ARCHITECT SYSTEM

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Toxo IgG Avidity

IVD REF 6L37

48-0339/R4

B6L370

Read Highlighted Changes
Revised November, 2008

Toxo IgG Avidity

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	*In Vitro* Diagnostic Medical Device	SN	Serial Number
LOT	Lot Number	CONTROL NO.	Control Number
	Expiration Date	REAGENT LOT	Reagent Lot
2°C 8°C	Store at 2-8°C	REACTION VESSELS	Reaction Vessels
	Consult instructions for use	SAMPLE CUPS	Sample Cups
		SEPTUM	Septum
	Manufacturer	REPLACEMENT CAPS	Replacement Caps

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

ABBOTT
Diagnostics Division

NAME

ARCHITECT Toxo IgG Avidity

INTENDED USE

The ARCHITECT Toxo IgG Avidity assay is a chemiluminescent microparticle immunoassay (CMIA) for the determination of the avidity 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 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. Low avidity results cannot be used to diagnose an acute toxoplasmosis.

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 Avidity assay consists of 2 single tests, that are both two-step immunoassays using CMIA technology with flexible assay protocols, referred to as Chemiflex. The avidity of anti-Toxo IgG in the sample is calculated using relative light units (RLUs) of both tests[7].

One aliquot of the sample is pretreated with blocking agent (Pre-Treatment 2).

A second aliquot of the sample is pretreated with buffer (Pre-Treatment 1) instead of blocking agent.

Each aliquot of the pretreated sample is combined with *Toxoplasma gondii* antigen coated microparticles (containing recombinant antigens P30(SAG1) and P35(GRA8)).

After washing, murine acridinium-labeled anti-human IgG conjugate is added. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as RLUs. The % Avidity is calculated from the RLUs obtained from the sample pretreated with the blocking agent and the RLUs obtained from the unblocked sample.

For the determination of the avidity of a sample, a grayzone or reactive ARCHITECT Toxo IgG result of the particular sample is required to select the correct dilution protocol for the ARCHITECT Toxo IgG Avidity assay. This is ensured by ordering an automated assay panel consisting of ARCHITECT Toxo IgG and ARCHITECT Toxo IgG Avidity. For details, refer to the **INSTRUMENT PROCEDURE** section of this package insert.

Use only specimens which were tested ≥ 1.6 IU/mL on ARCHITECT Toxo IgG.

Refer also to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS, Specimen Types** section of this package insert.

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

REAGENTS

Reagent Kit, 100 Tests (50 avidity determinations)

ARCHITECT Toxo IgG Avidity Reagent Kit (6L37)

- **MICROPARTICLES** 1 Bottle (6.6 mL) recombinant *Toxoplasma gondii* antigen coated microparticles in MES buffer. Minimum concentration: 0.02% solids. Preservative: ProClin 300.
- **CONJUGATE** 1 Bottle (5.9 mL) murine acridinium-labeled anti-human IgG in MES buffer. Minimum concentration: 0.05 µg/mL. Preservatives: antimicrobial agents.
- **ASSAY DILUENT** 1 Bottle (10.0 mL) Toxo IgG assay diluent containing TRIS buffer with protein stabilizers. Preservative: ProClin 300.
- **PRE-TREATMENT 1** 1 Bottle (2.9 mL) Pre-Treatment reagent 1 containing MES buffer with protein stabilizers and detergent. Preservative: ProClin 300.
- **PRE-TREATMENT 2** 1 Bottle (2.9 mL) Pre-Treatment reagent 2 containing blocking agent in MES buffer with protein stabilizers and detergent. 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

- **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 with appropriate biosafety practices.
- Microparticles, Pre-Treatment reagent 1, Pre-Treatment reagent 2 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.**
- **Do not have more than one lot of reagents on board.** If using a multi-modular ARCHITECT *i* System (e.g. *i* 4000), place ARCHITECT Toxo IgG Avidity reagents on one module only.
- Before loading the ARCHITECT Toxo IgG Avidity 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

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The ARCHITECT Toxo IgG Avidity 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 Avidity 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. Discard the reagent kit if the retested control result is out of the specified range. Associated test results are invalid and samples must be retested. 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 Avidity assay has following software requirements:

ARCHITECT *i* System	Required System Software	CD-ROM Version	CD-ROM List Number	Available Panels
*i*1000SR	5.0 or higher	4.0 or higher	1P61-04 or higher	Toxo G>A, Toxo G+M>A, Toxo G>M>A, Toxo M>G>A
all other *i* Systems	3.12 or higher	25 - 27	6E59-25 - 6E59-27	Toxo G>A
all other *i* Systems	3.12 or higher	28 or higher	6E59-28 or higher	Toxo G>A, Toxo G+M>A, Toxo G>M>A, Toxo M>G>A

- Install the following assay files using utilities diagnostic procedure 6114 (Install/Delete Assays). Choose “Congenital Disease” and then “All assays”. Alternatively the following assay files can be installed individually:
  - “Toxo IgG R”,
  - “Toxo IgM”,
  - “ToxoAvi1” and
  - “ToxoAvi2”.

