



ARCHITECT

SYSTEM

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Toxo IgG

REF 6C19

48-3427/R3

B6C190

Read Highlighted Changes
Revised January, 2009

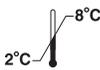
Toxo IgG

Customer Service

For additional product information, please contact your local customer service organization.

This Package insert must be read carefully prior to use. Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

REF	List Number	ASSAY CD-ROM	Assay CD-ROM
IVD	<i>In Vitro</i> Diagnostic Medical Device	CONTROL NO.	Control Number
LOT	Lot Number	REAGENT LOT	Reagent Lot
	Expiration Date	REACTION VESSELS	Reaction Vessels
	Store at 2-8°C	SAMPLE CUPS	Sample Cups
	Consult instructions for use	SEPTUM	Septum
SN	Serial Number	REPLACEMENT CAPS	Replacement Caps
	Manufacturer		

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

NAME

ARCHITECT Toxo IgG

INTENDED USE

The ARCHITECT Toxo IgG assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of IgG antibodies to *Toxoplasma gondii* in human serum and plasma.

SUMMARY AND EXPLANATION OF TEST

Toxoplasma gondii is an obligate intracellular protozoan parasite that infects most species of warm-blooded animals, including humans¹. Toxoplasmosis is primarily acquired by ingestion of undercooked, infected meat; via oocysts from fecally contaminated hands, food and water; and maternally through transplacental transmission². In addition, transmission associated with organ transplantation and during blood transfusion has been reported, although the risk of transmission through blood transfusion is extremely low³.

Acquired infection with *Toxoplasma gondii* in healthy individuals is commonly asymptomatic, however 10-20% of patients with acute infection may develop lymphadenopathy⁴.

Severe infections can occur in AIDS patients and adults immunocompromised by cancer chemotherapy or transplant recipients receiving immunosuppressive treatment. These infections can be fatal. Toxoplasmic encephalitis is the most common presentation and is the most frequent cause of focal central nervous system lesions in AIDS patients⁵.

Primary infection during pregnancy can result in transplacental transmission of the parasite resulting in congenital infection. The risk of congenital infection is lowest (10-25%) if acute maternal infection occurs during the first trimester and highest (60-90%) if it occurs during the third trimester². Severity of congenital infection is greatest when maternal infection is acquired early during pregnancy. Common outcomes of congenital toxoplasmosis include chorioretinitis, intracranial calcifications, and hydrocephalus. The majority of infants infected later in pregnancy are asymptomatic at birth, with sequelae occurring later in life.

Early treatment after prenatal diagnosis of *Toxoplasma gondii* infection has been shown to reduce the frequency and severity of congenital toxoplasmosis⁶. Serological tests can be used to identify seronegative women who then should be monitored during pregnancy.

The presence of IgG antibodies to *Toxoplasma gondii* indicates that infection has occurred but does not distinguish between recent and past infection. IgM antibodies are detected in individuals with a recently acquired infection, but antibodies may persist for up to 18 months post-infection². To differentiate between a recently acquired and a past infection, IgM and IgG positive specimens should be tested for IgG avidity. A high avidity index for IgG antibodies is a strong indication that an infection took place more than 4 months ago.

Toxo IgG	Toxo IgM	Toxo IgG Avidity	May indicate.../ Testing recommendation
nonreactive	nonreactive	N/A	no infection
nonreactive	reactive	N/A	obtain new sample 2-3 weeks after initial sample and test for Toxo IgG and Toxo IgM
reactive	nonreactive	high avidity	past infection. Strong indication that an infection took place more than 4 months ago
reactive	reactive	low avidity	obtain new sample 3 weeks after initial sample and test for Toxo IgG and Toxo IgM
reactive	reactive	high avidity	past infection. Strong indication that an infection took place more than 4 months ago

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Toxo IgG assay is a two-step immunoassay for the quantitative determination of IgG antibodies to *Toxoplasma gondii* in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

In the first step, pre-diluted sample, assay diluent, and recombinant *Toxoplasma gondii* antigen (containing recombinant antigens P30(SAG1) and P35(GRA8)) coated paramagnetic microparticles are combined. *Toxoplasma gondii* specific antibodies present in the sample bind to the recombinant *Toxoplasma gondii* antigen coated microparticles. After washing, murine acridinium-labeled anti-human IgG conjugate is added to create a reaction mixture in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture.

