using routine procedures and documented the results and test system used [5]. All results were recorded on the computer and statistically evaluated. When the results were in line with certified reference standards, a certificate was issued by INSTAND e.V. [4].

Table 2: Tetanus toxoid detection during the proficiency testing trials 2016

		Sample 31		Sample 32		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**ELISA** qual./quant. N=110/N=106	positive	100.0	positive	100.0	positive	100.0	positive	100.0
	Target value [IU/ml]	0.4		2.9		1.0		1.4	
	Target range	(0.22–0.51)	68.0	(1.71–4)	96.0	(0.6–1.4)	100.0	(0.84–1.96)	92.9
	Diagnostic N*=130		99.2		100.0		99.2		100.0

N=total number of participants
N*=average number of participants

2.3 Target values

The reference measurement procedure, which follows the guideline of the German Medical Association (RiLiBÄK), enables target values to be determined with the highest level of accuracy and precision. When a uniform target value cannot be determined for the quantitative test results, the robust mean of all participants is established as the target value. In terms of the qualitative test results, either the mode of the results of the reference laboratories, or the mode of the results of the participants is set as the target value [6], [7]. Qualitative test results are expressed as positive, negative or borderline, while semi-quantitative test results are provided in the form of titers, cut-off indices or U/ml. A specific assay or test method should be evaluated in a collective of more than eight participants. If the number of participants is less than eight, this could lead to statistically invalid assessments. Therefore, certificates for the test method are only issued for a collective of eight or more participants [6], [7].

3 Results

3.1 Tetanus toxoid (310)

3.1.1 Sample information

All samples (31, 32, 61 and 62) originated from clinically healthy blood donors.

3.1.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results, while in the case of the semi-quantitative test results, the robust mean of all participants was established as the target value. The corresponding target values, target ranges, test results and pass rates are listed in Table 2.

3.1.3 Overall diagnostic interpretation and commentary on the test results

ELISA was used to quantitatively determine antibodies against tetanus toxin and toxoid (TT) in the serum of clinically healthy donors. Antibody detection has no diagnostic relevance in determining a tetanus infection, however, it can be used to assess an individual's immune or vaccination status for tetanus toxoid [1]. Results of this trial show that samples 32, 61 and 62 had tetanus toxoid antibody titers ranging from 1 to 2.9 IU/ml, suggesting protective immunity against tetanus toxoid. However, the level of antibody titers in samples 32 and 62 indicated that a booster vaccination will be needed in 5 to 10 years for long-term protection, while in sample 61 a booster vaccination in 2 to 5 years will be needed to provide long-term protection. The level of antibodies in sample 31 was 0.4 IU/ml, suggesting that there was protective immunity; however, a booster vaccination will provide long-term immunity. It is important to note that vaccinations should primarily be in accordance with the recommendations of the German Standing Committee on Vaccination (STIKO) and not just based on measured antibody levels [1]. Pass rates for ELISA tests were 100% for the qualitative results and 99.2–100% for the quantitative results. The pass rate for the overall clinical diagnostic evaluation was between 99.2 and 100%.

3.2 Treponema pallidum antibodies (311)

3.2.1 Sample information

Samples 32 and 62 originated from healthy blood donors without any clinical evidence of syphilis. Sample 31 was taken from a clinically asymptomatic blood donor before a scheduled donation. The donor could not recall any previous infection or treatment. Sample 61 was donated by a blood donor treated for a syphilis infection several years ago.

3.2.2 Determination of the target values

The target value for the qualitative test results was the mode of the results of the reference laboratories, while in the case of the semi-quantitative test results, the results of the reference laboratories were established as the target value. The corresponding target values, target ranges, test results and pass rates are presented in Table 3.

Table 3: Treponema pallidum antibody detection during the proficiency testing trials 2016

			Sample 31		Sample 32		Sample 61		Sample 62	
			Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**ELISA/CLIA/CMIA** qual./quant.	N=174/N=106	positive	100.0	negative	100.0	positive	98.4	negative	98.4
	Target value [IU/ml]		27.0		0.1		25.1		0.1	
	Target range		17.3–36.7	100.0	0.077–0.163	100.0	16.1–34.1	100.0	0–0.1	100.0
	TPHA qual./quant.	N=274/N=166	positive	98.2	negative	96.4	positive	95.1	negative	97.6
	Target value [IU/ml]		2560.0		0.0		320.0		0.0	
	Target range		(640–10240)	88.4	(0–79.9)	97.6	(80–1280)	100.0	(0–79.9)	100.0
	TPPA qual./quant.	N=88/N=64	positive	100.0	negative	100.0	positive	95.5	negative	95.5
	Target value [IU/ml]		5120.0		0.0		1280.0		0.0	
	Target range		(1280–20480)	82.4	(0–79.9)	100.0	(320–5120)	73.3	(0–79.9)	100.0
	VDRL qual./quant.	N=244/N=206	positive	96.7	negative	98.3	negative	83.9	negative	98.4
	Target value [IU/ml]		16.0		0.0		0.0		0.0	
	Target range		(4–64)	94.3	(0–0.99)	90.2	(0–1)	92.0	(0–0.99)	91.8
	Cardiolipin qual./quant.	N=6/N=2	positive	100.0	negative		–	–	–	–
	Target value [IU/ml]		32.0		0.0		–		–	
	Target range		(8–128)	100.0	(0–4.99)	100.0	–	–	–	–
Specific IgG	**ELISA** qual./quant.	N=30/N=54	positive	100.0	negative	100.0	positive	85.7	negative	100.0
	Target value [IU/ml]		534.0		3.0		38.9		2.3	
	Target range		(390–678)	100.0	(2.17–3.77)	100.0	(28.4–49.4)	100.0	(1.69–2.93)	100.0
	Blot qual.	N=54	positive	100.0	negative	100.0	positive	100.0	negative	100.0
	FTA-ABS qual./quant.	N=74/N=58	positive	100.0	negative	95.7	positive	92.9	negative	100.0
	Target value [IU/ml]		1280.0		0.0		80.0		0.0	
	Target range		(320–5120)	58.3	(0–4.99)	100.0	(20–320)	52.9	(0–4.99)	100.0
Specific IgM	**ELISA** qual.	N=26	positive	71.4	negative	57.1	negative	100.0	negative	100.0
	Blot qual.	N=56	bl./positive	88.9	negative/bl.	77.8	negative	100.0	negative	100.0
	FTA-ABS qual./quant.	N=54/N=50	positive	70.6	negative	100.0	negative	100.0	negative	100.0
	Target value [IU/ml]		160.0		0.0		0.0		0.0	
	Target range		(40–640)	83.3	(0–4.99)	92.3	(0–4.99)	100.0	(0–4.99)	92.9
	Diagnostic	N*=337		92.7		85.9		79.9		97.3

