SIEMENS Healthineers

CMV IgM (CMV IgM)

Assay for the Detection of IgM Antibodies to Cytomegalovirus

Current Revision and Date[a]	Rev. 01, 2021-11	
Product Name	Atellica IM CMV IgM (CMV IgM)	REF 11202488 (50 tests)
Abbreviated Product Name	Atellica IM CMV IgM	
Test Name/ID	CMVIgM	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM CMV IgM QC	REF 11202489
Specimen Types	Serum, EDTA plasma, lithium heparin plasma	
Sample Volume	20 µL	
Measuring Interval	0.10–8.00 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 IgM (CMV IgM) assay is for *in vitro* diagnostic use in qualitative detection of IgM antibodies to cytomegalovirus (CMV) in human pediatric and adult serum and plasma (EDTA and lithium heparin) using the Atellica® IM Analyzer.

The assay is used as an aid in the diagnosis of recent or current CMV infection in individuals for whom a CMV IgM test was ordered.

Summary and Explanation

Human cytomegalovirus (CMV) is a member of the herpes virus group. The majority of CMV infections are asymptomatic, but the incidence and spectrum of the disease in immunocompromised individuals establishes this virus as a major opportunistic human pathogen.[1]

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. Ten percent of these infants will develop classic cytomegalic inclusion disease with jaundice, pneumonia, and central nervous system disorder. Infected infants may be asymptomatic at birth, but can develop neurological problems later in life.[2,3]

The incidence of intrauterine transmission of CMV is greatly reduced in women who have contracted the virus before pregnancy, even when the woman is re-infected during pregnancy, presumably because the maternal immune system is protective.[4]

Additionally, in immunocompromised individuals, CMV infection can result in pneumonia, hepatitis, encephalitis, myelitis, colitis, uveitis, retinitis, and neuropathy.[5] Primary or latent CMV infections in immunocompromised individuals, including HIV patients and organ recipients, can be life threatening.[6] CMV infection of an immunocompetent individual can result in flu-like symptoms, including malaise, fever, and sweats.[7]

Between 40%–100% of people have detectable CMV IgG antibody,[8] with the highest prevalence in developing countries. Presence of CMV IgM may indicate a current or recent infection, including reactivation after a past infection.[3]

Principles of the Procedure

The Atellica IM CMV IgM assay is a fully automated, 2-step sandwich immunoassay using indirect chemiluminescent technology. The patient sample is diluted with Atellica IM CMV IgM diluent and incubated with the Solid Phase and the Ancillary Well Reagent. The Solid Phase 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 fragment of an anti-human IgM 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 IgM-CMV antigen complex.

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
Atellica IM CMV IgM ReadyPack® primary reagent pack[a, b] **Lite Reagent** 7.5 mL/reagent pack Mouse monoclonal anti-human IgM fragment labeled with acridinium ester (~0.2 µg/mL); buffer; surfactant; sodium caseinate; sodium azide (< 0.1%) **Solid Phase** 5.0 mL/reagent pack Streptavidin-coated paramagnetic microparticles preformed with biotinylated CMV viral lysate antigens (~0.5 mg/mL); buffer; surfactants; sodium caseinate; preservatives **Ancillary Well Reagent** 5.0 mL/reagent pack buffer; surfactant; sodium caseinate; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 90 days
Atellica IM CMV IgM ReadyPack ancillary reagent pack[a, b] **Ancillary Reagent** 22.5 mL/reagent pack Buffer, surfactant, sodium caseinate, goat antiserum; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 90 days

Material Description	Storage	Stability
Atellica IM CMV IgM CAL[a, b] 2.0 mL/vial Processed human plasma containing low and high levels of anti-CMV IgM; sodium azide (< 0.1%); preservatives	Unopened at 2–8°C	Until expiration date on product
	Opened at 2–8°C	60 days
	At room temperature	8 hours

[a] Store in an upright position.

[b] Prevent exposure to sunlight and heat.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

For Prescription Use Only.

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

Warning! Potential Biohazard

Contains human source material.

