Elecsys Syphilis

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REF		Σ	SYSTEM
09015051190	09015051501	300	**cobas e** 402 **cobas e** 801

English

For use in the USA only

System information

Short name	ACN (application code number)
SYPHILIS	10212
SYPH E (for use with **cobas e** flow)	11212
SYPH R (for use with **cobas e** flow)	12035

Intended use

Immunoassay for the in vitro qualitative detection of total antibodies (IgG and IgM) to *Treponema pallidum* in human serum and plasma. The test is intended as an aid in the diagnosis of syphilis infection in conjunction with a nontreponemal laboratory test and clinical signs and symptoms.

The Elecsys Syphilis immunoassay is not intended for use in screening blood or tissue donors. The effectiveness of this assay in testing blood or tissue donors has not been established.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

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. 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.[2] In 2020, WHO estimated 7.1 million new syphilis infections globally.[3] In the US, 133945 cases of all stages of syphilis were reported in 2020. 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.[4] Certain European countries have also seen increases in the rate of infection and large localized outbreaks.[5]

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.[6] The estimated global maternal syphilis prevalence in 2016 was 0.69 %, resulting in 661000 total congenital syphilis cases, including 355000 adverse birth outcomes and 306000 non-clinical congenital syphilis cases (infants without clinical signs born to untreated mothers).[7] WHO and US Preventive Services Task Force recommend that all women be tested at their first prenatal visit and again in the third trimester.[8,9] If they are positive, sexual partners should be evaluated and offered treatment.[10] Syphilis infection facilitates HIV infection.[11]

In the early stage of infection, the clinical diagnosis of syphilis can be very difficult.[1] Typically, symptoms of syphilis 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). This is followed by a lengthy latent (asymptomatic) period. Eventually, tertiary syphilis ensues, characterized by the development of granulomatous dermal lesions, neurosyphilis, and/or cardiovascular syphilis (which can be fatal).[12] The immune response to *T. pallidum* is the main driver of lesion development.[12] The antibody response is directed not only against antigens specific to *T. pallidum* (treponemal antibodies), but antibodies are also generated against antigens which are not specific (non-treponemal antibodies); for example, antigens released during the cellular damage caused by the organism. Therefore, treponemal and non-treponemal tests co-exist for the diagnosis of syphilis.[1]

Non-treponemal tests use antigens comprising lecithin, cholesterol, and purified cardiolipin to detect antibodies against cardiolipin, which are present in many syphilis patients. Treponemal tests detect antibodies directed against *T. pallidum* proteins. A positive treponemal antibody test result indicates prior exposure to syphilis. Non-treponemal assays are useful for monitoring the progression of disease and response to therapy. Both tests are necessary as an aid of the diagnosis.[1]

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

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st 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.
- 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 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 - working solutions

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

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[b)] 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 labeled with ruthenium complex 0.7 mg/L; MES buffer 50 mmol/L, pH 6.5; preservative.

b) MES = 2-morpholino-ethane sulfonic acid

SYPHILIS Cal1 Negative calibrator 1 (lyophilized), 1 bottle for 1.0 mL:
Human serum, non-reactive for anti-TP antibodies; preservative.

SYPHILIS Cal2 Positive calibrator 2 (lyophilized), 1 bottle for 1.0 mL:
Human serum, reactive for anti-TP antibodies; preservative.

Precautions and warnings

For in vitro diagnostic use for health care professionals. 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 the safe disposal.

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:

Warning

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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.

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

All human material should be considered potentially infectious. All products derived from human blood are 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 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.[13,14]

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

Reagent handling

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

Calibrators:

Carefully dissolve the contents of one bottle 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 bottles.

Unless the entire volume is necessary for calibration on the analyzers, transfer aliquots of the reconstituted calibrators into empty snap-cap bottles (CalSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots at 2-8 °C or -20 °C (± 5 °C) for later use.

