



Read Highlighted Changes
Revised December, 2008


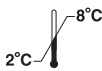


CMV IgG Avidity

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	<i>In Vitro</i> Diagnostic Medical Device	CONTROL NO.	Control Number
LOT	Lot Number	REAGENT LOT	Reagent Lot
	Expiration Date	REACTION VESSELS	Reaction Vessels
	Store at 2-8°C	SAMPLE CUPS	Sample Cups
	Caution, consult accompanying documents	SEPTUM	Septum
SN	Serial Number	REPLACEMENT CAPS	Replacement Caps
	Manufacturer		

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

NAME

ARCHITECT CMV IgG Avidity

INTENDED USE

The ARCHITECT CMV IgG Avidity assay is a chemiluminescent microparticle immunoassay (CMIA) for the determination of the avidity of IgG antibodies to Cytomegalovirus in human serum and plasma.

SUMMARY AND EXPLANATION OF TEST

Infections with Cytomegalovirus (CMV), a member of the herpesvirus family, are common in man and are usually mild and asymptomatic¹. However, in pregnant women², newborns³, and immunocompromised individuals⁴ CMV infections may pose a significant medical risk.

CMV infection remains difficult to diagnose on symptoms alone since a high percentage of infections remains asymptomatic. *In utero* infection may result in sequelae of varying degrees including mental retardation, chorioretinitis, hearing loss and neurologic problems⁵.

Since the risk of *in utero* virus transmission and CMV related damage of the fetus is markedly increased during primary infection, reliable recognition of primary CMV infection is of high importance for pregnant women⁵. An individual may undergo primary infection with CMV, reinfection with exogenous virus or reactivation of latent virus. Although presence of anti-CMV IgG reduces the likelihood of CMV related complications, it does not assure complete protection from disease.

CMV acquisition in infants can occur transplacentally following maternal infection, during birth by contact with the virus excreted from the cervix⁶ or following birth through the ingestion of infected maternal breast milk⁷. Both seronegative individuals and infants may acquire CMV through infected blood products^{3,8} or contact with an infected individual^{9,10}.

The functional binding affinity or avidity of IgG antibodies increases progressively over time after immunization, also known as maturation of the humoral immune response. High percentage of low avidity IgG antibodies may indicate a primary infection whereas high percentage of high avidity IgG antibodies may indicate a recurrent infection.

The ARCHITECT CMV IgG Avidity assay is a qualitative method for the determination of the avidity of IgG antibodies to Cytomegalovirus in human serum and plasma. It is used as an aid in the differentiation between primary and non-primary infection. If primary infection needs to be excluded, CMV IgG reactive samples should be tested for CMV IgM and CMV IgG Avidity. A positive CMV IgM result in combination with a low avidity result is a strong indicator for a primary CMV infection within the last 4 months.

CMV IgG	CMV IgM	CMV IgG Avidity	Indication for...
nonreactive	nonreactive	N/A	no infection
reactive	nonreactive	high avidity	past infection; low risk for <i>in utero</i> transmission
reactive	reactive	low avidity	primary infection; high risk for <i>in utero</i> transmission
reactive	reactive	high avidity	non-primary infection; low risk for <i>in utero</i> transmission

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT CMV 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. 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 CMV virus lysate (strain AD169) coated paramagnetic microparticles.

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 relative light units (RLUs)¹¹. The avidity of anti-CMV IgG in the sample is calculated using the RLUs of both tests.

To determine the avidity of a sample, a reactive ARCHITECT CMV IgG result of the respective sample is required to enable the ARCHITECT instrument to select the correct dilution protocol for the ARCHITECT CMV IgG Avidity assay. This is ensured by ordering automated assay panels consisting of at least ARCHITECT CMV IgG and ARCHITECT CMV IgG Avidity. For details refer to the **INSTRUMENT PROCEDURE** section.

It is strongly recommended to test only CMV IgM reactive samples with the ARCHITECT CMV IgG Avidity assay. This is imperative for samples with a low ARCHITECT CMV IgG concentration value between 6 to 15 AU/mL.

