

## Toxoplasma G (Toxo G)

### Assay for the Detection of IgG Antibodies to *Toxoplasma gondii*

Current revision and date <sup>a</sup>	Rev. Y, 2015-03	
Product Name	ADVIA Centaur® Toxoplasma G assay	REF 04520287 (120154)
Systems	ADVIA Centaur system ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur Toxo G Quality Control Material	REF 06317233 (120382)
	ADVIA Centaur Wash 1 (2 x 1500 mL)	REF 01137199
	ADVIA Centaur Wash 1 (2 x 2500 mL)	REF 03773025
	ADVIA Centaur Probe Wash 3	REF 03333963
Specimen Types	Serum, Heparinized Plasma, EDTA Plasma	
Assay Range	0.5–700 IU/mL	
Reagent Storage	2–8°C	
Reagent On-System Stability	28 days	

<sup>a</sup> In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.



#### WARNING

The calculated values for toxoplasma IgG in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the toxoplasma IgG assay used. Values obtained with different assay methods cannot be used interchangeably.

## Intended Use

The ADVIA Centaur® Toxoplasma G (Toxo G) assay is an IgG antibody capture microparticle direct chemiluminometric *in vitro* diagnostic immunoassay intended for the quantitative and qualitative detection of IgG antibodies to *Toxoplasma gondii* in serum or plasma (EDTA, heparin) using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems.

The measurement of toxoplasma IgG may be used to aid in the assessment of a patient's immunological response from individuals including women of childbearing age. This assay may be utilized with a toxoplasma IgM result to determine recent serological response to *Toxoplasma gondii*.

This assay is not intended for use in screening blood, plasma, or tissue donors.

## Summary and Explanation

*Toxoplasma gondii* is an intracellular parasitic protozoan that affects birds and mammals, with cats being the primary host. Infection is typically spread by eating raw or undercooked meat containing cysts or by coming in contact with oocyst-infected cat feces. Climate, dietary customs, and presence of cats influence the prevalence of *T. gondii*, which can vary considerably by geographical location and age. In healthy immunocompetent individuals, infections are usually asymptomatic or subclinical. If toxoplasmosis is diagnosed during the early stages of infection, the disease can be treated effectively with antibiotic therapy.

In pregnant women, *T. gondii* infection poses a potential threat to the fetus. The risk of a pregnant woman passing infection to the fetus is approximately 25% in the first trimester and increases to approximately 65% in the third trimester.<sup>1</sup> The earlier in the pregnancy that the mother is infected the greater the potential severity of congenital toxoplasmosis. If the fetus becomes infected, the infant may have symptoms such as lymphadenopathy, chorioretinitis, microcephaly and cerebral calcifications.

In immunosuppressed populations, such as cancer patients undergoing chemotherapy, transplants recipients, and AIDS patients, *T. gondii* has emerged as an important opportunistic pathogen leading to severe or fatal infections.<sup>2,3</sup> The immunosuppressed state of these patients is thought to allow reactivation of a latent infection,<sup>3</sup> and these patients may present symptoms such as headaches, confusion, fever, and focal neurological deficits.

Use of toxoplasma IgG assays has been shown to be a reliable method for establishing immune status and evaluating susceptibility to *T. gondii* infection. The presence of IgG antibodies indicates that the individual has been infected with toxoplasma in the past, but the level of reactivity does not indicate how recently the infection occurred. In the majority of AIDS patients, the IgG response to primary *T. gondii* infection often lacks a significant rise in IgG titers.<sup>4</sup>

## Principles of the Procedure

The ADVIA Centaur Toxo G assay is an immunoglobulin class-capture sandwich immunoassay using direct, chemiluminometric technology. The anti-human IgG<sub>FC</sub> monoclonal antibody is covalently coupled to paramagnetic particles in the Solid Phase. In the Lite Reagent, the purified *T. gondii* antigen is complexed to an anti-p30 monoclonal antibody (F(ab)<sub>2</sub> fragment) labeled with acridinium ester. Antibody-antigen complexes will form if toxoplasma IgG is present in the sample.

## Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur Toxo G ReadyPack® primary reagent pack; Lite Reagent	10.0 mL/reagent pack <i>T. gondii</i> p30 antigen (~0.75 µg/mL) complexed with mouse anti-p30 monoclonal antibody (F(ab) <sub>2</sub> fragment) labeled with acridinium ester in protein buffer with surfactant and preservatives	2–8°C	<b>Unopened:</b> Stable until the expiration date on the carton <b>On-system:</b> 28 days
ADVIA Centaur Toxo G ReadyPack primary reagent pack; Solid Phase Reagent	25.0 mL/reagent pack anti-human IgG <sub>FC</sub> monoclonal antibody (~0.3 mg/mL) covalently coupled to paramagnetic particles in protein buffer with surfactant and preservatives	2–8°C	<b>Unopened:</b> Stable until the expiration date on the carton <b>On-system:</b> 28 days
ADVIA Centaur Toxo G calibrator	1.0 mL/vial processed human plasma positive for toxoplasma IgG antibodies with preservatives	2–8°C	<b>Unopened:</b> Stable until the expiration date on the vial <b>On-system:</b> 8 hours
ADVIA Centaur Toxo G quality control material <sup>a</sup>	2.7 mL/vial processed human plasma negative and positive for toxoplasma IgG antibodies with preservatives	2–8°C	<b>Unopened:</b> Stable until the expiration date on the vial <b>On-system:</b> 8 hours
ADVIA Centaur Probe Wash 3 <sup>a</sup> <b>PW 3</b>	50.0 mL/pack sodium hypochlorite (0.5%), sodium hydroxide (< 0.5%), pH 11.0	2–8°C	<b>Unopened:</b> Stable until the expiration date on the vial <b>On-system:</b> 100 days
ADVIA Centaur Wash 1 <sup>a</sup> <b>WASH 1</b>	1500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	<b>Unopened:</b> Stable until the expiration date on the pack <b>On-system:</b> 1 month
ADVIA Centaur Wash 1 <sup>a</sup> <b>WASH 1</b>	2500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	<b>Unopened:</b> Stable until the expiration date on the pack <b>On-system:</b> 1 month

<sup>a</sup> See *Materials Required but Not Provided*.

## Warnings and Precautions

Safety data sheets (MSDS/SDS) available on [www.siemens.com/diagnostics](http://www.siemens.com/diagnostics).



### CAUTION POTENTIAL BIOHAZARD

Contains human source material. While each human serum or plasma donor unit used in the manufacture of this product was tested by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2, all products manufactured using human source material should be handled as potentially infectious. Because no test method can offer complete assurance that hepatitis B or C viruses, HIV, or other infectious agents are absent, these products should be handled according to established good laboratory practices.<sup>5–7</sup>



### CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

For *in vitro* diagnostic use.

## Preparing Reagents

All reagents are liquid and ready to use.

Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to the system operating instructions.

### Note

- Discard reagent packs at the end of the on-system stability interval.
- Do not use reagents beyond the expiration date.

## Storing and Stability

Store the reagents upright at 2–8°C.

Protect reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from heat and light sources.

All reagents are stable at 2–8°C until the expiration date on the packaging.

## Specimen Collection and Handling

Serum, heparinized plasma, or EDTA plasma are the recommended sample types for this assay. Do not use heat inactivated specimens. The performance of the ADVIA Centaur Toxo G assay has not been established with cord blood, neonatal specimens, cadaver specimens, or body fluids other than serum or plasma such as saliva, urine, amniotic, or pleural fluids.

- Handle all samples as if capable of transmitting disease.
- Test samples as soon as possible after collecting. Store samples at 2–8°C if not tested immediately.
- Store specimens at 2–8°C up to 7 days. Specimens may be stored on the clot.
- Freeze samples, devoid of red blood cells, at or below -20°C for longer storage. Do not store in frost-free freezer. When weakly positive samples and negative samples were subject to 3 freeze/thaw cycles, no qualitative differences were observed.
- Package and label samples for shipment in compliance with applicable federal and international regulations covering the transport of clinical samples and etiological agents. Samples maintained at room temperature up to 7 days or refrigerated up to 14 days demonstrated no qualitative differences. Store samples at 2–8°C upon arrival. If shipment is expected to exceed 7 days, ship specimens frozen.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

