Elecsys Toxo IgG Avidity

cobas®

REF		Σ	SYSTEM
07027974190	07027974500	100; equals to 50 Toxo IgG avidity determinations	**cobas e** 402 **cobas e** 801

English

System information

See section "**cobas e** flows".

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 **cobas e** immunoassay analyzers.

Summary

The Elecsys Toxo IgG Avidity assay is an immunoassay for the qualitative detection of the avidity of IgG antibodies to *Toxoplasma gondii* in human serum and plasma. The assay is intended to be used as an aid in the assessment of the immune status and in the estimation of the time of infection with *Toxoplasma gondii* in suspected patients and pregnant women.

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 identification of infection and initiation of appropriate 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 presence of IgG antibodies to *Toxoplasma gondii* is indicative of a latent or acute infection.[9] IgM is typically a marker of acute infection, but residual, long-lasting IgM can be detected months or even years after the primary infection.[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. To differentiate between a recently acquired and past infection, specimens that are positive for IgM and IgG may be tested for IgG avidity.[9] Toxoplasma IgG avidity assays are reliable methods to rule out recent infection occurring within the last 4 months.[10] The Toxoplasma IgG avidity assay measures the functional binding affinity of *Toxoplasma 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.[9] Avidity testing should be performed early in gestation; a high avidity result later than the fourth month cannot rule out whether a primary infection may have occurred earlier in gestation when low avidity *Toxoplasma gondii* IgG may have been present.[9]

Test principle

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

One aliquot of the sample is preincubated with PT1 (Diluent Universal) and this mixture serves as a reference.

A second aliquot of the sample is preincubated with PT2 (Avidity Diluent). During incubation with DilToxoAv, IgG antibodies directed against *Toxoplasma gondii* are bound to *T. gondii*-specific recombinant antigen present in the Avidity Diluent.

The Elecsys Toxo IgG Avidity assay uses the sandwich principle.

Total duration of the assay on the analyzer is 27 minutes for both the reference and DilToxoAv treated samples.

- 1st incubation: 2 x 18 µL of sample (each for the reference reaction and the avidity reaction), 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.
- The avidity (Avi%) is assessed by determining the ratio between the result (IU/mL) obtained from the aliquot diluted with Avidity Diluent and the result from the reference aliquot.

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

Reagents - working solutions

The **cobas e** pack (M, R1, R2, PT1, PT2) is labeled as TOXOAV.

M Streptavidin-coated microparticles, 1 bottle, 6.4 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Toxoplasma-Ag~biotin, 1 bottle, 9.9 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, 9.9 mL:
T. gondii-specific antigen (recombinant, E. coli) labeled with ruthenium complex > 400 µg/L; TRIS buffer 50 mmol/L, pH 7.5; preservative.

b) TRIS = Tris(hydroxymethyl)aminomethane

PT1 Diluent Universal, 1 bottle, 12.1 mL

PT2 Avidity Diluent (DilToxAv), 1 bottle, 4.7 mL:
T. gondii-specific antigen (recombinant, E. coli) in protein matrix, buffer, pH 7.4; preservative.

TOXOAV Cal1 Negative calibrator 1, 2 bottles of 1.0 mL each:
Human serum, non-reactive for anti-Toxoplasma IgG; buffer; preservative.

TOXOAV Cal2 Positive calibrator 2, 2 bottles of 1.0 mL each:
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.

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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:

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 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.[11,12]

The calibrators (TOXOAV Cal1, TOXOAV 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 (TOXOAV Cal2) was 0.2 micron filtrated.

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

Reagent handling

The reagents (M, R1, R2, PT1, PT2) 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 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 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.

Plasma tubes containing separating gel can be used.

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 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 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.

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 2.0 mL
- REF 04618823190, 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 **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

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- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- 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.

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.

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. Different **cobas e** flows are available to automatically perform all steps necessary for the determination of Toxo IgG avidity in a sample. An avidity result message will be reported.

Handling of sample for the Elecsys Toxo IgG Avidity assay:
Toxo IgG titer of the respective sample needs to be defined with the Elecsys Toxo IgG assay (REF 07028008190) prior to avidity measurement. Depending on the Toxo IgG titer the respective **cobas e** flow procedure has to be selected according to the table below.

Value in Elecsys Toxo IgG assay	**cobas e** flow to be selected	Description
≥ 6 to ≤ 500 IU/mL	TOXOA L	Toxo IgG Avidity Low Titer
> 500 to < 1500 IU/mL	TOXOA M	Toxo IgG Avidity Medium Titer
≥ 1500 IU/mL to < 4000 IU/mL	TOXOA H	Toxo IgG Avidity High Titer
≥ 4000 IU/mL	TOXOA VH	Toxo IgG Avidity Very High Titer

Please note:

- If the concentration of the sample is < 6 IU/mL the avidity calculation cannot be performed.
- If the result of the **cobas e** flow TOXOA VH is above the measuring range, a manual predilution of the sample is necessary.

Calibration

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

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

Calibration frequency: Calibration must be performed once per reagent lot using TOXOAV Cal1, TOXOAV 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 Toxo IgG for verification of calibration and PreciControl Toxo IgG Avidity for verification of functionality of the PT2 Avidity Diluent (DilToxoAv).

Use **cobas e** flow **TOXOA L** for determination of the PreciControl Toxo IgG Avidity.

- 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). The exact lot-specific target values and ranges are printed on the electronically available value sheet.
- Verification of functionality of the PT2 Avidity Diluent (DilToxoAv) using PreciControl Toxo IgG Avidity:
  As part of the **cobas e** flow **TOXOA L** the avidity (Avi%) is calculated from the reference measurement and the DilToxoAv-treated measurement automatically. The target range for the 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.

Calculation

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

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

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.

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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
Biotin	≤ 287 nmol/L or ≤ 70 ng/mL
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: Recovery 80-120 % (percent deviation based on IU/mL).

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.

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 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:

0.18-650 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.

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 %).

Specific performance data

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

Precision

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

cobas e 402 and **cobas e** 801 analyzers					
		Repeatability		**Intermediate precision**	
Sample	Mean Avi%	SD Avi%	CV %	SD Avi%	CV %
Human serum 1	38	1.30	3.4	2.07	5.4
Human serum 2	76	0.699	0.9	0.802	1.1
Human serum 3	91	0.351	0.4	0.388	0.4
PC[c)] Toxo IgG Avidity 1	57	1.61	2.8	1.76	3.1
PC Toxo IgG Avidity 2	88	0.418	0.5	0.543	0.6

c) PC = PreciControl

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*, Parvovirus 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 samples with the Elecsys Toxo IgG assay and the comparison test. 127 samples were found concordantly negative and 94 samples were found concordantly positive. 6 samples were found indeterminate either with the Elecsys Toxo IgG assay or the comparison test and were not included in the agreement calculation.

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

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

Clinical studies

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

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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	
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.

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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 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).

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

CE 0123

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

Roche