Elecsys Toxo IgG Avidity

cobas®

REF		Σ	SYSTEM
05802571190	05802571500	100; equals to 50 Toxo IgG avidity determinations	**cobas e** 411 **cobas e** 601 **cobas e** 602

English

System information

For **cobas e** 411 analyzer: test number 940
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 713

Intended use

Immunoassay for the in vitro qualitative determination of the avidity of IgG antibodies to *Toxoplasma gondii* in human serum and plasma.

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

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 also via organ 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.[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 intervention with drug therapy in cases of acute infection during pregnancy can prevent congenital damage or ameliorate the severity of clinical manifestations.[6,7] In the absence of acute clinical symptoms the diagnosis of Toxoplasma infection is based on serologic marker testing, namely IgG and IgM directed against T. gondii.[3,4,9] IgM is considered to be an acute-phase marker, but residual, long-lasting IgM can be detected months or even years after the primary infection.[8,9] Due to this fact, a complementary technique is needed to help refine the date of infection and thus enable appropriate counseling and management of pregnancy. Toxoplasma IgG avidity assays are currently the most reliable method to rule out infection occurring within the last 4 months.[10] The Elecsys Toxoplasma IgG avidity assay measures the functional binding affinity of T. gondii IgG in response to infection. The antibodies produced during the non-primary response or in the remote phase of infection have a higher antigen avidity than antibodies produced during the primary response.[3] No clinical interpretation can be deduced from a low or gray-zone avidity result. Avidity testing should be performed early in gestation; a high avidity result later than the fourth month cannot rule out a primary infection earlier in gestation when low avidity T. gondii IgG may have been present. The detection of high IgG avidity can be considered as a good indicator of past infection.[8]

Test principle

The test principle is based on two, parallel measurements with the Elecsys Toxo IgG Avidity assay.

One aliquot of the sample is diluted with Diluent Universal (DilUni) and this mixture serves as a reference.

A second aliquot of the sample is diluted with Diluent Toxo Avidity (DilToxoAv). During incubation with DilToxoAv, IgG antibodies directed against *Toxoplasma gondii* are bound to *T. gondii*-specific recombinant antigen present in the DilToxoAv diluent.

Both dilution steps have to be performed manually.

The Elecsys Toxo IgG Avidity assay uses the sandwich principle.

Total duration of the assay on the analyzer is 18 minutes for both the reference and DilToxoAv treated samples.

- 1st incubation: 10 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/ProCell 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 reagent barcode or e-barcode.
- The avidity (Avi%) is assessed by determining the ratio between the result (IU/mL) obtained from the aliquot diluted with Diluent Toxo Avidity and the result from the reference aliquot.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The reagent rackpack (M, R1, R2) is labeled as TOXO-AV.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Toxoplasma-Ag~biotin (gray cap), 1 bottle, 9 mL:
Biotinylated *T. gondii*-specific antigen (recombinant, *E. coli*), > 400 µg/L, TRIS buffer 50 mmol/L, pH 7.5; preservative.

R2 Toxoplasma-Ag~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 9 mL:
T. gondii-specific antigen (recombinant, *E. coli*) labeled with ruthenium complex > 400 µg/L; TRIS buffer 50 mmol/L, pH 7.5; preservative.

TOXO-AV Cal1 Negative calibrator 1 (white cap), 2 bottles of 1.0 mL each:
Human serum, non-reactive for anti-Toxoplasma IgG; buffer; preservative.

TOXO-AV Cal2 Positive calibrator 2 (black cap), 2 bottles of 1.0 mL each:
Human serum, reactive for anti-Toxoplasma IgG, approximately 100 IU/mL; buffer; preservative.

DilToxoAv Avidity Diluent (white cap) for manual dilutions, 1 bottle, 12 mL:
T. gondii-specific antigen (recombinant, *E. coli*) in protein matrix, buffer, pH 7.4; 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:

Elecsys Toxo IgG Avidity

cobas®

Warning

H317 May cause an allergic skin reaction.

Prevention:

Prevention:

P261 Avoid breathing mist or vapours.

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

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: all countries: +49-621-7590

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 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.[11,12]

Both calibrators (TOXO-AV Cal1, TOXO-AV 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 (TOXO-AV Cal2) was sterile filtrated.

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 (except for DilToxoAv).

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 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 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 for **cobas e** 602 analyzers: Both the vial labels, and the additional labels (if available) contain 2 different barcodes. Please turn the vial cap 180° into the correct position so that the barcode between the yellow markers can be read by the system. Place the vial on the analyzer 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 and DilToxoAv	
unopened at 2-8 °C	up to the stated expiration date
M, R1, R2, DilToxoAv after opening at 2-8 °C	12 weeks
M, R1, R2 on the analyzers DilToxoAv on bench	2 weeks or 12 weeks if stored alternately in the refrigerator and on the analyzers/on bench (up to 84 hours)

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

Criterion: Mean recovery of positive samples within 80-120 % of serum value.