No known test method can ensure that products derived from human source materials will not transmit infection. These materials should be handled using good laboratory practices and universal precautions.[9-11]

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.

Storage and Stability

Store all reagents in an upright position, away from light and heat. Do not use products beyond the expiration date printed on the product labeling.

For information about product storage and stability, refer to *Reagents*.

Onboard Stability

Discard products at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

For information about product onboard stability, refer to *Reagents*.

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.

Specimen Collection and Handling

Serum and plasma (EDTA and lithium heparin) are the recommended specimen 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.[11]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[12]
- Follow the instructions provided with your specimen collection device for use and processing.[13]
- Allow blood specimens to clot completely before centrifugation.[14]
- Keep tubes capped at all times.[14]

Storing the Specimen

- After centrifugation, specimens in the primary collection device are stable for up to 14 days at 2–8°C. Primary tube samples include serum stored on the clot, plasma stored on packed red cells, and samples processed and stored in gel-barrier tubes.
- Separated samples are stable for up to 48 hours at room temperature, and for up to 7 days at 2–8°C.
- Separated samples are stable at ≤ -20°C for up to 6 months. Do not store in a frost-free freezer.
- When samples were subjected to 3 freeze-thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed samples and centrifuge them before using. Thawed frozen specimens that are turbid must be clarified by centrifugation prior to testing.

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.

If during shipment, specimens may be subjected to temperatures > 25°C, then 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 a complete list of appropriate sample containers and information about determining the minimum required volume, refer to the system online help.

Do not use samples with apparent contamination.

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

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

Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[14]

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11202488	1 ReadyPack primary reagent pack containing Atellica IM CMV IgM Lite Reagent, Solid Phase, and Ancillary Well Reagent 1 ReadyPack ancillary reagent pack containing Atellica IM CMV IgM Ancillary Reagent (diluent) DIL Atellica IM CMV IgM master curve and test definition MC TDEF 1 vial Atellica IM CMV IgM CAL low calibrator CAL L 1 vial Atellica IM CMV IgM CAL high calibrator CAL H Atellica IM CMV IgM CAL calibrator assigned value sheet CAL LOT VAL	50

Materials Required but Not Provided

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

REF	Description
	Atellica IM Analyzer[a]

[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	
11202489	Atellica IM CMV IgM QC (quality control material)	2 x 2.7 mL negative quality control, level 1 CONTROL – 1 2 x 2.7 mL positive quality control, level 2 CONTROL + 2 Quality control assigned 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 450 µL of Atellica IM CMV IgM DIL into the cuvette with the specimen.
3. Removes 40 µL of the diluted specimen from the cuvette and dispenses it into a second cuvette.
4. Dispenses 100 µL of Solid Phase and 100 µL of Ancillary Well reagent, then incubates the mixture for 17 minutes at 37°C.
5. Separates the Solid Phase from the mixture, then aspirates the unbound reagent.
6. Washes the cuvette and resuspends the washed particles in 200 µL of Atellica IM Wash.
7. Dispenses 150 µL of Lite Reagent, then incubates the mixture for 18 minutes at 37°C.
8. Separates the Solid Phase from the mixture, washes the cuvette, and then aspirates the unbound reagent.

9. Dispenses 300 µL of Atellica IM Acid Reagent and 300 µL of Atellica IM Base Reagent to initiate the chemiluminescent reaction.
10. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading the packs onto the system, reagents require mixing. For information about mixing the reagents, refer to the system online help.

Note The Ancillary Reagent provided in this kit is matched to the Solid Phase, Lite Reagent, and Ancillary Well Reagent. Do not mix Ancillary Reagent lots with different lots of Solid Phase, Lite Reagent, and Ancillary Well Reagent.

Preparing the System

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided* and *Materials Required but Not Provided* for guidance about required reagents.

For information about loading products, refer to the system online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, enter the assay master curve and test definition by scanning the MC TDEF 2D barcodes. For information about entering the master curve and test definition, refer to the system online help.

Performing Calibration

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

Note Calibrators provided in an assay kit must only be used with the reagent lot provided in the same 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.

