

REF			SYSTEM
08814864119	08814864500	200	cobas e 411 cobas e 601 cobas e 602

English

System information

For **cobas e 411** analyzer: test number 2090

For **cobas e 601** and **cobas e 602** analyzers: Application Code Number 547

Intended use

Immunoassay for the in vitro qualitative determination of hepatitis B surface antigen (HBsAg) in human serum and plasma. This assay is indicated as an aid in the diagnosis of infection with HBV. This assay is also indicated as a donor screening test to detect HBV in serum or plasma specimens from individual human blood donors. It may also be used in testing serum or plasma specimens to screen individual organ donors when specimens are obtained while the donor's heart is still beating.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Note: Please note that the catalogue number appearing on the package insert retains only the first 8 digits of the licensed 11-digit Catalogue Number: 08814864190 for the HBsAg II assay. The last 3 digits -190 have been replaced by -119 for logistic purposes.

Summary

The hepatitis B surface antigen (HBsAg), a polypeptide of varying size, is a component of the external envelope of the hepatitis B virus (HBV) particle.^{2,3} The blood of persons infected with HBV contains, in addition to intact infectious HBV particles, an excess of smaller non-infectious 'empty' envelope particles, or filaments, formed from HBsAg.⁴

The HBsAg determinant 'a', against which the immune response is mainly directed, is common to all HBsAg particles. Within this 'a' determinant several HBsAg subtype determinants could be defined as d, y, w1-w4, r and q.⁵ Under selective pressure (caused by antiviral therapy or by the action of the immune system itself) the virus can express many different viable HBsAg mutants (so-called 'escape mutants'). Some mutants might lead to a loss of detection in commercially available HBsAg assays.^{3,6}

The Elecsys HBsAg II assay was specifically developed to detect a multitude of these mutants. HBsAg is the first immunologic marker of HBV infection and is generally present some days or weeks before clinical symptoms begin to appear. Detection of HBsAg in human serum or plasma indicates the presence of acute or chronic HBV infection.⁷

HBsAg assays are used within the scope of diagnostic procedures to identify persons infected with HBV and prevent the transmission of the virus by blood and blood products.^{4,8}

HBsAg assays can also be used to monitor the course of the disease and the efficacy of therapy in persons with acute or chronic HBV infections.⁹

In addition, HBsAg assays are recommended as part of prenatal care, in order to initiate suitable measures for preventing as far as possible the transmission of an HBV infection to the newborn child.¹⁰

The Elecsys HBsAg II assay uses monoclonal and polyclonal anti-HBs antibodies (mouse and sheep) to detect HBsAg.

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 50 µL of sample, two biotinylated monoclonal anti-HBsAg antibodies, and a mixture of monoclonal anti-HBsAg antibody and polyclonal anti-HBsAg antibodies labeled with a ruthenium complex^{a)} form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.

- Results are determined automatically by the software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by calibration.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex (Ru(bpy)₃²⁺)

Reagents - working solutions

The reagent rackpack (M, R1, R2) is labeled as HBSAGII2.

- M Streptavidin-coated microparticles (transparent cap), 1 bottle, 12 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Anti-HBsAg-Ab-biotin (gray cap), 1 bottle, 14 mL: Two biotinylated monoclonal anti-HBsAg antibodies (mouse) > 0.5 mg/L; phosphate buffer 100 mmol/L, pH 7.5; preservative.
- R2 Anti-HBsAg-Ab-Ru(bpy)₃²⁺ (black cap), 1 bottle, 12 mL: Monoclonal anti-HBsAg antibody (mouse), polyclonal anti-HBsAg antibodies (sheep) labeled with ruthenium complex > 1.5 mg/L; phosphate buffer 100 mmol/L, pH 8.0; preservative.

HBSAGII2 Cal1 Negative calibrator 1 (white cap), 1 bottle of 1.3 mL: Human serum; preservative.

HBSAGII2 Cal2 Positive calibrator 2 (black cap), 1 bottle of 1.3 mL: HBsAg approximately 0.5 IU/mL in human serum; preservative.