## Procedure

### Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
04520287 (120154)	1 ReadyPack primary reagent pack containing ADVIA Centaur Toxo G Lite Reagent and Solid Phase  ADVIA Centaur and ADVIA Centaur CP Toxo G Master Curve card  1 vial ADVIA Centaur Toxo G low calibrator <span>CAL L</span> 1 vial ADVIA Centaur Toxo G high calibrator <span>CAL H</span>  ADVIA Centaur and ADVIA Centaur CP Toxo G Calibrator Assigned Value cards	100

### Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description
REF 06317233 (120382)	ADVIA Centaur Toxo G quality control material 2 x 2.7 mL negative control <span>CONTROL -</span> 2 x 2.7 mL positive control <span>CONTROL +</span> Expected Value card
REF 01137199 (112351)	ADVIA Centaur Wash 1 <span>WASH 1</span> 2 x 1500 mL/pack
REF 03773025	ADVIA Centaur Wash 1 <sup>a</sup> <span>WASH 1</span> 2 x 2500 mL/pack
REF 03333963	ADVIA Centaur Probe Wash 3 <sup>a</sup> <span>PW 3</span> 50.0 mL

<sup>a</sup> For use with systems with 2500 mL capacity.

### Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following actions:

- Dispenses 10 µL of sample into a cuvette.
- Dispenses 250 µL of Solid Phase and incubates the mixture for 18 minutes at 37°C.
- Separates the Solid Phase from the mixture and aspirates the unbound reagent.
- Washes the cuvette with Wash 1.
- Dispenses 100 µL Lite Reagent and incubates the mixture for 18 minutes at 37°C.
- Separates the Solid Phase from the mixture and aspirates the unbound reagent.
- Washes the cuvette with Wash 1.
- Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
- Reports results according to the selected option, as described in the system operating instructions.

A direct relationship exists between the amount of toxoplasma IgG activity present in the patient sample and the amount of relative light units (RLUs) detected by the system. A result of reactive (positive) or nonreactive (negative) is determined using a clinical cutoff value of 10 IU/mL. Refer to *Interpretation of Results* for a description.

The system will wash the reagent probe with PW3 to mitigate potential interference between the ADVIA Centaur Toxo G assay and other assays.

## Preparing the System

Ensure that the system has sufficient primary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Load the ReadyPack primary reagent packs in the primary reagent compartment using the arrows on the packs as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about preparing the reagents for use, refer to the system operating instructions.

## Preparing the Samples

This assay requires 10 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For detailed information about determining the minimum required volume, refer to the system operating instructions.

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter. Remove particulates by filtration or centrifugation at 1000 x g for 10–15 minutes.
- Samples are free of bubbles.

## On-System Stability

The ADVIA Centaur Toxo G assay reagents are stable unopened until the expiration date on the carton or onboard the system for 28 days.

## Performing Calibration

For calibration of the ADVIA Centaur Toxo G assay, use ADVIA Centaur Toxo G Calibrators provided with each kit. The calibrators provided in this kit are matched to the ReadyPack primary reagent pack.

**Note** The Low and High Calibrators provided in this kit are matched to the ReadyPack primary reagent pack. Do not mix calibrator lots with different lots of reagent packs.

Each lot of calibrators contains a Calibrator Assigned Value card to facilitate entering the calibration values on the system. Enter the values using the barcode scanner or the keyboard.

Perform the calibration procedure using the following steps:

**Note** This procedure uses calibrator volumes sufficient to measure each calibrator in duplicate.

1. Schedule the calibrators to the worklist.
2. Label two sample cups with calibrator barcode labels: one for the low and another for the high.
3. Gently mix the Low and High Calibrators and dispense at least 3–4 drops into the appropriate sample cups.

**Note** Each drop from the calibrator vial is approximately 50 µL.

4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

**Note** Dispose of any calibrator remaining in the sample cups after 8 hours. Do not refill sample cups when the contents are depleted; if required, dispense fresh calibrators.

## Calibration Frequency

Calibrate the assay at the end of the 14-day calibration interval.

Additionally, the ADVIA Centaur Toxo G assay requires a two-point calibration:

- When changing lot numbers of primary reagent packs.
- When replacing system components.
- When quality control results are repeatedly out of range.

## Using Barcode Labels

Calibrator barcode labels are lot-number specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.

Use the ADVIA Centaur Toxo G Calibrator barcode labels to identify the Low and High Calibrator sample cups when performing the ADVIA Centaur Toxo G assay. Place the barcode label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

## Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

For quality control of the ADVIA Centaur Toxo G assay, use ADVIA Centaur Toxo G quality control material. Refer to the Expected Value card for the suggested expected values specific for the lot number of the positive and negative controls.

