ARCHITECT Rubella IgG

REF 6C17-26
REF 6C17-36

en
Rubella IgG
6C17
G80773R04
B6C1H0

Read Highlighted Changes: Revised May 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 Rubella IgG

INTENDED USE

ARCHITECT Rubella IgG is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination and qualitative detection of IgG antibodies to rubella virus in human serum and plasma on the ARCHITECT iSystem. The ARCHITECT Rubella IgG assay is intended to aid in the determination of immune status to rubella.

SUMMARY AND EXPLANATION OF THE TEST

Primary postnatal rubella virus infection is typically a mild self-limiting disease characterized by a maculopapular rash, fever, malaise and lymphadenopathy.[1] In contrast to postnatal infections, primary prenatal infections may have devastating effects. *In utero* infections may severely damage the fetus, particularly if occurring during the first four months of gestation. The congenitally infected infant may exhibit one or more of a variety of defects collectively known as the congenital rubella syndrome (CRS). Among these are low birth weight, cataracts, deafness, congenital heart disease, and mental retardation.[1] The World Health Organization (WHO) conducted a worldwide survey on rubella, CRS, and rubella vaccine in 1995 and 1996. They reported an incidence of CRS of 60 to 220 cases with 100000 live births during epidemics in developing countries, a rate similar to those of industrialized countries before vaccination.[2]

Both naturally acquired and vaccine induced immunity to rubella virus associated with antibody persistence have been shown to provide protection from clinical rubella upon reinfection.[3-6] The widespread use of highly effective and safe vaccines dramatically reduced the incidence of rubella and CRS in the United States. In spite of this reduction, rubella outbreaks continue to occur. The number of cases of rubella reported annually to the WHO Regional Office for Europe has remained fairly stable over the past decade, with 304320 cases reported during 2003. These occurrences indicate a need for continued serological surveillance to identify susceptible individuals and reduce the potential risk to CRS.[2]

Specific antibodies correlate with immunity, but it has not been possible to identify a specific type and level of antibodies which are invariably correlated with protection. Traditionally rubella IgG antibody levels >10-15 IU/mL were used as decision point for seropositivity. Due to the routine vaccination of young children and the absence of widespread virus circulation, individual antibody concentrations decline over time and there is an increasing number of true seropositive individuals who would be classified as seronegative if a concentration of 10 IU/mL is applied.[19-21, 23]

More recent studies have demonstrated that the presence of E1 antibodies as shown by immunoblot, corresponds well with neutralization assay results[18], and can be used as a measure of seropositivity irrespective of antibody levels, also in individuals with antibody levels below 10 IU/mL.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Rubella IgG assay is a two-step immunoassay for the quantitative determination and qualitative detection of IgG antibodies to rubella virus in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample, assay diluent, and partially purified rubella virus coated paramagnetic microparticles are combined. IgG antibodies to rubella present in the sample bind to the rubella virus coated microparticles.
2. After washing, anti-human IgG acridinium-labeled 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 IgG antibodies to rubella 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 Rubella IgG 6C17

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

REF	6C17-26	6C17-36
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 Partially purified rubella virus coated microparticles in TRIS buffer with surfactant. Preservatives: sodium azide and ProClin 950.

CONJUGATE Anti-human IgG (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with surfactant and protein (bovine) stabilizer. Minimum concentration: 16 ng/mL. Preservatives: antimicrobial agents.

ASSAY DILUENT Assay Diluent in TRIS buffer with surfactant and protein (bovine, goat, mouse) stabilizers. Preservatives: ProClin 950 and ProClin 300.

Other Reagents

MULTI-ASSAY MANUAL DILUENT 1 x 100 mL ARCHITECT Multi-Assay Manual Diluent, REF 7D82-50, containing phosphate buffered saline solution. Preservative: antimicrobial agent.