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

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

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 analyzers	16 weeks

Stability of the calibrators:	
lyophilized calibrators	up to the stated expiration date
reconstituted calibrators at 2-8 °C	28 days
reconstituted calibrators at -20 °C (± 5 °C)	6 months (3 freeze/thaw cycles possible)

Stability of the calibrators:	
on the analyzers 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, K_2-EDTA, K_3-EDTA, CPDA and Na-citrate plasma.

Li-heparin plasma tubes containing separating gel can be used.

Criterion: Mean recovery of positive samples within ± 20 % of serum value. Absolute deviation of samples with COI (cutoff index) values from 0.0-1.0 within ± 0.2 COI.

Sampling devices containing liquid anticoagulants have a dilution effect resulting in lower COI values for individual patient specimens. In order to minimize dilution effects it is essential that respective sampling devices are filled completely according to manufacturer's instructions.

Stable for 7 days at 20-25 °C, 14 days at 2-8 °C, 12 months at -20 °C (± 5 °C). The samples may be frozen 5 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 and thawed samples before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Ensure the samples and calibrators 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 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 or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Specimens should not be subsequently altered with additives (e.g. biocides, anti-oxidants or substances that could possibly change the pH or ionic strength of the sample) in order to avoid erroneous findings.

Materials provided

See "Reagents – working solutions" section for reagents.

- 2 x 6 bottle labels
- 4 empty labeled snap-cap bottles

Materials required (but not provided)

- REF 06923364190, PreciControl Syphilis, for 4 x 2.0 mL
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- General laboratory equipment
- **cobas e** analyzer
- Distilled or deionized water

Additional materials for **cobas e** 402 and **cobas e** 801 analyzers:

- REF 06908799190, ProCell II M, 2 x 2 L system solution
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
- REF 06908853190, PreClean II M, 2 x 2 L wash solution

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- REF 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- REF 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- REF 11298500160, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution (for USA)

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.

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 **cobas e** pack.

Calibrators:

Place the reconstituted calibrators (in the system-compatible bottles with barcoded labels) in the sample zone.

Read in all the information necessary for calibrating the assay.

Calibration

Calibration frequency: Calibration must be performed once per reagent lot using SYPHILIS Cal1, SYPHILIS Cal2 and fresh reagent (i.e. not more than 24 hours since the **cobas e** pack 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 12 weeks when using the same reagent lot
- after 28 days when using the same **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Syphilis.

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

Calculation

The analyzer automatically calculates the cutoff based on the measurement of SYPHILIS Cal1 and SYPHILIS 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 < 1.00 are non-reactive in the Elecsys Syphilis assay. These samples are considered negative for anti-*Treponema pallidum* antibodies.
Samples with a cutoff index ≥ 1.00 are considered reactive in the Elecsys Syphilis assay.
All initially reactive samples should be retested in duplicate with the Elecsys Syphilis assay. If cutoff index values < 1.00 are found in both cases, the samples are considered negative for anti-*Treponema pallidum* antibodies. Initially reactive samples giving cutoff index values of ≥ 1.00 in either of the retests are considered repeatedly reactive. Repeatedly reactive samples must be supplemented according to recommended confirmatory algorithms. Reactive treponemal test results alone are not diagnostic of syphilis, treponemal test results should always be interpreted in conjunction with additional treponemal or nontreponemal serologic test results (as appropriate), medical history, clinical presentation and other findings, as recommended by the Centers for Disease Control and Prevention (CDC) Sexually Transmitted Diseases Treatment Guidelines.

Retesting of samples with an initial cutoff index ≥ 1.00 can be automatically performed (see section "**cobas e** flows").

cobas e flows

cobas e flows are procedures 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 SYPH E). Both sub-results and the overall result message will be reported.