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

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 CMV IgG Avidity Reagent Kit (3L46)

- **MICROPARTICLES** 1 Bottle (6.6 mL) CMV virus lysate (strain AD169) coated microparticles in TRIS buffered saline. Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and antimicrobial agents.
- **CONJUGATE** 1 Bottle (5.9 mL) Murine acridinium-labeled anti-human IgG in MES buffer. Minimum concentration: 44 ng/mL. Preservatives: sodium azide and antimicrobial agents.
- **PRE-TREATMENT 1** 1 Bottle (3.4 mL) CMV IgG Avidity Pre-Treatment reagent 1 containing TRIS buffer. Preservatives: ProClin 300 and antimicrobial agents.
- **PRE-TREATMENT 2** 1 Bottle (3.4 mL) CMV IgG Avidity Pre-Treatment reagent 2 containing CMV virus lysate (strain AD169) in TRIS buffer. Preservatives: ProClin 300 and antimicrobial agents.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

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

ARCHITECT *i* Trigger Solution

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


ARCHITECT *i* Wash Buffer

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

WARNINGS AND PRECAUTIONS

- **IVD**

Safety Precautions

-  **CAUTION:** This product contains human-sourced infectious 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, it is recommended that all human-sourced materials be considered potentially infectious and handled with appropriate biosafety practices.
- Microparticles, Pre-Treatment 1 and Pre-Treatment 2 of this product 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.


- Some components of this product contain sodium azide. For a specific listing, refer to the **REAGENTS** section of this package insert. This material and its container must be disposed of in a safe way.
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.
- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.

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 CMV IgG Avidity reagents on one module only.
- Before loading the ARCHITECT CMV 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

-  The ARCHITECT CMV 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 CMV 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 CMV IgG Avidity assay has the following requirements.

ARCHITECT <i>i</i> Systems	Required System Software	CD-ROM Version	CD-ROM List Number
<i>i</i> 1000	5.0 or higher	4.0 or higher	1P61-04
All other <i>i</i> Systems	5.0 or higher	29 or higher	6E59-29

The assay files previously installed on the *i* 2000/*i* 2000SR from CD-ROM version 25 to 28 can still be used on system software versions 3.12 or higher.

- 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:
 - “CMV IgG R”,
 - “CMV IgM”,
 - “CMVAvi1” and
 - “CMVAvi2”.
- If assay files are individually installed, ensure that ARCHITECT “CMV IgG R” and “CMV IgM” are installed prior to “CMVAvi1” and “CMVAvi2” assays. Assay panels, calculated assay files and retest rules will be installed automatically together with the “CMVAvi1” and “CMVAvi2” assay files.
- **Do not modify the assay parameters** for assays starting with “zz” or “CMVAvidity”. In case an unintended modification occurs, delete all CMV panels, assays 3000-3009 as well as 540 and 550. Reinstall the Avidity assay files as described above.

- Enter the following information to configure result units, decimal places and interpretations for the “CMVAvidity” 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

- 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 CMV 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
 - Sodium citrate
 - Lithium heparin
 - Sodium heparin
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT CMV IgG Avidity assay.

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

It is strongly recommended to test only CMV IgM reactive samples with the ARCHITECT CMV IgG Avidity assay. This is imperative for samples with a low ARCHITECT CMV IgG concentration value between 6 to 15 AU/mL.

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 $\geq 10,000$ RCF (Relative Centrifugal Force) for 10 minutes before testing if
 - they contain fibrin, red blood cells, or other particulate matter,
 - they require repeat testing, or
 - they were frozen and thawed.

Transfer clarified specimen to a sample cup or secondary tube for testing.

- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.

Storage

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

- 3L46 ARCHITECT CMV IgG Avidity Reagent Kit

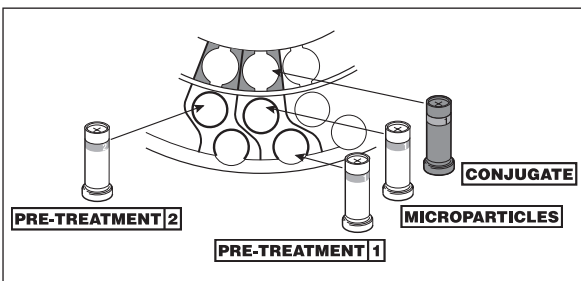
Materials Required but Not Provided

- ARCHITECT *i* System
- ARCHITECT *i* System **ASSAY CD-ROM**
- 3L46-11 ARCHITECT CMV IgG Avidity Calibrator and Controls
- 6C15 ARCHITECT CMV IgG Reagent Kit
- 6C15-01 ARCHITECT CMV IgG Calibrators
- 6C15-10 ARCHITECT CMV IgG Controls
- 6C16 ARCHITECT CMV IgM Reagent Kit (optional)
- 6C16-01 ARCHITECT CMV IgM Calibrator (optional)
- 6C16-10 ARCHITECT CMV 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.

