SIEMENS Healthineers

CMV IgG (CMV IgG)

Assay for the Detection of IgG Antibodies to Cytomegalovirus

Current Revision and Date[a]	Rev. 03, 2019-08	
Product Name	Atellica IM CMV IgG (CMV IgG)	REF 11202207
Abbreviated Product Name	Atellica IM CMV IgG	
Test Name/ID	CMVIgG	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM APW1	REF 10995458
Optional Materials	Atellica IM CMV IgG QC	REF 11202209
Specimen Types	Serum, dipotassium EDTA plasma, lithium heparin plasma	
Sample Volume	20 µL	
Measuring Interval	0.05–30.00 Index	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

CE 0197

Intended Use

The Atellica® IM CMV IgG (CMV IgG) assay is for *in vitro* diagnostic use in the qualitative and semi-quantitative determination of IgG antibodies to cytomegalovirus (CMV) in human pediatric and adult serum and plasma (dipotassium EDTA and lithium heparin) using the Atellica® IM Analyzer.

The assay is used to determine CMV IgG serological status and as an aid in the diagnosis of CMV infection.

Summary and Explanation

Human cytomegalovirus (CMV) is an enveloped DNA virus that is a member of the herpes virus group. Like other members of the herpesvirus family, CMV establishes lifelong latency following primary infection.[1] Subsequent viral reactivation or reinfection with a different CMV strain sometimes occurs, and is referred to as recurrent infection. CMV is spread through contact with infected bodily fluids, such as urine or saliva. Infection among pregnant women most frequently occurs through close contact with young children or through sexual transmission.

CMV is a universally distributed pathogen with approximately 40%–100% of the world's population having CMV antibody present in blood as evidence of infection. The highest prevalence is found in countries in the developing world.[2] By the age of 40, between 50%–85% of adults are infected by CMV.[3] The majority of CMV infections are asymptomatic, but CMV infection can cause serious disease among immunocompromised individuals, including but not limited to HIV-infected persons, organ transplant recipients on immunosuppressive therapy, and fetuses.

CMV is one of the most common intrauterine-transmitted viral agents, leading to congenital CMV infection in 0.3%–2.4% of live births in developed countries. Approximately 10% of congenitally infected infants exhibit symptoms of infection, such as jaundice, pneumonia, and central nervous system disorder at birth. Additionally, of the 90% who are asymptomatic, 10%–15% will develop neurological complications over the following months or even years.[4-6]

The incidence of intrauterine transmission of CMV is greatly reduced in women who have contracted the virus before pregnancy, even when the woman is reinfected during pregnancy, presumably because the maternal immune system is protective.[7] Therefore, it is critical that the diagnostician differentiate a primary infection from a latent infection, or reinfection in pregnant women.

Reactivation of latent CMV infection or acquisition of primary CMV infection in immunocompromised individuals can result in symptoms that include encephalitis, pneumonitis, hepatitis, uveitis, retinitis, colitis, and graft rejection.[8-9] To the contrary, in immunocompetent patients, primary CMV infection can result in flu-like symptoms, including malaise, fever, and sweats.[10]

Effective management of CMV infection in pediatric and adult patients is achieved by establishing the stage of CMV infection through accurate monitoring of the humoral response.

Principles of the Procedure

The Atellica IM CMV IgG assay is a fully automated, 2-step sandwich immunoassay using indirect chemiluminescent technology. The patient sample is diluted with Atellica IM CMV IgG DIL and incubated with the Solid Phase reagent. The Solid Phase reagent contains a heterogeneous mixture of biotinylated CMV viral lysate antigens, preformed to streptavidin-coated magnetic particles.

The antigen-coated particles subsequently capture CMV-specific antibodies in the sample. The antibody-antigen complex is washed and Lite Reagent is added. The Lite Reagent consists of an acridinium-ester-labeled anti-human IgG mouse monoclonal antibody. The entire complex is washed and the signal is generated in the presence of Lite Reagent bound to the Solid Phase via the CMV IgG-CMV antigen complex.

A direct relationship exists between the amount of bound anti-CMV IgG present in the patient specimen and the amount of relative light units (RLUs) detected by the system. A result of reactive or nonreactive is determined according to the Index Value established with the calibrators. Refer to *Interpretation of Results*.