For detailed information about entering quality control values, refer to the system operating instructions.

To monitor system performance and chart trends, as a minimum requirement, two levels of quality control material should be assayed on each day that samples are analyzed. Quality control samples should also be assayed when performing a two-point calibration. Treat all quality control samples the same as patient samples.

Perform the quality control procedure using the following steps:

**Note** This procedure uses control volumes sufficient to measure each control in duplicate.

1. Schedule the quality control samples to the worklist.
2. Label two sample cups with quality control barcode labels: one for the positive and another for the negative.
3. Gently mix the quality control materials and dispense at least 3–4 drops into the appropriate sample cups.

**Note** Each drop from the control vial is approximately 50 µL.

4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

**Note** Dispose of any quality control materials remaining in the sample cups after 8 hours. Do not refill sample cups when the contents are depleted; if required, dispense fresh quality control materials.

## Using Barcode Labels

Control barcode labels are lot-number specific. Do not use barcode labels from one lot of controls with any other lot of controls.

Use the ADVIA Centaur Toxo G quality control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur Toxo G assay. Place the barcode label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

## Taking Corrective Action

If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.

## Results

### Calculation of Results

For detailed information about how the system calculates results, refer to the system operating instructions.

The system reports toxoplasma IgG antibody results in IU/mL and as reactive (positive) or nonreactive (negative).

### Interpretation of Results

The clinical cutoff of the ADVIA Centaur Toxo G assay was determined by analysis of seronegative and seropositive samples that had been confirmed using a commercially available toxoplasma IgG EIA. The distribution of values was plotted after analysis, and the cutoff of the assay (10.0 IU/mL) was set at the point where relative specificity of > 99% and relative sensitivity of > 98% were achieved.

A Cutoff Value of 10.0 IU/mL is used to distinguish reactive (positive) from nonreactive (negative) samples:

- Samples with a calculated value of less than 6.4 IU/mL are considered nonreactive (negative).
- Samples with a calculated value between 6.4 and 9.9 IU/mL are equivocal.
- Samples with a calculated value greater than or equal to 10.0 IU/mL are considered reactive (positive).

Sample results are invalid and must be repeated if the controls are out of range.

The magnitude of the measured result above the cutoff is not indicative of the total amount of antibody present in the sample.

The detection of toxoplasma IgG in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagent specificity.



Interpretations for *Toxoplasma gondii* serology results are provided in the following table:

Anti- <i>T. gondii</i> IgG Result	Anti- <i>T. gondii</i> IgM Result	Interpretation
Negative	Negative	It is presumed that the patient has not been infected with and is not undergoing an acute infection with <i>T. gondii</i> . If symptoms persist, submit a new specimen within 3 weeks.
Positive	Negative	From these results, it cannot be determined whether the patient is or is not undergoing a reactivated <i>T. gondii</i> infection. It appears that the patient has been previously infected with <i>T. gondii</i> . Infection may have occurred more than one year ago. If the individual has not previously tested positive for <i>T. gondii</i> antibodies, confirm the result with a reference laboratory with experience in the diagnosis of toxoplasmosis.
Equivocal	Negative	Obtain a new specimen for further testing. Patient may not be undergoing an acute infection with <i>T. gondii</i> . Determining whether the patient has been previously infected with <i>T. gondii</i> is not possible.
Negative	Equivocal	Obtain a new specimen for determination of IgM antibodies to <i>T. gondii</i> . It cannot be determined if the patient is undergoing an acute <i>T. gondii</i> infection. It appears that the patient has not been previously infected with <i>T. gondii</i> . If the new specimen result is positive or equivocal for IgM antibodies, the specimen should be sent to a reference laboratory with experience in the diagnosis of toxoplasmosis for further testing.
Positive	Equivocal	Obtain a new specimen for determination of IgM antibodies to <i>T. gondii</i> . It cannot be determined if the patient is undergoing an acute <i>T. gondii</i> infection. It appears that the patient may have been previously infected with <i>T. gondii</i> . If the new specimen result is positive or equivocal for IgM antibodies, the specimen should be sent to a reference laboratory with experience in the diagnosis of toxoplasmosis for further testing.
Equivocal	Equivocal	Obtain a new specimen for further testing. It cannot be determined if the patient is undergoing an acute infection or has been previously infected with <i>T. gondii</i> . If the new specimen result is positive or equivocal for IgM and/or IgG antibodies to <i>T. gondii</i> , the specimen should be sent to a reference laboratory with experience in the diagnosis of toxoplasmosis for further testing.
Negative	Positive	Obtain a new specimen for further testing. The patient may or may not be acutely infected with <i>T. gondii</i> . Since the IgG antibodies to <i>T. gondii</i> are negative, the specimen may have been obtained too early in the disease process for an accurate determination. Retest the new specimen with a different anti- <i>T. gondii</i> IgM assay. If the new specimen result is still positive for <i>Toxoplasma</i> IgM antibodies, the specimen should be sent to a reference laboratory with experience in the diagnosis of toxoplasmosis for further testing.