N=total number of participants
N*=average number of participants
bl.=borderline

3.2.3 Overall diagnostic interpretation and commentary on the test results

Samples 32 and 62 showed no clinical or serological evidence of a syphilis infection. However, false reactive test results were reported for sample 32, mainly for IgM immunoblot, although the sample tested negative by the IgM-FTA-ABS test. The positive serological findings of sample 31 (target value (mode): TPPA: 5120, VDRL: positive, 16, IgM-FTA-ABS: positive, 160, EIA and immunoblot for IgG: positive and for IgM: borderline or positive), indicated a latent or possibly active infection. The overall pass rate of all test methods for sample 31 was 92.7%. The positive sample 61 (target value: TPPA: 1280, polyval. ELISA, IgG-ELISA: positive, VDRL: negative/borderline, FTA-ABS-IgG: 80, FTA-ABS-IgM and IgM-ELISA: negative) achieved an overall pass rate of 79.9%, indicating unsatisfactory test sensitivity. Findings in both samples 31 and 61 indicated that treatment was needed. The distribution of the immunoblot bands, as reported for the positive samples 31 (Figure 1, Figure 2) and 61 (Figure 3), are shown below [6], [7]. The overall diagnostic evaluation of the negative samples 32 and 62 showed pass rates between 85.9 and 97.3%, whereas those of the positive samples 31 and 61 were between 79.9 and 92.7%.

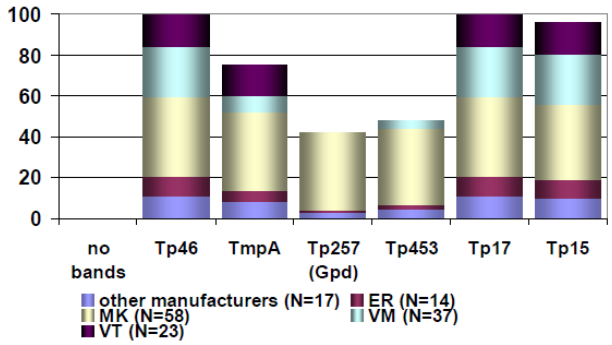

Figure 1: The distribution of the immunoblot bands reported for the positive sample 31 [7], [8]; recovery rate (%) of the submitted IgG immunoblot bands for sample 311/31 (May 2016); participants N=149

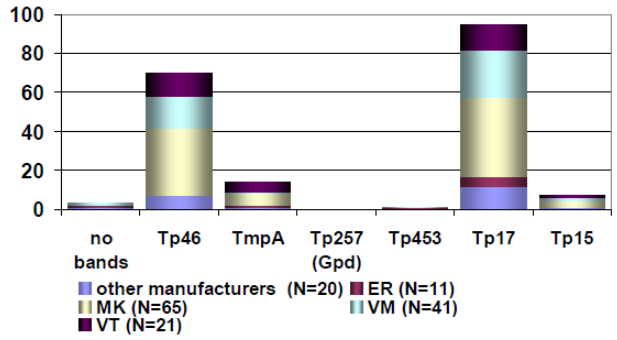

Figure 2: The distribution of the immunoblot bands reported for the positive sample 31 [7], [8]; recovery rate (%) of the submitted IgM immunoblot bands for sample 311/31 (May 2016); participants N=158

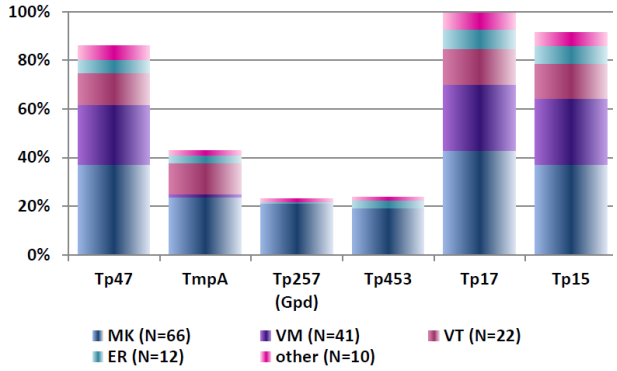

Figure 3: The distribution of immunoblot bands reported for the positive sample 61 [7], [8]; recovery rate (%) of the submitted IgG immunoblot bands for sample 311/61 (Nov. 2016); participants N=151

3.3 Chlamydia trachomatis antibodies (312)

3.3.1 Sample information

All samples (31, 32, 61 and 62) originated from clinically healthy blood donors.

3.3.2 Determination of the target values

The target value for the qualitative test results was the mode of the results of the reference laboratories; in the case of the semi-quantitative results, the results of the reference laboratories were set as the target value. The corresponding target values, target ranges, test results and pass rates are shown in Table 4.

3.3.3 Overall diagnostic interpretation and commentary on the test results

Samples 31 and 62 showed no serological evidence of a *C. trachomatis* infection. IgG antibodies were detected in sample 32, combined with negative test results for IgM antibodies and borderline results for IgA antibodies. IgG antibodies were detected in sample 61, combined with negative results for both IgM and IgA antibodies. Consequently, the test results for both samples 32 and 62 indicated an infection with *C. trachomatis*. In sample 61, the pass rate was between 33.3 and 100% for all tests, with the lowest pass rate (33.3%) for the qualitative detection of IgA antibodies by immunoblot. The overall diagnostic evaluation of the negative samples was 97.6–99.2% and thus in the range of previous years, while positive samples were more or less in the same range (98–99.6%).

3.4 Chlamydia trachomatis antibodies – direct detection by ELISA/PCR (313)

3.4.1 Sample information

All samples (31, 32, 61 and 62) originated from clinically healthy blood donors.

3.4.2 Determination of the target values

The mode of the results of all participants was set as the target value for the qualitative test results, while in the case of the semi-quantitative test results, the mode of the results of the reference laboratories was established as the target value. The corresponding target values, target ranges, test results and pass rates are presented in Table 5.

3.4.3 Overall diagnostic interpretation and commentary on the test results

Samples 31, 61 and 62 showed no clinical or serological evidence of *C. trachomatis*, while sample 32 tested positive for the pathogen, indicating a *C. trachomatis* infection. The overall diagnostic evaluation of the negative samples 31, 61 and 62 was between 92.9–100% and thus in line with previous years, while the positive sample 32 was 92.9%.

3.5 Chlamydia pneumonia antibodies (314)

3.5.1 Sample information

All samples (31, 32, 61 and 62) were taken from clinically healthy blood donors.

3.5.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results; in the case of the semi-quantitative test results, the results of the reference laboratories were specified as the target value. The corresponding target values, target ranges, test results and pass rates are shown in Table 6.