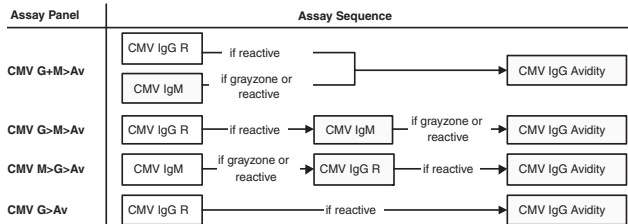
Assay Procedure

- Place ARCHITECT CMV IgG and CMV IgM (optional) Reagent Kits on the System. **Calibrate the “CMV IgG R” and “CMV IgM” assay.** For assay procedure, calibration and quality control procedure of these assays refer to the respective package inserts.
- Before loading the ARCHITECT CMV 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.
- Load the ARCHITECT CMV IgG Avidity Reagent Kit on the ARCHITECT *i* System according to the diagram below:



- 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.
 - Enter sample information and select the desired panel from the following assay panel list. The instrument will automatically select the assays required:



- It is strongly recommended to use the automated assay panels for ARCHITECT CMV IgG Avidity testing since this will ensure the correct selection of CMV assay testing steps and dilution protocols required for avidity determinations. Please contact Abbott for information on ordering the CMV assays using an LIS.
- ARCHITECT CMV IgG, CMV IgM, and one determination of CMV 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: 300 µL for the complete ARCHITECT CMV 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 CMV IgG Avidity Calibrator and Controls by gentle inversion before use.
 - To obtain the recommended volume requirements for the ARCHITECT CMV IgG Avidity Calibrator, use 2 sample cups, hold the calibrator bottle **vertically** and dispense 5 drops into each sample cup.
 - To obtain the recommended volume requirements for the ARCHITECT CMV 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 (retest 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 “CMV IgG R” assay will be placed for samples that have an ARCHITECT CMV IgG result of > 250 AU/mL. These samples will be tested automatically in a 1:10 dilution performed by the instrument. The D (dilution) and R (rerun) code is 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 CMV IgG Avidity assay.

Calibration

- To perform an ARCHITECT CMV IgG Avidity calibration, test one replicate of Calibrator 1 on assay files “CMVAvi1” and “CMVAvi2”. The instrument requires an individual sample cup per assay file. A single sample of each ARCHITECT CMV 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 CMV IgG Avidity constituent assays, “CMVAvi1” and “CMVAvi2”, 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 CMV 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 “CMVAvidity”. If multiple control replicates are required, note that only one avidity determination can be ordered per sample cup. Refer to the ARCHITECT CMV IgG Avidity Calibrator and Controls package insert for the expected mean (default value) and SD (default value). For configuration of multiconstituent controls, refer to 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 CMV IgG Avidity Control values must be within the acceptable ranges specified in the ARCHITECT CMV 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.

Verification of Assay Claims

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

RESULTS

The following results are reported depending on the panel chosen:

- ARCHITECT CMV IgG result in AU/mL.
- ARCHITECT CMV IgM result in Index (or S/CO).
- ARCHITECT CMV IgG Avidity (“CMVAvidity”) result in %Avi.

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

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.

$$\text{Avidity [\%]} = 100 \times (1 - (\text{CMVAvi1}/\text{CMVAvi2})).$$

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 CMV 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 (CMV IgG, CMV IgM), clinical impressions, etc.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.¹² 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)^{13,14} Specimens containing HAMA may produce anomalous values when tested with assay kits that employ mouse monoclonal antibodies¹².

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT CMV IgG Avidity assay is designed to show a total precision of ≤ 14% total** CV for a specimen representing the grayzone avidity range (50.0-59.9 %Avi). The study was performed at 1 internal and 1 external (Germany) 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 1 calibrator lot at each site. Each combination of reagent lots, panel members and instruments was tested in four runs across several days. Data from this study are summarized in the following table.*

Sample	N	Mean %Avi	Within Run		Total**	
			SD	%CV	SD	%CV
Low Control	288	25.5	2.19	8.59	2.41	9.46
High Control	288	80.8	0.72	0.89	0.89	1.10
Human Specimen	96	57.1	1.36	2.38	1.90	3.32

* 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 CMV IgG Avidity assay is designed to show a sensitivity equal to or better than a commercially available diagnostic kit when testing specimens from patients with documented primary CMV infection. Three commercially available seroconversion panels with a total number of 49 bleeds, of which 37 bleeds represent the acute CMV infection phase, were tested. The sensitivity was assessed to be 97.3% (36/37) on ARCHITECT CMV IgG Avidity (lower 95% confidence limit: 85.8%) compared to 75.7% (28/37) sensitivity on a commercially available diagnostic kit (lower 95% confidence limit: 58.8%). The following table shows data from the seroconversion panels tested.*