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 contains human-sourced and/or potentially infectious components. Refer to the **REAGENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. Therefore, all human-sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be 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.[8-11]

The following warnings and precautions apply to: MICROPARTICLES	
	
WARNING	Contains methylisothiazolones and sodium azide.
H317	May cause an allergic skin reaction.
EUH032	Contact with acids liberates very toxic gas.
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.

The following warnings and precautions apply to: ASSAY DILUENT	
	
DANGER:	Contains polyethylene glycol octylphenyl ether and methylisothiazolones.
H318	Causes serious eye damage.
H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.
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.
P273	Avoid release to the environment.
Response	
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310	Immediately call a POISON CENTER or doctor / physician.
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. Recalibration may be required to obtain maximum onboard reagent stability. 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

The ARCHITECT Rubella 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.

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	Potassium EDTA Lithium Heparin (plasma separator tube) Sodium Heparin Lithium Heparin Sodium Citrate*

* Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens. Sodium citrate specimens may result in a -16.8% bias when compared to serum specimens.

- 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 or plasma.
- 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
  - 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.

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 x 10000 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. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not 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
Human serum/ plasma	2-8°C	≤ 14 days
	-10°C or colder	--

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

If testing will be delayed more than 14 days, remove serum or plasma from clot, red blood cells, or separator gel and store frozen (-10°C or colder).

Specimens stored frozen for 1 month showed acceptable performance. Avoid multiple freeze/thaw cycles.

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 or dry ice.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

6C17 ARCHITECT Rubella IgG Reagent Kit

Materials Required but not Provided

- ARCHITECT Rubella IgG Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 6C17-03 ARCHITECT Rubella IgG Calibrators
- 6C17-13 ARCHITECT Rubella IgG Controls
- 7D82-50 ARCHITECT Multi-Assay Manual Diluent
- 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, place a septum on the bottle. For instructions about 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: 70 µL

    Sample volume for each additional test from same sample cup: 20 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 20 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 Rubella 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: 5 drops

    for each control: 5 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 concentrations greater than 500.0 IU/mL of IgG antibodies to rubella will be flagged as ">500.0 IU/mL" and may be diluted with either the Automated Dilution Protocol or the Manual Dilution Procedure.

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.

Manual Dilution Procedure

Suggested dilution: 1:10

1. Add 20 µL of the patient specimen to 180 µL of ARCHITECT Rubella IgG Calibrator A or ARCHITECT Multi-Assay Manual Diluent.
2. The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The result should be greater than 5 IU/mL before the dilution factor is applied.

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- Test calibrators A, B, C, D, E, and F in replicates of two. 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: 0.0 to 500.0 IU/mL.
- Once an ARCHITECT Rubella 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.
- 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 Rubella 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 Rubella IgG Control values must be within the acceptable ranges 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 Rubella IgG assay belongs to method group 1.

RESULTS

Standardization

The ARCHITECT Rubella IgG assay is referenced to the World Health Organization (WHO) 1st International Standard (RUBI-1-94) for Anti-Rubella Immunoglobulin.

The antibody levels of Rubella IgG for a given specimen may vary when determined by different assay methods and should not be used interchangeably. The absence of a reference measurement system and a well defined measurand for Rubella IgG contribute to the quantitative disagreement observed between assay methods.[22]

Calculation

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

Interpretation of Results

For details on configuring the ARCHITECT iSystem to use grayzone interpretations, refer to the ARCHITECT System Operations Manual, Section 2.

- Negative: 0.0 to 4.9 IU/mL
- *Grayzone (Equivocal): 5.0 to 9.9 IU/mL
- Positive: ≥10.0 IU/mL[7]

  * Specimens with grayzone results may contain low levels of Rubella specific antibodies. For confirmation, samples may be tested by other adequate assays, e.g. immunoblot for the presence of E1 antibodies.