Table 4: Chlamydia trachomatis antibody detection during the proficiency testing trials 2016

			Sample 31		Sample 32		Sample 61		Sample 62	
			Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Specific IgG	**ELISA** qual.	N=276	negative	98.1	positive	98.1	positive	95.2	negative	98.8
	ELISA C. spp qual./quant. Target value [IU/ml] Target range	N=12/N=30	negative 3.9 (2.48–5.26)	100.0 100.0	positive 69.5 (44.5–94.5)	100.0 100.0	positive 118.0 (75.5–160)	100.0 100.0	negative 3.5 (2.21–4.71)	100.0 100.0
	Blot qual.	N=18	negative	100.0	positive	100.0	positive	100.0	negative	80.0
	MIFT qual./quant. Target value [IU/ml] Target range	N=62/N=48	negative 0.0 (0–19.9)	93.8 76.9	positive 160.0 (40–640)	93.8 84.6	positive 80.0 (20–320)	100.0 90.9	negative 0.0 (0–19.9)	93.3 81.8
Specific IgA	**ELISA** qual.	N=264	negative	100.0	negative/bl.	82.9	negative	94.5	negative	94.5
	ELISA C. spp qual.	N=8	–	100.0	bl.	100.0	negative	100.0	negative	100.0
	Blot qual.	N=22	negative	100.0	negative/bl.	80.0	negative	33.3	negative	100.0
	MIFT qual./quant. Target value [IU/ml] Target range	N=22/N=68	negative 0.0 (0–19.9)	90.0 100.0	negative/bl. 0.0 (0–20)	80.0 94.1	negative 9.3 (0–19.9)	77.8 82.4	negative 0.0 (0–19.9)	88.9 100.0
Specific IgM	**ELISA** qual.	N=76	negative	100.0	negative	85.0	negative	100.0	negative	100.0
	ELISA C. spp qual.	N=10	negative	100.0	bl.	100.0	negative	100.0	negative	100.0
	Blot qual.	N=38	negative	100.0	negative	100.0	negative	100.0	negative	100.0
	MIFT qual./quant. Target value [IU/ml] Target range	N=78/N=72	negative 0.0 (0–19.9)	95.2 100.0	negative 0.0 (0–19.9)	90.5 100.0	negative 0.0 (0–19.9)	100.0 94.1	negative 0.0 (0–19.9)	94.4 94.1
	Diagnostic	N*=248		99.6		99.2		97.6		98.0

N=total number of participants
N*=average number of participants
bl.=borderline

Table 5: Chlamydia trachomatis antibody detection during the proficiency testing trials 2016

			Sample 31		Sample 32		Sample 61		Sample 62	
			Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
313	**ELISA Ag** qual.	N=30	negative	88.9	positive	77.8	negative	100.0	negative	100.0
	DNA hybridisation without amplification qual.	N=24	negative	100.0	positive	100.0	negative	100.0	negative	100.0
	Antigen-detection techniques (others) qual.	N=26	negative	100.0	positive	71.4	negative	100.0	negative	100.0
	Diagnostic	N*=14		92.9		92.9		100.0		100.0
316	**IFT** qual.	N=84	positive	100.0	negative	95.5	negative	80.0	negative	85.0
	Diagnostic	N*=84		100.0		95.5		80.0		90.0

N=total number of participants
N*=average number of participants

3.5.3 Overall diagnostic interpretation and commentary on the test results

No evidence of an infection with *C. pneumonia* was detected in samples 32 and 61, while samples 31 and 62 tested positive for the pathogen. In sample 31, IgG antibodies and borderline results for IgA and IgM antibodies were detected, while in sample 62, IgG antibodies were detected along with borderline results for IgA antibodies. Test results in both samples indicated an infection with *C. pneumonia*. All four samples had qualitative results of 86.3–100% for all ELISA tests, while all MIFT tests were in a range of 70.6–100% for qualitative results and 78.6–100% for quantitative results. The qualitative results of all immunoblot tests for all samples except for sample 62 were 100%. In sample 62, immunoblot had a pass rate of 60% for detecting IgG antibodies. The overall diagnostic evaluation of the negative samples 32 and 61 was 97.3%, while for the positive samples 31 and 62 it was 97.7–98.7%.

3.6 Yersinia antibodies (315)

3.6.1 Sample information

Sample 31 was obtained from a patient with reactive arthritis. Sample 32 was collected from a clinically asymptomatic seronegative blood donor.

3.6.2 Determination of the target values

The mode of the results of all participants was set as the target value for the qualitative test results, while in the case of the semi-quantitative test results, the results of the reference laboratories were set as the target value.

Table 6: Chlamydia pneumonia antibody detection during the proficiency testing trials 2016

		Sample 31		Sample 32		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**CFT** qual./quant. N=12/N=28 Target value [IU/ml] Target range	negative – (0–9.9)	100 100	negative – (0–9.9)	100 100	negative – (0–0)	100 100	negative 3.5 (2.24–4.76)	100 100
Specific IgG	**ELISA** qual. N=212	positive	93.0	negative	93.0	negative	100	positive	98.4
	Blot N=16	positive	100	negative	100	negative	100	positive	60
	MIFT qual./quant. N=42/N=56 Target value [IU/ml] Target range	positive 160 (40–640)	100 85.7	negative – (0–19.9)	100 78.6	negative – (0–19.9)	100 100	positive 160 (40–640)	100 92.9
Specific IgA	**ELISA** qual. N=228	neg./bl./pos.	96.6	negative	93.2	negative	98.2	bl./positive	94.5
	Blot N=20	neg./bl./pos.	100	negative	100	negative	100	neg./bl./pos.	100
	MIFT qual./quant. N=36/N=72 Target value [IU/ml] Target range	neg./bl./pos. 20 (0–80)	100 94.1	negative – (0–19.9)	100 100	negative (0–19.9)	100 100	bl./positive 80 (20–320)	100 78.9
Specific IgM	**ELISA** qual. N=204	neg./bl./pos.	94.1	negative	96.1	negative	86.3	negative	92.2
	Blot N=50	neg./bl./pos.	100	negative	100	negative	100	negative	100
	MIFT qual./quant. N=70/N=64 Target value [IU/ml] Target range	neg./bl./pos. 40 (0–160)	100 86.7	negative – (0–19)	100 100	negative – (0–19)	88.2 100	negative – (0–19)	70.6 88.2
	Diagnostic N*=221		97.7		97.3		97.3		98.7

N=total number of participants
N*=average number of participants
bl.=borderline

Table 7: Yersinia antibody detection during the proficiency testing trials 2016

		Sample 31		Sample 32	
		Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**Y. enter. 03** qual./quant. N=52/N=20 Target value [IU/ml] Target range	negative 1 (0–99)	88.5 80	negative 1 (0–99)	88.5 100
	Y. enter. 09 qual./quant. N=50/N=20 Target value [IU/ml] Target range	negative 1 (0–99)	96.0 90	negative 1 (0–99)	92.0 100
	Y. pseudotub. qual./quant. N=48/N=18 Target value [IU/ml] Target range	negative 1 (0–99)	91.7 100	negative 1 (0–99)	100 100
Specific IgG	**ELISA** qual. N=46	positive	95.7	negative	100
	Blot qual. N=26	positive	100	negative	100
Specific IgM	**ELISA** qual. N=24	bl./positive	41.7	negative	91.7
	Blot qual. N=20	bl./positive	80	negative	100
Specific IgA	**ELISA** qual. N=42	positive	90.5	negative	100
	Blot qual. N=22	positive	100	negative	100
	Diagnostic N*=227		96.0		99.6

N=total number of participants
N*=average number of participants
bl.=borderline

The corresponding target values, target ranges, test results and pass rates are listed in Table 7.