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	≤ 1129 µmol/L or ≤ 66 mg/dL
Hemoglobin	≤ 0.310 mmol/L or ≤ 500 mg/dL
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/mL or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1500 IU/mL
IgG	≤ 3.2 g/dL
IgA	≤ 2.8 g/dL
IgM	≤ 1.0 g/dL
Human serum albumin	≤ 10 g/dL

Criterion: Mean recovery of positive samples within ± 15 %. Absolute deviation of samples with COI values from 0.0-1.0 within ± 0.2 COI.

Specimens that contain biotin at a concentration of 1200 ng/mL, demonstrate less than or equal to 10 % negative bias in COI values. Pharmacokinetic studies have shown that serum concentrations of biotin can reach up to 355 ng/mL within the first hour after biotin ingestion for subjects consuming supplements of 20 mg biotin per day[15] and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.[16]

No false negative result due to high-dose hook effect was found with the Elecsys Syphilis assay.

Drug interference

A drug interference study was performed with 16 commonly used therapeutic drugs. No interference was observed at the levels tested.

Drug tested	No interference up to
Acetylcystein	150 mg/L
Ampicillin-Na	1000 mg/L
Ascorbic Acid	300 mg/L
Cyclosporine	5 mg/L
Cefoxitin	2500 mg/L
Heparin	5000 U/L
Levodopa	20 mg/L
Methyldopa + 1.5	20 mg/L
Metronidazole	200 mg/L
Phenylbutazone	400 mg/L
Doxycyclin	50 mg/L
Acetylsalicylic Acid	1000 mg/L
Rifampicin	60 mg/L
Acetaminophen	200 mg/L
Ibuprofen	500 mg/L

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Drug tested	No interference up to
Theophylline	100 mg/L

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

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.

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

A negative 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 negative findings.

Specific performance data

Representative performance data on the analyzers are given below. The precision data was generated on the **cobas e** 801 analyzer. However, since the **cobas e** 801 analyzer is a member of the Elecsys instrument family of analyzers, some of the data below may have been generated on other members of the Elecsys instrument family. Results obtained in individual laboratories may differ.

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:

cobas e 801 analyzer[c]					
		Repeatability		**Intermediate precision**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS[d], negative 1	0.125	0.00192	1.5	0.00210	1.7
HS, negative 2	0.888	0.0175	2.0	0.0264	3.0
HS, positive 1	1.09	0.0173	1.6	0.0260	2.4
HS, positive 2	4.11	0.0983	2.4	0.126	3.1
HS, positive 3	6.88	0.198	2.9	0.249	3.6
HS, positive 4	15.8	0.395	2.5	0.574	3.6
HS, positive 5	16.4	0.395	2.4	0.540	3.3
PC[e] Syphilis 1	0.0951	0.00107	1.1	0.00130	1.4
PC Syphilis 2	5.90	0.126	2.1	0.155	2.6

c) The precision data generated on the **cobas e** 402 analyzer was equivalent to that of the **cobas e** 801 analyzer.

d) HS = human serum

e) PC = PreciControl

Analytical specificity

Specimens from individuals diagnosed with other diseases were obtained from commercial vendors. The results of the study are shown below.

Potential Interference	Number tested	Number of reactive samples
Borrelia	50	0
EBV IgG	21	1
Rubella IgG	17	1
E. coli	18	1
Hepatitis A	25	1
Hepatitis B	10	2
Hepatitis C	13	0
ANA	15	1
RF	19	0
HSV-1/2	12	1
CMV IgG	20	0
HIV-1	25	1
Toxo IgG	21	0
Total	266	9

The 9 samples that were reactive with the Elecsys Syphilis assay were confirmed as coinfected and positive for anti-*Treponema pallidum* antibodies with another syphilis total antibody assay. No cross-reactivity was found.

Clinical performance

A total of 2282 prospectively collected specimens from the intended use population were tested at 3 sites using the Elecsys Syphilis assay, including 1524 subjects sent for routine syphilis testing, 457 HIV positive subjects and 301 pregnant women. In addition, all samples were tested according to a composite testing algorithm using FDA-cleared tests that included the predicate syphilis immunoassays, the Rapid Plasma Reagin (RPR) non-treponemal specific assay and the *Treponema pallidum* Particle Agglutination Treponema-specific assay.

