Elecsys Toxo IgG

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REF		Σ	SYSTEM
07028008190	07028008501	300	**cobas e** 402 **cobas e** 801

English

For use in the USA only

System information

Short name	ACN (application code number)
TOXOIGG	10047

Intended use

Immunoassay for the in vitro quantitative determination of IgG antibodies to Toxoplasma gondii in human serum and heparin, EDTA and citrate plasma. The test is intended for use as an aid in the assessment of immune status and as an aid in the diagnosis of Toxoplasma gondii infection.

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

NOTE: This assay has not been cleared by the FDA for blood/plasma donor screening.

Summary

Toxoplasmosis is a relatively common infection caused by the protozoan parasite Toxoplasma gondii.

The infection is mainly acquired by ingestion of food or water contaminated by mature oocysts shed by cats or by undercooked meat containing tissue cysts.[1,2,3,4] Infection can also be transmitted congenitally if a woman is newly infected during or just prior to pregnancy, and via organ transplant or blood transfusion from an infected donor.[4]

Primary, acute infection in healthy individuals is mostly mild or even asymptomatic and is followed by life-long latency.[3,4] Reactivation of a latent Toxoplasma infection can occur as a result of immunosuppression (e.g. in organ transplant recipients, patients with cancer or HIV) and can be associated with high morbidity and mortality.[3,4] Reactivated disease in immunocompromised hosts frequently presents with brain lesions, especially in patients with advanced HIV-related immunosuppression.[3,4,5]

Primary maternal Toxoplasma infection occurring during pregnancy may have significant implications for the fetus as the parasite can be transmitted across the placenta.[3,6] The majority of infants with congenital infection do not present clinical symptoms at birth but may develop severe sequelae later in life such as chorioretinitis, intellectual and psychomotor disabilities, visual and hearing impairment and hearing loss.[3,6,7,8] The fetal infection rate increases with gestational age, but the risk of severe clinical manifestations is higher in the case of early maternal infection.[3,6,7,8]

Early drug therapy in acute infection during pregnancy can prevent congenital damage or ameliorate the severity of clinical manifestations.[6,7]

The diagnosis of Toxoplasma infection is most commonly made by the detection of anti-Toxoplasma-specific IgG and IgM antibodies.[3,4,9]

The determination of Toxo IgG antibodies is used to assess the serological status of T. gondi infection and their presence is indicative of a latent or acute infection.[4,9]

Detection of Toxo IgM antibodies is presumptive of an acute or recent Toxoplasma infection.[3,4,9]

The diagnosis of the acute acquired infection during pregnancy is established by a seroconversion or a significant rise in antibody titers (IgG and/or IgM) in serial samples.[8,9]

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 6 µL of sample, a biotinylated recombinant T. gondii-specific antigen, and a T. gondii-specific recombinant antigen 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 II M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the **cobas** link.

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 TOXOIGG.

M Streptavidin-coated microparticles, 1 bottle, 14.1 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Toxoplasma-Ag~biotin, 1 bottle, 19.7 mL:
Biotinylated T. gondii-specific antigen (recombinant, E. coli) > 400 µg/L, TRIS[b)] buffer 50 mmol/L, pH 7.5; preservative.

R2 Toxoplasma-Ag~$Ru(bpy)_3^{2+}$, 1 bottle, 19.7 mL:
T. gondii-specific antigen (recombinant, E. coli) labeled with ruthenium complex > 400 µg/L; TRIS buffer 50 mmol/L, pH 7.5; preservative.

b) TRIS = Tris(hydroxymethyl)aminomethane

TOXOIGG Cal1 Negative calibrator 1, 1 bottle of 1.0 mL:
Human serum, non-reactive for anti-Toxoplasma IgG; buffer; preservative.

TOXOIGG Cal2 Positive calibrator 2, 1 bottle of 1.0 mL:
Human serum, reactive for anti-Toxoplasma IgG, approximately 100 IU/mL; buffer; 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.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

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

Warning

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing mist or vapours.

P272 Contaminated work clothing should not be allowed out of the workplace.