Precautions and warnings

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

2-methyl-2H-isothiazol-3-one hydrochloride

EUH 208 May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.

All human material should be considered potentially infectious.

The calibrators have been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg (HBSAGII2 Cal1 only) and antibodies to HCV and HIV.

The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

The serum containing HBsAg (HBSAGII2 Cal2) was inactivated using β-propiolactone and UV-radiation.

However, as no inactivation or testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.^{11,12}

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

The reagents in the kit are ready-for-use and are supplied in bottles compatible with the system.

cobas e 411 analyzer: The calibrators should only be left on the analyzer during calibration at 20-25 °C. After use, close the bottles as soon as possible and store upright at 2-8 °C.

Due to possible evaporation effects, not more than 5 calibration procedures per calibrator bottle set should be performed.

cobas e 601 and **cobas e 602** analyzers: Unless the entire volume is necessary for calibration on the analyzers, transfer aliquots of the

Elecsys HBsAg II



ready-for-use calibrators into empty snap-cap bottles (CalSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots at 2-8 °C for later use.

Perform **only one** calibration procedure per aliquot.

All information required for correct operation is read in from the respective reagent barcodes.

Please note: Both the vial labels, and the additional labels (if available) contain 2 different barcodes. The barcode between the yellow markers is for **cobas** 8000 systems only. If using a **cobas** 8000 system, please turn the vial cap 180° into the correct position so the barcode can be read by the system. Place the vial on the instrument as usual.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the reagent rackpack	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	8 weeks
on cobas e 601 and cobas e 602	4 weeks
on cobas e 411	4 weeks
on cobas e 411	6 weeks if stored alternately in the refrigerator and on the analyzers (up to 42 hours at 20-25 °C)

Stability of the calibrators	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	8 weeks
on cobas e 411 at 20-25 °C	up to 5 hours
on cobas e 601 and cobas e 602 at 20-25 °C	use only once

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the snap-cap.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin, Na-heparin, K₂-EDTA, K₃-EDTA, ACD, CPD, CP2D, CPDA and Na-citrate plasma.

Plasma tubes containing separating gel can be used.

Criterion: Correct assignment of negative and positive samples.

Stable for 7 days at 20-25 °C, 14 days at 2-8 °C, 6 months at -20 °C (± 5 °C). The samples may be frozen 6 times.

The sample types listed were tested with a selection of sample collection tubes or systems that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in

primary tubes (sample collection systems), follow the instructions of the tube/collection system manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples and calibrators on the analyzers should be analyzed/measured within 2 hours.

The performance of the Elecsys HBsAg II assay has not been established with cadaveric samples or body fluids other than serum and plasma.

Materials provided

See "Reagents – working solutions" section for reagents.

- 2 x 6 bottle labels

Materials required (but not provided)

- [REF](#) 04687876190, PreciControl HBsAg II, for 16 x 1.3 mL

- [REF](#) 11820648122, HBsAg Confirmatory Test, 2 x 1.0 mL each of confirmatory and control reagent

- [REF](#) 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles

- General laboratory equipment

- cobas e** analyzer

Additional materials for the **cobas e** 411 analyzer:

- [REF](#) 11662988122, ProCell, 6 x 380 mL system buffer

- [REF](#) 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution

- [REF](#) 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive

- [REF](#) 11933159001, Adapter for SysClean

- [REF](#) 11706802001, AssayCup, 60 x 60 reaction cups

- [REF](#) 11706799001, AssayTip, 30 x 120 pipette tips

- [REF](#) 11800507001, Clean-Liner

Additional materials for **cobas e** 601 and **cobas e** 602 analyzers:

- [REF](#) 04880340190, ProCell M, 2 x 2 L system buffer

- [REF](#) 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution

- [REF](#) 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use

- [REF](#) 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change

- [REF](#) 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags

- [REF](#) 03023150001, WasteLiner, waste bags

- [REF](#) 03027651001, SysClean Adapter M

Additional materials for all analyzers:

- [REF](#) 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Place the calibrators in the sample zone.

