Elecsys Syphilis

cobas®

Materials provided

REF			IVD	Rx only	SYSTEM
09015051162	09015051502	20 x 300			**cobas pro** serology solution

- 2 x 2 empty labeled snap-cap vials

For reagents, refer to the "Reagents" section.

Materials required (but not provided)

REF	Description
06923364162	PreciControl Syphilis, 4 x 2.0 mL
09366903190	PreciControl Release Syphilis, 6 x 2.0 mL
	General laboratory equipment
	Distilled or deionized water
	The **cobas pro** serology solution is a combination of the **cobas pro** serology controller, **cobas pro** integrated solutions (**cobas** e 801 analytical units only), and applicable licensed or cleared donor screening assays.

Additional materials for **cobas** e 801 analytical unit:

REF	Description
06908799190	ProCell II M, 2 x 2 L system solution
04880293190	CleanCell M, 2 x 2 L measuring cell cleaning solution
07485409001	Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
06908853190	PreClean II M, 2 x 2 L wash solution
05694302001	Assay Tip / Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
07485425001	Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution / Elecsys SysClean for Liquid Flow Cleaning Detection Unit
07485433001	PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution / Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
11298500160	ISE Cleaning Solution / Elecsys SysClean, 5 x 100 mL system cleaning solution

For use in the USA only

System information

Short name	ACN (application code number)
SYPHB	10503
SYPHBE (embedded application)	11503
SYPHBR (for use with **cobas** e flow)	12503

Intended use

Elecsys Syphilis is an in vitro immunoassay for the qualitative detection of total antibodies (IgG and IgM) to *Treponema pallidum* in human serum and plasma. Elecsys Syphilis is intended to screen individual human donors, including volunteer donors of whole blood, blood components and source plasma. This test is also intended to be used to screen organ, tissue and cell donors, when donor samples are obtained while the donor's heart is still beating.

It is not intended for use on cord blood specimens.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use with the **cobas pro** serology solution equipped with a **cobas** e 801 analytical unit.

Summary

Syphilis is caused by the intracellular Gram-negative spirochete bacterium *Treponema pallidum* (TP) subspecies pallidum.[1]

Syphilis is mainly transmitted sexually, but also can be transmitted from mother to fetus during pregnancy or birth, or rarely via transfusion of blood or blood products or organ transplant.[2,3] Based on prevalence data from 2009 to 2016, the estimated global prevalence of syphilis in both men and women was 0.5 %, with regional values ranging from 0.1 to 1.6 %, corresponding to 19.9 million syphilis cases.[4] In 2020, WHO estimated 7.1 million new syphilis infections globally.[5] In the US, in 2020, 133,945 cases of all stages of syphilis were reported. Since reaching a historic low in 2000 and 2001, the rate of primary and secondary syphilis has increased almost every year, increasing 6.8 % during 2019-2020.[6] Certain European countries have also seen increases in the rate of infection[6] and large localized outbreaks.[7]

Elecsys Syphilis

Congenital syphilis in the newborn is still common in the developing world, as many women do not receive prenatal care or the care does not include syphilis screening.[8] The estimated global maternal syphilis prevalence in 2016 was 0.69 %, resulting in 661,000 total congenital syphilis cases, including 355,000 adverse birth outcomes and 306,000 non-clinical congenital syphilis cases (infants without clinical signs born to untreated mothers).[9] Septicemia, abortion, or neonatal death can occur, and congenital syphilis is associated with significant morbidity. The World Health Organization recommends all women should be tested at their first prenatal visit and again in the third trimester.[10,11] If they are positive, sexual partners should be evaluated and offered treatment.[12,13] Syphilis infection facilitates HIV infection.[14] In the early stage of infection, the clinical diagnosis of syphilis can be very difficult.[1] Typically, the symptoms start with a painless ulcer at the site of entry to the body (primary syphilis) followed by a widespread rash as the bacteria disseminate (secondary syphilis). A lengthy latent (asymptomatic) period follows. Eventually, tertiary syphilis ensues, characterized by the development of granulomatous dermal lesions, neurosyphilis, and/or cardiovascular syphilis (which can be fatal).

The immune response to *T. pallidum* is the main driver of lesion development.[15] The antibody response is directed not only against antigens specific to *T. pallidum* (treponemal antibodies) but also against antigens that are not specific to *T. pallidum* (non-treponemal antibodies), for example, antigens released during the cellular damage caused by the organism.