Reagents

Material Description	Storage	Stability[a]
Atellica IM CMV IgG ReadyPack® primary reagent pack **Lite Reagent** 10.0 mL/reagent pack Mouse monoclonal anti-human IgG antibody labeled with acridinium ester (~0.06 µg/mL) in buffer with surfactant; bovine serum albumin (BSA); sodium azide (< 0.1%) **Solid Phase** 20.0 mL/reagent pack Streptavidin-coated paramagnetic microparticles preformed with biotinylated CMV viral lysate antigens (~0.5 mg/mL) in buffer with surfactants; sodium caseinate; sodium azide (< 0.1%)	Unopened at 2–8°C Onboard	Until expiration date on product 60 days
Atellica IM CMV IgG DIL ReadyPack ancillary reagent pack 19.5 mL/reagent pack Potassium thiocyanate (~0.55 M); surfactant; sodium caseinate; BSA; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 60 days
Atellica IM CMV IgG CAL 2.0 mL/vial Processed human plasma containing low and high levels of anti-CMV IgG; sodium azide (< 0.1%); preservatives	Unopened at 2–8°C Opened at 2–8°C At room temperature Atellica® Sample Handler[b]	Until expiration date on product 60 days after opening product 8 hours
Atellica IM APW1 ReadyPack ancillary reagent pack[c] 25.0 mL/pack 0.4 N sodium hydroxide	Unopened at 2–8°C Onboard	Until expiration date on product 14 days

[a] Refer to *Storage and Stability*.

[b] Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

[c] Refer to *Materials Required but Not Provided*.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens.com/healthineers.

H317
P272, P280, P302+P352, P333+P313, P363, P501

Warning!
May cause an allergic skin reaction.
Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/protective clothing/eye protection/face protection. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Wash contaminated clothing before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: reaction mass of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1) (in Atellica IM CMV IgG DIL)

H290, H319, H315
P280, P264, P305+P351+P338, P310, P390, P501

Warning!
May be corrosive to metals. Causes serious eye irritation. Causes skin irritation.
Wear protective gloves/protective clothing/eye protection/face protection. Wash hands thoroughly after handling. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor/physician. Absorb spillage to prevent material damage. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: sodium hydroxide (in Atellica IM APW1)

CAUTION POTENTIAL BIOHAZARD

Contains human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2), as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions.[11–12]

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Note For information about reagent preparation, refer to *Preparing the Reagents* in the *Procedure* section.

Note For information about calibrator preparation, refer to *Preparing the Calibrators*.

Storage and Stability

Store reagents in an upright position. Protect the product from heat and light sources. Unopened reagents are stable until the expiration date on the product when stored at 2–8°C.

Store calibrators in an upright position. Unopened calibrators are stable until the expiration date on the product when stored at 2–8°C. Opened calibrators are stable for 60 days at 2–8°C. Calibrators are stable for 8 hours at room temperature.

Store Atellica IM CMV IgG DIL in an upright position. Unopened Atellica IM CMV IgG DIL is stable until the expiration date on the product when stored at 2–8°C.

Store Atellica IM APW1 in an upright position. Unopened Atellica IM APW1 is stable until the expiration date on the product when stored at 2–8°C.

Do not use products beyond the expiration date printed on the product labeling.

Onboard Stability

Reagents are stable onboard the system for 60 days. Discard reagents at the end of the onboard stability interval.

Note Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

Atellica IM CMV IgG DIL is stable onboard the system for 60 days.

Atellica IM APW1 is stable onboard the system for 14 days.

Do not use products beyond the expiration date printed on the product labeling.

Specimen Collection and Handling

Serum and plasma (dipotassium EDTA and lithium heparin) are the recommended sample types for this assay.

Do not use heat-inactivated specimens.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[12]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[13]
- Follow the instructions provided with your specimen collection device for use and processing.[14]
- Keep tubes capped at all times.[15]
- Complete clot formation should take place before centrifugation.[15] Serum should be physically separated from cells as soon as possible, with a maximum limit of 24 hours from the time of collection.
- Test specimens as soon as possible after collecting. Store specimens at 2–8°C if not tested immediately.

Storing the Specimen

- Specimens may be stored on the clot for up to 14 days at 2–8°C.
- Separated specimens are stable for up to 48 hours at room temperature, and for up to 7 days at 2–8°C. For longer storage, specimens devoid of red blood cells may be frozen for up to 12 months at -20°C to -70°C. Do not store in a frost-free freezer.
- Thoroughly mix all thawed specimens and centrifuge before using. Thawed frozen specimens that are turbid must be clarified by centrifugation prior to testing. When specimens were subjected to 3 freeze-thaw cycles, no clinically significant differences were observed.