Note When loading a new primary reagent pack, a calibration is not required if there is a valid lot calibration. For information about lot calibration and pack calibration, refer to the system online help.

Stability Interval	Days
Lot Calibration	70
Pack Calibration	56
Reagent Onboard Stability	90

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. Allow the calibrators to equilibrate to room temperature. Gently mix and invert the vials to ensure homogeneity of the material.

Use calibrators within the stability limits specified in *Reagents* 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 system 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 lot with reagents from a different assay kit lot.
- For the calibrator definitions, refer to the calibrator assigned 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 system online help.

Performing Quality Control

For quality control of the Atellica IM CMV IgM assay, use the Atellica IM CMV IgM QC or an equivalent product at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use. For the assigned values, refer to the quality control assigned value sheet provided CONTROL LOT VAL.

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration
- With use of a new lot of reagent
- When troubleshooting test results that do not match clinical conditions or symptoms

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

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

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 system online help.

Taking Corrective Action

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

Results

Calculation of Results

The system determines the result using the calculation procedure described in the system 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 IgM assay results in Index Values and as Nonreactive or Reactive:

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

The cut-off value for the Atellica IM CMV IgM assay was verified based on clinical agreement of results generated from clinical studies. The magnitude of the measured result above the cut-off value is not indicative of the total amount of IgM 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 assay is limited to the detection of IgM antibodies to CMV. Additional information may be required for diagnosis.
- Results obtained with the assay may not be used interchangeably with values obtained with different assay methods.
- A nonreactive CMV IgM test result does not exclude possible acute cytomegalovirus infection. Because individual immune responses can vary, detectable levels of CMV IgM antibodies may not be present in the early stage of infection.[15,16]
- The detection of IgM antibodies against CMV in a single sample is not sufficient to prove an acute CMV infection. In some cases, elevated IgM antibody levels may persist for six months or longer after initial infection.[2]
- The performance of the assay has not been established with cord blood, neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic fluid, or pleural fluid.
- As with any serological assay, be alert to possible interference from various medications or endogenous substances in the patient sample.
- Patient samples may contain heterophilic antibodies that could react in immunoassays and cause falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[17,18]

Expected Values

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur systems. Expected values were established using the ADVIA Centaur XP 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 IgG antibody present in blood. Age, socioeconomic status, and geographic location have all been suggested to play a role in the overall incidence of CMV IgM.[19-21]

A population of 1031 male and female subjects from the United States (aged 6 months to 87 years) was tested using the ADVIA Centaur CMV IgM assay. The subjects tested included those who were pregnant, pediatric, and adult/not pregnant.

Population	N[a]	Reactive	Nonreactive
Pregnant women (18–42 years)	361	13 (3.60%)	348 (96.40%)
HIV-positive patients (18–67 years) (70.6% male and 29.4% female)	85	4 (4.71%)	81 (95.29%)
Transplant patients (retrospective: 17–80 years) (58.7% male and 41.1% female)	175	10 (5.71%)	165 (94.29%)
Pediatric subjects (2–21 years) (21.2% male and 78.8% female)	170	2 (1.18%)	168 (98.82%)
Subjects sent for CMV IgM testing (6 months–87 years) (35.0% male and 65.0% female)	240	14 (5.83%)	226 (94.17%)
Total	**1031**	**43 (4.17%)**	**988 (95.83%)**

[a] Number of samples tested.

Results are representative of the population tested. Consider this information as guidance only.

Performance Characteristics on the ADVIA Centaur® XP System

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

Measuring Interval

0.10–8.00 Index is reported as nonreactive or reactive.