Stable for 3 weeks at 2-8 °C, 3 days at 25 °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 altered subsequently with additives (biocides, anti-oxidants or substances possibly changing 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 and heat-inactivated samples can be used.

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 1 hour after manual processing (avidity sample handling).

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

- REF 10394246001, 20 x 250 sample cups, needed for the manual dilution step
- REF 05802580190, PreciControl Toxo IgG Avidity, 6 x 1.0 mL
- REF 04618823190, PreciControl Toxo IgG, 16 x 1.0 mL
- REF 11732277122, Diluent Universal, 2 x 16 mL sample diluent or REF 03183971122, Diluent Universal, 2 x 36 mL sample diluent
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles

Elecsys Toxo IgG Avidity

cobas®

- 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.

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

Handling of specimen for the Elecsys Toxo IgG Avidity assay:

Sample concentration needs to be defined with the Elecsys Toxo IgG assay (REF 04618815190) prior to avidity measurement.

Samples found to be reactive using the Elecsys Toxo IgG assay with a concentration between 6-500 IU/mL are split into two aliquots.

If a patient sample is reactive using the Elecsys Toxo IgG assay and has a concentration > 500 IU/mL, the sample must be pre-diluted manually with Diluent Universal according to the following table **before** being split into two aliquots.

Value in Elecsys Toxo IgG assay (IU/mL)	Pre-dilution steps
≥ 6 to ≤ 500 IU/mL	**no** pre-dilution required
> 500 to < 1500 IU/mL	1:20
≥ 1500 IU/mL to < 4000 IU/mL	1:50
≥ 4000 IU/mL	1:100

Dilute one aliquot of the sample 1:2 with Diluent Universal (1 Vol. sample + 1 Vol. DilUni) and mix the diluted aliquot gently by pipetting the mixture up and down once. Dilute the second aliquot of the sample 1:2 with Diluent Toxo Avidity (1 Vol. sample + 1 Vol. DilToxoAv) and mix as described above. Allow both aliquots to stand for at least 10 minutes at ambient temperature (20-25 °C) before placing in the analyzer. Complete all determinations on the analyzer within 1 hour of preparing the dilutions.

Measure both aliquots with the Elecsys Toxo IgG Avidity assay. The operator must ensure that the measurements are performed consecutively with the same reagent lot, the same calibration and on the same analyzer.

Calibration

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

Every Elecsys Toxo IgG Avidity reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using TOXO-AV Cal1 and TOXO-AV Cal2.

Calibration frequency: Calibration must be performed once per reagent lot using TOXO-AV Cal1, TOXO-AV 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 with PreciControl Toxo IgG Avidity outside the defined limits
- more frequently when this is required by pertinent regulations

Quality control

For quality control, use PreciControl Toxo IgG for verification of calibration and PreciControl Toxo IgG Avidity for verification of correctly performed dilution steps and of functionality of the Diluent Toxo Avidity (DilToxoAv).

Please note: PreciControl Toxo IgG Avidity is not barcode-labeled and requires manual preparation. These controls should be prepared in the same way as the specimen samples. For the recommended procedure please refer to the "Assay" section of this document.

- Verification of calibration using PreciControl Toxo IgG:

  The target values and ranges (IU/mL) of the PreciControl Toxo IgG were determined and evaluated by Roche. They were obtained using the Elecsys Toxo IgG Avidity assay reagents and analyzers available at the time of testing. The control values obtained during testing must be within the control ranges (IU/mL) stated in the value sheet. The exact lot-specific target values and ranges are printed on the enclosed (or electronically available) value sheet.

- Verification of correctly performed 1:2 dilution using PreciControl Toxo IgG Avidity:

  The target values and ranges (IU/mL) of the PreciControl Toxo IgG Avidity diluted 1:2 with Diluent Universal were determined and evaluated by Roche. They were obtained using the Elecsys Toxo IgG Avidity assay reagents and analyzers available at the time of testing. The control values obtained during testing must be within the control ranges (IU/mL) stated in the value sheet. The exact lot-specific target values and ranges are printed on the enclosed (or electronically available) value sheet.

- Verification of functionality of the Diluent Toxo Avidity (DilToxoAv) using PreciControl Toxo IgG Avidity:

  The avidity (Avi%) is calculated from the reference measurement and the DilToxoAv-treated measurement as per the "Calculation" section of this document. The target range for the manually calculated avidity result (Avi%) of PreciControl Toxo IgG Avidity 1 is < 70 Avi%, while the respective range for PreciControl Toxo IgG Avidity 2 is ≥ 80 Avi%.