All the information necessary for calibrating the assay is automatically read into the analyzer.

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After calibration has been performed, store the calibrators at 2-8 °C or discard (**cobas e 601** and **cobas e 602** analyzers).

Calibration

Traceability: This method has been standardized against the NIBSC standard (code number: 00/588; WHO Second International Standard for HBsAg, subtype adw2, genotype A; IU/mL).

The following reference materials from the Paul-Ehrlich-Institute, Langen (Germany), were also measured (U/mL) and compared with the WHO standard:

PEI Standard AD (information sheet 1985, subtype AD; 1000 U/mL; inactivated)

PEI Standard AY (information sheet 1985, subtype AY; 1000 U/mL; inactivated)

(1 IU/mL WHO Standard corresponds to 0.34 U/mL PEI Standard AY and 1 IU/mL WHO Standard corresponds to 0.44 U/mL PEI Standard AD)

Calibration frequency:

Calibration must be performed once per reagent lot using HBSAGII2 Cal1, HBSAGII2 Cal2 and fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 1 month (28 days) when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings outside the defined limits

Range for the electrochemiluminescence signals (counts) for the calibrators:

Negative calibrator (HBSAGII2 Cal1): 600-1700

Positive calibrator (HBSAGII2 Cal2): 3000-11000

Quality control

For quality control, use PreciControl HBsAg II.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Note:

For technical reasons re-assigned target values valid only for a specific reagent and control lot combination must be entered manually on all analyzers (except for the **cobas e 602** analyzer). Therefore always refer to the value sheet included in the reagent kit or PreciControl kit to make sure that the correct target values are used.

When a new reagent or control lot is used, the analyzer will use the original values encoded in the control barcodes.

Calculation

The analyzer automatically calculates the cutoff based on the measurement of HBSAGII2 Cal1 and HBSAGII2 Cal2.

The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index (signal sample/cutoff).

Interpretation of the results

Samples with a cutoff index < 0.90 are non-reactive in the Elecsys HBsAg II assay. These samples are considered negative for HBsAg and do not need further testing.

Samples having a cutoff index in the range ≥ 0.90 to < 1.0 are considered borderline in the Elecsys HBsAg II assay.

Samples with a cutoff index ≥ 1.0 are considered reactive.

All initially reactive or borderline samples should be redetermined in duplicate using the Elecsys HBsAg II assay. If cutoff index values < 0.90 are found in both cases, the sample is considered negative for HBsAg. Initially reactive or borderline samples giving cutoff index values of ≥ 0.90 in either of the redeterminations are considered repeatedly reactive.

Repeatedly reactive samples must be investigated using an independent neutralization test (Elecsys HBsAg Confirmatory Test).

Samples confirmed by neutralization with human anti-HBs are regarded as positive for HBsAg.

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 684 μmol/L or ≤ 40 mg/dL
Hemoglobin	≤ 1.24 mmol/L or ≤ 2000 mg/dL
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 6210 IU/mL
IgG	≤ 3817 mg/dL
IgA	≤ 3250 mg/dL
IgM	≤ 3678 mg/dL

Criterion for all substances but biotin: Correct assignment of negative and positive samples.

Criterion for biotin: Correct assignment of negative and positive samples. Samples with a COI (cutoff index) < 0.7: recovery < COI + 0.3; samples with a COI ≥ 0.7: recovery 80-140 %.

No false negative result due to high-dose hook effect was found with the Elecsys HBsAg II assay up to a concentration of 1.5 million IU/mL.

No significant interfering effects of 21 commonly used therapeutic drugs could be detected.