The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of anti-Toxo IgG in the sample and the RLUs detected by the ARCHITECT *i* System optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 100/500 Tests

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT *i* Systems. Please contact your local distributor.

ARCHITECT Toxo IgG Reagent Kit (6C19)

- **MICROPARTICLES** 1 Bottle (6.6 mL per 100-test bottle/27.0 mL per 500-test bottle) Recombinant *Toxoplasma gondii* antigen coated microparticles in MES buffer with protein stabilizers. Minimum concentration: 0.03% solids. Preservative: ProClin 300.
- **CONJUGATE** 1 Bottle (5.9 mL per 100-test bottle/26.3 mL per 500-test bottle) Murine acridinium-labeled anti-human IgG in MES buffer with protein stabilizers. Minimum concentration: 0.05 µg/mL. Preservatives: antimicrobial agents.
- **ASSAY DILUENT** 1 Bottle (10.0 mL per 100-test bottle/ 50.9 mL per 500-test bottle) Toxo IgG assay diluent containing TRIS buffer with protein stabilizers. Preservative: ProClin 300.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35 N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

WARNINGS AND PRECAUTIONS

- **IVD**
- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled with appropriate biosafety practices.

Safety Precautions

- Microparticles and Assay Diluent contain methylisothiazolones which are components of ProClin. These components are classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases:



- R43 May cause sensitization by skin contact.
- S24 Avoid contact with skin.
- S35 This material and its container must be disposed of in a safe way.
- S37 Wear suitable gloves.
- S46 If swallowed, seek medical advice immediately and show this container or label.

- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.
- For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between reagent kits.**
- Before loading the ARCHITECT Toxo IgG Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend the microparticles that have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
 - When handling conjugate vials, change gloves that have contacted human serum or plasma, since introduction of human IgG will result in a neutralized conjugate.
 - Once a septum has been placed on the reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
 - Over time, residual liquids may dry on the septum surface. These are typically dried salts, which have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

- The ARCHITECT Toxo IgG Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT Toxo IgG Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** After reagents are removed from the system, initiate a reagent scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

Depending on the ARCHITECT *i* System used, the ARCHITECT Toxo IgG assay has the following requirements:

ARCHITECT <i>i</i> Systems	Assay	Required System Software	CD-ROM List Number	CD-ROM Version
<i>i</i> 1000	Toxo IgG	4.01 or higher	1P61-03 or higher	3.0 or higher
	Toxo IgG R	5.0 or higher	1P61-04 or higher	4.0 or higher
All other <i>i</i> Systems	Toxo IgG	1.0 or higher	6E59-24 to 6E59-28	24 - 28
	Toxo IgG	2.6 or higher	6E59-29 or higher	29 or higher
	Toxo IgG R	2.6 or higher	6E59-24 to 6E59-28	24 - 28
	Toxo IgG R	5.0 or higher	6E59-29 or higher	29 or higher

- An ARCHITECT Toxo IgG assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* System Assay CD-ROM before performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- The following assay files are available for testing:
 - "Toxo IgG" – which does not automatically dilute and retest specimens with an anti-Toxo IgG concentration of > 200 IU/mL.
 - "Toxo IgG R" – which automatically dilutes and retests specimens with an anti-Toxo IgG concentration of > 200 IU/mL. **To configure the retest rule, delete the maximum value of "2000.0" of the Result Range.**
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen collection tubes listed below were verified to be used with the ARCHITECT Toxo IgG assay. Other specimen collection tubes have not been tested with this assay.

- Human serum (including serum collected in serum separator tubes)
- Human plasma collected in:
 - Plasma separator tubes (lithium heparin)
 - Potassium EDTA
 - Sodium citrate
 - Lithium heparin
 - Sodium heparin
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT Toxo IgG assay.