Treponemal (and/or nontreponemal) tests are furthermore also used to screen donors of blood, blood components, cells, tissue, and organs when donor samples are obtained while the donor's heart is still beating.[16,17,18,19,20,21,22,23,24]

The Elecsys Syphilis assay uses recombinant antigens representing the lipoproteins TpN17, TpN15 and TpN47 for the detection of anti-*Treponema pallidum* antibodies.

Test principle

Double antigen sandwich principle. Total duration of assay: 18 minutes.

- First incubation: 6 µL of sample, biotinylated TP-specific recombinant antigens and TP-specific recombinant antigens labeled with a ruthenium complex[a)] react to form a sandwich complex.
- Second incubation: After streptavidin-coated microparticles have been added, 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 II 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 ($Ru(bpy)_3^{2+}$)

Reagents

The **cobas** e pack (M, R1, R2) is labeled as SYPHB.

M	Streptavidin-coated microparticles, 1 bottle, 14.1 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
R1	TP-specific recombinant antigens (E. coli)~biotin, 1 bottle, 19.7 mL: Biotinylated TP-specific recombinant antigens (E. coli) 0.7 mg/L; MES[A)] buffer 50 mmol/L, pH 6.5; preservative.
R2	TP-specific recombinant antigens (E. coli)~$Ru(bpy)_3^{2+}$, 1 bottle, 19.7 mL: TP-specific recombinant antigens (E. coli) labeled with ruthenium complex 0.7 mg/L; MES buffer 50 mmol/L, pH 6.5; preservative.
SYPHB Cal1	Non-reactive calibrator 1 (lyophilized), 2 vials each for 1.0 mL: Human serum, non-reactive for anti-TP antibodies; preservative.
SYPHB Cal2	Reactive calibrator 2 (lyophilized), 2 vials each for 1.0 mL: Human serum, reactive for anti-TP antibodies; preservative.

A) MES = 2-morpholinoethane sulfonic acid

Warnings and precautions

For in vitro diagnostic use.

This test is not intended for use as an aid in diagnosis of syphilis infection.

Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste

Warning: Handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards

Apply all relevant local disposal regulations to determine safe disposal.

The Safety Data Sheet is available for professional users on request.

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

Elecsys Syphilis

Warning

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P261	Avoid breathing mist or vapours.
P273	Avoid release to the environment.
P280	Wear protective gloves.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Hazardous components:

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

Product safety labeling follows EU GHS guidance.

Contact phone: +1-866-744-6397

All human material should be considered potentially infectious.

The calibrators (SYPHB Cal1 and SYPHB Cal2) have been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.

The testing methods use assays that have been approved or cleared by the FDA or that are in compliance with the legal rules of the European Union (IVDR 2017/746/EU, IVDD 98/79/EC, Annex II, List A).

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 donor specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[25,26]

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

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the **cobas** e pack **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the cobas e pack:

unopened at 2-8 °C	up to the stated expiration date
on the **cobas** e 801 analytical unit	16 weeks

Stability of the calibrators:

unopened at 2-8 °C	up to the stated expiration date
reconstituted at 2-8 °C	3 days
on the **cobas** e 801 analytical unit at 20-25 °C	use only once, stable onboard for up to 5 hours

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the lid of the vials.

Calibration

Calibration frequency: Calibration must be performed once per reagent lot using SYPHB Cal1, SYPHB Cal2 and fresh reagent (i.e. not more than 24 hours since the **cobas** e pack was registered on the analytical unit).

Recalibration is required as follows:

- every 12 weeks when using the same reagent lot
- every 28 days when using the same **cobas** e pack on the analytical unit
- as required, such as when quality control findings are outside the defined limits

Quality control

For quality control, use PreciControl Syphilis.

Controls for the various concentration ranges must be run individually at least once every 24 hours when the test is in use, once per **cobas** e pack, and following each calibration.

PreciControl Syphilis values must be within the ranges specified in the control value sheet.

When the assay control values are within range, sample results are generated, and a valid release control result is required to release test results. If an assay control value is not within range, sample results are not generated for in-process or scheduled samples. For troubleshooting information, refer to User Assistance **cobas pro** serology solution or contact US Customer Technical Support.

Release control

For release control, use PreciControl Release Syphilis.

Result validation is based on test result batches that are concluded by release control measurements. A release control result within defined limits is required to validate a batch of previously measured test results utilizing the **cobas pro** serology controller software. Initial reactive results will not be invalidated by a failed release control and must be retested in duplicate. Repeatedly reactive results will not be invalidated by a failed release control and stay reactive. Other results rendered invalid due to a failed release control result must be retested after resolving the cause for the failed control measurement.