The handling and storage information provided here is based on data or references maintained by the manufacturer. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

Store specimens stoppered at 2–8°C upon arrival. If shipment is expected to exceed 7 days, ship specimens frozen.

Preparing the Samples

This assay requires 20 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For information about determining the minimum required volume, refer to the online help.

Note Do not use specimens with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[15]

Note For a complete list of appropriate sample containers, refer to the online help.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11202207	1 ReadyPack primary reagent pack containing Atellica IM CMV IgG Lite Reagent and Solid Phase 1 ReadyPack ancillary reagent pack containing Atellica IM CMV IgG DIL DIL Atellica IM CMV IgG master curve and test definition MC TDEF 1 vial Atellica IM CMV IgG CAL low calibrator CAL L 1 vial Atellica IM CMV IgG CAL high calibrator CAL H Atellica IM CMV IgG CAL calibrator lot-specific value sheet CAL LOT VAL	100

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

REF	Description	
	Atellica IM Analyzer[a]	
10995458	Atellica IM APW1 (probe wash)	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack WASH

[a] Additional system fluids are required to operate the system: Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner. For system fluid instructions for use, refer to the Document Library.

Optional Materials

The following materials may be used to perform this assay, but are not provided:

REF	Description	
11202209	Atellica IM CMV IgG QC (quality control material)	2 x 2.7 mL negative quality control (Control 1) CONTROL 1 – 2 x 2.7 mL positive quality control (Control 2) CONTROL 2 + Quality control lot-specific value sheet CONTROL LOT VAL

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 20 µL of specimen into a cuvette.
2. Dispenses 195 µL of Atellica IM CMV IgG DIL into the cuvette with the specimen.
3. Removes 100 µL of the diluted specimen from the cuvette and dispenses it into a second cuvette.
4. Dispenses 200 µL of Solid Phase, then incubates the mixture for 18 minutes at 37°C.
5. Separates the Solid Phase from the mixture, then aspirates the unbound reagent.
6. Washes the cuvette with Atellica IM Wash.
7. Resuspends the washed particles in 250 µL of Atellica IM Wash.
8. Dispenses 100 µL of Lite Reagent, then incubates the mixture for 18 minutes at 37°C.
9. Separates the Solid Phase from the mixture, then aspirates the unbound reagent.
10. Washes the cuvette with Atellica IM Wash.
11. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
12. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading primary reagent packs onto the system, mix them by hand and visually inspect the bottom of the reagent pack to ensure that all particles are resuspended. For information about preparing the reagents for use, refer to the online help.

Note The ancillary reagent (Atellica IM CMV IgG DIL) provided in this kit is matched to the Solid Phase and Lite Reagent. Do not mix ancillary reagent lots with different lots of Solid Phase and Lite Reagent.

Preparing the System

Ensure that the system has sufficient reagent packs loaded in the reagent compartment. The system automatically mixes reagent packs to maintain homogeneous suspension of the reagents. For information about loading reagent packs, refer to the online help.

Ensure that Atellica IM CMV IgG DIL is loaded in the reagent compartment.

Master Curve Definition

Before initiating calibration on each new lot of reagent, load the assay master curve and test definition values by scanning the MC TDEF 2D barcodes. For loading instructions, refer to the online help.

Performing Calibration

For calibration of the Atellica IM CMV IgG assay, use the calibrators provided with each kit.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

At the end of the onboard stability interval, replace the reagent pack on the system with a new reagent pack. Recalibration is not required, unless the lot calibration interval is exceeded.

Stability Interval	Days
Lot Calibration	77
Pack Calibration	60
Reagent Onboard Stability	60

For information about lot calibration and pack calibration intervals, refer to the online help.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Preparing the Calibrators

Calibrators are liquid and ready to use. Gently mix and invert the vials to ensure homogeneity of the material.

Note Use calibrators within the stability limits specified in *Storage and Stability* and discard any remaining material.

Calibration Procedure

The calibrators are provided in dropper vials. Each dispensed drop is approximately 50 µL.

The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the online help.

Use the following lot-specific materials to perform calibration:

- For the master curve and assay test definitions, refer to the lot-specific master curve and test definition sheet MC TDEF provided with the assay reagents.
- Calibrators provided in an assay kit must only be used with reagents from that assay kit lot. Do not use calibrators from one assay kit with reagents from a different assay kit lot.
- For the calibrator definitions, refer to the lot-specific value sheet CAL LOT VAL provided with the calibrator materials.
- Generate lot-specific barcode labels to use with the calibrator samples.