According to the present state of knowledge, it can be assumed that available assays for the detection of HBsAg cannot identify all infected blood samples or persons. A negative test result does not exclude with certainty a possible exposure to or an infection with the hepatitis B virus. Negative test results obtained for persons with a past exposure may be caused by an antigen concentration below the detection limit of this assay or the lack of reactivity of the antigens to the antibodies used in this assay.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

cobas e 601 and cobas e 602 analyzers:

Make sure that in the Special Wash List (Screen → Utility → Special Wash → Immune) the Elecsys HBsAg II assay is combined with all assays performed on the analyzer - including the Elecsys HBsAg II assay itself:

From test	Step	To test	Step 0	Step 1	Step 2
Elecsys HBsAg II	1	Elecsys HBsAg II	x	x	x
Elecsys HBsAg II	1	each other assay	x	x	x

If new tests are installed make sure that the Special Wash List is updated accordingly.

For the Elecsys Anti-HBs II assay make sure that "Step 1" and "Step 2" are activated:

From test	Step	To test	Step 0	Step 1	Step 2
Elecsys Anti-HBs II	1	Elecsys HBsAg II	-	x	x

The described additions to the Special Wash List have to be entered manually. Please refer to the operator's manual.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Limits and ranges

Detection limit

In order to determine the sensitivity, the HBsAg concentration which corresponds to the measuring signal of the cutoff value was read off the standard curves of serial dilutions of HBsAg standards (ad and ay) in human HBV-negative serum.

Sample	Paul-Ehrlich-Institute standards				WHO standard 00/588	
	Subtype ad, 1985		Subtype ay, 1985		Subtype ad	
	COI	U/mL	COI	U/mL	COI	IU/mL
1	88.4	1.999	566	10.0	39.4	2.00
2	44.7	1.005	289	5.04	19.9	0.998
3	3.09	0.047	12.7	0.200	1.64	0.052
4	0.396	0.000	0.421	0.000	0.409	0.000
Cutoff sensitivity (cutoff = 0.9)	≤ 0.04 U/mL		≤ 0.04 U/mL		≤ 0.1 IU/mL	

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

cobas e 411 analyzer					
Sample	Mean COI	Repeatability ^{b)}		Intermediate precision ^{c)}	
		SD COI	CV %	SD COI	CV %
HS ^{d)} , negative	0.267	0.033	12.5	0.060	22.5
HS, high negative	0.695	0.035	5.0	0.066	9.6
HS, weakly positive	1.00	0.039	3.9	0.076	7.6
HS, positive	7.74	0.147	1.9	0.432	5.6
PreciControl HBsAg II 1	0.454	0.045	9.9	0.066	14.4
PreciControl HBsAg II 2	3.14	0.060	1.9	0.206	6.6

b) Repeatability = within-run precision

c) Intermediate precision = between-run precision

d) HS = human serum

cobas e 601 and cobas e 602 analyzers					
Sample	Mean COI	Repeatability		Intermediate precision	
		SD COI	CV %	SD COI	CV %
HS ^{d)} , negative	0.235	0.024	10.3	0.043	18.2
HS, high negative	0.899	0.040	4.5	0.077	8.6
HS, weakly positive	1.01	0.035	3.4	0.082	8.1
HS, positive	8.00	0.253	3.2	0.589	7.4
PreciControl HBsAg II 1	0.353	0.029	8.2	0.052	14.6
PreciControl HBsAg II 2	3.01	0.085	2.8	0.245	8.1

Analytical specificity

1596 samples containing potentially interfering substances were tested with the Elecsys HBsAg II assay comprising specimens:

- containing antibodies against HAV, HCV, HIV, HTLV, CMV, EBV, HSV, Rubella, Parvo virus, VZV, Toxoplasma gondii, Treponema pallidum, Borrelia, Listeriosis
- containing autoantibodies (ANA, SLE), elevated titers of rheumatoid factor or HAMA antibodies
- positive for Mumps, Measles, Malaria
- after vaccination against HBV and influenza
- from patients with monoclonal gammopathy and multiple myeloma/lymphoma, patients undergoing dialysis or patients suffering from alcoholic liver disease
- from pregnant women

No false positive result was found. 14 samples were found to be positive for HBsAg (1 out of each group of the HAV, HIV, HTLV and EBV antibody positive patients; 1 from a patient undergoing dialysis and 9 from pregnant women). 2 samples (1 after HBV vaccination and 1 with elevated RF) were initially positive, but negative after performing a second measurement. The overall specificity was 100 % (lower confidence limit 95 %, one-sided: 99.81 %).

