510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K220949

B Applicant

Abbott Laboratories

C Proprietary and Established Names

Architect CMV IgG

D Regulatory Information

1. Regulation section: 21 CFR 866.3175
2. Classification: Class II
3. Product code(s): LFZ – Cytomegalovirus serological reagents JJE – Discrete photometric chemistry analyzer for clinical use
4. Panel: Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain 510k clearance for the Abbott ARCHITECT CMV IgG Reagent Kit, ARCHITECT CMV IgG Calibrators and ARCHITECT CMV IgG Controls to be used on the ARCHITECT i 2000SR analyzer.

B Measurand:

CMV IgG

C Type of Test:

chemiluminescent microparticle immunoassay

III Intended Use:

A Intended Use(s):

The ARCHITECT CMV IgG assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgG antibodies to cytomegalovirus in human serum, serum separator, and plasma tubes (lithium heparin, lithium heparin separator, and tripotassium EDTA) on the ARCHITECT i System.

The ARCHITECT CMV IgG assay is to be used as an aid in the diagnosis of infection with cytomegalovirus and as an aid in the determination of serological status to cytomegalovirus in individuals including women of child-bearing age.

The ARCHITECT CMV IgG assay has not been cleared for use in screening blood, plasma, or tissue donors.

ARCHITECT CMV IgG Calibrators
The ARCHITECT CMV IgG Calibrators are for the calibration of the ARCHITECT i System when used for the qualitative detection of IgG antibodies to cytomegalovirus in human serum and plasma.

ARCHITECT CMV IgG Controls
The ARCHITECT CMV IgG Controls are for the estimation of test precision and the detection of systematic analytical deviations of the ARCHITECT i System when used for the qualitative detection of IgG antibodies to cytomegalovirus in human serum and plasma.

B Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

C Special Instrument Requirements:

ARCHITECT i System

IV Device/System Characteristics:

A Device Description:

The ARCHITECT i System is regulated under 21 CFR 862.2160 as Class I devices exempt from premarket notification. The ARCHITECT i System is a fully automated immunoassay system that allows random and continuous access as well as priority and automated retest processing. The ARCHITECT CMV IgG Reagents, Calibrator, and Controls are designed to be used on the ARCHITECT i2000SR instrument.

The ARCHITECT CMV IgG reagent kit contains:

- **Microparticles:** (1 bottle x 6.6 mL per 100-test / 1 bottle x 27.0 mL per 500-test) CMV virus lysate (strain AD169) coated microparticles in TRIS buffered saline with protein (bovine). Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and antimicrobial agents.

- **Conjugate:** (1 bottle x 5.9 mL per 100-test / 1 bottle x 26.3 mL per 500-test). Murine anti-human IgG acridinium-labeled conjugate in MES buffer with protein (bovine). Minimum concentration: 44 ng/mL. Preservatives: sodium azide and antimicrobial agents.
- **Assay Diluent:** (1 bottle x 10.0 mL per 100-test / 1 bottle x 50.9 mL per 500-test). Calf serum and MES buffer with protein (bovine). Preservatives: ProClin 300 and ProClin 950.

Calibrators

The ARCHITECT CMV IgG Calibrators:

- Calibrator A - 1 Bottle (4.0 mL): contains recalcified human plasma with protein (ovine) stabilizer. Preservative: sodium azide.
- Calibrators B through F - 5 bottles (4.0 mL each): contain recalcified human plasma and are reactive for IgG antibodies to cytomegalovirus (anti-CMV IgG). Preservative: sodium azide.

Calibrators cover the calibration range of the assay (0.0 to 250.0 AU/mL). The calibrators are at the following anti-CMV IgG concentrations:

Table 1. Calibrator concentration

Calibrator	Target Anti-CMV IgG Concentration (AU/mL)
A	0.0
B	10.0
C	50.0
D	75.0
E	125.0
F	250.0

The Calibrators B through F are referenced to internal reference standards at each concentration level.

Controls

The ARCHITECT CMV IgG Controls:

- Negative Control - 1 Bottle (8.0 mL): contains recalcified human plasma with protein (ovine) stabilizer. Preservative: sodium azide.
- Positive Control 1 - 1 Bottle (8.0 mL): contains recalcified human plasma and is reactive for IgG antibodies to cytomegalovirus (anti-CMV IgG). Preservative: sodium azide.