Panel Member	Days after first draw	ARCHITECT CMV IgG [AU/ml]	ARCHITECT CMV IgM [Index]	ARCHITECT CMV IgG Avidity [%Avi]	Commercially Available Diagnostic Kit [% Avidity]
Low Avidity/ Non-reactive		< 6.0	< 0.85	< 50.0	< 35
Grayzone		N/A	0.85-0.99	50.0-59.9	35-45
High Avidity/ Reactive		≥ 6.0	≥ 1.00	≥ 60.0	> 45
RP-003-01	1	8.1	1.60	1.0	N/A
RP-003-02	4	21.8	4.71	2.4	N/A
RP-003-03	8	51.1	5.70	10.5	N/A
RP-003-04	51	86.2	1.74	25.4	24.1
RP-003-05	55	94.1	1.44	24.7	31.2
RP-003-06	59	91.2	1.29	30.4	27.9
RP-003-07	65	84.0	1.20	31.8	29.6
RP-003-08	67	85.1	1.18	32.7	30.3
RP-003-09	72	80.8	1.08	37.9	50.2
RP-003-10	74	78.4	1.05	39.9	28.4
RP-003-11	79	80.3	1.07	40.5	31.0
RP-003-12	84	85.1	1.07	39.4	43.3
RP-003-13	88	94.7	1.15	40.3	26.7
RP-003-14	95	87.1	1.05	45.1	45.7
RP-003-15	99	89.4	1.02	44.9	44.1
RP-019-01	1	1.2	0.26	N/A	N/A
RP-019-02	5	1.1	0.24	N/A	N/A
RP-019-03	8	1.1	0.25	N/A	N/A
RP-019-04	12	1.1	0.27	N/A	N/A
RP-019-05	15	1.1	0.24	N/A	N/A
RP-019-06	21	1.4	0.35	N/A	N/A
RP-019-07	26	1.8	0.41	N/A	N/A
RP-019-08	29	3.3	0.99	N/A	N/A
RP-019-09	33	10.9	4.22	1.2	N/A

Panel Member	Days after first draw	ARCHITECT CMV IgG [AU/ml]	ARCHITECT CMV IgM [Index]	ARCHITECT CMV IgG Avidity [%Avi]	Commercially Available Diagnostic Kit [% Avidity]
RP-019-10	36	18.6	6.30	8.3	N/A
RP-019-11	43	76.5	7.05	12.9	14.0
RP-019-12	50	88.1	6.06	9.2	12.9
RP-019-13	57	98.0	5.30	18.8	13.0
RP-019-14	68	107.4	4.11	30.1	13.7
RP-019-15	75	109.9	3.68	21.9	18.1
RP-019-16	82	108.0	2.98	22.8	18.5
RP-019-17	86	107.8	3.19	28.3	17.8
RP-019-18	89	102.7	2.87	29.5	18.2
RP-019-19	96	106.4	2.66	28.3	24.3
RP-019-20	104	100.1	2.50	29.9	22.1
RP-019-21	109	93.8	2.24	34.1	24.5
RP-019-22	113	101.4	2.43	31.9	21.6
RP-019-23	116	108.9	2.66	32.4	20.5
RP-019-24	121	101.8	2.12	39.1	21.3
RP-019-25	124	104.2	2.18	37.6	18.2
PTC901-01	0	3.2	0.15	N/A	N/A
PTC901-02	2	2.0	0.12	N/A	N/A
PTC901-03	7	1.9	0.13	N/A	N/A
PTC901-04	10	1.7	0.13	N/A	N/A
PTC901-05	17	3.6	3.09	N/A	16.1
PTC901-06	24	42.8	5.29	15.8	16.8
PTC901-07	32	77.0	4.87	25.3	17.7
PTC901-08	51	101.1	4.50	22.7	17.3
PTC901-09	67	126.1	4.07	29.7	19.3

N/A in the table indicates that anti-CMV IgG was either not detectable (on a commercially available diagnostic kit) or the result was nonreactive (on the ARCHITECT CMV IgG assay). Therefore no avidity result could be generated.