For instructions about how to perform the calibration procedure, refer to the online help.

Performing Quality Control

For quality control of the Atellica IM CMV IgG assay, use the Atellica IM CMV IgG QC or an equivalent product with at least 2 levels (negative and positive) at least once during each day that samples are analyzed. Additional quality control material of known analyte concentration can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

For the assigned values, refer to the lot-specific value sheet CONTROL | LOT | VAL provided. A satisfactory level of performance is achieved when the analyte values obtained are within the expected control interval for the system or within your interval, as determined by an appropriate internal laboratory quality control scheme. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the online help.

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Test quality control samples after a successful calibration.

Taking Corrective Action

If the quality control results do not fall within the assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

Results

Calculation of Results

The system determines the result using the calculation scheme described in the online help. Refer to *Interpretation of Results*.

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Interpretation of Results

The system reports Atellica IM CMV IgG assay results in Index Values and as Nonreactive or Reactive:

- **Nonreactive:** Samples with a value < 1.00 Index are considered nonreactive for CMV IgG antibodies.
- **Reactive:** Samples with a value ≥ 1.00 Index are considered reactive for CMV IgG antibodies.

The cut-off value for the Atellica IM CMV IgG assay was verified based on results generated from clinical studies. The magnitude of the measured result above the cut-off value is not indicative of the total amount of IgG antibody present in the sample.

Note If the controls are out of range, the sample results are invalid. Do not report results.

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

Limitations

The following information pertains to limitations of the assay:

- The Atellica IM CMV IgG assay is limited to the detection of IgG antibodies to CMV.
- The use of the Atellica IM CMV IgG assay to diagnose recent infection by testing acute and convalescent serum samples has not been validated.

- Specimens taken early during the acute phase of infection may not contain detectable levels of IgG antibodies to cytomegalovirus. Patients suspected of having recent infection should be tested for the presence of IgM antibodies to cytomegalovirus.
- The performance of the Atellica IM CMV IgG assay has not been established with cadaver specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic fluid, or pleural fluid.
- Assay performance characteristics have not been established when the Atellica IM CMV IgG assay is used in conjunction with other manufacturers' assays for specific cytomegalovirus serological markers.
- Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[16,17] Additional information may be required for diagnosis.

Expected Values

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur® system. Expected values were established using the ADVIA Centaur system and confirmed by assay comparison. Refer to *Performance Characteristics on the Atellica IM Analyzer*.

CMV is a universally dispersed pathogen with approximately 40%–100% of the world's population having CMV antibody present in blood. Age, socioeconomic status, and geographic location have all been suggested to play a role in the overall incidence of CMV IgG.[18-20]

A population of 1842 male and female subjects, including those who were pregnant, pediatric, or adult/not pregnant, were tested.

Population	N[a]	Reactive	Nonreactive
Pregnant women (20–45 years)	348	288 (82.8%)	60 (17.2%)
HIV-positive patients (prospective: 25–73 years)	44	43 (97.7%)	1 (2.3%)
HIV-positive patients (retrospective: 18–70 years)	143	135 (94.4%)	8 (5.6%)
Transplant patients (13–91 years)	394	257 (65.2%)	137 (34.8%)
Pediatric subjects (2–21 years)	229	82 (35.8%)	147 (64.2%)
Other subjects sent for CMV IgG testing (6 months–85 years)	684	388 (56.7%)	296 (43.3%)
Total	**1842**	**1193 (64.8%)**	**649 (35.2%)**

[a] Number of samples tested.

Assay results obtained at individual laboratories may vary from the data presented. Consider this information as guidance only.

Performance Characteristics

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur system. Some performance characteristics for the Atellica IM assay were established using the ADVIA Centaur system.

Performance Characteristics on the ADVIA Centaur System

Specificity

The assay was evaluated for potential cross-reactivity with other viral antibodies and disease state specimens. The CMV IgG status of each sample was verified using a comparative CMV IgG assay (Comparative Assay 1). Discordant samples were further evaluated using alternate comparative assays (Comparative Assays 2 and 3).