The controls are at the following proposed target anti-CMV IgG concentrations and ranges:

Table 2. Control Concentrations and Ranges

Control	Target Anti-CMV IgG Concentration (AU/mL)	Control Range (AU/mL)
Negative Control (Control −)	N/A	≤ 3.1
Positive Control 1 (Control +1)	30.0	15.0 to 45.0

The Positive Control 1 is referenced to an internal reference standard.

Interpretation of Results

Table 3. Results and Interpretation

Result AU/mL	Interpretation
< 6.0	Nonreactive for anti-CMV IgG. Individuals with such results are presumed to be not infected with CMV and susceptible to primary infection.
6.0 to < 15.0	Grayzone/Equivocal It is recommended to confirm results of specimens with concentration values between 6.0 and < 15.0 AU/mL using a CMV IgM test or draw a second sample, if possible, within a reasonable period of time (e.g., 2 weeks) to repeat ARCHITECT CMV IgG testing.
≥ 15.0	Reactive for anti-CMV IgG. Reactivity for anti-CMV IgG indicates past or acute infection. Such individuals are potentially at risk of transmitting CMV infection but are not necessarily currently contagious.

B Principle of Operation:

This assay is an automated, two-step immunoassay for the qualitative detection of IgG antibodies to CMV (anti-CMV IgG) in human serum and plasma using chemiluminescent microparticle immunoassay (CMIA) technology.

Pre-diluted sample, CMV virus lysate (strain AD169) coated paramagnetic microparticles, and assay diluent are combined and incubated. The anti-CMV IgG present in the sample binds to the CMV virus lysate (strain AD169) coated microparticles. The mixture is washed. Murine anti-human IgG acridinium-labeled conjugate is added to create a reaction mixture and incubated. Following a wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as a relative light unit (RLU).

The presence or absence of anti-CMV IgG in the sample is determined by comparing the chemiluminescent RLU in the reaction to the cutoff RLU determined from an active calibration.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ADVIA Centaur CMV IgG Assay

B Predicate 510(k) Number(s):

K181213

C Comparison with Predicate(s):

Table 4. Comparison to Predicate – Similarities and Differences

Device & Predicate Device(s):		

	Device: ARCHITECT CMV IgG (K220949)	Predicate Device: ADVIA Centaur CMV IgG Assay (K181213)
General Device Characteristic Similarities		
Intended Use	The ARCHITECT CMV IgG assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgG antibodies to cytomegalovirus in human serum, serum separator, and plasma tubes (lithium heparin, lithium heparin separator, and tripotassium EDTA) on the ARCHITECT i System. The ARCHITECT CMV IgG assay is to be used as an aid in the diagnosis of infection with cytomegalovirus and as an aid in the determination of serological status to cytomegalovirus in individuals including women of child-bearing age. The ARCHITECT CMV IgG assay has not been cleared for use in screening blood, plasma, or tissue donors.	The ADVIA Centaur CMV IgG (CMV IgG) assay is for *in vitro* diagnostic use in the qualitative detection of IgG antibodies to cytomegalovirus (CMV) in human pediatric and adult serum and plasma (dipotassium EDTA, lithium heparin) using the ADVIA Centaur CP system. This assay is used to determine CMV IgG serological status and as an aid in the diagnosis of CMV infection in individuals for whom a CMV IgG test was ordered, including pregnant women. The ADVIA Centaur CMV IgG assay is not intended for blood and tissue donor screening.
Controls	Same	2 (Negative and Positive)
Methodology	Same	Chemiluminometric Technology
Type of Specimen	Same	Serum and Plasma
General Device Characteristic Differences		
Antigen Used	CMV Virus lysate (strain AD169)	Heterogeneous mixture of CMV viral lysate antigens
Interpretation of Results	Nonreactive: < 6.0 AU/mL Grayzone/Equivocal: 6.0 to <15.0 AU/mL Reactive: ≥ 15.0 AU/mL	Negative: < 1.00 Index Reactive: ≥ 1.00 Index
Components	Microparticles – CMV virus lysate (strain AD169) coated microparticles in TRIS buffered saline with protein (bovine). Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and antimicrobial agents. Conjugate – Murine anti-human IgG acridinium-labeled conjugate in MES buffer with protein (bovine). Minimum concentration: 44 ng/mL. Preservatives: sodium azide and antimicrobial agents. Assay Diluent – Calf serum and MES buffer with protein (bovine).	Solid Phase Reagent – Streptavidin-coated paramagnetic microparticles preformed with biotinylated CMV viral lysate antigens (~0.5 mg/mL) in buffer with surfactants, sodium caseinate, and sodium azide (< 0.1%) Lite Reagent - Mouse monoclonal anti-human IgG antibody labeled with acridinium ester (~0.06 µg/mL) in buffer with surfactant, bovine serum albumin (BSA), and sodium azide (< 0.1%)