3.6.3 Overall diagnostic interpretation and commentary on the test results

No evidence of an infection with *Yersinia* was detected in sample 32, while sample 31 tested positive for the pathogen. Sample 31 had negative Widal test results, but clear reactive results for the immunoglobulin classes IgG and IgA by ELISA and immunoblot. Borderline results for IgM antibodies were detected by ELISA and immunoblot. The constellation of findings in sample 31 was consistent with both a previous *Yersinia* infection (this probably occurred a long time ago because the Widal test was negative) and with a *Yersinia*-associated secondary disease [6], [7]. The overall diagnostic evaluation of the negative sample 32 was 99.6%, while it was 96% for the positive sample 31.

Table 8: Bordetella pertussis antibody detection during the proficiency testing trials 2016

			Sample 61		Sample 62	
			Test result	Pass rate [%]	Test result	Pass rate [%]
Specific IgG	**ELISA (PT+FHA)** qual.	N=24	positive	91.7	negative	83.3
	ELISA (PT) qual.	N=116	neg./bl./pos.	98.3	negative	94.8
	Blot qual.	N=18	positive	88.9	negative	88.9
Specific IgM	**ELISA** qual.	N=40	neg./bl./pos.	100	negative	95
	Blot qual.	N=8	negative	100	negative	100
Specific IgA	**ELISA (PT+FHA)** qual.	N=34	neg./bl./pos.	100	negative	100
	ELISA (PT) qual.	N=100	negative	88.0	negative	100
	Blot qual.	N=18	neg./bl./pos.	100	negative	100
	Diagnostic	N*=211		100		98.6

N=total number of participants
N*=average number of participants
bl.=borderline

3.7 Chlamydia trachomatis antibodies – direct detection by IFT (316)

3.7.1 Sample information

All samples (31, 32, 61 and 62) were taken from clinically healthy blood donors.

3.7.2 Determination of the target values

The mode of the results of all participants was established as the target value for the qualitative test results. The corresponding target values, target ranges, test results and pass rates are listed in Table 5.

3.7.3 Overall diagnostic interpretation and commentary on the test results

Samples 32, 61 and 62 showed no serological evidence of *C. trachomatis*, while sample 31 tested positive for the pathogen, indicating an infection with *C. trachomatis*. The overall diagnostic evaluation of the negative samples 32, 61 and 62 was between 80–95.5% and thus in the line with previous years, while the pass rate of positive sample 31 was 100%.

3.8 Bordetella pertussis antibodies (317)

3.8.1 Sample information

Sample 61 was donated by a non-immunized blood donor without evidence of any respiratory infections in his recent medical history. Sample 62 originated from a healthy vaccinated blood donor without any respiratory infections in his recent medical history.

3.8.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results, while in the case of the semi-quantitative test results, the robust mean of all participants was stipulated as the target value. The corresponding target values, target ranges, test results and pass rates are listed in Table 8.

3.8.3 Overall diagnostic interpretation and commentary on the test results

Sample 62 tested negative for specific antibodies against *B. pertussis*; therefore, no evidence of infection was detected. Sample 61 tested positive for the pathogen. This sample exhibited an interesting constellation of findings in different assay systems and yielded weakly reactive results for IgG as well as for IgM and IgA. PT-based tests resulted in borderline or positive results (IgG-ELISA, IgG-immunoblot). The quantitative PT-IgG-ELISA result was 44.6 IU/ml, indicating a doubtful result or the possibility of a past infection according to the guidelines [6], [7]. Due to the overall variability of the findings, however, the survey was generous and the clinical commentary as to a recent infection was accepted. The overall diagnostic evaluation of the negative sample 62 was 98.6%, while for the positive sample 61 it was 100%.

3.9 Diphtheria toxoid antibodies (318)

3.9.1 Sample information

Samples 31 and 32 were donated by healthy pre-immunized blood donors, while samples 61 and 62 originated from clinically healthy blood donors.

3.9.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results, while in the case of the semi-quantitative test results, the robust mean of all participants was stipulated as the target value. The corresponding target values, target ranges, test results and pass rates are shown in Table 9.

Table 9: Diphtheria toxoid antibody detection during the proficiency testing trials 2016

		Sample 31		Sample 32		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**ELISA** qual./quant. N=116/N=124 Target value [IU/ml] Target range	positive 1.033 (0.661–1.4)	96.8 79.5	neg./bl./pos. 0.081 (0–0.11)	100 79.5	positive 1.36 (0.87–1.85)	100 82.6	neg./bl./pos. 0.036 (0–0.099)	100 100
	Diagnostic N*=121		100.0		100.0		99.2		94.1

N=total number of participants
N*=average number of participants
bl.=borderline

Table 10: Campylobacter antibody detection during the proficiency testing trials 2016

		Sample 31		Sample 32	
		Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**CFT** qual./quant. N=38/N=40 Target value [IU/ml] Target range	negative 0.0 (0–9.99)	94.7 95.0	neg./bl./pos. 0.0 (0–20)	78.9 94.4
Specific IgG	**ELISA** qual./quant. N=22/N=118 Target value [IU/ml] Target range	negative 8.24 (5.27–11.2)	100 100	bl./positive 41.6 (26.6–56.6)	90.9 100
	Blot qual. N=12	negative	83.3	positive	83.3
	IFT qual./quant. N=4/N=4 Target value [IU/ml] Target range	negative 0.0 (0–0)	100 100	borderline 1000.0 (640–1360)	100 100
Specific IgM	**ELISA** qual. N=8	negative	100	negative	50
	IFT qual./quant. N=2/N=2 Target value [IU/ml] Target range	negative 0.0 (0–0)	100 100	negative 0.0 (0–0)	100 100
Specific IgA	**ELISA** qual. N=22	negative	100	neg./bl./pos.	100
	Blot qual. N=12	negative	100	neg./bl./pos.	100
	IFT qual./quant. N=4/N=4 Target value [IU/ml] Target range	negative 0.0 (0–0)	100 100	bl. 320.0 (205–435)	100 100
	Diagnostic N*=112		98.2		84.4

N=total number of participants
N*=average number of participants
bl.=borderline

3.9.3 Overall diagnostic interpretation and commentary on the test results

Antibodies against the diphtheria toxin and toxoid (DT) can be quantitatively detected in serum.
Antibody detection is not suitable for identifying an acute case of diphtheria; it can only be used to assess the immune and vaccination status of diphtheria [1].
The titer level (1.033 IU/ml) of sample 31 indicated protective immunity, however, a booster vaccination would provide long-term immunity. The high titer level of 1.36 IU/ml in sample 61 indicated that there was active protective immunity against tetanus, however a booster vaccination in 5 to 10 years would be needed to provide long-term protection. Low titer levels of 0.081 IU/ml and 0.036 IU/ml in samples 32 and 62 respectively suggested that there was no protective immunity; therefore, a booster vaccination was recommended. Vaccination recommendations should primarily be made following STIKO recommendations and based on measured antibody levels [1]. ELISA tests had qualitative results of 96.8–100% and quantitative results of 79.5–100%. The overall diagnostic evaluation was in the range of 94.1–100%.