Total percent agreement for the following clinical categories was 99.0% (295/298). The following results were obtained:

Clinical Category	Number Tested	Number of Reactive Anti-CMV IgG Results	
		ADVIA Centaur CMV IgG	Comparative Assay 1
Antinuclear Antibody (ANA)	1	0	0
Chlamydia	11	4	4
CMV IgM	10	6	6
Epstein Barr virus (EBV) IgG	13	0	0
Epstein Barr virus (EBV) IgM	10	4	4
Graves' disease	3	0	0
Hepatitis A infection (HAV)	10	3	3
Hepatitis B core antibody (HBcAb)	10	3[a]	4
Hepatitis C infection (HCV)	10	1	1
Herpes simplex virus 1 (HSV1) IgG	13	3	3
Herpes simplex virus 2 (HSV2) IgG	12	0	0
Human anti-mouse antibody (HAMA)	14	7[b]	6
Human chorionic gonadotropin (hCG)	11	0	0
Human herpes virus (HHV6) IgG	11	0	0
Human immunodeficiency virus (HIV)[c]	16	9	9
Influenza	11	7	7
Measles IgG	11	0	0
Multiparity	20	18	18
Multiple myeloma	23	11	11
Parvovirus B19 IgG	11	3	3
Rheumatoid factor (RF)	10	1	1
Rubella IgG	13	0	0
Sjogren's syndrome	4	0	0
Systemic lupus erythematosus (SLE)	3	0	0
Syphilis IgG	11	4	4
Toxoplasma IgG	10	4	4

Clinical Category	Number Tested	Number of Reactive Anti-CMV IgG Results	
		ADVIA Centaur CMV IgG	Comparative Assay 1
Varicella zoster virus (VZV) IgG	16	0	0
Total	298	88	88

[a] One sample resolved as reactive.
[b] One sample resolved as nonreactive.
[c] One sample was nonreactive on the ADVIA Centaur CMV IgG assay and equivocal on Comparative Assay 1. Resolution testing did not confirm reactive or nonreactive serological status of CMV IgG.

Assay results obtained at individual laboratories may vary from the data presented.

Relative Sensitivity and Specificity

Relative sensitivity and specificity were determined by comparing the performance of the ADVIA Centaur CMV IgG assay to Comparative Assay 1. A total of 1842 samples were analyzed, including 1699 prospectively collected specimens (ages 6 months–91 years) and 143 HIV-positive retrospectively collected specimens from the following sources:

- 348 pregnant subjects
- 44 (prospective) and 143 (retrospective) HIV-positive subjects
- 394 transplant patients
- 229 pediatric subjects (2–21 years old)
- 684 other subjects sent for CMV IgG testing

Initial Relative Sensitivity and Specificity

Of the 1699 clinical prospective routine specimens analyzed, 14 samples that tested equivocal on Comparative Assay 1 were removed from the study calculations. A total of 1038 prospective samples were used to calculate initial relative sensitivity, and a total of 647 prospective samples were used to calculate initial relative specificity.

The ADVIA Centaur CMV IgG assay demonstrated initial relative sensitivity of 99.9% (1037/1038) with a 95% confidence interval of 99.5%–99.9%.

The ADVIA Centaur CMV IgG assay demonstrated initial relative specificity of 98.5% (637/647) with a 95% confidence interval of 97.2%–99.3%.

Initial Relative Sensitivity and Specificity

ADVIA Centaur CMV IgG Assay	Comparative Assay 1			
	Reactive	Equivocal	Nonreactive	Total
Reactive	1037	11	10	1058
Nonreactive	1	3	637	641
Total	**1038**	**14**	**647**	**1699**

Resolved Relative Sensitivity and Specificity

Eleven samples that were discordant were further tested using Comparative Assay 2. Of these 11 samples, 7 changed in interpretation to agree with the ADVIA Centaur CMV IgG assay, and 1 did not agree with the ADVIA Centaur CMV IgG assay. Three samples resolved equivocal and were removed from the calculations.

The ADVIA Centaur CMV IgG assay demonstrated resolved relative sensitivity of 100.0% (1044/1044) with a 95% confidence interval of 99.6%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated resolved relative specificity of 99.8% (637/638) with a 95% confidence interval of 99.1%–99.9%.

Resolved Relative Sensitivity and Specificity

	Resolved CMV IgG Assay Results			
ADVIA Centaur CMV IgG Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	1044	2	1	1047
Nonreactive	0	1	637	638
Total	**1044**	**3**	**638**	**1685**

Pregnant Women Study

Prospective serum samples were obtained from 348 pregnant subjects to assess initial relative sensitivity and initial relative specificity using the ADVIA Centaur CMV IgG assay and Comparative Assay 1.