Sensitivity and Specificity

Specificity and sensitivity were determined by comparing the performance of the ADVIA Centaur CMV IgM assay to a consensus of 3 commercially available, comparative CMV IgM assays at 3 evaluation sites. A total of 1138 clinical serum specimens, including 1031 prospective specimens (from males and females, aged 6 months to 87 years), and 107 retrospectively collected specimens (from subjects aged 16–75 years) were evaluated from the following populations:

1031 prospective specimens

- 361 pregnant subjects
- 85 HIV-positive subjects
- 175 transplant patients
- 170 pediatric subjects (2–21 years old)
- 240 other subjects sent for CMV IgM testing

107 retrospective specimens

- 16 pediatric subjects (2–21 years old)
- 91 other subjects sent for CMV IgM testing

Of the 1031 prospective samples analyzed, 12 samples tested reactive on the consensus of 3 comparative assays. Four samples tested equivocal on the consensus of 3 comparative assays and were removed from the study calculations. A total of 107 retrospective samples were used to calculate sensitivity, and 1015 prospective samples were used to calculate specificity.

Prospective Population

	Consensus of CMV IgM Comparative Assays			
ADVIA Centaur CMV IgM Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	9	3	31	43
Nonreactive	3	1	984	988
Total	**12**	**4**	**1015**	**1031**

Sensitivity: 75.00% (9/12); 95% Confidence Interval: 42.81%–94.51%

Specificity: 96.95% (984/1015); 95% Confidence Interval: 95.69%–97.92%

Retrospective Population

	Consensus of CMV IgM Comparative Assays			
ADVIA Centaur CMV IgM Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	106	0	0	106
Nonreactive	1	0	0	1
Total	**107**	**0**	**0**[a]	**107**

[a] Because of the lack of nonreactive specimens in the retrospective population, specificity could not be assessed in the retrospective population.

Sensitivity: 99.07% (106/107); 95% Confidence Interval: 94.90%–99.99%

The results obtained for subgroups of different populations are presented in the sections that follow.

Pregnant Women Subgroup

Serum specimens sent for CMV IgM testing from 361 pregnant women were prospectively collected from 3 sites. There were 2 equivocal samples that were removed from the calculation. A total of 359 nonreactive specimens were used to calculate specificity. Because of the lack of reactive specimens in the prospective pregnant population, sensitivity could not be assessed.

	Consensus of CMV IgM Comparative Assays			
ADVIA Centaur CMV IgM Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	0	1	12	13
Nonreactive	0	1	347	348
Total	**0**	**2**	**359**	**361**

Specificity: 96.66% (347/359); 95% Confidence Interval: 94.23%–98.26%

Pediatric Subgroup

Serum specimens from 170 pediatric subjects were prospectively collected from 3 sites. Subjects who were females who were not pregnant, and males. The subjects ranged in the age from 2–21 years. One reactive sample was used to calculate sensitivity, and 169 nonreactive samples were used to calculate specificity.

	Consensus of CMV IgM Comparative Assays			
ADVIA Centaur CMV IgM Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	1	0	1	2
Nonreactive	0	0	168	168
Total	**1**	**0**	**169**	**170**

Sensitivity: 100% (1/1); 95% Confidence Interval: 2.50%–100%

Specificity: 99.41% (168/169); 95% Confidence Interval: 96.75%–99.99%

Human Immunodeficiency Virus (HIV) Subgroup

Serum specimens were obtained from 85 HIV-positive subjects sent for CMV IgM testing were prospectively collected from 3 sites. Two positive samples were used to calculate sensitivity, and 83 nonreactive samples were used to calculate specificity.

	Consensus of CMV IgM Comparative Assays			
ADVIA Centaur CMV IgM Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	2	0	2	4
Nonreactive	0	0	81	81
Total	**2**	**0**	**83**	**85**

Sensitivity: 100% (2/2); 95% Confidence Interval: 15.81%–100%

Specificity: 97.59% (81/83); 95% Confidence Interval: 91.57%–99.71%

Transplant Patient Subgroup

Serum specimens from 175 transplant patients were prospectively collected from 3 sites in the United States that perform kidney, pancreas, bone and marrow stem cell, liver, face and limb, heart, and lung transplants. One sample tested equivocal on the consensus comparative assays and was removed from othe calculations. A total of 6 reactive samples were used to calculate sensitivity, and 168 samples were used to calculate initial specificity.