P280 Wear protective gloves.

Response:

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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.

The calibrators (TOXOIGG Cal1, TOXOIGG 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 serum containing anti-Toxoplasma IgG (TOXOIGG Cal2) was sterile filtrated.

The testing methods used assays approved by the FDA or that are in compliance with the legal rules applicable to placing in vitro diagnostic medical devices for human use on the market in the European union.

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.[10,11]

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

The calibrators are supplied ready-for-use in bottles compatible with the system.

Unless the entire volume is necessary for calibration on the analyzer, transfer aliquots of the 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 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 **cobas e** analyzers	16 weeks

Stability of the calibrators:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	16 weeks
on the **cobas e** 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, K_2-EDTA, K_3-EDTA and Na-citrate plasma.

When citrated plasma is used, the values found are approximately 15 % lower.

Criterion: Slope 0.9-1.1 + intercept within ≤ ± 0.5 IU/mL + coefficient of correlation ≥ 0.95.

Stable for 3 days at 20-25 °C, 3 weeks at 2-8 °C, 3 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 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 manufacturer.

Specimens should not be subsequently altered with additives (biocides, anti-oxidants or substances that could possibly change the pH of the sample) in order to avoid erroneous findings. Pooled samples and other artificial material may have different effects on different assays and thus may lead to discrepant findings.

Centrifuge samples containing precipitates and thawed samples before performing the assay. Lyophilized samples, heat-inactivated samples and samples and controls stabilized with azide (up to 0.1 %) can be used.

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.

Sample stability claims were established by experimental data by the manufacturer 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.

Materials provided

See "Reagents – working solutions" section for reagents.

- 2 x 6 bottle labels

Materials required (but not provided)

- REF 04618823160, PreciControl Toxo IgG, 16 x 1.0 mL
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- REF 07299001190, Diluent Universal, 36 mL sample diluent
- General laboratory equipment
- **cobas e** analyzer

Additional materials for the **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
- 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

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 calibrators in the sample zone.

Read in all the information necessary for calibrating the assay.

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Calibration

Traceability: This method has been standardized against the 3rd International Standard for anti-Toxoplasma serum (TOXM) from NIBSC, UK.

The predefined master curve is adapted to the analyzer using TOXOIGG Cal1 and TOXOIGG Cal2.

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

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 with PreciControl Toxo IgG outside the defined limits

Quality control

For quality control, use PreciControl Toxo IgG.

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 analyte concentration of each sample in IU/mL.

Interpretation of the results

The cutoff for the Elecsys Toxo IgG assay was established by measuring a total of 2645 samples from clinical routine in a multi-center study at 5 European study sites in France, Switzerland and Germany. The majority of samples were from pregnant women who were tested for toxoplasma during pregnancy screening. The distribution of positive, equivocal and negative results was compared to results from various reference assays and the cutoffs were set as noted below. This setting revealed an excellent separation of negative and positive samples exhibiting only 14 equivocal results out of 2645. The cutoff was verified internally with an additional set of 2121 samples and applied to the performance evaluation studies described below.

Results obtained with the Elecsys Toxo IgG assay can be interpreted as follows:

Non-reactive:	< 1 IU/mL
Equivocal:	≥ 1 - < 3 IU/mL
Reactive:	≥ 3 IU/mL

Samples with concentrations < 1 IU/mL are considered non-reactive in the Elecsys Toxo IgG assay.
Samples with concentrations between 1 IU/mL and < 3 IU/mL are considered equivocal. The sample should be retested. In case the result is still equivocal, a second sample should be collected e.g. within 2 weeks.
Samples with concentrations ≥ 3 IU/mL are considered positive for IgG antibodies to T. gondii. The diagnosis of acute Toxoplasma infection may be supported by a significant increase of the Toxo IgG antibody titer from a first to a second sample taken e.g. within 2 weeks and in addition by Toxoplasma-specific IgM results. To obtain additional serological data to aid in the diagnosis of a recent infection, the laboratory is advised to evaluate the samples for the presence of a significant level of IgM antibody to T. gondii. For additional information concerning the interpretation of Toxoplasma serology results, refer to CLSI document M36-A.