A total of 287 reactive samples were used to calculate initial relative sensitivity, and a total of 61 nonreactive samples were used to calculate initial relative specificity.

The ADVIA Centaur CMV IgG assay demonstrated initial relative sensitivity of 100.0% (287/287) with a 95% confidence interval of 98.7%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated initial relative specificity of 98.4% (60/61) with a 95% confidence interval of 91.2%–99.9%.

One discordant sample was further tested on Comparative Assay 2 and resolved in agreement with the ADVIA Centaur CMV IgG assay.

The ADVIA Centaur CMV IgG assay demonstrated resolved relative sensitivity of 100.0% (288/288) with a 95% confidence interval of 98.7%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated resolved relative specificity of 100.0% (60/60) with a 95% confidence interval of 94.0%–100.0%.

Pregnant Women Study - Resolved Relative Sensitivity and Specificity

	Resolved CMV IgG Assay Results			
ADVIA Centaur CMV IgG Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	288	0	0	288
Nonreactive	0	0	60	60
Total	**288**	**0**	**60**	**348**

Human Immunodeficiency Virus (HIV) Study

Serum specimens were prospectively collected from 44 HIV-positive subjects, and retrospectively collected from 143 HIV-positive subjects. Fifteen of the retrospective specimens collected from 1 site in the United States were from subjects who were not United States residents. The samples were tested using the ADVIA Centaur CMV IgG assay and Comparative Assay 1.

The ADVIA Centaur CMV IgG assay demonstrated relative sensitivity of 100.0% (43/43) for the prospective HIV-positive population with a 95% confidence interval of 91.8%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated relative specificity of 100.0% (1/1) for the prospective HIV-positive population with a 95% confidence interval of 2.5%–100.0%.

HIV Study - Prospective Specimens

	Comparative Assay 1			
ADVIA Centaur CMV IgG Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	43	0	0	43
Nonreactive	0	0	1	1
Total	**43**	**0**	**1**	**44**

The ADVIA Centaur CMV IgG assay demonstrated relative sensitivity of 100.0% (135/135) for the retrospective HIV-positive population with a 95% confidence interval of 97.3%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated relative specificity of 100.0% (8/8) for the retrospective HIV-positive population with a 95% confidence interval of 63.1%–100.0%.

HIV Study - Retrospective Specimens

	Comparative Assay 1			
ADVIA Centaur CMV IgG Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	135	0	0	135
Nonreactive	0	0	8	8
Total	**135**	**0**	**8**	**143**

Transplant Patient Study

Prospective serum samples from 394 transplant patients were tested using the ADVIA Centaur CMV IgG assay and Comparative Assay 1. Five samples that tested equivocal on Comparative Assay 1 were removed from the calculations.

A total of 252 reactive samples were used to calculate initial relative sensitivity, and a total of 137 samples were used to calculate initial relative specificity.

The ADVIA Centaur CMV IgG assay demonstrated initial relative sensitivity of 100.0% (252/252) with a 95% confidence interval of 98.5%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated initial relative specificity of 99.3% (136/137) with a 95% confidence interval of 96.0%–99.9%.

One discordant sample was further tested on Comparative Assay 2 and resolved in agreement with the ADVIA Centaur CMV IgG assay.

The ADVIA Centaur CMV IgG assay demonstrated resolved relative sensitivity of 100.0% (253/253) with a 95% confidence interval of 98.6%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated resolved relative specificity of 100.0% (136/136) with a 95% confidence interval of 97.3%–100.0%.

Transplant Patient Study - Resolved Relative Sensitivity and Specificity

	Resolved CMV IgG Assay Results			
ADVIA Centaur CMV IgG Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	253	0	0	253
Nonreactive	0	0	136	136
Total	**253**	**0**	**136**	**389**

Pediatric Study

A total of 229 clinical prospective routine pediatric serum samples were tested. Samples were obtained from male and non-pregnant female subjects (in the age range of 2–21 years). Two samples that tested equivocal on Comparative Assay 1 were removed from the calculations.

Eighty reactive samples were used to calculate initial relative sensitivity, and a total of 147 nonreactive samples were used to calculate initial relative specificity.