  If assay files are individually installed, ensure that ARCHITECT “Toxo IgG R” and “Toxo IgM” are installed prior to “ToxoAvi1” and “ToxoAvi2” assays. Assay panels, calculated assay files and retest rules will be installed automatically together with the “ToxoAvi1” and “ToxoAvi2” assay files.
- **Do not modify the assay parameters** for assays starting with “zz” or “ToxoAvi”. In case an unintended modification occurs, delete all Toxo assay panels, assays 3010 - 3019 as well as 817 and 818. Reinstall the Avidity assay files as described above.
- Enter the following information to configure result units, decimal places and interpretations for the “ToxoAvi” assay file according to the ARCHITECT System Operations Manual:
  - Result unit: %Avi
  - Number of decimal places: 1
  - Interpretation of results:

Name to enter	Range to enter
Low Avidity	-
Grayzone	50
High Avidity	60

- To configure the retest rule for the “Toxo IgG R” assay, delete the maximum value “2000.0” of the *Result range*.
- For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For 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 Avidity 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
  - Lithium heparin
  - Sodium heparin
  - Sodium citrate (only suitable if no ARCHITECT Toxo IgM testing is performed)
- 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 Avidity assay.

To determine the avidity of a sample, a grayzone or reactive ARCHITECT Toxo IgG result of the respective sample is required to enable the ARCHITECT instrument to select the correct dilution protocol for the ARCHITECT Toxo IgG Avidity assay. This is ensured by ordering automated assay panels consisting of ARCHITECT Toxo IgG and ARCHITECT Toxo IgG Avidity.

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 (calibrator, controls, and patient specimens) should be tested within 5 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 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.

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 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

- 6L37 ARCHITECT Toxo IgG Avidity Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System
- ARCHITECT *i* System **ASSAY CD-ROM**
- 6L37-11 ARCHITECT Toxo IgG Avidity Calibrator and Controls
- 6C19 ARCHITECT Toxo IgG Reagent Kit
- 6C19-01 ARCHITECT Toxo IgG Calibrators
- 6C19-10 ARCHITECT Toxo IgG Controls
- 6C20 ARCHITECT Toxo IgM Reagent Kit (optional)
- 6C20-01 ARCHITECT Toxo IgM Calibrator (optional)
- 6C20-10 ARCHITECT Toxo IgM Controls (optional)
- 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

- Place ARCHITECT Toxo IgG and Toxo IgM (optional) Reagent Kits on the System. **Calibrate the "Toxo IgG R" and "Toxo IgM" assays.** For assay procedure, calibration and quality control procedure of this assay, refer to the respective package insert.
- Before loading the ARCHITECT Toxo IgG Avidity 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.
- The reagent carousel has color coded rings which match the colored bands on the reagent bottle labels.
- Verify that all necessary assay reagents are present.
- **Ensure that only one lot of reagents is present**.
- Ensure that septums are present on all reagent bottles.

- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the **Calibration** section and 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.
  - For information on ordering controls, refer to the **QUALITY CONTROL PROCEDURES** section of this reagent package insert.
  - Enter sample information and select the desired assay panel from the following assay panel list. The instrument will automatically select the assays required. Refer to Figure 1.
- It is strongly recommended to use the automated assay panel for ARCHITECT Toxo IgG Avidity testing since this will ensure the correct selection of Toxo assay testing steps and dilution protocols required for avidity determinations. Please contact Abbott for information on ordering the Toxo assays using an LIS.
- ARCHITECT Toxo IgG, Toxo IgM, and one determination of Toxo IgG Avidity can be sampled from the same sample cup. If multiple avidity determinations are required for the same sample, place the respective number of differently barcoded sample cups with aliquots of the same sample on the instrument. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the tests.
  - ≤ 3 hours on board: 280 µL for the complete ARCHITECT Toxo assay panel testing using one 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 calibrator and controls.
  - Mix the ARCHITECT Toxo IgG Avidity Calibrator and Controls by gentle inversion before use.
  - To obtain the recommended volume requirements for the ARCHITECT Toxo IgG Avidity Calibrator, use 2 sample cups, hold the calibrator bottle **vertically** and dispense 8 drops into each sample cup.
  - To obtain the recommended volume requirements for the ARCHITECT Toxo IgG Avidity Controls, hold the bottles **vertically** and dispense 8 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.
  - If the result(s) of the initial test(s) meet(s) the retest criteria of the assay panel, the ARCHITECT system generates a rerun order. Tests scheduled for rerun are displayed on the Order status, Rerun status, and Sample status screens. The R (rerun) code is assigned to the test. If the system is configured with an RSH (robotic sample handler), the system can be configured to automatically reposition the sample(s) for retest. If the system is not configured for automatic repositioning, sample(s) to be retested must be reloaded. If the system is configured with an SSH (standard sample handler) or LAS (laboratory automation system), the sample(s) must be reloaded to perform the auto retest.
  - A rerun order for the "Toxo IgG R" assay will be placed for samples that have an ARCHITECT Toxo IgG result of > 200 IU/mL. These samples will be tested automatically in a 1:10 dilution performed by the instrument. The D (dilution) and R (rerun) codes are assigned to the test.
- 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 must not be diluted manually prior to running the ARCHITECT Toxo IgG Avidity assay.

Calibration

- To perform an ARCHITECT Toxo IgG Avidity calibration, test two replicates of Calibrator 1 on assay files "ToxoAvi1" and "ToxoAvi2". The instrument requires an individual sample cup per assay file. A single sample of each ARCHITECT Toxo IgG Avidity control level must be tested. Ensure that control values are within the control ranges specified in the calibrator and controls package insert. Calibrator 1 should be priority loaded.
- Once a calibration of the Toxo IgG Avidity constituent assays, "ToxoAvi1" and "ToxoAvi2", is accepted and stored, all subsequent samples may be tested without further calibration unless a reagent kit with a new lot number is used.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

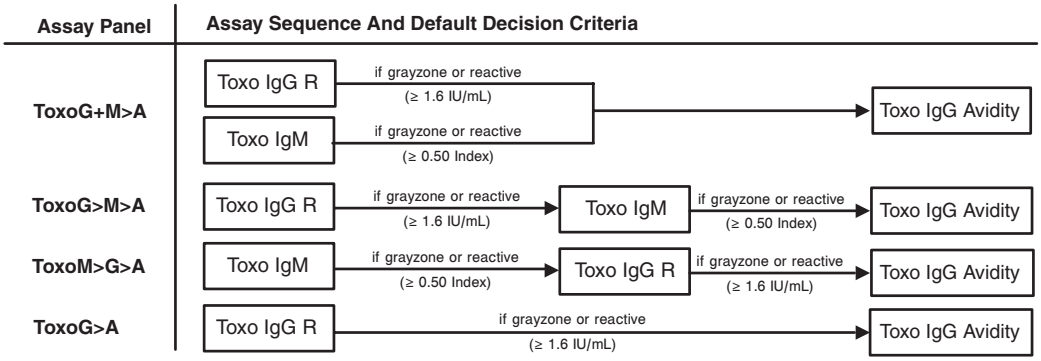
QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT Toxo IgG Avidity assay is that a single sample of each control be tested once every 24 hours each day of use. Controls are ordered as multiconstituent controls for "ToxoAvi". If multiple control replicates are required, note that only one avidity determination can be ordered per sample cup. Refer to the ARCHITECT Toxo IgG Avidity Calibrator and Controls package insert for the expected mean (default value) and SD (default value). For configuration of multiconstituent controls, refer to the ARCHITECT System Operations Manual, Section 5.

If laboratory quality control procedures require more frequent use of controls to verify test results, follow those procedures.

The ARCHITECT Toxo IgG Avidity Control values must be within the acceptable ranges specified in the ARCHITECT Toxo IgG Avidity Calibrator and Controls package insert. If a control is out of its specified range, the associated test results are invalid and samples must be retested. It may be indicated to use a new reagent kit.

Figure 1 "Assay Sequence And Default Decision Criteria"



Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT Operations Manual, Appendix B. The ARCHITECT Toxo IgG Avidity assay belongs to method group 5 (except functional sensitivity).

RESULTS

The following results are reported depending on the panel chosen:

- ARCHITECT Toxo IgG result in IU/mL.
- ARCHITECT Toxo IgM result in Index (S/CO).
- ARCHITECT Toxo IgG Avidity ("ToxoAvi") result in %Avi.