	Consensus of CMV IgM Comparative Assays			
ADVIA Centaur CMV IgM Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	3	1	6	10
Nonreactive	3	0	162	165
Total	**6**	**1**	**168**	**175**

Sensitivity: 50.0% (3/6); 95% Confidence Interval: 11.81%–88.19%

Specificity: 96.43% (162/168); 95% Confidence Interval: 92.39%–98.68%

Subjects Sent for CMV IgM Testing

Serum samples from 240 members of the general population who were sent for CMV IgM testing were prospectively collected from 3 sites. The subjects ranged in age from 6 months to 87 years. One sample tested equivocal on consensus comparator assays and was removed from the calculations. A total of 3 reactive samples were used to calculate sensitivity, and 236 nonreactive samples were used to calculate specificity.

	Consensus of CMV IgM Comparative Assays			
ADVIA Centaur CMV IgM Assay	**Reactive**	**Equivocal**	**Nonreactive**	**Total**
Reactive	3	1	10	14
Nonreactive	0	0	226	226
Total	**3**	**1**	**236**	**240**

Sensitivity: 100.0% (3/3); 95% Confidence Interval: 29.24%–100.0%

Specificity: 95.76% (226/236); 95% Confidence Interval: 92.35%–97.95%

Reproducibility

Reproducibility was evaluated according to CLSI document EP05-A3.[22] A reproducibility study was conducted at 3 external sites, with each site evaluating 2 reagent lots. The protocol was run over 5 days, 2 runs per day. There were 3 replicates per run for the serum pools and 6 replicates per run for negative and positive control materials. Reproducibility data was pooled across 3 sites. The data presented is for 1 representative reagent lot.

			Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
Specimen Type	**N[a]**	**Mean (Index)**	**SD[b] (Index)**	**CV[c] (%)**	**SD (Index)**	**CV (%)**	**SD (Index)**	**CV (%)**	**SD (Index)**	**CV (%)**	**SD (Index)**	**CV (%)**
Serum 1	90	0.39	0.01	1.6	0.01	1.4	0.02	4.9	0.02	5.2	0.03	7.4
Serum 2	90	0.80	0.02	2.4	0.02	1.9	0.01	0.6	0.01	1.1	0.03	3.3
Serum 3	90	1.15	0.03	2.3	0.02	1.7	0.01	1.1	0.02	1.3	0.04	3.4
Serum 4	90	2.39	0.06	2.5	0.02	0.8	0.05	2.1	0.08	3.2	0.11	4.7
Serum 5	90	5.14	0.13	2.6	0.10	2.0	0.06	1.2	0.19	3.8	0.26	5.1
Control 1 (negative)	180	0.14	0.04	N/A[d]	0.00	N/A	0.00	N/A	0.04	N/A	0.02	N/A
Control 2 (positive)	180	2.57	0.07	2.9	0.03	1.1	0.03	1.1	0.08	3.3	0.05	1.8

[a] Number of measurements.
[b] Standard deviation.
[c] Coefficient of variation.
[d] Not applicable. The results remained nonreactive throughout the study.

The assay was designed to have reproducibility precision of ≤ 15% CV for for samples > 0.70–≤ 8.00. For specimens ≤ 0.70 Index, the assay must not show a change in clinical interpretation.

Specimen Equivalency

Specimen equivalency was determined with the ordinary least squares model in accordance in accordance with CLSI Document EP09c-ed3.[23] Agreement of the specimen types may vary depending on the study design and population tested.

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval	N[a]	r[b]
Dipotassium EDTA plasma	y = 0.97 (x) + 0.06	0.81–7.02 Index	36	0.996
Lithium heparin plasma	y = 0.99 (x) + 0.01	0.76–7.38 Index	36	0.998

[a] Number of samples tested.
[b] Correlation coefficient.

The assay is designed to have a correlation coefficient ≥ 0.95, with a slope of 1.0 ±0.10, and an intercept of ≤ ±0.20 Index, for samples between > 0.70 and ≤ 8.00 Index. Negative samples (≤ 0.70 Index) shall remain negative.

IgM Specificity

To assess that the ADVIA Centaur CMV IgM assay specifically detects CMV IgM antibodies, performance was evaluated by testing 3 CMV IgM samples (high negative, low positive, and high positive), which were spiked with high CMV IgG, against the same 3 unspiked CMV IgM samples. Percent bias was calculated.