The ADVIA Centaur CMV IgG assay demonstrated initial relative sensitivity of 100.0% (80/80) with a 95% confidence interval of 95.5%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated initial relative specificity of 99.3% (146/147) with a 95% confidence interval of 96.3%–99.9%.

One discordant sample was further tested on Comparative Assay 2 and did not agree with the ADVIA Centaur CMV IgG assay. Resolved relative sensitivity and specificity remained the same as the initial relative sensitivity and specificity.

Pediatric Study - Resolved Relative Sensitivity and Specificity

	Resolved CMV IgG Assay Results			
ADVIA Centaur CMV IgG Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	80	0	1	81
Nonreactive	0	0	146	146
Total	**80**	**0**	**147**	**227**

Other Subjects Sent for CMV IgG Testing

A total of 684 other prospective serum samples were tested. The subjects' ages ranged from 6 months–91 years. Seven samples that tested equivocal on Comparative Assay 1 were removed from the calculations.

A total of 376 reactive samples were used to calculate initial relative sensitivity, and a total of 301 nonreactive samples were used to calculate initial relative specificity.

The ADVIA Centaur CMV IgG assay demonstrated initial relative sensitivity of 99.7% (375/376) with a 95% confidence interval of 98.5%–99.9%.

The ADVIA Centaur CMV IgG assay demonstrated initial relative specificity of 97.7% (294/301) with a 95% confidence interval of 95.3%–99.1%.

Eight discordant samples were further tested using Comparative Assay 2. Of these 8 samples, 5 changed in interpretation to agree with the ADVIA Centaur CMV IgG assay, and 3 resolved as equivocal and were removed from the calculations.

The ADVIA Centaur CMV IgG assay demonstrated resolved relative sensitivity of 100.0% (380/380) with a 95% confidence interval of 99.0%–100.0%.

The ADVIA Centaur CMV IgG assay demonstrated resolved relative specificity of 100.0% (294/294) with a 95% confidence interval of 98.8%–100.0%.

Other Subjects Sent for CMV IgG Testing - Resolved Relative Sensitivity and Specificity

	Resolved CMV IgG Assay Results			
ADVIA Centaur CMV IgG Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	380	2	0	382
Nonreactive	0	1	294	295
Total	**380**	**3**	**294**	**677**

Interferences

Interference testing was performed in accordance with CLSI Document EP07-A2.[21]

Hemolysis, Icterus, Lipemia (HIL), and Other Interferences

The assay is designed to have no change in clinical interpretation when testing samples containing the compounds listed below.

Serum specimens that are, or that contain. . .	Have an insignificant effect on the assay up to . . .
hemolyzed	500 mg/dL of hemoglobin
icteric	20 mg/dL of conjugated bilirubin
icteric	20 mg/dL of unconjugated bilirubin
lipemic	3000 mg/dL of intralipids (Triglycerides)
biotin	4500 ng/mL of biotin
cholesterol	400 mg/dL of cholesterol

Total protein was tested using 21 samples with a total protein concentration greater than 9 g/dL. A single reactive sample was identified compared to the clinical status established with the comparative assay.

Results were established using the ADVIA Centaur system.

Performance Characteristics on the Atellica IM Analyzer

Measuring Interval

The Atellica IM CMV IgG assay provides results from 0.05–30.00 Index. The system flags all values that are outside the specified measuring interval.

Relative Sensitivity

Relative sensitivity was determined by comparing the Atellica IM CMV IgG assay using the Atellica IM Analyzer to the ADVIA Centaur CMV IgG assay using the ADVIA Centaur XP system.

A population of 205 ADVIA Centaur CMV IgG reactive samples was tested using the Atellica IM CMV IgG assay. One discordant sample that was further tested on Comparative Assay 1 resulted as nonreactive. The performance of the Atellica IM CMV IgG assay is shown in the following table:

Number	Nonreactive	Reactive	Resolved Relative Sensitivity (%)
205	1	204	100% (204/204)

The resolved relative sensitivity of the Atellica IM CMV IgG assay was 100% (204/204) with a 95% confidence interval of 98.2%–100%.

Assay results obtained at individual laboratories may vary from the data presented.

Relative Specificity

Relative specificity was determined by comparing the Atellica IM CMV IgG assay using the Atellica IM Analyzer to the ADVIA Centaur CMV IgG assay using the ADVIA Centaur XP system.