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

Specificity

The ARCHITECT CMV IgG Avidity assay is designed to show a specificity comparable to a commercially available diagnostic kit when testing anti-CMV IgG reactive and anti-CMV IgM nonreactive specimens (indicating the absence of a primary infection). A total of 492 specimens from pregnant females, diagnostic/hospitalized patients and randomly selected volunteer blood donors were evaluated. 33 specimens grayzone on either assay were not included in the calculation of specificity. Data for specificity are summarized in the following table.*

Sample Type	ARCHITECT CMV IgG Avidity		Commercially Available Diagnostic Kit	
	Observed Specificity	Lower 95% Confidence Limit	Observed Specificity	Lower 95% Confidence Limit
Pregnant Females	100.0% (399/399)	99.1%	99.5% (397/399)	98.2%
Diagnostic/Hospitalized Patients	96.8% (61/63)	89.0%	98.4% (62/63)	91.5%
Blood Donors	96.7% (29/30)	82.8%	100.0% (30/30)	88.4%
Total	99.4% (489/492)	98.2%	99.4% (489/492)	98.2%

* 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). Potential interference was further assessed on specimens from patients with diseases unrelated to CMV infection. High avidity results can be expected since all specimens were anti-CMV IgG reactive and anti-CMV IgM nonreactive thus indicating the absence of a primary infection. Data are summarized in the table below.*

Interfering Substance	Total per Category [N]	High Avidity [N]	Grayzone Avidity [N]	Low Avidity [N]
Anti-nuclear antibody	9	9	0	0
Epstein-Barr virus	8	8	0	0
Influenza vaccinees	2	2	0	0
Human anti-mouse antibody	5	4	0	1
Herpes simplex virus type 1	9	8	1	0
Herpes simplex virus type 2	9	8	1	0
Hyperpolyclonal IgG	9	9	0	0
Hyperpolyclonal IgM	8	8	0	0
Measles	6	6	0	0
Rheumatoid factor	6	5	1	0
Systemic lupus erythematosus	6	5	1	0
Varicella zoster virus	7	7	0	0

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

BIBLIOGRAPHY

- Hecker M, Qui D, Marquardt K, Bein G, Hackstein H. Continuous cytomegalovirus seroconversion in a large group of healthy blood donors. *Vox Sang*. 2004 Jan;86(1):41-44.
- Munro SC, Hall B, Whybin LR, Leader L, Robertson P, Maine GT, Rawlinson WD. Diagnosis of and screening for cytomegalovirus infection in pregnant women. *J Clin Microbiol*. 2005 Sep;43(9):4713-4718.
- Cannon MJ, Davis KF. Washing our hands of the congenital cytomegalovirus disease epidemic. *BMC Public Health*. 2005 Jun 20;5:70.
- Pass R, Griffiths C, August A. Antibody Response to Cytomegalovirus after Renal Transplantation: Comparison of Patients with Primary and Recurrent Infections. *J Infect Dis* 1983;147:40-46.
- Lazzarotto T, Gabrielli L, Lanari M, Guerra B, Bellucci T, Sassi M, Landini MP. Congenital cytomegalovirus infection: recent advances in the diagnosis of maternal infection. *Hum Immunol*. 2004 May;65(5):410-415.
- Reynolds D, Stagno S, Hosty T, Tiller M, Alford C. Maternal Cytomegalovirus Excretion and Perinatal Infection. *N Engl J Med* 1973;289:1-5.
- Stagno S, Reynolds D, Pass R, Alford C. Breast Milk and the Risk of Cytomegalovirus Infection. *N Engl J Med* 1980;302:1073-1076.
- Bowden R, Sayers M, Flournoy N, Newton R, Banaji M, Thomas E, et al. Cytomegalovirus Immune Globulin and Seronegative Blood Products to Prevent Primary Cytomegalovirus Infection After Bone Marrow Transplantation. *N Engl J Med* 1986;314:1006-1010.

- Yow M, White N, Taber L, Frank A, Gruber W, May R, et al. Acquisition of Cytomegalovirus Infection From Birth to 10 Years: A Longitudinal Serologic Study. *J Pediatr* 1987; 10:37-42.
- Adler S. Molecular Epidemiology of Cytomegalovirus: Viral Transmission Among Children Attending A Day Care Center, Their Parents, and Caretakers. *J Pediatr* 1988;122:366-371.
- Maine G.T., Hsu S.T. et al. Methods of the determination of antibody IgG avidity. Patent PCT/US2006/042818.
- Boscato, LM and Stuart, MC. Heterophilic antibodies: A problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.
- 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;34:261-4.
- Schroff RW, Foon KA, Beatty SM, et al. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45:879-85.

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.

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