Anti- <i>T. gondii</i> IgG Result	Anti- <i>T. gondii</i> IgM Result	Interpretation
Positive	Positive	The patient may or may not be acutely infected with <i>T. gondii</i> . Obtain a new specimen for further testing. Since the IgG and IgM antibodies to <i>T. gondii</i> are positive, it appears the patient may be acutely infected with <i>T. gondii</i> . The new specimen should be repeated with a different anti- <i>T. gondii</i> IgG and IgM assay. If the new specimen is still positive for IgG and IgM antibodies to <i>T. gondii</i> , the specimen should be sent to a reference laboratory with experience in the diagnosis of toxoplasmosis for further testing.
Equivocal	Positive	It cannot be determined if the patient is acutely infected with <i>T. gondii</i> . Obtain a new specimen for further testing. Determining whether the patient has been previously infected with <i>T. gondii</i> is not possible. The specimen may have been collected too early during the disease process for an accurate determination. Retest the new specimen with a different anti- <i>T. gondii</i> IgM and IgG assay. If the new specimen result is still positive for IgM and the IgG is positive/negative/equivocal for antibodies to <i>T. gondii</i> , the specimen should be sent to a reference laboratory with experience in the diagnosis of toxoplasmosis for further testing.

## Limitations

The following information pertains to limitations of the assay:

The ADVIA Centaur Toxo G assay is limited to the detection of IgG antibodies to *T. gondii* in human serum or plasma.

Specimens collected in the early stages of infection may have IgG levels that are classified as negative.

Do not use heat inactivated specimens. The performance of the ADVIA Centaur Toxo G assay has not been established with cord blood, neonatal specimens, cadaver specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic, or pleural fluids.

The use of the assay to diagnose recent infection by testing acute and convalescent samples has not been validated.

Because toxoplasma IgG may remain in serum for many months after infection, use caution in interpreting results from patients who may have received blood transfusions or infusion of other blood products within the past several months.

In geographic regions that have an apparent low prevalence of toxoplasma IgG in asymptomatic populations, the positive predictive value of any assay is reduced due to the increased possibility that a positive result is actually falsely positive.<sup>8</sup> As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.<sup>9</sup>

Human anti-mouse antibodies (HAMA) or heterophile antibodies may be present in samples from individuals exposed to mouse or animal immunoglobulins from natural sources or as part of disease therapies. These antibodies may interfere with the ADVIA Centaur Toxo G assay and give falsely positive or falsely negative results.<sup>10</sup> These samples should not be tested.

The presence of anti-nuclear antibodies (ANA) and anti-mitochondrial antibodies (AMA) in samples from patients with autoimmune syndrome may interfere with the ADVIA Centaur Toxo G assay and give falsely positive or falsely negative results. These samples should not be tested.

For patient samples measuring at or around the cutoff value of 10 to 17 IU/mL, significantly elevated or increasing concentrations of total IgG may change a positive qualitative interpretation to equivocal, or rarely, may result in a negative interpretation.

## Expected Values

The prevalence of IgG antibody to *T. gondii* varies considerably by geographic location and the age of the patient. The following seroprevalence rates for various populations have been reported in the literature:

Location	Seroprevalence Rate
<b>Europe</b>	
France, Italy	50–85%, by region
Germany	20–72%, by region
United Kingdom	20%
Japan	24%
Africa	20–65%, by country
S. America	36–82%, by country
N. America	8–38%, by region

In clinical trials, the seropositive rates for IgG antibody to *T. gondii* of samples obtained in the U.S. from pregnant women (N = 494) and low risk and healthy individuals (N = 1224) were 15.0% and 18.6%, respectively.