	Preservatives: ProClin 300 and ProClin 950.	Diluent – Potassium thiocyanate (~0.55 M), surfactant, sodium caseinate, BSA, and preservatives
Calibrators	6 Calibrators	2 Calibrators
Calibration Storage	Maximum of 30 days	14 days

VI Standards/Guidance Documents Referenced:

- CLSI. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. CLSI Document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
- CLSI. *Interference Testing in Clinical Chemistry*. 3rd ed. CLSI Guideline EP07. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
- CLSI. *User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline—Second Edition.* CLSI Document EP12-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
- CLSI. *Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline*. CLSI Document EP25-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.
- CLSI. *Supplemental Tables for Interference Testing in Clinical Chemistry*. 1st ed. CLSI supplement EP37. Wayne, PA: Clinical and Laboratory Standards Institute; 2018

Guidance Title

Format for Traditional and Abbreviated 510(k)s - Guidance for Industry and FDA Staff issued on September 13, 2019.

eCopy Program for Medical Device Submissions: Guidance for Industry and Food and Drug Administration Staff, issued on April 27, 2020.

Guidance for Industry and FDA Staff – Replacement Reagent and Instrument Family Policy issued on December 19, 2017.

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices issued on May 11, 2005.

Design Considerations and Pre-Market Submission Recommendations for Interoperable Medical Devices, issued September 6, 2017.

General Principles of Software Validation; Final Guidance for Industry and FDA Staff Document, issued on January 11, 2002.

Content of Premarket Submissions for Management of Cybersecurity in Medical Devices Guidance for Industry and Food and Drug Administration Staff; issued on October 18, 2018.

Guidance for Industry: Cybersecurity for Networked Medical Devices Containing Off-the-Shelf (OTS) Software; issued on January 14, 2005.

Postmarket Management of Cybersecurity in Medical Devices Guidance for Industry and Food and Drug Administration Staff; issued on December 28, 2016.

Guidance for Industry, FDA Reviewers Compliance on Off-the-Shelf Software Use in Medical Devices, September 27, 2019.

Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics issued on September 24, 2018.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision:

The purpose of this study was to evaluate the precision performance of the ARCHITECT CMV IgG assay. In addition, this study evaluated the acceptability of a calibration generated using the ARCHITECT CMV IgG assay and stored on the ARCHITECT i2000SR System for a minimum of 31 days. Precision was performed based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP05-A3. The following samples were tested, Table 4:

Table 5. Precision Panel Members and Concentrations

Sample	Sample Matrix#	Mean Value (AU/mL)
Negative Control	Sheep Serum with Recalcified Plasma	0.0 AU/mL
Positive Control 1	Recalcified Plasma	27.9 AU/mL
Panel 1 (Nonreactive)	Recalcified Plasma	0.3 AU/mL
Panel 2 (High Nonreactive)	Recalcified Plasma	3.3 AU/mL
Panel 3 (Grayzone/Equivocal)	Recalcified Plasma	7.0 AU/mL
Panel 4 (Low Reactive)	Recalcified Plasma	18.1 AU/mL
Panel 5 (Moderate Reactive)	Recalcified Plasma	38.2 AU/mL
Panel 6 (High Reactive)	Recalcified Plasma	193.9 AU/mL

Testing was performed using 1 instrument, 3 Reagent lots, 3 Calibrator lots, and 3 Control lots. Each reagent lot was paired with a different lot of calibrators and controls. A calibration per reagent lot was performed on the instrument by testing the calibrators in replicates of 2. The samples were tested in a minimum of 2 replicates (from separate sample cups), 2 times per day (separated by a minimum of 2 hours), on at least 20 different days, for a minimum of 80 required measurements.
Note: Three replicates per run were tested for each sample and therefore, the total number of measurements in may be up to 120 measurements.