3.10 Campylobacter antibodies (319)

3.10.1 Sample information

Samples 31 and 32 originated from clinically healthy blood donors.

3.10.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results, while in the case of the semi-quantitative test results, the robust mean of all participants was stipulated as the target value. The corresponding target values, target ranges, test results and pass rates are listed in Table 10.

Table 11: Procalcitonin detection during the proficiency testing trials 2016

		Sample 31		Sample 32		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**All methods** qual. N=94	negative	100	positive	100	negative	100	positive	100
	Method 1 semi-quant. [ng/ml] N=14	<0.5 ng/ml	100	≥2 ng/ml	100	<0.5 ng/ml	100	≥2 ng/ml	75
	Method 2 quant. N=194 Target value [IU/ml] Target range	– (0–0.499)	92.2	7.033 (5.13–8.93)	76.5	0.05 (0–0.499)	100	3.6 (2.52–4.68)	77.8
	Diagnostic N*=129		98.5		97.0		99.2		89.3

N=total number of participants
N*=average number of participants

3.10.3 Overall diagnostic interpretation and commentary on the test results

Specific IgG, IgM and IgA antibodies were detected using the commercially available ELISA, immunoblot and IFT tests. No evidence of an infection with *C. jejuni* was detected in sample 31, while sample 32 had borderline results for IgG and IgA antibodies against the tested pathogen, indicating a *Campylobacter* infection. In sample 31, qualitative and quantitative results for ELISA were 100% for IgG, IgM and IgA antibodies against *C. jejuni*, while in sample 32 they were in the range of 50–100%. Sample 32 had a low qualitative result of 50% for IgM antibodies using the ELISA method. The overall diagnostic evaluation of the negative sample 31 was 98.2%, while it was 84.4% for the positive sample 32.

3.11 Procalcitonin (320)

3.11.1 Sample information

Samples 31, 32 and 61 were donated by a healthy blood donor without signs of infection. Sample 62 was pooled from backup samples of septic patients.

3.11.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results, while the robust mean of all participants was stipulated as the target value for the semi-quantitative test results. The corresponding target values, target ranges, test results and pass rates are presented in Table 11.

3.11.3 Overall diagnostic interpretation and commentary on the test results

Findings for samples 31 and 61 indicated that a local bacterial infection was possible in both samples, while findings for samples 32 and 62 indicated the likelihood of a systemic infection (sepsis). Semi-quantitative results of method 1 for samples 31 and 61 were <0.5 ng/ml with a pass rate of 100%, while samples 32 and 62, at ≥2 ng/ml, had pass rates of 100% and 75% respectively. In samples where a local bacterial infection was likely, the overall diagnostic evaluation was between 98.5 and 99.2%, while in samples where sepsis was possible, it was between 89.3 and 97%.

3.12 Streptococci antibodies (321)

3.12.1 Sample information

All samples (31, 32, 61 and 62) were donated by a healthy blood donor.

3.12.2 Determination of the target values

Different testing methods were used to determine the streptococcal antibodies (DNSAse and the anti-Streptolysin-O) against streptococcal antigens. For the qualitative test results, the mode of the results of the reference laboratories was set as the target value and it depended on the method used. In the case of the semi-quantitative test results, the robust mean of all participants was specified as the target value. The range of acceptance for the semi-quantitative results was ±25%. The corresponding target values, target ranges, test results and pass rates are displayed in Table 12.

3.12.3 Overall diagnostic interpretation and commentary on the test results

In the qualitative evaluation, titers of streptococcal antibodies above the cut-off value (200 IU/ml) indicated an infection with *Streptococcus*. Titers between 200 and 400 indicated a past or recent infection [5]. A much higher titer occurs when there is severe infection or an acute secondary disease. The pass rate of Streptococcus-O-lysine antibody detection was between 57.3 and 100%, and the pass rate of streptodornase detection was between 60 and 100%.

3.13 Rheumatoid factor (323)

3.13.1 Sample information

All samples (31, 32, 61 and 62) were taken from clinically healthy blood donors.

Table 12: Streptococci antibody detection during the proficiency testing trials 2016

		Sample 31		Sample 32		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Streptococcus-O-Lysine	**All methods** qual. N=248	positive	83.3	negative	100	negative	100	positive	100
	Method 1 qual./quant. N=82/N=70	bl./pos.	68.8	negative	100	negative	100	positive	95.8
	Target value [IU/ml]	300		–		–		800	
	Target range	(200–400)	93.3	(0–199)	100	(0–199)	100	(400–1600)	80
	Method 2 qual./quant. N=14/N=22	positive	100	negative	100	negative	100	positive	100
	Target value [IU/ml]	423		–		33.6		1159	
	Target range	(321–525)	100	(0–199)	100	(0–199)	100	(881–1437)	100
	Method 3 qual./quant. N=48/N=14	negative	87.5	negative	100	negative	100	positive	100
	Target value [IU/ml]	–		–		–		–	
	Target range	(0–199)	57.1	(0–199)	100	–	–	–	–
Streptodornase	**All methods** qual. N=158	negative	83.5	negative	100	–	–	–	–
	Method 1 quant. N=50	–	–	–	–	–	–	–	–
	Target value [IU/ml]	–		–		–		165	
	Target range	–	–	–	–	(0–199)	100	(0–200)	100
	Method 2 quant. N=16	–	–	–	–	–	–	–	–
	Target value [IU/ml]	–		–		–		202	
	Target range	(0–199)	100	(0–199)	100	(0–199)	100	(154–250)	100
	Method 3 quant. N=12	–	–	–	–	–	–	–	–
	Target value [IU/ml]	–		–		–		127	
	Target range	(0–199)	60	(0–199)	100	(0–199)	100	(96.5–157)	0

N=total number of participants
bl.=borderline
Method 1: latex particle agglutination, method 2: endpoint nephelometry, method 3: kinetic nephelometry

Table 13: Rheumatoid factor detection during the proficiency testing trials 2016

	Sample 31		Sample 32		Sample 61		Sample 62	
	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
All methods qual. N=278	positive	98.1	negative	96.2	positive	100	negative	96.6
All methods quant. N=454								
Target value [IU/ml]	46		–		40.8		3.89	
Target range	(36.8–55.2)	65	(0–19.9)	92.5	(32.6–49.0)	91.4	(0–19.9)	96.8

N=total number of participants

3.13.2 Determination of the target values

The mode of the results of reference laboratories was set as the target value for the qualitative test results, while the robust mean of all participants was stipulated as the target value for the semi-quantitative test results. The corresponding target values, target ranges, test results and pass rates are indicated in Table 13.

3.13.3 Overall diagnostic interpretation and commentary on the test results

The quantitative and qualitative test results for all methods were between 65–100%, with the worst qualitative results being 65% for sample 31.