The distribution of ADVIA Centaur Toxo G classifications observed in the clinical trials are summarized below:

Population	N	Positive
Pregnant women	494	74 (15.0%)
Random Hospital/Clinical patients	1224	228 (18.6%)
Total	1718	302 (17.6%)

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.<sup>9</sup>

## Performance Characteristics

### Analytical Measuring Range

The ADVIA Centaur Toxo G assay measures IgG antibodies to *Toxoplasma gondii* concentrations from 0.5–700 IU/mL.

### Clinical Sensitivity and Specificity

The performance of the ADVIA Centaur Toxo G assay was determined by testing a total of 1804 samples at three sites. The ADVIA Centaur results were compared to test results generated on a commercially available, automated toxoplasma IgG EIA. Fresh and frozen samples were used. The samples included the following populations: prenatal (N = 494), asymptomatic blood donors (N = 418), asymptomatic hospital patients (N = 806), and 86 patients with confirmed toxoplasma IgG positive status.

### Initial Relative Sensitivity

Using the alternative method, 388 tested positive for toxoplasma IgG antibody. Of the specimens that tested positive, 12 were equivocal, 363 were positive, and 13 were negative using the ADVIA Centaur Toxo G assay. The initial relative sensitivity was 96.5%.

## Initial Relative Specificity

Using the alternative method, 1400 tested negative for toxoplasma IgG antibody. Of the specimens that tested negative, 11 were equivocal, 19 were positive, and 1370 were negative using the ADVIA Centaur Toxo G assay. The initial relative specificity was 98.6%.

**Note** Samples giving equivocal results were not included in the calculation of relative sensitivity, relative specificity, and relative agreement.

## Relative Sensitivity, Specificity, and Agreement Before Resolution of Discordant Samples

Site	N	Initial Relative Sensitivity (%)	Initial Relative Specificity (%)	Initial Relative Agreement (%)
1	804	99.5 (210/211)	98.4 (568/577)	98.7 (778/788)
2	500	94.7 (89/94)	97.7 (384/393)	97.1 (473/487)
3	500	90.1 (64/71)	99.8 (418/419)	98.4 (482/490)
<b>Total</b>	<b>1804</b>	<b>96.5 (363/376)</b>	<b>98.6 (1370/1389)</b>	<b>98.2 (1733/1765)</b>

**Note** *Relative* refers to a direct comparison of ADVIA Centaur Toxo G results to that of a similar assay. No attempt has been made to correlate with disease presence or absence, and no judgement can be made regarding the predicate assay's accuracy to predict toxoplasma disease.

## Resolution of Discordant Samples

Samples with discordant results were tested using another commercially available test for toxoplasma IgG. The resolved results are shown in the following table.

**Note** Samples giving equivocal results were not included in the calculation of relative sensitivity, relative specificity, and relative agreement.

## Relative Sensitivity, Specificity, and Agreement after Resolution of Discordant Samples

Site	N	Relative Sensitivity (%)	Relative Specificity (%)	Relative Agreement (%)
1	804	99.5 (210/211)	99.3 (571/575)	99.4 (781/786)
2	500	95.8 (92/96)	99.7 (387/388)	99.0 (479/484)
3	500	94.1 (64/68)	99.8 (422/423)	99.0 (486/491)
<b>Total</b>	<b>1804</b>	<b>97.6 (366/375)</b>	<b>99.6 (1380/1386)</b>	<b>99.1 (1746/1761)</b>

**Note** Initially discordant samples in the trial (N = 32) were repeated in duplicate using the predicate device, and repeat discordant samples were tested on a secondary toxoplasma IgG EIA. Relative agreement, sensitivity, and specificity calculations are based on observations after resolution testing was conducted. Calculations of relative specificity and sensitivity do not include specimens that gave equivocal results on either the ADVIA Centaur Toxo G assay or predicate EIA. Relative agreement calculations are based on the number of concordant positive and negative samples for the ADVIA Centaur Toxo G assay and EIA.