A summary of the serological test profile for all prospectively-collected specimens in the intended use population is presented in the following table.

Predicate Syphilis Immunoassay	RPR	TPPA	Final Comparator Results	Elecsys Syphilis	N
NR[f]	NR	N/A[g]	Negative	NR	2023
NR	NR	Inconclusive	Negative	NR	1
NR	NR	NR	Negative	NR	1
NR	NR	NR	Negative	Reactive	1
NR	NR	Reactive	Negative	Reactive	4
NR	Reactive	NR	Negative	NR	4
Reactive	NR	Inconclusive	Negative	Reactive	2
Reactive	NR	NR	Negative	NR	9
Reactive	NR	NR	Negative	Reactive	9
Reactive	NR	Reactive	Positive	Reactive	166
Reactive	Reactive	N/A[f]	Positive	Reactive	62

f) NR = Non-reactive

g) test not performed

The comparison between the Elecsys Syphilis results and the final comparator results for the prospective specimens in the intended use population is shown in the following table.

	Final Comparator Results		
Elecsys Syphilis	Positive for Syphilis	Negative for Syphilis	Total
Reactive	228	16	244
Non-reactive	0	2038	2038
Total	228	2054	2282

The positive percent agreement was 100 % (228/228) with a 95 % confidence interval of 98.40 to 100 %. The negative percent agreement was 99.22 % (2038/2054) with a 95 % confidence interval of 98.74 to 99.58 %. The percent agreement for the individual cohorts is given below.

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Percent agreement by category for prospective cohorts

Cohort	Positive Percent Ageement		PPA 95 % CI	Negative Percent Agreement		NPA 95 % CI
	%	Ratio		%	Ratio	
Routine Syphilis	100	66/66	94.56 to 100	99.8	1455/1458	99.40 to 99.96
HIV	100	162/162	97.75 to 100	95.6	282/295	92.58 to 97.63
Pregnant	N/A	0/0	N/A	100	301/301	98.78 to 100
Total	100	228/228	98.40 to 100	99.2	2038/2054	98.74 to 99.55

Clinical performance in retrospective medically diagnosed individuals

Clinical performance in the pre-selected retrospective cohort included a total of 169 specimens, including 15 pregnant positive women and 154 subjects medically diagnosed with syphilis at different stages. The comparison between the Elecsys Syphilis results and the final comparator results is given in the following table.

Performance of Elecsys Syphilis compared with Final Comparator

	Final Comparator Result		
Elecsys Syphilis	**Positive for Syphilis**	**Negative for Syphilis**	**Total**
Reactive	155	0	155
Non-reactive	2	12	14
Total	157	12	169

The positive percent agreement was 98.73 % (155/157) with a 95 % confidence interval of 95.47 to 99.85 %. The negative percent agreement was 100 % (12/12) with a 95 % confidence interval of 73.54 to 100 %. The percent agreement for the individual cohorts is given in the following table.

Percent agreement by category for retrospective cohorts

Cohort	Positive Percent Ageement		PPA 95 % CI	Negative Percent Agreement		NPA 95 % CI
	%	Ratio		%	Ratio	
Pregnant	100	15/15	78.20 to 100	N/A	0/0	N/A
Staged	98.6	140/142	95.00 to 99.83	100	12/12	73.54 to 100
Total	98.7	155/157	95.47 to 99.85	100	12/12	73.54 to 99.55

Clinical performance in medically diagnosed individuals

Samples were collected from 154 individuals diagnosed with primary, secondary or latent syphilis. They included 10 females and 144 males. Results of the Elecsys Syphilis assay for this cohort are summarized below.