Clinical sensitivity

A total of 1025 selected HBsAg confirmed positive samples in various stages of the disease were tested with the Elecsys HBsAg II assay. 1024 samples were correctly identified (1 sample was repeatedly negative (COI 0.81-0.88), positively neutralized with the Elecsys HBsAg Confirmatory Test; negative in a 3rd HBsAg assay, anti-HBs negative, anti-HBe negative, HBeAg negative, anti-HBc positive). The sensitivity in that group of 1025 samples is 99.9 %.

A total of 156 genotyped samples (genotype A (30), B (8), C (11), C/E (1), D (68), E (17), F (17), G (3), not assigned (1)) and all known HBsAg subtypes (CNTS "Centre National de la Transfusion Sanguine", n = 9 subtype panels) were tested with the Elecsys HBsAg II assay. All of them were positive except for 6 samples (2 of genotype A, 1 of genotype D and 3 of genotype E) with negative or low HBV-DNA (also negative in other HBsAg tests). A total of 115 samples comprising different HBsAg mutations were tested with the Elecsys HBsAg II assay and compared to 3 registered HBsAg assays.

Mutant panel	Elecsys HBsAg II tested/positive
Native mutant panel 1 (strains displaying amino acid substitutions either linked to vaccine resistance, resistance to therapy with human HB immunoglobulin or impaired HBsAg reactivity)	41/40 ^{e)}
Native mutant panel 2 (strains displaying other amino acid changes)	24/24
Native mutant panel 3	19/17 ^{f)}
Recombinant mutant panel	31/31
Total	115/112

e) sample (mutation G145R) negative in all assays (COI 0.1-0.8); all measurements were performed in 1:40 dilution (FCS: fetal calf serum)

f) samples (mutation M133L/M143T/G145R and mutation T45S/I49R/113T/114/1186P, respectively) negative in all assays tested; 1st mutation tested in 3 assays (COI 0.03-0.76), 2nd mutation tested in 4 assays (COI 0.03-0.78)

For 8 performance panels (Boston Biomedica, Inc.) the Elecsys HBsAg II assay shows a very good concordance with the data given in the respective product information (140 positives out of 150 samples tested). All positive assigned samples were positive with the Elecsys HBsAg II assay, resulting in a 100 % sensitivity.

Clinical specificity

The specificity of the Elecsys HBsAg II assay in a group of 6360 blood donors was found to be as follows: initially reactive (IR) specificity 99.91 %; repeatedly reactive (RR) specificity 99.98 %.

Elecsys HBsAg II

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In the group of the 3593 daily routine samples (hospitalized patients, outpatients, pre-surgery, health care workers and anonymous testing), the specificity (IR and RR) was 99.88 %.

Group	Number	Initially reactive	Repeatedly reactive	Confirmed positive
Blood donors	6360	8	3	2
Hospitalized patients	3593	181	176 ^{g)}	122 ^{h)}

g) 5 samples could not be repeated due to insufficient sample volume

h) 55 samples could not be neutralized due to insufficient sample volume; 1 sample was negative with the Elecsys HBsAg II assay

Seroconversion panels

Seroconversion sensitivity of the Elecsys HBsAg II assay has been shown by testing 56 commercial seroconversion panels in comparison to registered HBsAg assays. In all panels the Elecsys HBsAg II assay shows detection of seroconversion equal to or earlier than other HBsAg assays.

References

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- US Preventative Services Task Force. Screening for hepatitis B virus infection in pregnancy: US Preventative Services Task Force Reaffirmation Recommendation Statement. Ann Int Med 2009;150:569-873.
- Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.
- Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog. Roche.com for definition of symbols used):

CONTENT Contents of kit

SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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