To configure result units, decimal places and interpretations refer to the **INSTRUMENT PROCEDURE** section of this package insert.

NOTE: Results with the unit of measurement "AdjRLU" or results from assay files starting with "zz" may be reported. These results are intermediate and not relevant for sample evaluation.

Calculation

The ARCHITECT *i* System calculates the avidity per the following formula and stores the result.

Avidity [%] = 100 x (1- (ToxoAvi2/ToxoAvi1))

Interpretation of Results

< 50.0 %Avi:	low avidity
50.0 – 59.9 %Avi:	grayzone
≥ 60.0 %Avi:	high avidity

No clinical interpretation can be drawn from a grayzone result. It is recommended to take a second sample within an appropriate period of time (e.g. 2 weeks) and repeat 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 Toxo IgG Avidity 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 IgG, Toxo IgM), clinical impressions, etc.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[8] 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)[9,10]. Specimens containing HAMA may produce anomalous values when tested with assay kits that employ mouse monoclonal antibodies[9].

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Toxo IgG Avidity assay is designed to have a within run precision of ≤ 10% CV and a total** precision of ≤ 14% CV for samples with ≥ 50% Avidity. The study was performed at one internal and one external (France) evaluation site each using one instrument. Precision was assessed on a panel consisting of three different control lots and one human plasma specimen.

Panel members were tested in replicates of four across three reagent lots and one calibrator lot at each site. Each combination of instruments, panel members, and reagent lots was tested in four runs across several days.

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

Member	N	Mean Avidity [%]	Within Run SD	Within Run %CV	Total ** SD	Total ** %CV
High Avidity Control	288	79.7	0.80	1.00	0.93	1.17
Low Avidity Control	288	21.8	2.70	12.39	2.70	12.39
Human Plasma Specimen	96	54.6	1.80	3.30	1.80	3.30

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

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

Sensitivity

The ARCHITECT Toxo IgG Avidity assay is designed to have a sensitivity of > 98.0% when testing samples drawn from patients within four months since seroconversion (samples from patients drawn within this period are not expected to generate a high avidity result). A total of 125 samples have been evaluated and 100% of these samples (95% confidence interval of 97.1% to 100%)* have been tested with a low or grayzone avidity result.

In addition, 89 samples drawn later than four months since seroconversion have been evaluated. The distribution of all samples is given in the following table*:

	Seroconversion < 4 months	Seroconversion > 4 months	Total
Low Avidity	124	54	178
Grayzone	1	7	8
High Avidity	0	28	28
Total	125	89	214

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

Relative Agreement

Relative Agreement was assessed on 175 Toxo IgG positive and Toxo IgM negative specimens from pregnant females.

Five specimens giving grayzone/borderline results on ARCHITECT or the other commercially available Toxo IgG Avidity assay were not included in the calculation of relative agreement.

From the 170 specimens evaluated, two specimens were tested discordant between ARCHITECT Toxo IgG Avidity and the commercially available Toxo IgG Avidity assay resulting in a relative agreement of 98.8% (168/170) with a 95% confidence interval of 95.8% to 99.9%.*

		ARCHITECT Toxo IgG Avidity		
		High	Low	Total
Commercially Available Toxo IgG Avidity Assay	High	167	2	169
	Low	0	1	1
	Total	167	3	170

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

Interference

No interference was observed between experimental controls and Low Avidity or High Avidity 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 Avidity assay.

A total of 65 specimens containing the following potentially interfering substances have been tested.*

Category	N tested	High Avidity	Grayzone	Low Avidity
Anti-nuclear antibody	5	5	0	0
Cytomegalovirus	1	1	0	0
Epstein-Barr Virus	4	4	0	0
Influenza Vaccinees	3	3	0	0
HAMA	4	4	0	0
Herpes Simplex Virus 1	3	3	0	0
Herpes Simplex Virus 2	2	2	0	0
Hyperpolyclonal IgG	4	4	0	0
Hyperpolyclonal IgM	7	7	0	0
Measles	3	3	0	0
Parvovirus B19	5	5	0	0
Rheumatoid Factor	5	4	1	0
Rubella	2	2	0	0
Systemic Lupus Erythematosus	3	2	0	1[a]
Syphilis	2	2	0	0
Varicella Zoster Virus	3	1	0	2[b]
Monoclonal IgG	5	4	0	1[b]
Monoclonal IgM	4	4	0	0

[a] Further testing was not performed due to insufficient sample volume.

[b] High Avidity result with a commercially available Toxo IgG Avidity assay.

* 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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