Please note

The measured anti-Toxo IgG value of a patient's sample can vary depending on the testing procedure used. The laboratory finding must therefore always contain a statement on the Toxo IgG assay method used. Anti-Toxo IgG values determined on patient samples by different testing procedures cannot be directly compared with one another and could be the cause of erroneous medical interpretations.

Therefore, the results reported by the laboratory to the physician should include: "The following results were obtained with the Elecsys Toxo IgG assay. Results from assays of other manufacturers cannot be used interchangeably."

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	≤ 0.62 mmol/L or ≤ 1000 mg/dL
Intralipid	≤ 2000 mg/dL
Rheumatoid factors	≤ 1200 IU/mL
Albumin	≤ 7.0 g/dL
IgG	≤ 7.0 g/dL
IgA	≤ 1.6 g/dL
IgM	≤ 1.0 g/dL

Criterion: For concentrations < 3.0 IU/mL the deviation is ≤ 0.3 IU/mL. For concentrations ≥ 3.0 IU/mL the deviation is ≤ ± 20 %.

A negative test result does not completely rule out the possibility of an infection with T. gondii. Individuals may not exhibit any detectable IgG antibodies at the early stage of acute infection.

The detection of Toxoplasma-specific IgG antibodies in a single sample indicates a previous exposure to T. gondii but is not sufficient to distinguish between an acute or latent infection (irrespective of the level of the IgG antibody titer).

For monitoring of the Toxoplasma-specific IgG antibody titer it is recommended to test serial samples by parallel measurements.

If a treatment is prescribed early enough, antibody production may not increase. IgG and IgM levels may remain low and can coexist for years.

Elecsys Toxo IgG results should be used in conjunction with the patient's medical history, clinical symptoms and other laboratory tests, e.g. Toxoplasma-specific IgM results, Toxoplasma avidity results.

The results in HIV patients, in patients undergoing immunosuppressive therapy, or in patients with other disorders leading to immune suppression, should be interpreted with caution.

Specimens from neonates, cord blood, pretransplant patients or body fluids other than serum and plasma, such as urine, saliva or amniotic fluid have not been tested.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

Biotin interference

% Bias for samples containing various concentrations of Biotin					
Sample (IU/mL)	Biotin concentration (ng/mL)				
	360	500	600	700	720
2.27	0.110	0.047	-0.036	-0.146	-0.141
273	104	104	102	96.0	94.3
600	108	108	104	99.7	98.4

% Bias for samples containing various concentrations of Biotin				
Sample (IU/mL)	Biotin concentration (ng/mL)			
	750	800	1080	1440
2.27	-0.206	-0.330	-0.984	-1.30
273	95.2	87.7	60.4	51.4
600	94.3	85.2	64.1	51.3

Specimens with biotin concentrations up to 750 ng/mL demonstrated ≤ 10 % bias. Biotin concentrations greater than 750 ng/mL lead to higher

negative bias. 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[12] and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.[13]

Pharmaceutical substances
In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.

In addition, the following special drugs used in Toxoplasmosis therapy during pregnancy were tested. No interference with the assay was found.

Special drugs

Drug	Concentration tested mg/L
Spiramycine	≤ 3000
Sulfadiazine	≤ 2500
Pyrimethamine	≤ 500
Folinic acid	≤ 3

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.

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

Measuring range

0.18-650 IU/mL (defined by the Limit of Detection and the maximum of the master curve). Values below the Limit of Detection are reported as < 0.18 IU/mL. Values above the measuring range are reported as > 650 IU/mL.