3.14 Mycoplasma pneumonia antibodies (324)

3.14.1 Sample information

Sample 61 originated from a patient with several known respiratory infections in his recent medical history. Sample 62 was donated by a healthy blood donor in the summer months.

3.14.2 Determination of the target values

The mode of the results of all participants was set as the target value for the qualitative test results, while for the semi-quantitative test results, the robust mean of all participants was stipulated as the target value. The corresponding target values, target ranges, test results and pass rates are presented in Table 14.

3.14.3 Overall diagnostic interpretation and commentary on the test results

No evidence of an infection with *M. pneumonia* was detected in sample 62, while in sample 61 both the reference laboratories and most participants detected a pronounced IgG seroreactivity combined with negative test results for specific IgM and IgA antibodies. Consequently, the test results pointed to a past infection with *M. pneumonia*. The overall diagnostic evaluation of the negative sample 62 was 84.4%, while for sample 61 it was 98.2%.

Table 14: Mycoplasma pneumonia antibody detection during the proficiency testing trials 2016

			Sample 61		Sample 62	
			Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**ELISA-IgA+IgM** qual.	N=20	positive	100.0	negative	100.0
	PHA qual./quant. Target value [IU/ml] Target range	N=2/N=8	positive 320.0 (160–640)	100.0 100.0	negative 0.0 (0–39.9)	100.0 100.0
Specific IgG	**ELISA** qual./quant. Target value [IU/ml] Target range	N=106/N=106	positive 27 (17.3–36.7)	75.5 100.0	negative 7.68 (4.92–10.4)	73.6 100.0
	Blot qual.N=8		positive	100.0	negative	100.0
	CLIA qual./quant. Target value [IU/ml] Target range	N=80/N=60	positive 28.4 (28.4–38.6)	96.3 100.0	negative 0.432 (0.276–0.588)	96.3 100.0
	IFT qual./quant. Target value [IU/ml] Target range	N=8/N=8	positive – –	100.0 100.0	negative – –	100.0 100.0
Specific IgM	**ELISA** qual.	N=130	negative	90.8	negative	98.5
	Blot qual.	N=12	negative	100.0	negative	100.0
	CLIA qual.	N=80	negative	90.0	negative	97.5
	IFT qual./quant. Target value [IU/ml] Target range	N=8/N=8	negative – –	100.0 100.0	negative – –	100.0 100.0
Specific IgA	**ELISA** qual.	N=76	negative	92.1	negative	100.0
	Blot qual.	N=10	negative	100.0	negative	100.0
	IFT qual./quant. Target value [IU/ml] Target range	N=4/N=4	negative – –	100.0 100.0	negative – –	100.0 100.0
	Diagnostic	N*=257		98.2		84.4

N=total number of participants
N*=average number of participants

3.15 Coxiella burnetii antibodies (325)

3.15.1 Sample information

Sample 61 was donated by a patient shortly after an acute infection with *C. burnetii*. Sample 62 was donated by a healthy blood donor without evidence of a recent infection.

3.15.2 Determination of the target values

The mode of the results of all participants was set as the target value for the qualitative test results, while the robust mean of all participants was stipulated as the target value of the semi-quantitative test results. The corresponding target values, target ranges, test results and pass rates are shown in Table 15.

3.15.3 Overall diagnostic interpretation and commentary on the test results

Sample 62 tested negative for *C. burnetii*, while sample 61 tested positive. The positive sample 61 had CFT titers of 1280 for phase I and 640 for phase II (median), IgG phase I – IFT titers of 10240 and IgG phase II – IFT titers of 5120 (median), positive IgM test results as well as weakly reactive IgA test results. This indicated an acute infection with *C. burnetii* [6], [7].

The overall diagnostic evaluation of the negative sample 62 was 100% and thus in line with previous years, while the pass rate of positive sample 61 was 88.5%.

3.16 Salmonella antibodies (331)

3.16.1 Sample information

All samples (31, 32, 61 and 62) originated from clinically healthy blood donors.

3.16.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results, while in the case of the semi-quantitative results, the results of the reference laboratories were set as the target value. The corresponding target values, target ranges, test results and pass rates are listed in Table 16.

3.16.3 Overall diagnostic interpretation and commentary on the test results

No evidence of a *Salmonella* infection was detected in samples 31, 32 and 61. In sample 62 borderline results for Salmonella Ag. Gr A, Salmonella typhim. and (O)H-Ag Gr. B antibodies against the tested pathogen were detected using WIDAL tests. The borderline results were also detected for the specific polyvalent ELISA.

Table 15: Coxiella burnetii antibody detection during the proficiency testing trials 2016

		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**CFT Phase I** qual./quant. N=12/N=18 Target value [IU/ml] Target range	positive 1280 (320–5120)	83.3 88.9	negative 0 (0–19.9)	100 100
Specific IgG	**ELISA Phase I** qual. N=62	positive	96.8	negative	100
	ELISA Phase II qual. N=10	positive	80	negative	100
	IFT Phase I qual./quant. N=76/N=84 Target value [IU/ml] Target range	positive 10240 (2560–40960)	100 73.8	negative 0 (0–79.9)	100 97.5
	IFT Phase II qual./quant. N=78/N=82 Target value [IU/ml] Target range	positive 5120 (1280–20480)	97.4 75.6	negative 0 (0–79.9)	97.4 97.4
Specific IgM	**ELISA** qual. N=10	positive	100	negative	100
	IFT qual./quant. N=74/N=80 Target value [IU/ml] Target range	positive 160 (40–640)	75 60	negative 0 (0–19.9)	97.3 97.4
Specific IgA	**ELISA** qual. N=50	bl./positive	96	negative	100
	IFT qual./quant. N=16/N=20 Target value [IU/ml] Target range	positive 160 (40–640)	100 100	negative 0.0 (0–19.9)	100 100
	Diagnostic N*=89		88.5		100

N=total number of participants
N*=average number of participants
bl.=borderline

Table 16: Salmonella antibody detection during the proficiency testing trials 2016