Specimen Conditions

- Do not use specimens with the following conditions:
 - heat-inactivated
 - pooled
 - grossly hemolyzed (> 500 mg/dL)
 - obvious microbial contamination
 - cadaver specimens or any other body fluids
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, or other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.
- All samples (calibrators, controls, and patient specimens) should be tested within 3 hours of being placed on board the ARCHITECT *i* System.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix completely thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at $\geq 10,000$ RCF (Relative Centrifugal Force) for 10 minutes before testing if
 - they contain fibrin, red blood cells, or other particulate matter,
 - they require repeat testing, or
 - they were frozen and thawed.Transfer clarified specimen to a sample cup or secondary tube for testing.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.

Storage

- Specimens may be stored on or off the clot, red blood cells or separator gel for up to 3 days at 15-30°C or 14 days refrigerated at 2-8°C.
- If specimens are stored at 15-30°C and testing will be delayed more than 3 days, remove serum or plasma from the clot, red blood cells or separator gel and store frozen at -10°C or colder.
- If specimens are stored at 2-8°C and testing will be delayed more than 14 days, remove serum or plasma from the clot, red blood cells or separator gel and store frozen at -10°C or colder.
- No qualitative performance differences were observed between experimental controls and nonreactive or reactive specimens subjected to 6 freeze/thaw cycles; however, multiple freeze/thaw cycles should be avoided.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped on wet ice or dry ice. Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

- 6C19 ARCHITECT Toxo IgG Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System
- ARCHITECT *i* System **ASSAY CD-ROM**
- 6C19-01 ARCHITECT Toxo IgG Calibrators
- 6C19-10 ARCHITECT Toxo IgG Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the volumes specified in the protocol.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT Toxo IgG Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend the microparticles that have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
 - **Invert the microparticle bottle 30 times.**
 - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain adhered to the bottle, continue inverting the bottle until the microparticles have been completely resuspended.
 - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
- Once the microparticles have been resuspended, place a septum on the bottle. For instructions on placing septums on bottles, refer to the **Handling Precautions** section of this package insert.

- Load the ARCHITECT Toxo IgG Reagent Kit on the ARCHITECT *i* System.
 - Verify that all necessary assay reagents are present.
 - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
 - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
 - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
 - Priority: 75 µL for the first ARCHITECT Toxo IgG test plus 25 µL for each additional ARCHITECT Toxo IgG test from the same sample cup.
 - ≤ 3 hours on board: 150 µL for the first ARCHITECT Toxo IgG test plus 25 µL for each additional ARCHITECT Toxo IgG test from the same sample cup.
 - > 3 hours on board: additional sample volume is required. For information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
 - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrators and controls.
 - Mix ARCHITECT Toxo IgG Calibrators and Controls by gentle inversion before use.
 - To obtain the recommended volume requirements for the ARCHITECT Toxo IgG Calibrators and Controls, hold the bottles **vertically** and dispense 6 drops of each calibrator or 4 drops of each control into each respective sample cup.
- Load samples.
 - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. When a laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens with an anti-Toxo IgG concentration of > 200.0 IU/mL will be flagged as “> 200.0 IU/mL” and may be diluted with the Automated Dilution Protocol:

- The system performs a 1:10 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.
- When testing is conducted using the “Toxo IgG R” assay file, specimens flagged as “> 200.0 IU/mL” will be automatically retested in 1:10 dilution.
- For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- To perform an ARCHITECT Toxo IgG calibration, test Calibrators A to F in replicates of two. A single sample of each ARCHITECT Toxo IgG control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the control package insert. Calibrators should be priority loaded.
- Calibration Range: 0 – 200.0 IU/mL.

- Once an ARCHITECT Toxo IgG calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
 - A reagent kit with a new lot number is used.
 - Controls are out of range.
- It is recommended that the assay be calibrated every 30 days.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT Toxo IgG assay is that a single sample of each control level be tested once every 24 hours each day of use. If laboratory quality control procedures require more frequent use of controls to verify test results, follow those procedures.

The ARCHITECT Toxo IgG Control values must be within the acceptable ranges as specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and samples must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims refer to the ARCHITECT Operations Manual, Appendix B. The ARCHITECT Toxo IgG belongs to method group 5.