Lower limits of measurement

Limit of Blank and Limit of Detection

An internal study was performed based on guidance from the CLSI protocol EP17-A2. Limit of Blank and Limit of Detection were determined to be the following:

Limit of Blank ≤ 0.10 IU/mL

Limit of Detection ≤ 0.18 IU/mL

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

Expected values

In a prospective study of 515 subjects from a United States reference laboratory, the prevalence of IgG antibodies to T. gondii was shown to be 37.1 %. The prevalence was 42.7 % in pregnant women, 43.6 % in males and 36.6 % in females.
The prevalence from a European study of 470 prospectively collected samples was 37.4 %. The prevalence was 9.6 % in pregnant women, 41.2 % in males and 11.2 % in females. Prevalence in the group of unknown gender was 65.1 %.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data is 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, 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 801 analyzer[c]					
		Repeatability		**Intermediate precision**	
Sample	Mean IU/mL	SD IU/mL	CV %	SD IU/mL	CV %
HS[d], negative	0.585	0.034	5.8	0.045	7.7
HS, positive	21.8	0.380	1.7	0.586	2.7
HS, positive	324	8.49	2.6	12.2	3.8
PC[e] Toxo IgG 1	1.19	0.044	3.7	0.056	4.7
PC Toxo IgG 2	46.6	0.590	1.3	1.04	2.2

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

Clinical performance data

A multi-center study was conducted in the U.S. and Europe to characterize the performance of the Elecsys Toxo IgG immunoassay. All subjects were tested with the Elecsys Toxo IgG assay on the Elecsys 2010 analyzer and with an FDA cleared reference method in strict accordance with the manufacturers' package insert instructions.
In the U.S. study, 515 samples were obtained from a reference laboratory; representing subjects from whom anti-Toxoplasma testing had been ordered per clinical routine. Of those samples, 512 were fresh serum, 2 were frozen serum and one was frozen plasma; 39 samples were from males ranging in age from 1 to 74. 475 were from females ranging in age from 4 to 87. 234 females were known to be pregnant. The gender of one 19 year old subject was not known.
The following table summarizes the results for the U.S. cohort:

Reference Toxo IgG Assay				
Elecsys Toxo IgG Immunoassay		Positive	Equivocal	Negative
	Positive	183	2	7
	Equivocal	0	0	13
	Negative	0	0	310

Agreement classification[f]	Numerator/ Denominator	Percent agreement (%)	95 % confidence interval
Positive agreement	183/183	100	98.0 - 100
Negative agreement	310/332	93.4	90.1 - 95.8

f) Repeated equivocals are counted as discrepant results against the Elecsys immunoassay.

898 samples were collected in a multi-center study in Europe. 468 fresh serum samples were collected prospectively from the daily routine collective of hospital laboratories in Berlin, Germany and Lausanne, France.
426 frozen serum samples were gathered retrospectively from the archived repository of these labs. 4 samples were without characterization with regard to fresh or frozen status. Only 457 subjects had full characterization with regard to age and gender. Of those, 53 were male and 404 were female. Of the 404 female subjects, 388 were of childbearing age and 352 were pregnant.

The following table summarizes the results obtained with the fresh serum samples from the prospective portion of the European study:

Reference Toxo IgG Assay				
Elecsys Toxo IgG Immunoassay		Positive	Equivocal	Negative
	Positive	151	4	20
	Equivocal	0	0	4
	Negative	1	0	288

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Agreement classification[f]	Numerator/ Denominator	Percent agreement (%)	95 % confidence interval
Positive agreement	151/152	99.3	96.4 - 100
Negative agreement	288/316	91.1	87.5 - 94.0

The following table summarizes the results obtained with the frozen serum samples from the retrospective portion of the European study. Based on serological evidence and clinical information, this cohort included 21 subjects never infected with Toxoplasmosis; 214 subjects with a previous Toxoplasmosis infection, 79 with an acute infection, and 68 with a remote infection. Further categorization was unavailable for the remaining 44 subjects from this cohort.