		Sample 31		Sample 32		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
S. Typhi O-Ag	**WIDAL** qual./quant. N=94/N=96 Target value [IU/ml] Target range	negative – (0–99)	96.0 100.0	negative – (0–99)	96.0 96.0	negative – (0–99)	100.0 100.0	negative – (0–99)	95.5 95.7
S. Typhi (O)H-Ag	**WIDAL** qual./quant. N=96/N=98 Target value [IU/ml] Target range	negative – (0–99)	92.3 96.0	negative – (0–99)	96.2 100	negative – (0–99)	100.0 100	negative – (0–99)	90.9 91.7
S. Enterit. (O)H-Ag	**WIDAL** qual./quant. N=60/N=60 Target value [IU/ml] Target range	negative – (0–99)	92.9 92.3	negative – (0–99)	92.9 92.3	negative – (0–99)	100 100	negative – (0–99)	100 100
S. O-Ag, Gr. A	**WIDAL** qual./quant. N=62/N=76 Target value [IU/ml] Target range	negative – (0–99)	100 100	negative – (0–99)	100 100	negative – (0–99)	100 100	negative – (0–99)	100 100
S. O-Ag, Gr. B	**WIDAL** qual./quant. N=72/N=84 Target value [IU/ml] Target range	negative – (0–99)	100 94.7	negative – (0–99)	100 94.7	negative – (0–99)	100 100	negative/bl. – (0–100)	100 95.7
S. parat. B (O)H-Ag	**WIDAL** qual./quant. N=92/N=96 Target value [IU/ml] Target range	negative – (0–99)	91.3 95.8	negative – (0–99)	95.7 100	negative – (0–99)	95.7 95.8	negative – (0–99)	100 100
S. typhim. (O)H-Ag Gr. B	**WIDAL** qual./quant. N=56/N=54 Target value [IU/ml] Target range	negative – (0–99)	100 100	negative – (0–99)	100 100	negative – (0–99)	93.3 100	negative/bl. – (0–100)	86.7 93.3
S. O-Ag, Gr. C	**WIDAL** qual./quant. N=60/N=60 Target value [IU/ml] Target range	negative – (0–99)	100 100	negative – (0–99)	100 100	negative – (0–99)	100 100	negative – (0–99)	82.4 77.8
ELISA	**Polyvalent** N=20	negative	80	negative	80	negative	100	negative/bl.	80
	IgA N=10	negative	100	negative	66.7	negative	100	negative	100
	Diagnostic N*=83		95.4		95.4		98.7		92.3

N=total number of participants
N*=average number of participants
bl.=borderline

Table 17: Borrelia burgdorferi antibody detection during the proficiency testing trials 2016

		Sample 31		Sample 32		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Specific polyvalent test system	**PHA** qual./quant. N=24/N=26	negative	100	positive	100	negative	100	positive	100
	Target value [IU/ml]	–		5120		–		640	
	Target range	(0–79.9)	100	(1280–20480)	100	(0–79.9)	100	(320–1280)	100
	ELISA qual. N=12	negative	100	positive	100	negative	100	positive	100
	Line immunoblot qual. N=22	negative	83.3	positive	100	negative	75	positive	100
Specific IgG	**ELISA** qual. N=168	negative	97.3	positive	100	negative	100	positive	100
	Blot qual. N=184	negative	97.8	positive	100	negative	91.5	positive	89.4
	CLIA qual. N=24	negative	100	positive	100	negative	100	positive	100
	IFT qual./quant. N=42/N=36	negative	81.8	positive	90.9	negative	100	bl./pos.	100
	Target value [IU/ml]	–		1280		–		160	
	Target range	(0–39.9)	72.7	(320–5120)	63.6	(0–39.9)	100	(40–640)	100
Specific IgM	**ELISA** qual. N=162	negative	95.1	negative	82.9	negative	100	negative	100
	Blot qual. N=200	negative	96	negative	96	negative	94	negative	96
	CLIA qual. N=18	negative	100	negative	100	negative	75	negative	75
	IFT qual./quant. N=34/N=34	negative	88.9	negative	77.8	negative	100	negative	100
	Target value [IU/ml]	–		–		–		–	
	Target range	(0–19.9)	100	(0–19.9)	87.5	(0–19.9)	100	(0–19.9)	100
	Diagnostic N*=385		99.7		97.7		98.2		90.2

N=total number of participants
N*=average number of participants
bl.=borderline

These results pointed to a possible infection or no infection. The pass rates for the Widal test system were between 91.5 and 100%, while for ELISA they were between 80 and 100%. The overall diagnostic pass rates were between 92.3 and 100%, showing better results than in previous years.

3.17 Borrelia burgdorferi antibodies (332)

3.17.1 Sample information

Samples 31, 61 and 62 originated from a healthy blood donor without evidence of a tick bite or clinical Lyme borreliosis in his medical history. Sample 32 was donated by a patient with recent neuroborreliosis (CSF pleocytosis, positive borrelia-specific antibody index).

3.17.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results, while in the case of the semi-quantitative test results, the mode of the results of all participants was set as the target value. The corresponding target values, target ranges, evaluation and pass rates are listed in Table 17.

3.17.3 Overall diagnostic interpretation and commentary on the test results

No evidence of an infection with *B. burgdorferi* was detected in samples 31 and 61, while pathogens were detected in samples 32 and 62, indicating an infection with *B. burgdorferi*.
Sample 62 showed isolated reactivity for specific IgG antibodies against *B. burgdorferi* in ELISA, immunoblot and CLIA, with borderline test results in IFT and negative test results for specific IgM antibodies in all tests systems.
Sample 32 showed positive test results for specific IgG antibodies and negative test results for specific IgM antibodies against *B. burgdorferi*. Consequently, the test results of samples 32 and 62 point to an infection with *B. burgdorferi*. The distribution of immunoblot bands reported for the positive sample 62 is depicted below in Figure 4. Figure 5 shows the distribution of the reported immunoblot bands as obtained by the different manufacturers' assays [6], [7]. The overall diagnostic evaluation of the negative samples 31 and 61 was 98.2–99.7%, while it was 90.2–97.7% for the positive samples 32 and 62.

3.18 Helicobacter pylori antibodies (334)

3.18.1 Sample information

Samples 31 and 62 originated from clinically healthy blood donors without evidence of an infection.
Samples 32 and 61 were taken from a helicobacter-positive patient after finishing eradication therapy.

3.18.2 Determination of the target values

The mode of the results of the reference laboratories was set as the target value for the qualitative test results. The corresponding target values, target ranges, test results and pass rates are shown in Table 18.

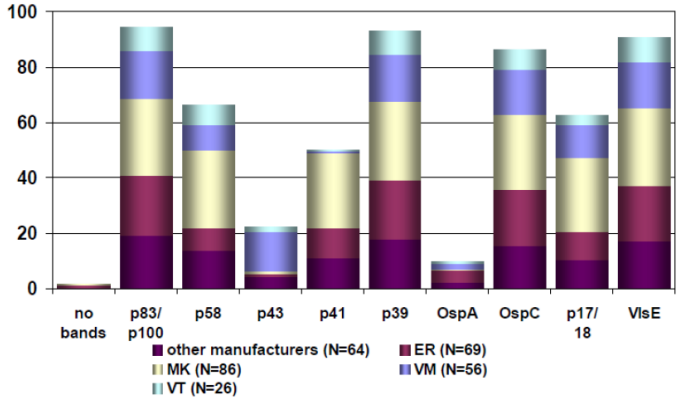

Figure 4: The distribution of the immunoblot bands reported for the positive sample 62 [7], [8]; recovery rate (%) of the submitted IgG immunoblot bands for sample 332/32 (May 2016), participants N=301