Reactivity of Elecsys Syphilis in subjects medically diagnosed with syphilis

			Elecsys Syphilis Results	
Syphilis stage	**Treatment status**	**N**	**Reactive**	**Non-reactive**
Primary	Treated	29	16	13[h)]
	Untreated	25	25	0
Secondary	Treated	25	24	1
	Untreated	25	25	0
Latent	Treated	25	25	0
	Untreated	25	25	0

h) 12 of these samples also tested negative for syphilis with the composite testing algorithm

Clinical performance in pregnant women

A total of 316 pregnant female samples were tested in the study. Of these samples, 301 were prospectively collected and 15 were retrospectively collected. The percent agreement between the Elecsys Syphilis results and the final comparator results is shown below stratified by pregnancy trimesters.

Percent agreement in pregnant women

Cohort	Positive Percent Ageement		PPA 95 % CI	Negative Percent Agreement		NPA 95 % CI
	%	Ratio		%	Ratio	
Pregnant (Prospective)	N/A	0/0	N/A	100	301/301	98.78 to 100
1st Trimester	N/A	0/0	N/A	100	100/100	96.38 to 100
2nd Trimester	N/A	0/0	N/A	100	125/125	97.09 to 100
3rd Trimester	N/A	0/0	N/A	100	76/76	95.26 to 100
Pregnant (Retrospective)	100	15/15	78.20 to 100	N/A	0/0	N/A
1st Trimester	100	7/7	59.04 to 100	N/A	0/0	N/A
3rd Trimester	100	8/8	63.06 to 100	N/A	0/0	N/A

In addition, 40 samples from pregnant women, non-reactive for *T. pallidum* antibodies, were spiked with serum with *T. pallidum* antibodies and analyzed with the Elecsys Syphilis assay. All samples tested reactive.

Performance in apparently healthy individuals

Specimens were collected from 209 apparently healthy individuals. Of these 80 were from female subjects and 129 were from male subjects. The results of the Elecsys Syphilis assay in this cohort are shown below.

Results of Elecsys Syphilis assay in apparently healthy individuals

	Elecsys Syphilis Results		
Gender	**Reactive**	**Non-reactive**	**Total**
	N	**N**	
Female	9 (11.3 %)	71 (88.7 %)	80
Male	11 (8.53 %)	118 (91.5 %)	129
Total	20 (9.57 %)	189 (90.4 %)	209

Expected values

In this clinical study, there were a total of 2282 prospectively collected specimens for the intended use population that were tested with the Elecsys Syphilis assay. There were 244 reactive samples for a 10.7 % prevalence of *Treponema pallidum* antibodies in the study population. The distribution of the Elecsys Syphilis reactive and non-reactive results is summarized below by age and gender.

		Elecsys Syphilis Results		
Age Range (years)	**Gender**	**Reactive**	**Non-reactive**	**Total**
18-21	Female	0 (0.00 %)	247 (100 %)	247
	Male	6 (3.5 %)	165 (96.5 %)	171

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		Elecsys Syphilis Results		
Age Range (years)	**Gender**	**Reactive**	**Non-reactive**	**Total**
22-29	Female	0 (0.00 %)	358 (100 %)	358
	Male	19 (10.7 %)	159 (89.3 %)	178
30-39	Female	10 (3.7 %)	261 (96.3 %)	271
	Male	13 (12.3 %)	93 (87.7 %)	106
40-49	Female	29 (12.1 %)	210 (87.9 %)	239
	Male	29 (20.0 %)	116 (80.0 %)	145
50-59	Female	47 (20.8 %)	179 (79.2 %)	226
	Male	55 (27.1 %)	148 (72.9 %)	203
60-69	Female	11 (23.9 %)	35 (76.1 %)	46
	Male	23 (29.5 %)	55 (70.5 %)	78
70-79	Female	0 (0.00 %)	5 (100 %)	5
	Male	2 (22.2 %)	7 (77.8 %)	9
Combined	Total	244 (10.7 %)	2038 (89.3 %)	2282

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

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

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