Flags

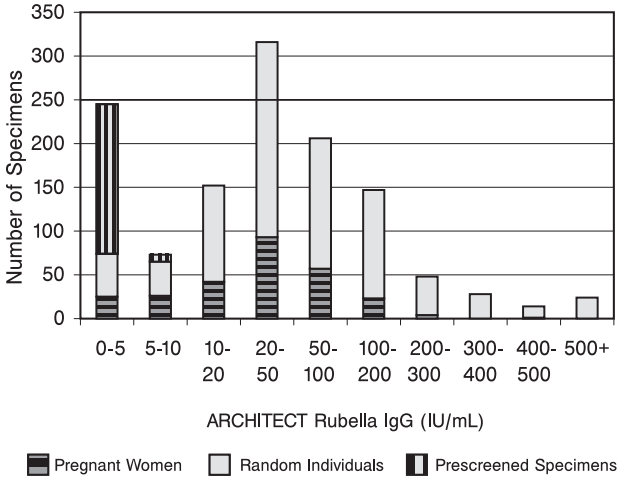
Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, 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.[12]
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Specimens containing HAMA may produce anomalous values when tested with assay kits (such as ARCHITECT Rubella IgG) that employ mouse monoclonal antibodies.[13, 14]

EXPECTED VALUES

The incidence of Rubella IgG antibodies varies among populations depending on vaccination practices. In this study, an asymptomatic population composed of 1253 specimens (fresh and frozen) from pregnant women, random individuals, and negative samples were tested. Of these specimens, 935 (75%) were positive, 74 (6%) were equivocal and, 244 (19%) were negative by ARCHITECT Rubella IgG assay. The distribution of this population is shown below.*



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

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Rubella IgG assay is designed to have a precision of ≤ 10% total CV within the range of 15.0 to 180.0 IU/mL and ≤ 20% total CV from greater than 180.0 IU/mL to 500.0 IU/mL.

A study was performed with the ARCHITECT Rubella IgG assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) document EP5-A2.[15] A total of six levels of panels and controls were assayed, using three lots of reagents, on three instruments, in replicates of two at two separate times per day for 20 days. Data from this study are summarized in the following table.* The Negative Control concentration ranged from 0.0 to 0.1 IU/mL.

				Mean	Within Run		Total	
Sample	Instrument	Reagent Lot	n	Concentration (IU/mL)	SD	%CV	SD	%CV
Positive Control 1	1	1	80	26.3	1.1	4.0	1.8	7.0
		2	80	24.4	1.5	6.2	1.9	7.7
		3	80	25.6	1.5	5.7	1.8	6.9
	2	1	80	27.1	1.0	3.7	2.4	8.9
		2	80	24.2	1.0	4.1	1.2	5.1
		3	80	25.7	1.3	5.1	1.7	6.4
	3	1	80	26.7	1.1	4.2	2.0	7.5
		2	80	26.2	1.2	4.8	1.6	6.2
		3	80	26.4	2.0	7.7	2.1	8.1
Positive Control 2	1	1	80	323.2	25.7	7.9	47.4	14.7
		2	80	278.8	30.7	11.0	33.3	11.9
		3	80	296.4	27.5	9.3	33.0	11.1
	2	1	80	319.5	16.8	5.3	29.5	9.2
		2	80	288.2	18.6	6.5	21.7	7.5
		3	80	301.6	19.1	6.3	23.0	7.6
	3	1	80	301.4	22.6	7.5	42.4	14.1
		2	80	304.0	32.6	10.7	36.9	12.1
		3	80	295.1	29.4	10.0	32.1	10.9
Panel 1	1	1	80	107.7	6.3	5.8	9.2	8.5
		2	80	97.7	5.7	5.9	7.1	7.3
		3	80	101.0	6.7	6.6	8.6	8.5
	2	1	80	117.9	5.7	4.8	7.1	6.0
		2	80	97.6	3.9	4.0	5.3	5.4
		3	80	100.8	4.2	4.2	5.9	5.8
	3	1	80	112.2	5.4	4.8	8.6	7.6
		2	80	104.6	7.6	7.3	9.2	8.8
		3	80	105.6	5.5	5.2	6.5	6.2
Panel 2	1	1	80	378.0	42.1	11.1	43.6	11.5
		2	80	346.2	44.5	12.8	50.7	14.6
		3	80	378.4	57.3	15.1	64.4	17.0
	2	1	80	367.8	29.2	7.9	33.5	9.1
		2	80	360.7	26.8	7.4	32.1	8.9
		3	80	378.1	25.0	6.6	37.5	9.9
	3	1	80	387.6	37.5	9.7	56.9	14.7
		2	80	383.8	42.2	11.0	43.4	11.3
		3	80	367.4	30.5	8.3	33.2	9.0
Panel 3	1	1	80	12.7	0.8	6.6	1.2	9.1
		2	80	11.4	0.6	5.4	0.7	6.5
		3	80	12.0	0.8	6.5	1.0	8.6
	2	1	80	12.5	0.6	4.8	1.0	8.1
		2	80	11.3	0.4	3.8	0.7	6.3
		3	80	12.2	0.5	4.0	0.8	6.2
	3	1	80	12.4	0.6	5.0	0.9	7.6
		2	80	12.4	0.7	5.6	1.0	8.5
		3	80	12.2	0.6	4.6	1.0	8.0