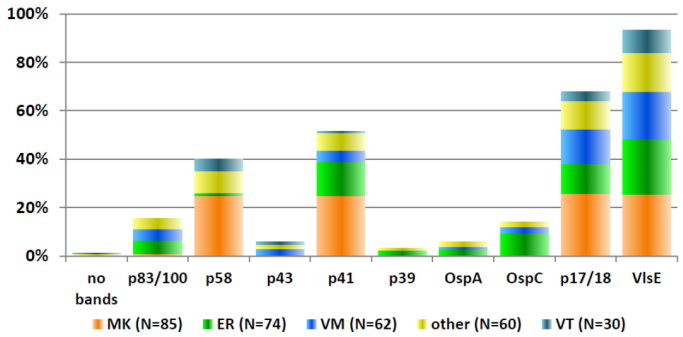

Figure 5: Distribution of the reported immunoblot bands as obtained by the different manufacturers' assays [7], [8]; recovery rate (%) of the reported IgG immunoblot bands for sample 332/62 (Nov. 2016); participants N=311

Table 18: Helicobacter pylori antibody detection during the proficiency testing trials 2016

		Sample 31		Sample 32		Sample 61		Sample 62	
		Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]	Test result	Pass rate [%]
Specific IgG	**ELISA** qual./quant. N=174/N=130 Target value [IU/ml] Target range	negative 3.68 (2.36–5)	95.6 100	positive 64.8 (41.5–88.1)	95.6 100	positive 35.4 (22.7–48.1)	92.9 100	negative 1.57 (1–2.14)	100 100
	Blot qual. N=34	negative	100	positive	100	positive	100	negative	100
Specific IgA	**ELISA** qual. N=108	negative	93.3	positive	86.7	bl./pos.	45.8	negative	100
	Blot qual. N=24	negative	100	positive	100	bl./pos.	60	negative	100
	Diagnostic N*=181		98.9		94.0		92.2		98.9

N=total number of participants
N*=average number of participants
bl.=borderline

3.18.3 Overall diagnostic interpretation and commentary on the test results

No evidence of an infection with *H. pylori* was detected in samples 31 and 62. In sample 61, borderline results for IgA and positive results for IgG antibodies against the tested pathogen were detected, and in sample 32, positive results for IgA and IgG antibodies were detected, indicating a *Helicobacter* infection in both samples 32 and 61. Both expert laboratories and participants interpreted this constellation of results as pointing to a possible infection or colonization with *H. pylori*. In sample 61, the qualitative results for IgA antibodies for ELISA were 45.8% and for immunoblot they were 60%. The overall diagnostic evaluation of the negative samples 31 and 62 was 98.9%, while for the positive samples 32 and 61 it was 92.2–94.0%.

4 Discussion and conclusion

EQA is becoming increasingly important as a basis for developing strategies to improve diagnostic processes. The results of the EQA presented in this report generally show moderate to very good diagnostic quality. The average overall pass rate of the above-mentioned serological testing samples was over 90% in both proficiency testing trials. However, some special comments on serology need to be made:

In the case of the *Treponema pallidum* serology (311), the overall pass rate in the positive sample 61 for all test methods was 79.9%, indicating an unsatisfactory result. The lowest pass rate of 52.9% was seen in the quantitative detection of IgG antibodies by FTA-ABS. In the positive sample 31, the lowest pass rate of 58.3% was observed for the quantitative detection of IgG antibodies by FTA-ABS. In terms of the qualitative results of the negative sample 32, the lowest pass rate (57.1%) was observed for the ELISA test. These results are striking and could be problematic in the context of blood donor screening or screening during pregnancy. Regarding *Chlamydia trachomatis* serology (312), the overall pass rate was between 33.3% and 100% for all tests in sample 61. A pass rate of 33.3% was observed for the qualitative detection of IgA antibodies by immunoblot. With respect to the *Coxiella burnetii* serology (325), in the diagnostic assessment of the positive sample 61, the overall pass rate was between 73.8% and 100% for all test methods with the lowest pass rates for IgG or IgM analysis by IFT. In the case of the *Borrelia burgdorferi* serology (332), an overall pass rate of 97.7% was recorded for all test methods in the diagnostic assessment of the positive sample 32. The lowest pass rate of 63.6% was observed in the quantitative detection of IgG antibodies for IFT. In the *Helicobacter pylori* serology (334), the overall pass rate for sample 61 was between 45.8% and 100%. However, in terms of the qualitative result, the pass rate was 45.5% for ELISA and 60% for immunoblot, but only with respect to IgA antibody detection.

The above-mentioned findings and comments show the need for further improvement in certain diagnostic procedures in order to achieve more standardized and higher quality testing in Germany. This would ensure even better diagnostic test results in the routine clinical setting.

Notes

Competing interests

The authors declare that they have no competing interests.

References

1. Wellinghausen N, Abele-Horn M, Donoso Mantke O, Enders M, Fingerle V, Gärtner B, Hagedorn J, Rabenau HF, Reiter-Owona I, Tintelnot K, Weig M, Zeichhardt H, Hunfeld KP. MiQ 35a–c Qualitätsstandards in der mikrobiologisch-infektiologischen Diagnostik: Infektionsimmunologische Methoden Teil 1–3. München, Jena: Urban & Fischer; 2016.
2. Mai M, Müller I, Hunfeld KP. Qualität bakteriologisch-infektionsserologischer Verfahren in Deutschland: Auswertung der infektionsserologischen Ringversuche 2011 – Beitrag der Qualitätssicherungskommission der Deutschen Gesellschaft für Hygiene und Mikrobiologie (DGHM). GMS Z Forder Qualitatssich Med Lab. 2014;5:Doc04. DOI: 10.3205/lab000014
3. Bundesärztekammer (German Medical Association); Instand e.V. Guidelines of the German Medical Association on quality assurance in medical laboratory testing. GMS Z Forder Qualitatssich Med Lab. 2015;6:Doc03. DOI: 10.3205/lab000018
4. Müller I, Besier S, Hintereder G, Brade V, Hunfeld KP. Zur Qualität der bakteriologischen Infektionsserologie in Deutschland: eine Metaanalyse der infektionsserologischen Ringversuche des Jahres 2006 – Beitrag der Qualitätssicherungskommission der DGHM. GMS Z Forder Qualitatssich Med Lab. 2009;1:Doc04. DOI: 10.3205/lab000004
5. Müller I, Hunfeld KP. Manual May 2016 Testing Information Bacteriology Infection Serology DAkkS. D-EP-15027-02-00 – May 2016. Düsseldorf: INSTAND e.V.; 2016 [accessed 2020 Jan 20]. Available from: https://www.instand-ev.de/uploads/tx_nfextinstandpdf/Begleitheft_Mai_eng_01.pdf
6. Müller I, Hunfeld KP. Report on INSTAND e.V. EQAS 310-334 – May 2016. Düsseldorf: INSTAND e.V.; 2016 [accessed 2020 Jan 20]. Available from: https://www.instand-ev.de/uploads/tx_nfextinstandpdf/RV_310-334_Mai_en_01.pdf
7. Müller I, Hunfeld KP. Report on INSTAND e.V. EQAS 310-334 – November 2016. Düsseldorf: INSTAND eV; 2016 [accessed 2020 Jan 20]. Available from: https://www.instand-ev.de/System/rv-files/RV_310-334_Nov_en.pdf

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