A population of 155 ADVIA Centaur CMV IgG nonreactive samples was tested using the Atellica IM CMV IgG assay. One discordant sample that was further tested on Comparative Assay 1 was indeterminate and was removed from the study calculations. The performance of the Atellica IM CMV IgG assay is shown in the following table:

Number	Nonreactive	Reactive	Resolved Relative Specificity (%)
155	154	0	100% (154/154)

The resolved relative specificity of the Atellica IM CMV IgG assay was 100% (154/154) with a 95% confidence interval of 97.6%–100%.

Assay results obtained at individual laboratories may vary from the data presented.

Centers for Disease Control (CDC) Panel

A panel of 80 previously characterized mix-titered serum samples was obtained from the CDC and evaluated with the Atellica IM CMV IgG assay to determine the performance of the assay. The observed results showed 100% (39/39) positive percent agreement and 100% (41/41) negative percent agreement to the serological status provided by the CDC.

	CDC Panel Results		
Atellica IM CMV IgG Assay	**Positive**	**Negative**	**Total**
Reactive	39	0	39
Nonreactive	0	41	41
Total	**39**	**41**	**80**

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[22] Samples were assayed on an Atellica IM Analyzer in duplicate in 2 runs per day for 20 days. The assay was designed to have repeatability precision of ≤ 8.0% CV and within-laboratory precision of ≤ 12.0% CV for samples > 0.70–≤ 30.00 Index. For samples ≤ 0.70 Index, the Atellica IM CMV IgG assay must not show a change in clinical interpretation. The following results were obtained:

			Repeatability		Within-Laboratory Precision	
Sample Type	**N[a]**	**Mean (Index)**	**SD[b] (Index)**	**CV[c] (%)**	**SD (Index)**	**CV (%)**
Serum A	80	0.04	0.00	N/A[d]	0.00	N/A
Serum B	80	0.74	0.01	1.3	0.02	2.9
Serum C	80	1.18	0.02	1.5	0.04	3.4
Serum D	80	1.93	0.03	1.6	0.06	3.2
Serum E	80	9.17	0.12	1.3	0.28	3.0

			Repeatability		Within-Laboratory Precision	
Sample Type	N[a]	Mean (Index)	SD[b] (Index)	CV[c] (%)	SD (Index)	CV (%)
Control 1	80	0.05	0.00	N/A	0.00	N/A
Control 2	80	4.23	0.05	1.3	0.11	2.5

[a] Number of samples tested.
[b] Standard deviation.
[c] Coefficient of variation.
[d] Not applicable. Results must not show a change in clinical interpretation.

Assay results obtained at individual laboratories may vary from the data presented.

Standardization

The Atellica IM CMV IgG assay standardization is based upon clinical agreement with a commercially available CMV IgG assay. Refer to *Performance Characteristics*. Assigned values for calibrators and controls are traceable to this standardization.

Technical Assistance

For customer support, contact your local technical support provider or distributor.

siemens.com/healthineers

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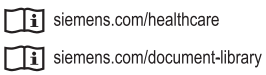
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
	Version of instructions for use
	Internet URL address to access the electronic instructions for use
	Revision

Symbol	Symbol Title and Description
	Caution Consult instructions for use or accompanying documents for cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device.
	Biological risks Potential biological risks are associated with the medical device.
	Corrosive
	Dangerous to environment
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable
	Oxidizing
	Explosive
	Toxic
	Compressed gas
	Keep away from sunlight Prevent exposure to sunlight and heat.
	Up Store in an upright position.
	Do not freeze
	Temperature limit Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines.
	Handheld barcode scanner

Symbol	Symbol Title and Description
IVD	*In vitro* diagnostic medical device
Σ (n)	Contains sufficient for <n> tests Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol.
RxOnly	Prescription device (US only) Applies only to United States-registered IVD assays. CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.
	Mixing of substances Mix product before use.
g mL	Reconstitute and mix lyophilized product before use.
	Target
	Interval
	Legal Manufacturer
EC REP	Authorized Representative in the European Community
	Use-by date Use by the designated date.
LOT	Batch code
REF	Catalog number
	Recycle
PRINTED WITH SOY INK	Printed with soy ink
CE	CE Mark
CE 0088	CE Mark with notified body ID number Notified body ID number can vary.
YYYY-MM-DD	Date format (year-month-day)
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
UNITS C	Common Units
UNITS SI	International System of Units

Symbol	Symbol Title and Description
MATERIAL	Material
MATERIAL ID	Unique material identification number
CONTROL NAME	Name of control
CONTROL TYPE	Type of control

Legal Information

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