For a valid batch of sample results, the release control is tested at user-defined intervals with a maximum span of every 300 samples or 350 determinations within 24 hours from the PreciControl and must be tested in order to release the test results. Reactive results will not be invalidated.

The release control must meet specifications defined in the PreciControl Release Syphilis value sheet in order to validate the system functionality and release test results.

For troubleshooting information, refer to User Assistance **cobas pro** serology solution or contact US Customer Technical Support.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum and Li-heparin, K2 EDTA, K3 EDTA, CPD and Na-citrate plasma collected using standard sampling tubes.

Serum and Li-heparin and K2 EDTA plasma collected in tubes containing separating gel.

Samples on-the-clot are stable for 7 days at 15-30 °C, 14 days at 2-8 °C. Do not freeze samples on-the-clot.

Samples off-the-clot are stable for 7 days at 15-30 °C, 14 days at 2-8 °C, 12 months at -20 °C (± 5 °C). Samples off-the-clot may be frozen up to 4 times.

Specimens collected by plasmapheresis, which have not been frozen, do not require centrifugation. All other whole blood samples and samples containing precipitates need to be centrifuged before performing the assay for 10 to 15 minutes at 2000 to 4000 RCF (relative centrifugal force = x g).

The sample types listed were tested with a selection of sample collection tubes or systems that were commercially available at the time of testing. Not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials that 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.

Do not use pools of samples.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

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

Sample stability claims were established by experimental data by the manufacturer only for the temperatures/time frames as stated in the method sheet.

Test procedure

The reagents (M, R1, R2) in the kit are ready for use and are supplied in **cobas** e packs.

For optimum performance of the assay follow the directions given in this document for the analytical unit concerned. Refer to the appropriate user guide for analytical unit specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use.

Place the cooled (stored at 2-8 °C) **cobas** e pack on the reagent manager.

Avoid foam formation.

The system automatically regulates the temperature of the reagents and the opening/closing of the reagent pack.

Calibrators

Carefully dissolve the contents of one vial by adding exactly 1.0 mL of distilled or deionized water and allow to stand closed for 15 minutes to reconstitute. Mix carefully, avoiding foam formation.

Transfer the reconstituted calibrators into the supplied empty labeled snap-cap vials.

Read in all the information necessary for calibrating the assay.

Perform **only 1** calibration procedure per vial.

All information required for correct operation is available via **cobas** link.

Place the calibrators in the sample zone.

Calculation

The analytical unit automatically calculates the cutoff based on the measurement of SYPHB Cal1 and SYPHB 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 results

Initial result

Numeric result	Result	Interpretation / further steps
COI < 1.00	Non-reactive	Non-reactive for anti-*Treponema pallidum* antibodies. No further testing needed.
COI ≥ 1.00	Reactive	Reactive in the Elecsys Syphilis assay. All initially reactive samples should be retested in duplicate with the Elecsys Syphilis assay. Redetermination of samples with an initial COI ≥ 1.00 can be performed automatically (see section **cobas** e flow).

Final result

Numeric result	Result	Interpretation / further steps
One or both of the duplicate retests have a COI ≥ 1.00	Repeatedly reactive	Repeatedly reactive samples must be confirmed according to supplementary algorithms.
Both of the duplicate retests have a COI < 1.00	Non-reactive	Non-reactive for anti-*Treponema pallidum* antibodies. No further testing needed.

cobas e flow

A **cobas** e flow is a procedure programmed into the system to enable a fully automated sequence of measurements and the calculation of assay combinations to perform decision algorithms. A **cobas** e flow is available to perform a repetition of measurements in duplicate automatically for samples with an initial cutoff index ≥ 1.00 (short name SYPHBR).

Limitations of the test

A non-reactive test result does not completely rule out the possibility of an infection with *Treponema pallidum*. Serum or plasma samples from the very early (pre-seroconversion) phase or the late phase of a syphilis infection can occasionally yield non-reactive findings.

The detection of anti-*T. pallidum* antibodies is not a diagnosis of syphilis. It is recommended that repeatedly reactive specimens are confirmed by supplemental testing. Individuals who are repeatedly reactive should be referred for medical evaluation which may include additional testing.

The performance of the Elecsys Syphilis assay has not been established with cord blood, neonatal specimens, cadaveric specimens, heat-inactivated specimens, or body fluids other than serum and plasma.