RESULTS

The ARCHITECT Toxo IgG assay uses a 4 Parameter Logistic Curve fit (4PLC, Y-weighted) data reduction method to generate a calibration curve.

Calculation

The ARCHITECT *i* System calculates the Calibrator A through F mean chemiluminescent signal from two Calibrator A through F replicates, generates a calibration curve and stores the result.

The default result unit for the ARCHITECT Toxo IgG assay is IU/mL.

Interpretation of Results

- Specimens with concentration values < 1.6 IU/mL are considered nonreactive for IgG antibodies to *Toxoplasma gondii*. Individuals with such results are presumed to be not infected with *Toxoplasma gondii* and susceptible to acute infection. A negative result does not always exclude the possibility of *Toxoplasma gondii* infection. Patients with negative results in suspected early disease cases should be retested in 3 weeks.
- Specimens with concentration values ≥ 3.0 IU/mL are considered reactive for IgG antibodies to *Toxoplasma gondii* and indicate past or acute infection.
- Specimens with concentration values from 1.6 to < 3.0 IU/mL are considered grayzone and may contain low levels of IgG. It is recommended to test those specimens using a Toxo IgM test, and/or a second sample should be taken within a reasonable period of time (e.g. two weeks) and used to repeat ARCHITECT Toxo IgG testing.

Flags

- Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- If the ARCHITECT Toxo IgG results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, results should be used in conjunction with other data; e.g., results of other tests (Toxo IgM, Toxo IgG Avidity), clinical impressions, etc.

- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.⁷ Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).^{8,9} Such specimens may show either falsely elevated or depressed values when tested with assay kits that employ mouse monoclonal antibodies. ARCHITECT Toxo IgG reagents contain a component that reduces the effect of HAMA reactive specimens.
- Assay to assay variation in results: **The concentration values for Toxo IgG in a given specimen can vary based on the assay method and standardization and should not be used interchangeably.** Note: The ARCHITECT Toxo IgG Calibrators are referenced to the World Health Organization (WHO) First International Standard (01/600) for Anti-Toxoplasma IgG¹⁰.
- IgG antibodies to *Toxoplasma gondii* might not dilute linearly in all samples. Do not use different dilution protocols when analyzing sequential samples taken from an individual.

EXPECTED VALUES

The prevalence of Toxo IgG antibody to *Toxoplasma gondii* will vary with age and geographic location. In this study 1270 specimens from pregnant women and 1297 specimens from random individuals were tested. Of these specimens 1115 (43.4%) were positive, 83 (3.2%) were grayzone and 1369 (53.3%) were nonreactive by the ARCHITECT Toxo IgG assay.

IU/mL	N (%) Overall Specimen Categories	N (%) Blood Donor	N (%) Diagnostic/Hospitalized	N (%) Pregnant Women
0.0 to < 1.6	1369 (53.3)	278 (45.8)	270 (39.1)	821 (64.6)
1.6 to < 3.0	83 (3.2)	16 (2.6)	38 (5.5)	29 (2.3)
3.0 to < 10.0	450 (17.5)	134 (22.1)	161 (23.3)	155 (12.2)
10.0 to < 50.0	554 (21.6)	160 (26.4)	182 (26.4)	212 (16.7)
50.0 to < 100.0	59 (2.3)	9 (1.5)	26 (3.8)	24 (1.9)
100.0 to < 150.0	22 (0.9)	5 (0.8)	6 (0.9)	11 (0.9)
150.0 to < 200.0	7 (0.3)	2 (0.3)	0 (0.0)	5 (0.4)
> 200.0	23 (0.9)	3 (0.5)	7 (1.0)	13 (1.0)
Total	2567 (100.0)	607 (100.0)	690 (100.0)	1270 (100.0)

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Toxo IgG assay is designed to have precision of < 10% total** CV for representative specimens within the ranges of 3.0 to 120.0 IU/mL. The study was performed at 1 internal and 1 external (France) evaluation site each using one instrument. Precision was assessed on a panel consisting of 3 different control lots and 1 human plasma specimen. Panel members were tested in replicates of 4 across 3 reagent lots and 2 calibrator lots at each site. Each combination of instruments, panel members, and reagent lots was tested in four runs.