## Precision

Reproducibility of the ADVIA Centaur Toxo G assay was determined as described in CLSI protocol EP5-A2.<sup>11</sup> A 5-member panel was assayed two times in two separate daily runs, over a period of 20 days (N = 80). The following results were obtained using one reagent lot and a stored calibration curve:

Panel Member	N	Mean Concentration (IU/mL)	Within-run		Total <sup>a</sup>	
			SD	%CV	SD	%CV
Negative Control	80	0.37	0.06	NA <sup>b</sup>	0.09	NA
Positive Control	80	27.54	0.89	3.2	0.98	3.6
1	80	1.67	0.09	5.2	0.12	7.3
2	80	8.22	0.14	1.7	0.33	4.0
3	80	20.00	0.27	1.3	0.65	3.3

a Includes within-run and run-to-run.

b Not applicable.

System reproducibility was determined by testing a 6 member panel with 3 reagent lots including 5 instruments and 3 sites over multiple days. The panel was assayed three times in each of 40 runs. The following results were obtained:

Panel Member	N	Mean Concentration (IU/mL)	Within-run		Total <sup>a</sup>	
			SD	%CV	SD	%CV
Negative Control	210	0.20	0.23	NA <sup>b</sup>	0.25	NA
Positive Control	210	29.91	0.61	2.05	0.75	2.51
1	120	18.32	0.44	2.42	0.53	2.91
2	120	45.02	0.84	1.86	1.12	2.50
3	120	50.57	0.96	1.89	1.15	2.27
4	120	123.71	7.84	6.33	7.88	6.37

a Includes within-run and run-to-run.

b Not applicable.

## Interferences

Following the Clinical and Laboratory Standards Institute (CLSI) guidelines,<sup>12</sup> toxoplasma IgG positive and negative samples were tested for interference as follows:

Serum specimens that are . . .	Demonstrate ≤ 10% change in results . . .
hemolyzed	up to 500 mg/dL of hemoglobin
lipemic	up to 1000 mg/dL of triglycerides
icteric	up to 60 mg/dL of conjugated bilirubin up to 40 mg/dL of unconjugated bilirubin
hypo/hyperproteinemia	between 3–12 g/dL of protein

## Evaluation of Potentially Interfering Disease States

Potentially cross-reactive or interference samples were evaluated using the ADVIA Centaur Toxo G assay and a commercially available, automated toxoplasma IgG EIA. Populations evaluated included RF, CMV, EBV, HSV, VZV, syphilis, multiple myeloma, parvovirus B19, measles, and influenza vaccinees. Of the 93 samples tested, 93 (100%) were negative by the EIA. Using the ADVIA Centaur Toxo G assay, specificity of 100% was achieved on the EIA negative samples. No significant interference or cross-reactivity for these disease states was indicated.

## Linearity

The linearity of the ADVIA Centaur Toxo G assay was determined using a differential dilution series from two serum pools with anti-*T. gondii* titers of 8 and 930 IU/mL. Linear regression analysis of expected versus observed values indicated less than 5% recovery bias across the range.

## Standardization

The ADVIA Centaur Toxo G assay standardization is traceable to World Health Organization (WHO) 3rd International standard for human anti-toxoplasma serum (TOXM). A comparison over the range of 0 to 500 IU/mL using four lots of reagents gave the following correlation:

$$\begin{aligned}\text{ADVIA Centaur Toxo G} &= 1.02 (\text{WHO}) + 10.7 \text{ IU/mL} \\ r &= 0.99\end{aligned}$$

Assigned values for calibrators and controls are traceable to this standardization.

## Technical Assistance

For customer support, please contact your local technical support provider or distributor.

[www.siemens.com/diagnostics](http://www.siemens.com/diagnostics)














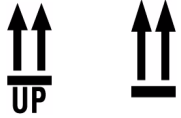










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## Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
	<i>In vitro</i> diagnostic medical device	 <b>REF</b>	Catalog number
	Legal manufacturer		Authorized Representative in the European Community
	CE Mark		CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat		Up
	Use by		Contains sufficient for (n) tests
	Batch code		Shake the reagent pack vigorously. Refer to <i>Preparing Reagents</i> in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	<b>Rev.</b>	Revision
	Master Curve Definition		Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
	Lot Details		Green dot
	Recycle		Printed with soy ink



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US Pats 5,609,822; 5,788,928

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