Specific performance data

Representative performance data is given below. Results obtained in individual laboratories may differ.

Reproducibility

A study was performed based on guidance from CLSI EP05-A3 (n = 270). Testing was conducted at 3 external sites using 3 lots of the Elecsys Syphilis assay and 1 lot of PreciControl Syphilis. Panel members and controls were tested in 2 runs per day for 5 days with 3 sample replicates per run. The precision and reproducibility for the Elecsys Syphilis assay are presented in the following tables.

Elecsys Syphilis

Overall repeatability and reproducibility for Elecsys Syphilis

Sample	Mean (COI)	Repeatability SD (COI)	Repeatability % CV	Between run SD (COI)	Between run % CV	Between day SD (COI)	Between day % CV	Intermediate precision SD (COI)	Intermediate precision % CV
HSP 01 A)	1.63	0.030	1.84	0.012	0.715	0.021	1.31	0.039	2.37
HSP 02	10.7	0.186	1.74	0.098	0.916	0.107	0.999	0.235	2.21
PC SYPH1 B B)	0.085	0.001	1.19	0.000	0.000	0.001	0.814	0.001	1.44
PC SYPH2 B	5.05	0.074	1.47	0.048	0.959	0.054	1.07	0.104	2.05

A) HSP = human specimens

B) PC = PreciControl

Overall repeatability and reproducibility for Elecsys Syphilis

Sample	Mean (COI)	Between site SD (COI)	Between site % CV	Between lot SD (COI)	Between lot % CV	Reproducibility SD (COI)	Reproducibility % CV
HSP 01	1.63	0.006	0.374	0.031	1.90	0.050	3.06
HSP 02	10.7	0.046	0.432	0.097	0.911	0.259	2.43
PC SYPH1 B	0.085	0.001	1.03	0.001	1.75	0.002	2.49
PC SYPH2 B	5.05	0.017	0.345	0.125	2.47	0.163	3.23

Results: The precision and reproducibility of the Elecsys Syphilis assay demonstrated minor variability from run to run, day to day and between reagent lots.

Precision

Precision was determined using Elecsys reagents, pooled human sera 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:.

Overall precision for Elecsys Syphilis

Sample	Mean (COI)	Repeatability SD (COI)	Repeatability % CV	Between run SD (COI)	Between run % CV	Between day SD (COI)	Between day % CV	Intermediate precision SD (COI)	Intermediate precision % CV
HSP 01	0.125	0.002	1.5	0.000	0.4	0.001	0.6	0.002	1.7
HSP 02	0.888	0.018	2.0	0.016	1.8	0.012	1.3	0.026	3.0
HSP 03	1.09	0.017	1.6	0.011	1.0	0.016	1.5	0.026	2.4
HSP 04	4.11	0.098	2.4	0.079	1.9	0.000	0.0	0.126	3.1
HSP 05	6.88	0.198	2.9	0.073	1.1	0.133	1.9	0.249	3.6
HSP 06	15.8	0.395	2.5	0.216	1.4	0.357	2.3	0.574	3.6
HSP 07	16.4	0.395	2.4	0.158	1.0	0.332	2.0	0.540	3.3
PC SYPH1 B	0.095	0.001	1.1	0.000	0.0	0.001	0.8	0.001	1.4
PC SYPH2 B	5.90	0.126	2.1	0.087	1.5	0.025	0.4	0.155	2.6

Analytical specificity

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

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 753 µmol/L or ≤ 44 mg/dL
Hemoglobin	≤ 0.311 mmol/L or ≤ 500 mg/dL
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Albumin	≤ 7.0 g/dL

Additionally, naturally elevated samples for bilirubin, rheumatoid factor, triglycerides (lipemic), hemoglobin and albumin were tested; no false reactive results were found.
No false non-reactive result due to high-dose hook effect was found with the Elecsys Syphilis assay.
In rare cases, interference due to extremely high titers of antibodies to immunological components, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

Clinical specificity

The initial and repeat reactive rates were 0.10 % (2/2052) for the serum specimens and 0.24 % (6/2504) for the plasma specimens.