It is recommended to run PreciControl Toxo IgG 1 and 2 as well as PreciControl Toxo IgG Avidity 1 and 2 at the beginning of each working day and after every calibration.

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.

Elecsys Toxo IgG Avidity

cobas®

Calculation

The analyzer automatically calculates the analyte concentration of each sample in IU/mL for both measurements (reference measurement and DilToxoAv-treated measurement).

To calculate the avidity (Avi%) please use the formula given below.

$$\text{Avi(\%)} = 100 - \frac{\text{IU/mL of aliquot treated with DilToxoAv}}{\text{IU/mL of aliquot treated with DilUni}} \times 100$$

Please note:

- If the concentration of the sample diluted with DilUni is < 3 IU/mL (indeterminate result) the avidity calculation cannot be performed.
- If the concentration of the sample diluted with DilToxoAv is < 0.130 IU/mL (< lower detection limit) the avidity calculation cannot be performed.

Interpretation of the results

Results obtained with the Elecsys Toxo IgG Avidity assay are interpreted as follows:

Avidity (Avi%)	Interpretation
< 70	low avidity
70-79	gray-zone
≥ 80	high avidity

No clinical interpretation can be deduced from a low or gray-zone result.

The recommendation in these cases is to take a follow-up sample within an appropriate period of time (e.g. 2-4 weeks) and repeat testing. Elecsys Toxo IgG Avidity results should be used in conjunction with the patient's medical history, clinical symptoms, and other laboratory tests, e.g. Toxo-specific IgG and IgM results. If a Toxo IgG avidity result is discordant with the patient's medical history, clinical symptoms and other laboratory tests, e.g. Toxo-specific IgG and IgM results, further tests should be performed to verify the result and testing of a follow-up sample is recommended. The Toxo IgG avidity results in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagents used. Therefore, the results reported by the laboratory to the physician should include the statement: "The following results were obtained using the Elecsys Toxo IgG Avidity assay. Results from assays provided by other manufacturers cannot be used interchangeably." In rare cases a value of 0 % avidity or negative percentage avidity might be observed; these results are classified as low avidity.

Limitations - interference

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, pre-transplant patients or body fluids other than serum and plasma, such as urine, saliva or amniotic fluid have not been tested.

The assay is unaffected by icterus (bilirubin < 684 µmol/L or < 40 mg/dL), hemolysis (Hb < 1.24 mmol/L or < 2 g/dL), lipemia (Intralipid < 2000 mg/dL) and biotin (< 246 nmol/L or < 60 ng/mL).

Criterion: Mean recovery of positive samples within ± 20 % of serum value.

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.

No interference was observed from rheumatoid factors up to a concentration of 6210 IU/mL.

Among a panel of 30 positive samples within the measuring range (0.13-650 IU/mL) no high-dose hook effect was observed (no increasing signals upon dilution).

In vitro tests were performed on 18 commonly used pharmaceuticals and in addition on spiramycine, sulfadiazine, folic acid and pyrimethamine. No interference with the assay was found.

In rare cases, interference due to extremely high titers of antibodies to 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

Reference measurement:

0.13-650 IU/mL (defined by the lower detection limit and the maximum of the master curve). Values below the lower detection limit are reported as < 0.13 IU/mL. Values above the measuring range are reported as > 650 IU/mL.

Lower limits of measurement

Lower detection limit of the test

Lower detection limit: 0.13 IU/mL

The Lower Detection Limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying two standard deviations above that of the lowest standard (master calibrator, standard 1 + 2 SD, repeatability study, n = 21).

Dilution

Samples with Toxo IgG concentrations > 500 IU/mL must be pre-diluted with Diluent Universal prior to testing with the Elecsys Toxo IgG Avidity assay. Please refer to the "Assay" section of this document for the recommended procedure.

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 executing single avidity measurements for each sample including the manual assay handling according to the assay workflow.

Repeatability (within-run precision): n = 21 single determinations (sample handling was performed by single operator).