Representative data from this study are summarized in the following table*.

Member	N	Mean IU/mL	Within Run		Total **	
			SD	%CV	SD	%CV
NC	576	0.1	0.03	N/A	0.03	N/A
PC 1	576	6.4	0.14	2.17	0.16	2.55
PC 2	576	119.2	3.69	3.10	4.74	3.98
Human Specimen	192	3.3	0.09	2.74	0.10	3.10

* Representative data; results in individual laboratories may vary from these data.

** Total is an accumulation of within run, between run and between day.

Resolved Relative Sensitivity, Specificity and Relative Agreement

Resolved relative sensitivity/specificity and relative agreement was assessed on 2464 specimens from pregnant females, diagnostic/hospitalized specimens and randomly selected volunteer blood donors.

103 specimens giving grayzone results using ARCHITECT and/or AxSYM Toxo IgG and/or any other Toxo assay were not included in the calculation of resolved relative sensitivity, specificity and relative agreement.

Resolved Relative Sensitivity

From 2464 specimens evaluated, 1099 were classified as positive. 1096 were reactive by ARCHITECT Toxo IgG and 3 specimens were nonreactive by ARCHITECT Toxo IgG. The resolved relative sensitivity was 99.7% (1096/1099) with a 95% confidence interval of 99.2% to 99.9%.

Resolved Relative Specificity

From 2464 specimens evaluated, 1365 were classified as negative. 1359 were nonreactive by ARCHITECT Toxo IgG and 6 specimens were reactive by ARCHITECT Toxo IgG. The resolved relative specificity was 99.6% (1359/1365) with a 95% confidence interval of 99.0% to 99.8%.

Relative Agreement

From the 2464 specimens evaluated, 12 specimens were tested discordant between ARCHITECT Toxo IgG and AxSYM Toxo IgG resulting in a relative agreement of 99.5% (2452/2464) with a 95% confidence interval of 99.2% to 99.7%.

	ARCHITECT Toxo IgG		
	REA***	NR***	Total
AxSYM Toxo IgG POS***	1094	4**	1098
NEG***	8*	1358	1366
Total	1102	1362	2464

* Two specimens out of 8 specimens reactive on ARCHITECT Toxo IgG and nonreactive on AxSYM Toxo IgG were confirmed reactive by testing with a commercially available assay, the Sabin-Feldman Dye Test and the HS Agglutination test. Six specimens out of 8 specimens reactive on ARCHITECT Toxo IgG and nonreactive on AxSYM Toxo IgG were confirmed non-reactive by testing with a commercially available assay, the Sabin-Feldman Dye Test and the HS Agglutination test. Four specimens out of these 6 unconfirmed specimens showed reactivity to GRA8 (p35) on a commercially available blot.

** One specimen out of 4 specimens reactive on AxSYM Toxo IgG and nonreactive on ARCHITECT Toxo IgG could not be confirmed by additional testing as outlined above whereas 3 specimens were confirmed reactive.

*** REA = reactive, NR = nonreactive, POS = positive, NEG = negative

Interference

No interference was observed between experimental controls and nonreactive or reactive specimens tested with elevated levels of bilirubin (20 mg/dL), triglycerides (3000 mg/dL), protein (12 g/dL), red blood cells (0.4% v/v), or hemoglobin (500 mg/dL).

Other Potential Interferents

Additional studies were performed to evaluate other potential interfering disease states on the ARCHITECT Toxo IgG assay. Eight specimens grayzone on either ARCHITECT Toxo IgG or AxSYM Toxo IgG were not included in the calculation of the relative agreement.