The nonreactive panel was CMV IgG negative human plasma. The high nonreactive panel (Panel 2), grayzone/equivocal panel (Panel 3), low reactive panel (Panel 4), moderate reactive panel (Panel 5), and high reactive panel (Panel 6) were prepared by diluting recalcified CMV IgG

positive human plasma with recalcified CMV IgG negative human plasma.
The precision of the ARCHITECT CMV IgG assay was considered acceptable if the within-laboratory imprecision (repeatability [within-run], between-run, and between-day) was

- ≤ 10 %CV for samples within the range of 15.0 AU/mL to 250.0 AU/mL and
- SD ≤ 0.6 AU/mL for samples less than 6.0 AU/mL and
- SD ≤ 1.5 AU/mL for samples between 6.0 AU/mL and less than 15.0 AU/mL.

Calibration Storage

The calibration generated using the ARCHITECT CMV IgG assay was considered acceptable if the result from each control replicate met the following specifications, when the calibration curve was stored on board the instrument for up to 31 days.
Table 6. Control Value Specifications

Control	Lower Limit (AU/mL)	Upper Limit (AU/mL)
Negative Control	NA	3.10
Positive Control 1	15.0	45.0

Results
The within-laboratory imprecision results, which include within-run, between-run, and between-day, are presented in Table 6 below.
There were no results outside of the control specifications when the calibration was stored on the instrument for 35 calendar days for the calibration curve storage study.

Table 7. Precision of the ARCHITECT CMV IgG assay

Sample	n	Mean (AU/mL)	Within-Run (Repeatability)		Within-Laboratory[a]	
			SD	%CV	SD (Range[b])	%CV (Range[b])
Negative Control	118	0.1	0.04	NA[c]	0.04 (0.00-0.04)	NA[c]
Positive Control 1	118	27.2	0.75	2.8	0.81 (0.71-0.89)	3.0 (2.6-3.0)
Panel 1	117	0.4	0.05	NA[c]	0.05 (0.04-0.05)	NA[c]
Panel 2	118	3.3	0.13	NA[c]	0.14 (0.13-0.15)	NA[c]
Panel 3	120	6.8	0.24	NA[c]	0.25 (0.23-0.25)	NA[c]
Panel 4	119	17.6	0.47	2.7	0.52 (0.50-0.54)	2.9 (2.8-2.9)
Panel 5	120	37.3	0.79	2.1	0.96 (0.96-1.06)	2.6 (2.6-2.8)
Panel 6	118	200.9	4.14	2.1	4.86 (4.05-5.00)	2.4 (2.2-2.5)

[a] Includes within-run (repeatability), between-run, and between-day variability.
[b] Minimum and maximum SD or %CV across all reagent lot/calibrator lot combinations.
[c] Not applicable

2. Linearity:

NA

3. Analytical Specificity/Interference:

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed. and CLSI EP37, 1st ed. Each substance was tested at 3 levels of the analyte (approximately 4.0 AU/mL, 12.0 AU/mL, and 20.0 AU/mL).

Table 8. Endogenous Interferents

Potentially Interfering Substance	**Interferent Level**
Unconjugated Bilirubin	40 mg/dL
Conjugated Bilirubin	40 mg/dL
Hemoglobin	1000 mg/dL
Total Protein	15 g/dL

Interference greater than +0.6 AU/mL for samples < 6.0 AU/mL was observed at the concentration shown below for the following substance.