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

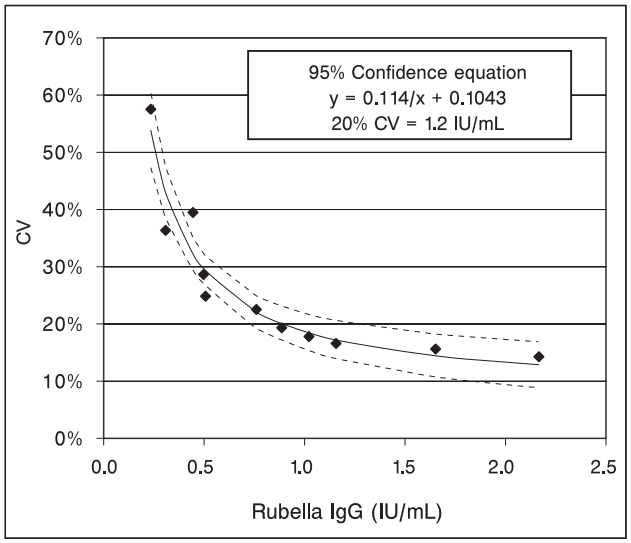
Dilution Linearity

The ARCHITECT Rubella IgG assay is designed to be linear between 5 and 500 IU/mL based on a study performed with guidance from the CLSI document EP6-A.[16]

Functional Sensitivity

The ARCHITECT Rubella IgG assay is designed to have a 20% CV at the upper 95% confidence limit of less than 5.0 IU/mL.

In this study, 11 human serum panels ranging in Rubella IgG concentrations from 0.2 - 2.2 IU/mL were tested in replicates of two over ten days on two instruments using two reagent lots and three calibrations for a total of 40 replicates per panel. At the upper 95% confidence limit, the lowest ARCHITECT Rubella IgG assay value exhibiting a 20% CV was calculated to be 1.2 IU/mL, as shown in the graph below.*



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

Interference

Potential interference in the ARCHITECT Rubella IgG assay from bilirubin, hemoglobin, total protein, and triglycerides at the levels indicated below is designed to be ≤10% as demonstrated by a study based on guidance from the CLSI document EP7-A2.[17] Data from this study are summarized in the following table.*

Potentially Interfering Substance	Concentration	% Interference
Bilirubin	20 mg/dL	≤ 10.0
Hemoglobin	500 mg/dL	≤ 10.0
Red Blood Cells	0.4% v/v	≤10%
Total protein	3 to 12 g/dL	≤ 10.0
Triglycerides	3000 mg/dL	≤ 10.0

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

Other Potential Interferents

Additional studies were performed to evaluate other potential interfering disease states on the ARCHITECT Rubella IgG assay.*

Potential Interfering Disease States	% Agreement[a]	Number of specimens[b]
ANA	100.0	9
Epstein-Barr Virus	96.0	25
HAMA	100.0	9
Herpes Simplex Virus	100.0	20
Hyper IgG	100.0	9
Hyper IgM	100.0	11
Influenza Vaccinees	100.0	10
Measles Virus	100.0	10
Parvovirus B19	100.0	7
Rheumatoid Factor	100.0	7
Systemic Lupus Erythematosis	100.0	6
Varicella Zoster Virus	100.0	10

[a] Compared to a commercially available Rubella IgG assay.