Interfering Substance	N	*Relative Agreement between ARCHITECT Toxo IgG and AxSYM Toxo IgG
Anti-nuclear antibody	8	100 %
Cytomegalovirus	10	100 %
Epstein-Barr Virus	10	100 %
Influenza Vaccines	10	90 %
HAMA	10	100 %
Herpes Simplex Virus 1	10	80 %
Herpes Simplex Virus 2	9	100 %
Hyperpolyclonal IgG	9	100 %
Hyperpolyclonal IgM	10	100 %
Measles	10	100 %
Parvovirus B19	10	100 %
Rheumatoid Factor	10	100 %
Rubella	8	100 %
Syphilis	10	100 %
Varicella Zoster Virus	8	100 %
anti ds DNA antibodies	7	100 %
Monoclonal IgG	10	90 %
Monoclonal IgM	9	100 %

* Representative data; results in individual laboratories may vary from these data.

After discordant resolution of ARCHITECT Toxo IgG nonreactive or reactive results, 2 discordant specimens from patients infected with anti-HSV-1 and 1 discordant specimen containing monoclonal IgG were confirmed by an additional commercially available assay, the Sabin-Feldman Dye Test, HS Agglutination test and/or a commercially available blot.

Functional Sensitivity

The assay is designed to have a functional sensitivity (20% CV at the 95% confidence limit) of less than 1.6 IU/mL.

In this study 7 human serum panels with Toxo IgG concentrations ranging from 0.5 IU/mL to 3.3 IU/mL and the ARCHITECT Toxo IgG Negative Control and PC1 were tested on 3 different ARCHITECT Toxo IgG reagent lots using one calibrator lot and one control lot over 5 days. The functional sensitivity ranged from 0.03 to 0.25 IU/mL.

Seroconversion Sensitivity

A total of 50 bleeds from 12 different seroconversion panels were tested. ARCHITECT Toxo IgG showed comparable seroconversion sensitivity to AxSYM Toxo IgG on the panels tested in this study.

During an acute infection, the ARCHITECT Toxo IgG assay typically shows a substantial rise in anti-Toxo IgG concentrations in consecutive draws. Data from selected seroconversion panels are shown in the following table.*

Sample ID	Months after last negative bleed	ARCHITECT Toxo IgG IU/mL	AxSYM Toxo IgG IU/mL	Sabin-Feldman Dye Test IU/mL	HS Agglutination Test IU/mL	Isaga (Toxo-M) Index
GZ range		1.6 - 2.9	2.0 - 2.9		1	6 - 8
Reactive cutoff		3.0	3.0	2	2	9
29944022	0.0	0.8	0.3	< 2	< 1	0
29944023	1.1	5.0	19.4	40	8	12
29944024	1.4	18.7	54.8	200	16	12
29944025	1.7	21.9	60.8	400	32	12
29944029	0.0	0.6	0.4	< 2	< 1	0
29944030	1.2	6.8	7.6	10	2	12
29944031	0.0	0.4	0.4	< 2	< 1	0
29944032	2.1	172.6	482.2	1600	200	12
29944033	4.1	141.2	466.5	1600	400	12
29944034	8.4	39.6	84.8	400	50	12
29944035	0.0	0.4	0.1	< 2	< 1	0
29944036	2.3	1.6	2.3	5	1	12
29944037	2.4	5.8	6.7	10	1	12
29944038	0.0	0.4	0.1	< 2	< 1	0
29944039	1.0	9.1	9.9	10	2	12
29944040	0.0	0.3	0.3	< 2	< 1	0
29944041	1.6	15.1	21.8	40	16	12
29944042	11.8	21.9	28.1	80	32	12
29944043	0.0	0.5	0.4	< 2	< 1	0
29944044	1.5	3.2	2.9	10	1	11
29944045	1.8	9.4	10.1	20	2	11
00006214	0.0	0.8	0.4	< 2	< 1	0
00006215	3.5	46.3	140.9	400	200	12
00006216	4.2	125.2	342.9	1600	400	12
00006217	0.0	0.5	0.2	< 2	< 1	0
00006218	3.2	28.4	38.1	100	16	12
00006219	7.0	20.3	18.6	100	100	12

* Representative data; results in individual laboratories may vary from these data.

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The following US Patents are relevant to the ARCHITECT *i* System or its components. There are other such patents and patent applications in the United States and worldwide.

5 468 646	5 543 524	5 545 739
5 565 570	5 669 819	5 783 699

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