Interference Observed			
Potentially Interfering Substance	**Interferent Level**	**Analyte Level**	**Interference (95% CI)**
Triglycerides	2475 mg/dL	4.0 AU/mL	0.7 AU/mL (0.6 AU/mL, 0.8 AU/mL)

Potentially Interfering Drugs and Other Substances

A study was performed based on guidance from CLSI EP07, 3rd ed. and CLSI EP37, 1st ed. Each substance was tested at 3 levels of the analyte (approximately 4.0 AU/mL, 12.0 AU/mL, and 20.0 AU/mL).

No significant interference (interference ≤ +0.6 AU/mL for samples < 6.0 AU/mL, ≤ +1.5 AU/mL for samples between 6.0 AU/mL and < 15.0 AU/mL, and ≥ -10% for samples ≥ 15.0 AU/mL) was observed for the following drugs and other substances.

Table 9. Drug and Other Substances Interference

No Significant Interference	
Potentially Interfering Substance	**Interferent Level**
Acetaminophen	250 mg/L

No Significant Interference	
Potentially Interfering Substance	**Interferent Level**
Ascorbic Acid	300 mg/L
Beta Carotene	6 mg/L
Biotin	3510 ng/mL
Cidofovir	240 mg/L
Diphenhydramine	77.4 µg/dL
Folic Acid	100 nmol/L
Foscarnet	4320 mg/L
Gangciclovir	800 mg/L
Ibuprofen	500 mg/L
Valganciclovir	900 mg/L

Potentially Interfering Other Conditions

A total of 187 specimens from individuals with medical conditions unrelated to cytomegalovirus infection and specimens containing potentially interfering substances were evaluated. One specimen tested resulted in a reactive result.

Table 10. Interference due to Unrelated Medical Conditions

Category	**N**	**Number of ARCHITECT CMV IgG Reactive Results**
Anti-dsDNA Antibodies	10	0
Anti-nuclear Antibody (ANA)	8	0
Epstein-Barr Virus (EBV) IgG	10	0
Hepatitis A	9	0
Hepatitis B	10	0
Hepatitis C	10	0
Herpes Simplex Virus Types 1 (IgG)	10	0
Herpes Simplex Virus Types 2 (IgG)	6	0
High titer CMV IgM	1	0
HAMA	10	0
Human Herpesvirus 6 (HHV6)	10	0
Human Immunodeficiency Virus (HIV)	6	0
Hyper IgG	7	0
Influenza vaccine recipient	10	0
Measles (IgG)	10	0
Parvovirus B19 (IgG)	10	0[a]
Rheumatoid Factor	10	0
Rubella (IgG)	10	0
Syphilis	10	0
Toxoplasmosis (IgG)	10	1[b]
Varicella Zoster Virus	10	0

Category	N	Number of ARCHITECT CMV IgG Reactive Results
Total	187	1

[a] One parvovirus B19 (IgG) specimen was equivocal with the ARCHITECT CMV IgG assay and positive with the comparator assay.
[b] One toxoplasmosis (IgG) specimen was reactive with the ARCHITECT CMV IgG assay and positive with the comparator assay.

4. Assay Reportable Range:

This qualitative test has an assay reportable range of 0.0 to 250.0 AU/mL

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Table 11. Reagent Storage

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	2 to 8°C	Until expiration date	Store in upright position.
Onboard	System Temperature	30 days	
Opened	2 to 8°C	Until expiration date	Store in upright position. 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.

Table 12. Specimen Storage

Specimen Type	Temperature	Maximum Storage Time	Special Instructions
Serum/Plasma	Room temperature (15 to 30°C)	3 days	Specimens may be stored on or off the clot, red blood cells, or separator gel.
	2 to 8°C	7 days	Specimens may be stored on or off the clot, red blood cells, or separator gel.
	-20°C or colder	28 days	Remove serum or plasma from the clot, red blood cells, or separator gel.

Expected Values

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

It is recommended that each laboratory determine its own reference range based upon its particular locale and population characteristics.

Of the 989 specimens included in the ARCHITECT CMV IgG clinical study, 791 were from the intended use population in the US. Of the 791 specimens, 591 (74.7%) were routine order (325 female and 266 male, 0 to 91 years old) and 200 (25.3%) were pregnant females (19 to 45 years old). The mean age across the 791 subjects was 40 years.