Inter-Module precision: n = 8 single results per sample (two runs per module, 4 modules). The following results were obtained:

cobas e 411 analyzer			
	Repeatability		
Sample	Mean Avi%	SD Avi%	CV %
Human serum 1	49	2.1	4.3
Human serum 2	75	1.3	1.7
Human serum 3	93	0.6	0.6
PC[b)] Toxo IgG Avidity 1	42	3.0	7.3
PC Toxo IgG Avidity 2	86	0.9	1.0

b) PC = PreciControl

cobas e 601 and **cobas e** 602 analyzers			
	Inter-Module precision		
Sample	Mean Avi%	SD Avi%	CV %
Human serum 1	42	2.2	5.2
Human serum 2	51	4.3	8.7
Human serum 3	56	1.5	2.7
Human serum 4	80	1.2	1.5
Human serum 5	79	0.8	1.0
Human serum 6	87	0.5	0.5
Human serum 7	92	0.5	0.5

Elecsys Toxo IgG Avidity

cobas®

cobas e 601 and **cobas e** 602 analyzers			
	Inter-Module precision		
Sample	Mean Avi%	SD Avi%	CV %
Human serum 8	94	0.0	0.0
PC Toxo IgG Avidity 1	53	1.5	2.8
PC Toxo IgG Avidity 2	90	0.5	0.5

Analytical specificity

232 potentially cross reacting samples were tested with the Elecsys Toxo IgG assay (equivalent to the Elecsys Toxo IgG Avidity formulation) and a comparison Toxo IgG assay comprising specimens:

- containing antibodies against HBV, HCV, HIV**, CMV, EBV, HSV, VZV**, Parvo B19, Rubella, Treponema pallidum, Malaria*, Amebiasis, Chlamydia and Gonorrhea
- containing autoantibodies (AMA, ANA)
- after vaccination against HBV and Influenza

An overall agreement of 97.8 % (221/226) was found in these specimens with the Elecsys Toxo IgG assay and the comparison test. 127 samples were found concordantly negative and 94 samples were found positive. 6 samples were found indeterminate either with the Elecsys Toxo IgG assay or the comparison test.

* Malaria: 3 samples which were found discordant positive with the Elecsys Toxo IgG assay, revealed also a positive result by a direct agglutination assay.

**VZV: 1 discordant positive sample; HIV: 1 discordant negative sample with the Elecsys Toxo IgG assay

Clinical studies

Overall 455 single and sequential samples (collected and classified by reference laboratories) were investigated with Elecsys Toxo IgG Avidity assay and two commercially available comparison methods. The presumed onset of infection of investigated specimen samples was determined as accurately as possible based on diagnostic testing and if available, clinical indications. The following 3 sample groups were analyzed:

- 135 samples from pregnant women with a presumed onset of infection within less than 4 months (referred to as acute infection).
- 159 samples from pregnant women with a presumed onset of infection within more than 4, but less than 9 months (referred to as late acute infection).
- 161 samples from pregnant women with a presumed onset of infection later than 9 months ago (referred to as remote infection).

The distribution of samples tested within the indicated assays is given in the table below:

Clinical status	Avidity	Elecsys Toxo IgG Avidity assay	Comparison method A	Elecsys Toxo IgG Avidity assay	Comparison method B
		n = 239 samples; site 1		n = 216 samples; site 2	
Acute infection	Low	64	68	65	65
	Gray zone	4	0	2	2
	High	0	0	0	0
Late acute infection	Low	58	61	50	52
	Gray zone	30	19	8	5
	High	12	20	1	2
Remote infection	Low	9	4	31	27
	Gray zone	16	3	10	10
	High	46	64	49	53

References

1 Montoya JG, Liesenfeld O. Toxoplasmosis. Lancet 2004;363:1965-1976.

2 Jones JL, Dubey JP. Foodborne toxoplasmosis. Clin Infect Dis 2012;55:845-851.

3 Halonen SK, Weiss LM. Toxoplasmosis. Handb Clin Neurol 2013;114:125-145.

4 Jones JL, Parise ME, Fiore AE. Neglected parasitic infections in the United States: toxoplasmosis. Am J Trop Med Hyg 2014;90:794-799.

5 Luft BJ, Remington JS. Toxoplasmic encephalitis in AIDS. Clin Infect Dis 1992;15:211-222.

6 Kieffer F, Wallon M. Congenital toxoplasmosis. Handb Clin Neurol 2013;112:1099-1101.

7 Moncada PA, Montoya JG. Toxoplasmosis in the fetus and newborn: an update on prevalence, diagnosis and treatment. Expert Rev Anti Infect Ther 2012;10:815-828.

8 Robert-Gangneux F, Dardé ML. Epidemiology of and diagnostic strategies for toxoplasmosis. Clin Microbiol Rev 2012;25:264-296.

9 Murat JB, Hidalgo HF, Brenier-Pinchart MP, et al. Human toxoplasmosis: which biological diagnostic tests are best suited to which clinical situations? Expert Rev Anti Infect Ther 2013;11:943-956.

10 Murat JB, L'Ollivier C, Fricker Hidalgo H, et al. Evaluation of the new Elecsys Toxo IgG avidity assay for toxoplasmosis and new insights into the interpretation of avidity results. Clin Vaccine Immunol. 2012;19:1838-1843.

11 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

12 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 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.

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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

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

CE 0123

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606

Roche