The presence of a high CMV IgG titer did not affect the clinical interpretation of CMV IgM samples. The negative samples remained negative. The positive samples showed a bias of less than 10% in the presence of a high CMV IgG titer.

	ADVIA Centaur CMV IgM		
CMV IgM Samples	Unspiked Samples (Index)	Spiked Samples (Index)	Bias (%)
Sample 1	0.72	0.73	1.39
Sample 2	1.47	1.45	1.36
Sample 3	5.23	4.94	5.54

Interferences

Interference testing was performed in accordance with CLSI Document EP07-ed3.[24]

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

Interference by endogenous substances in the ADVIA Centaur CMV IgM assay was evaluated at 3 CMV IgM levels (low negative, low positive, and high positive). No change in clinical serological status was observed for all samples tested in the presence of the interfering substances listed. The following results are representative of the performance of the assay:

Substance	Substance Test Concentration
Hemoglobin	1000 mg/dL (10.0 g/L)
Bilirubin, conjugated	40 mg/dL (474 µmol/L)
Bilirubin, unconjugated	40 mg/dL (684 µmol/L)
Triglycerides	3000 mg/dL (33.9 mmol/L)
Biotin	3510 ng/mL (14.4 µmol/L)
Cholesterol	400 mg/dL (10.4 mmol/L)
High IgG (human serum albumin)	6 g/dL (60 g/L)
High protein	15 g/dL (150 g/L)

Cross-Reactivity

The assay was evaluated for potential cross-reactivity with other viral and microbial antibodies and disease state specimens. The ADVIA Centaur CMV IgM status of each sample was assessed using a comparator CMV IgM assay. The following results are representative of the performance of the assay:

		Number of Reactive Anti-CMV IgM Results	
Clinical Category	**Number Tested**	**ADVIA Centaur CMV IgM**	**Comparator CMV IgM Assay**
Autoimmune disease - antinuclear antibodies (ANA)	8	1[a]	0
Autoimmune disease - Graves' disease	5	0	0
Autoimmune disease - Systemic lupus erythematosus (SLE)	5	0	0
Chlamydia IgM positive	16	0	0
Cytomegalovirus (CMV) IgG positive	19	0	0
Epstein Barr virus (EBV) IgG positive	13	0	0
Epstein Barr virus (EBV) IgM positive	10	0	0
Hepatitis A virus IgM positive	10	0	0
Hepatitis B core IgM positive	12	0	0
Hepatitis C antibody positive	15	0	0
Herpes simplex virus (HSV) IgM positive	13	0	0
Herpes virus type 6 (HHV6) antibody positive	10	0	0
Human anti-mouse antibodies (HAMA)	10	0	0
Human chorionic gonadotropin (HCG) antibody positive	13	0	0
Human immunodeficiency virus (HIV) antibody positive	11	0	0
Influenza	11	0	0
Measles IgG positive	10	0	0
Measles IgM positive	15	0	0
Multiparity	10	0	0
Multiple myeloma	15	0	0
Parvovirus B19 IgG positive	10	0	0
Rheumatoid factor (RF) positive	10	0	0
Rubella IgM positive	12	0	0
Syphilis IgM positive	10	0	0
Toxoplasma IgM positive	10	0	0

Clinical Category	Number Tested	Number of Reactive Anti-CMV IgM Results	
		ADVIA Centaur CMV IgM	Comparator CMV IgM Assay
Varicella zoster virus (VSV) IgM positive	16	0	0
Total	**299**	**1**	**0**

[a] A discordant sample was further evaluated using an alternate comparative CMV IgM assay, and was confirmed as discordant.

Performance Characteristics on the Atellica IM Analyzer

Assay Comparison

To demonstrate equivalence of the Atellica IM Analyzer CMV IgM assay between the ADVIA Centaur XP system and Atellica IM Analyzer, 331 specimens were evaluated on both systems using 1 reagent lot. Testing was performed in accordance with CLSI Document EP12-A2.[25]

Agreement of the assays may vary depending on the study design, comparative assay, and population tested.