The ARCHITECT CMV IgG assay was reactive in 508 (64.2%) of the collected specimens in the intended use population in the US (n = 791). Testing of the specimens was performed at 3 clinical testing sites located in Indianapolis Indiana, Lewisville Texas, and Palo Alto California.

The distribution of ARCHITECT CMV IgG reactive, grayzone/equivocal, and nonreactive results by age and sex is summarized in Table 11.

Table 13. Expected Values

		ARCHITECT CMV IgG Result			
Age Range (Years)	**Sex**	**Number of Reactive (%)**	**Number of Grayzone/Equivocal (%)**	**Number of Nonreactive (%)**	**Total**
0 to 12	Female	4 (33.3)	1 (8.3)	7 (58.3)	12
	Male	7 (38.9)	0 (0.0)	11 (61.1)	18
13 to 21	Female	16 (47.1)	0 (0.0)	18 (52.9)	34
	Male	12 (60.0)	1 (5.0)	7 (35.0)	20
22 to 29	Female	90 (65.2)	0 (0.0)	48 (34.8)	138
	Male	17 (63.0)	0 (0.0)	10 (37.0)	27
30 to 39	Female	85 (50.0)	3 (1.8)	82 (48.2)	170
	Male	21 (56.8)	0 (0.0)	16 (43.2)	37
40 to 49	Female	38 (82.6)	0 (0.0)	8 (17.4)	46
	Male	25 (59.5)	2 (4.8)	15 (35.7)	42
50 to 59	Female	44 (81.5)	1 (1.9)	9 (16.7)	54
	Male	29 (72.5)	1 (2.5)	10 (25.0)	40
60 to 64	Female	16 (88.9)	0 (0.0)	2 (11.1)	18
	Male	24 (80.0)	0 (0.0)	6 (20.0)	30
65 to 100	Female	40 (75.5)	1 (1.9)	12 (22.6)	53
	Male	40 (76.9)	0 (0.0)	12 (23.1)	52
Total		508 (64.2)	10 (1.3)	273 (34.5)	791

6. Detection Limit:

   NA

7. Assay Cut-Off:

   Data obtained from 530 specimens used in the OUS ARCHITECT CMV IgG verification study was used to confirm that the cutoff from the original Abbott AxSYM CMV IgG would maintain assay sensitivity in the ARCHITECT CMV IgG assay. Each sample was tested using all 3 reagent lots, on both the OUS ARCHITECT CMV IgG assay and the Abbott AxSYM CMV IgG assay (1590 samples total). AxSYM was utilized as truth. It was determined that an implementation of a lower decision limit of 6 AU/mL with an upper

decision limit of 15 AU/mL was necessary based on this internal data for the OUS ARCHITECT CMV IgG assay. The cutoff was validated in the clinical studies performed in the US to support the substantial equivalence determination of the ARCHITECT CMV IgG assay to the predicate device.

Nonreactive: < 6.0 AU/mL
Grayzone/Equivocal: 6.0 to <15.0 AU/mL
Reactive: ≥ 15.0 AU/mL

B Comparison Studies:

1. Method Comparison with Predicate Device:

A clinical study (method comparison) was performed in the US based on guidance from CLSI EP12-A2, 2nd ed. to evaluate the percent agreement between the ARCHITECT CMV IgG investigational assay and a current, FDA-cleared, commercially available anti-CMV IgG assay with routine order specimens collected in the US (n = 591) and outside of the US (n= 198) and specimens collected from pregnant females in the US (n = 200).

Further evaluation of 4 specimens (3 from routine order and 1 from pregnant females) with an equivocal/grayzone result by comparator assay was performed with 2 additional current, FDA-cleared, commercially available anti-CMV IgG assays.

Clinical Testing Sites

There were three testing sites in California, Indiana, and Texas. Testing with the ARCHITECT CMV IgG assay was performed using 3 ARCHITECT i2000SR instruments (one at each external clinical testing site). Three lots of ARCHITECT CMV IgG Reagents, 2 lots of ARCHITECT CMV IgG Calibrators, and 1 lot of ARCHITECT CMV IgG Controls were used at each of the 3 external clinical testing sites. Comparator testing using the FDA cleared assay was performed at Site 1 only.

