ARCHITECT Toxo IgG

REF 6C19-25
REF 6C19-35

en
Toxo IgG
6C19
G47734R06
B6C190

Read Highlighted Changes: Revised July 2019.

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.

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 THE TEST

Toxoplasma gondii is an obligate intracellular protozoan parasite that infects most species of warm-blooded animals, including humans.[1] Toxoplasmosis is primarily acquired by ingestion of undercooked, infected meat; via oocysts from fecally contaminated hands, food and water; and maternally through transplacental transmission.[2] In addition, transmission associated with organ transplantation and during blood transfusion has been reported, although the risk of transmission through blood transfusion is extremely low.[3]

Acquired infection with *Toxoplasma gondii* in healthy individuals is commonly asymptomatic, however 10-20% of patients with acute infection may develop lymphadenopathy.[4]

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 patients.[5]

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 trimester.[2] 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 toxoplasmosis.[6] 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-infection.[2] 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.

1. 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.
2. After washing, murine acridinium-labeled anti-human IgG conjugate is added to create a reaction mixture.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of anti-Toxo IgG in the sample and the RLUs detected by the ARCHITECT iSystem optics.

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

REAGENTS

Kit Contents

ARCHITECT Toxo IgG 6C19

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

REF	6C19-25	6C19-35
Σ	100	500
MICROPARTICLES	1 x 6.6 mL	1 x 27.0 mL
CONJUGATE	1 x 5.9 mL	1 x 26.3 mL
ASSAY DILUENT	1 x 10.0 mL	1 x 50.9 mL

MICROPARTICLES Recombinant *Toxoplasma gondii* antigen coated microparticles in MES buffer with protein stabilizers. Minimum concentration: 0.03% solids. Preservative: ProClin 300.

CONJUGATE Murine acridinium-labeled anti-human IgG in MES buffer with protein stabilizers. Minimum concentration: 0.05 µg/mL. Preservatives: antimicrobial agents.

ASSAY DILUENT Toxo IgG assay diluent containing TRIS buffer with protein stabilizers. Preservative: ProClin 300.

Other Reagents

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

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

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

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[7-10]

The following warnings and precautions apply to: MICROPARTICLES / ASSAY DILUENT

WARNING	Contain methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
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 in accordance with local regulations.

Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may 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.
  - Once a septum has been placed on an open 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 and have no effect on assay efficacy.
- When handling conjugate vials, change gloves that have contacted human serum or plasma, since introduction of human IgG will result in a neutralized conjugate.

For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Reagent Storage

When stored and handled as directed, reagents are stable until the expiration date.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8°C	Until expiration date	May be used immediately after removal from 2-8°C storage. Store in upright position.
On board	System temperature	30 days	Discard after 30 days. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

* Reagents may be stored on or off the ARCHITECT iSystem. 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.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

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 iSystem used, the ARCHITECT Toxo IgG assay has the following requirements:

ARCHITECT iSystems	Assay	Required System Software	CD-ROM List Number	CD-ROM Version
i1000	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 iSystems	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

The ARCHITECT Toxo IgG assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem Assay CD-ROM prior to performing the assay.

For detailed information on assay file installation and 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

Verified specimen types to be used with this assay:

Specimen Types	Collection Tubes
Human serum	Serum
	Serum separator tubes
Human plasma	Plasma separator tubes (lithium heparin)
	Potassium EDTA
	Sodium citrate
	Lithium heparin
	Sodium heparin

- Other specimen collection tube types have not been tested with this assay.
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum and plasma.
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The instrument 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 assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed (> 500 mg/dL hemoglobin)
  - obvious microbial contamination
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.
- All samples (calibrators, controls, and patient specimens) should be tested within 3 hours of being placed on board the ARCHITECT iSystem.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix 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 ≥ 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.
- 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.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	15-30°C	≤ 3 days
	2-8°C	≤ 14 days
	-10°C or colder	--

Specimens may be stored on or off the clot, red blood cells, or separator gel.