Specificity of Elecsys Syphilis

Specimen category	Number tested	Number initally reactive (% of tested)	Number repeatedly reactive (% of tested)	Number positive by supplemental testing (% of repeatedly reactive)	Specificity (%) (95 % CI)
Volunteer blood donors - serum	2052	2 (0.10)	2 (0.10)	2 (100)	100 (2050/2050) (99.81, 100)
Volunteer blood donors - plasma	2504	6 (0.24)	6 (0.24)	2 (33.3)	99.84 (2498/2502) (99.59, 99.94)
Total donors	4556	8 (0.18)	8 (0.18)	4 (50.0)	99.91 (4548/4552) (99.77, 99.97)

Clinical specificity - Source plasma

A total of 3089 source plasma samples from donors with a non-reactive nontreponemal (lipoidal antigen) test of record were collected and tested using the Elecsys Syphilis assay. All initial reactive samples were repeat reactive; therefore, the initial negative percent agreement to the non-reactive nontreponemal (lipoidal antigen) test of record for the source plasma specimens was 97.83 % (3022/3089) with a 95 % confidence interval of 97.25 % to 98.29 %. The 67 repeatedly reactive specimens were further tested using treponemal syphilis immunoassays. Based on the additional test results, 59 specimens were positive and 8 specimens were negative for anti-treponemal antibodies. The false reactive rate in source plasma donors was estimated in this study to be 0.26 % (8/3030). Therefore, the negative percent agreement to the treponemal test for the source plasma specimen was calculated to be 99.74 % (3022/3030) with a 95 % confidence interval of 99.48 % to 99.87 %.

Clinical Sensitivity

All 552 specimens (201 serum, 351 plasma) showing a positive syphilis specimen status were congruently repeatedly reactive with the Elecsys Syphilis assay. The sensitivity was calculated to be 100 % (552/552) with a 95 % confidence interval of 99.31 % to 100 %.

Sensitivity of Elecsys Syphilis - Combined

Specimen category	Specimen status positive	Number repeatedly reactive	Sensitivity (%) (95 % CI)
Latent infection	97	97	100 (96.19, 100)
Primary infection	76	76	100 (95.19, 100)
Secondary infection	64	64	100 (94.34, 100)
Uncharacterized syphilis infection	315	315	100 (98.80, 100)
Total	552	552	100 (99.31, 100)

Sensitivity of Elecsys Syphilis - Serum

Specimen category	Specimen status positive	Number repeatedly reactive	Sensitivity (%) (95 % CI)
Latent infection	70	70	100 (94.80, 100)
Primary infection	50	50	100 (92.87, 100)
Secondary infection	63	63	100 (94.25, 100)
Uncharacterized syphilis infection	18	18	100 (82.41, 100)
Total	201	201	100 (98.12, 100)

Sensitivity of Elecsys Syphilis - Plasma

Specimen category	Specimen status positive	Number repeatedly reactive	Sensitivity (%) (95 % CI)
Latent infection	27	27	100 (87.54, 100)
Primary infection	26	26	100 (87.13, 100)
Secondary infection	1	1	100 (20.65, 100)
Uncharacterized syphilis infection	297	297	100 (98.72, 100)
Total	351	351	100 (98.92, 100)

Other specimen conditions and disease states

170 samples containing potentially interfering factors were tested with the Elecsys Syphilis assay comprising specimens:

- containing antibodies against HAV, HBV, HCV, HIV, HTLV-I/II, CMV, EBV, HSV-1/2, Rubella
- containing autoantibodies (ANA) and elevated titers of rheumatoid factor
- containing antibodies against *Escherichia coli*, *Toxoplasma gondii* , *Borrelia burgdorferi*
- after vaccination against influenza
- from pregnant women and multiparous pregnancies

Results showed no interference from the above agents.

Additional information

For further information, refer to the User Guide for the corresponding analytical unit and to the Method Sheets of all necessary components (if available in your country).

Report any serious incident that has occurred in relation to the device to the manufacturer and the competent authority of the member state in which the user and/or patient is established.

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product meets the specifications stated in the labeling when used in accordance with the labeling and is free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL, OR CONSEQUENTIAL DAMAGES.

Symbols

For definition of symbols used, refer to navifyportal.roche.com.

In addition to the ISO 15223-1 standard, Roche Diagnostics uses the following symbols and signs:

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent

CALIBRATOR	Calibrator
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

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Change log

Due to technical reasons, changes that have been made since the last version of this document are listed in the following table instead of indicated by change bars in the margin.

Document Revision Information

Doc. Rev. 4.0	1. Changes due to source plasma were added to the following new and existing sections: Intended use, Specimen collection and preparation, and Clinical specificity. 2. Hazardous components added to Warnings and precautions. 3. Format changes made to references and reference #7 in previous version deleted due to duplication. 4. Editorial and layout updates due to change in software.