[b] Specimens giving equivocal results removed.

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

CDC Panel Results

The following information is from a panel of coded serum specimens (n=100) provided by the Center for Disease Control (CDC) and tested in a blind study. The sera panel was titered by Hemagglutination Inhibition. The ARCHITECT Rubella IgG assay results on this sera panel consists of 82 positive tests on 82 positive sera and 18 negative tests on 18 negative sera. This does not imply an endorsement of the assay by the CDC.

Initial Relative Agreement

The presence of IgG antibodies to rubella virus in 1253 specimens (fresh and frozen) was determined at three sites using the ARCHITECT Rubella IgG assay. In addition, each specimen was tested using another commercially available Rubella IgG assay.

Specimens with results of ≥ 10.0 IU/mL were considered positive, specimens with results of 5.0 - 9.9 IU/mL were considered grayzone and specimens with results of < 5.0 IU/mL were considered negative to calculate sensitivity and specificity.

Of the 1253 specimens evaluated, 113 were equivocal by ARCHITECT and/or the commercially available assay and removed from analysis. Seventeen specimens yielded discordant results between ARCHITECT and the commercially available assay. The relative agreement was 98.5% (1123/1140) (95% confidence interval: 97.6% to 99.1%).

Initial Relative Sensitivity

The initial relative sensitivity was 98.4% (932/947) (95% confidence interval: 97.4% to 99.1%).

Initial Relative Specificity

The initial relative specificity was 99.0% (191/193) (95% confidence interval: 96.3% to 99.9%).

Comparison of ARCHITECT Rubella IgG with another commercially available Rubella IgG assay.*

	Initial Relative Agreement (%)			
	Site I	Site II	Site III	Total
Mean	99.5	95.6	96.2	98.5
95% CI	(98.8-99.9)	(91.1-98.2)	(92.1-98.6)	(97.6-99.1)
N	819/823	151/158	153/159	1123/1140
	Initial Relative Sensitivity (%)			
Mean	99.4	96.6	95.9	98.4
95% CI	(98.4-99.8)	(92.3-98.9)	(91.5-98.5)	(97.4-99.1)
N	648/652	143/148	141/147	932/947
	Initial Relative Specificity (%)			
Mean	100.0	80.0	100.0	99.0
95% CI	(98.3-100)	(44.4-97.5)	(77.9-100)	(96.3-99.9)
N	171/171	8/10[a]	12/12	191/193

NOTE: Specimens giving equivocal results using ARCHITECT and another commercially available assay were not included in the calculation of relative agreement, relative sensitivity and relative specificity.

[a] Specificity 100% following consensus testing.

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

Consensus Testing

Further evaluation of the 17 discordant samples was performed using another commercially available Rubella IgG assay (Comparison Assay). From this testing, two samples were equivocal, 13 were negative and two were positive.

		Comparison Assay	
		+	-
ARCHITECT Result	+	2	0
	-	0	13

After this additional testing, the consensus relative sensitivity of the ARCHITECT Rubella IgG assay was 100% (95%CI: 99.4%-100%), the consensus relative specificity was 100% (95%CI: 98.5%-100%), and the consensus relative agreement was 100% (95%CI: 99.5%-100%).*

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

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Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
ASSAY DILUENT	Assay Diluent
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL NO.	Control Number
ECO HAZARD	Ecological hazard
GTIN	Global Trade Item Number
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
MULTI-ASSAY MANUAL DILUENT	Multi-Assay Manual Diluent
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCT OF IRELAND	Product of Ireland
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

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