Remove serum or plasma from the clot, red blood cells, or separator gel if stored longer than the maximum 15-30°C or maximum 2-8°C storage time 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.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- It is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- Ship 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 Toxo IgG Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 6C19-01 ARCHITECT Toxo IgG Calibrators
- 6C19-10 ARCHITECT Toxo IgG Controls
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

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

Assay Procedure

- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may 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 are still adhered to the bottle, continue to invert 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, discard the cap and place a septum on the bottle. For instructions on placing septums on bottles, refer to the **Reagent Handling** section of this package insert.
- Load the reagent kit on the ARCHITECT iSystem.
  - Verify that all necessary 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.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 10
  - Priority:

    Sample volume for first test: 75 µL

    Sample volume for each additional test from same sample cup: 25 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 25 µL
  - > 3 hours on board: Additional sample volume 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 ARCHITECT Toxo IgG Calibrators and Controls.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 6 drops

    for each control: 4 drops
- 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. Perform maintenance more frequently when required by laboratory 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.

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

- Test Calibrators A to F in replicates of two. The calibrators should be priority loaded.

  A single sample of each control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the respective control package insert.
- 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 or
  - 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 the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific 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 System Operations Manual, Appendix B.

The ARCHITECT Toxo IgG assay belongs to method group 5.

RESULTS

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

Calculation

The ARCHITECT iSystem 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

Concentration values	Instrument Interpretation	Interpretation of Results and Retest Procedure
< 1.6 IU/mL	Nonreactive	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.
1.6 to < 3.0 IU/mL	Grayzone	Specimens that are considered grayzone 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.
≥ 3.0 IU/mL	Reactive	Specimens that are considered reactive for IgG antibodies to *Toxoplasma gondii* indicate past or acute infection.

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. 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.[11]
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as ARCHITECT Toxo IgG that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.[12, 13]

  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 IgG.[14]
- 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 SD	Within Run %CV	Total** SD	Total** %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 Vaccinees	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.

BIBLIOGRAPHY

1. Willis MS, Southern P, Latimer MJ. Toxoplasma infection. Making the best use of laboratory tests. *Infect Med* 2002; 19: 522-532.
2. Jones JL et al. Congenital Toxoplasmosis: A Review. *CME Review Article* Vol. 56, Number 5 2001; 296-305.
3. Shulman IA. Parasitic infections and their impact on blood donor selection and testing. *Arch Pathol Lab Med.* 1994; 118: 366-370.
4. Montoya J.G. Laboratory Diagnosis of Toxoplasma gondii Infection and Toxoplasmosis. *Journal of Infectious Diseases* 2002; 185 (Suppl 1) 73-82.
5. Israelski DM, Remington JS. Toxoplasmosis in the non-AIDS immunocompromised host. *Curr Clin Top Infect Dis* 1993; 13: 322-356.
6. Wong SY and Remington. Toxoplasmosis in Pregnancy. *Clinical Infectious Diseases* 1994; 18:853-862.
7. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
8. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
9. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
10. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline–Third Edition.* CLSI Document M29-A3. Wayne, PA: CLSI; 2005.
11. Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.
12. Primus FJ, Kelley EA, Hansen HJ, et al. “Sandwich”-type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy. *Clin Chem* 1988;34(2):261-264.
13. Schroff RW, Foon KA, Beatty SM, et al. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45(2):879-885.
14. Rigsby et al. 2004. Evaluation of a Candidate International Standard Preparation for Human Anti-Toxoplasma Immunoglobulin G. J. *Clin. Microbiol. 42*, No. 11:5133-5138.

Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
ASSAY DILUENT	Assay Diluent
CONJUGATE	Conjugate
CONTROL NO.	Control Number
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCT OF GERMANY	Product of Germany
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WARNING: SENSITIZER	Warning: May cause an allergic reaction.
WASH BUFFER	Wash Buffer

Abbott GmbH & Co. KG
Max-Planck-Ring 2
65205 Wiesbaden
Germany
+49-6122-580

CE 0123

Customer Service: Contact your local representative or find country-specific contact information on www.abbottdiagnostics.com

Revised July 2019.

Abbott