Atellica IM Analyzer	ADVIA Centaur XP system		
	Reactive	Nonreactive	Total
Reactive	121	0	121
Nonreactive	2	208	210
Total	**123**	**208**	**331**

Sensitivity: 98.37% (121/123); 95% Confidence Interval: 94.31%–99.56%

Specificity: 100% (208/208); 95% Confidence Interval: 98.19%–100%

Overall Agreement: 99.40% (329/331); 95% Confidence Interval: 97.38%–99.83%

Centers for Disease Control (CDC) Panel

A panel of 60 previously characterized mix-titered serum samples was obtained from the CDC and evaluated with the ADVIA Centaur CMV IgM assay to determine the performance of the assay using the Atellica IM Analyzer. The observed results showed 96.55% (28/29) positive percent agreement and 100% (31/31) negative percent agreement with the ADVIA Centaur XP system.

CDC Panel Results on the Atellica IM Analyzer	CDC Panel Results on the ADVIA Centaur XP System		
	Reactive	Nonreactive	Total
Reactive	28	0	28
Nonreactive	1	31	32
Total	**29**	**31**	**60**

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[22] Samples were assayed in duplicate in 2 runs per day for 20 days. Precision was evaluated by testing negative and positive controls (plasma) and serum samples. The following results are representative of the performance of the assay:

			Repeatability		Within-Laboratory Precision	
Sample Type	N[a]	Mean (Index)	SD[b] (Index)	CV[c] (%)	SD (Index)	CV (%)
Serum 1	80	0.35	0.006	N/A[d]	0.013	N/A
Serum 2	80	0.74	0.012	1.6	0.029	3.9
Serum 3	80	1.09	0.019	1.7	0.040	3.7
Serum 4	80	2.61	0.050	1.9	0.107	4.1
Serum 5	80	4.90	0.078	1.6	0.202	4.1
Control 1 (negative)	80	0.10	0.003	N/A	0.004	N/A
Control 2 (positive)	80	2.80	0.049	1.8	0.109	3.9

[a] Number of measurements.
[b] Standard deviation.
[c] Coefficient of variation.
[d] Not applicable. The results remained nonreactive throughout the study.

The assay was designed to have repeatability precision of ≤ 8.0% CV and within-laboratory precision of ≤ 12.0% CV for samples > 0.70–≤ 8.00 Index. For samples ≤ 0.70 Index, the Atellica IM CMV IgM assay must not show a change in clinical interpretation.

Standardization

The Atellica IM CMV IgM assay standardization is based on clinical agreement with a consensus of commercially available CMV IgM assays. Refer to *Performance Characteristics on the ADVIA Centaur® XP System* and *Performance Characteristics on the Atellica IM Analyzer*.

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-healthineers.com

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Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Symbol	Symbol Title
	Manufacturer		Authorized representative in the European Community
	Use-by date		Batch code
	Catalog number		Contains sufficient for <n> tests
	Consult Instructions for Use		Version of Instructions for Use
	Internet URL address to access the electronic instructions for use		Revision
	*In vitro* diagnostic medical device		Unique Device Identifier
	Prescription device (US only)		CE Marking
	CE Marking with Notified Body		Keep away from sunlight
	Temperature limit		Lower limit of temperature
	Upper limit of temperature		Do not freeze
	Do not re-use		This way up
	Recycle		Caution
	Biological risks		Document face up[a]
	Common Units		International System of Units
YYYY-MM-DD	Date format (year-month-day)	**YYYY-MM**	Date format (year-month)
	Handheld barcode scanner		Mixing of substances

Symbol	Symbol Title	Symbol	Symbol Title
	Target		Interval
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	MATERIAL	Material
MATERIAL ID	Unique material identification number	CONTROL NAME	Name of control
CONTROL TYPE	Type of control	CAL LOT VAL	Calibrator lot value
CONTROL LOT VAL	Quality control lot value		

[a] Indicates Assay-eNote

Legal Information

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