Reference Toxo IgG Assay				
Elecsys Toxo IgG Immunoassay		Positive	Equivocal	Negative
	Positive	378	2	10
	Equivocal	0	0	3
	Negative	1	0	32

Agreement classification[f]	Numerator/ Denominator	Percent agreement (%)	95 % confidence interval
Positive agreement	378/379	99.7	98.5 - 100
Negative agreement	32/47	68.1	52.9 - 80.9

Evaluation of CDC reference panel

A panel of 100 samples was obtained through the U.S. Centers for Disease Control and Prevention (CDC) and was tested for Toxo IgG on the Elecsys 2010 analyzer. As evaluated by the CDC, the Elecsys 2010 analyzer showed 100 % agreement, with 70/70 positive tests on 70 positive sera and 30/30 negative tests on 30 negative sera.
The results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. This does not imply an endorsement of the assay by the CDC.

Cross reactivity

The specificity of the Elecsys Toxo IgG assay was evaluated by testing a total of 193 specimens representing a variety of disease states (AMA, ANA, Chlamydia, CMV, EBV, Gonorrhea, HAV, HBV, HCV, HIV, HSV, Influenza, Malaria, Parvo B19, Rubella, Syphilis, TPAH and VZV). The testing results are summarized in the table below.

Cross-reactant	No. tested	Elecsys Toxo IgG/ Reference Neg/Neg	Elecsys Toxo IgG/ Reference Pos/Neg	Elecsys Toxo IgG/ Reference Neg/Pos	Elecsys Toxo IgG/ Reference Pos/Pos
AMA[g]	15	3	0	0	11
ANA[h]	26	8	1	0	15
Chlamydia	4	2	0	0	2
CMV	8	0	0	0	8
EBV[i]	9	4	0	0	4
Gonorrhea	5	2	0	0	3
HAV	10	7	0	0	3
HBV	23	14	1	0	8
HCV[g]	11	5	0	0	5
HIV	13	10	1	0	2
HSV[i]	8	1	0	0	6
Influenza	16	12	0	0	4
Malaria	10	4	0	0	6
Parvo B19	10	9	0	0	1
Rubella	10	4	0	0	6
Syphilis	5	3	0	0	2
TPAH[j]	3	1	0	0	1
VZV	7	4	1	0	2
Sub-total	186	93	4	0	89
Total	193	186			

g) One sample was repeatedly equivocal by the Elecsys Toxo IgG immunoassay.

h) Two samples were repeatedly equivocal by the reference method.

i) One sample was repeatedly equivocal by the reference method.

j) One equivocal sample was not repeated on the reference method.

Serum and plasma comparison

The following tables summarize the results for the comparison between serum and 3 plasma matrices.

Plasma matrix	Number of positive specimens showing differences in recovery to serum within various ranges		
	< 10 %	10 % - 20 %	> 20 %
Li-heparin	19	1	0
K_3-EDTA	26	0	0
sodium citrate	6	18	2

Plasma matrix	Number of negative specimens showing differences in recovery to serum within various ranges		
	< 0.1 IU/mL	0.1 - 0.3 IU/mL	> 0.3 IU/mL
Li-heparin	13	1	0
K_3-EDTA	24	1	0
sodium citrate	24	2	0

Linearity with WHO Standard

10 dilutions of the WHO 3rd International Standard for anti-Toxoplasma serum were prepared using human serum and measured. The percent recovery was calculated, with results shown in the table below. Linear regression yielded the following equation: y = 1.04x - 4.50; r = 0.9996.

Dilution percentage	WHO value, IU/mL	Percent recovery %
0	0.00	100
10	58.6	103
20	117	98.0
30	176	98.0
40	234	101
50	293	101
60	351	97.0
70	410	96.0
80	468	96.0
90	527	95.0
100	585	97.0

Method comparison

A comparison of the Elecsys Toxo IgG assay on the **cobas e** 801 analyzer (y), with the Elecsys Toxo IgG assay on the **cobas e** 601 analyzer (x), gave the following correlations (IU/mL):

Number of samples measured: 210

Passing/Bablok[14]	Linear regression
y = 1.01x - 0.000	y = 1.02x - 1.03
τ = 0.979	r = 0.999

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The sample concentrations were between 0.000 and 620 IU/mL.

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For further information, please refer to the appropriate 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.

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 for reconstitution
GTIN	Global Trade Item Number

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be 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.

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