Results

Results were interpreted per the package insert for each assay and are shown in the following table:

Table 14. Results Method Comparison Study

Specimen Category	ARCHITECT CMV IgG Result	Comparator Result			Positive % Agreement (95% CI)[a]	Negative % Agreement (95% CI)[a]
		Positive	Equivocal	Negative		
Routine Order	Reactive	514	0	0	97.7 (514/526) (96.1, 98.7)	99.2 (261/263) (97.3, 99.8)
	Equivocal	7	0	2		
	Nonreactive	2	3[c]	261		
Pregnant Females	Reactive	98[b]	0	0	99.0 (98/99) (94.5, 99.8)	100.0 (102/102) (96.4, 100.0)
	Equivocal	1	1[d]	0		
	Nonreactive	0	0	102		

[a] The 95% confidence interval (CI) for negative percent agreement and positive percent agreement were estimated using the Wilson Score method.

[b] Two routine order specimens were from pregnant females and therefore, were also included in the pregnant female category.
[c] Of the 3 specimens that were nonreactive by ARCHITECT CMV IgG and equivocal/grayzone by comparator assay, 2 were negative and 1 was equivocal/grayzone by consensus testing. One specimen that was concordant equivocal/grayzone by ARCHITECT CMV IgG and comparator assay was negative by consensus testing.
[d] One specimen from pregnant females that was concordant grayzone/equivocal by ARCHITECT CMV IgG and comparator assay was negative based on the consensus result from the comparator assay and 2 additional current, FDA-cleared, commercially available anti-CMV IgG assays.

One Centers for Disease Conctrol and Prevention (CDC) CMV IgG human serum panel, comprised of 80 samples that are either CMV IgG negative or CMV IgG positive, was obtained from the Centers for Disease Control and Prevention (CDC) and tested using the ARCHITECT CMV IgG assay. The results were submitted to the CDC. The CDC added their result interpretation for each sample.
The percent (%) agreement values of the ARCHITECT CMV IgG assay relative to the CDC results were calculated. The positive % agreement and corresponding two-sided 95% CI was 100% (91.59%, 100%). The negative % agreement and corresponding two-sided 95% CI was 92.11% (78.62%, 98.34%). The overall % agreement and corresponding two-sided 95% CI was 96.25% (89.43%, 99.22%).

The results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. This does not imply endorsement of the assay by the CDC.

3. Matrix Comparison:

Samples were obtained from a specimen vendor from a minimum of 40 donors (at least 20 CMV IgG negative and 20 CMV IgG positive donors) in the control tube type (serum, plastic) and in the following evaluation tube types:

Table 15. Tube Types for Matrix Comparison Study

Evaluation Tube Types
Serum separator, plastic (SSP)
Lithium heparin (LIH)
Lithium heparin plasma separator (PST)
Tripotassium EDTA (TED)

For each donor set, the mean concentration was calculated for the control tube type.

For each donor set, the difference between the evaluation tube first replicate concentration and the control tube mean concentration was calculated using the following equation:

$$\text{Difference} = \text{Evaluation Tube First Replicate} - \text{Control Tube Mean}$$

For each donor set, the percent (%) difference was calculated using the following equation:

$$\%\ \text{Difference} = \frac{\text{Difference}}{\text{Control Tube Mean}} \times 100$$

Control Tube Mean

The mean of the differences/% differences across donors and the two-sided 95% CI across donors are summarized by analyte level and tube type

The tube types under evaluation were considered acceptable if, when compared to the control tube type, the mean difference in measured CMV IgG concentration were

- ≤ + 0.6 AU/mL for samples with concentrations less than 6.0 AU/mL,
- ≤ + 1.5 AU/mL for samples with concentrations between 6.0 AU/mL and less than 15.0 AU/mL, and
- ≥ -10% for samples with concentrations greater than or equal to 15.0 AU/mL.

All tube types tested met the evaluation criteria and are suitable for use with the ARCHITECT CMV IgG assay.

C Clinical Studies:

1. Clinical Sensitivity:

   NA

2. Clinical Specificity:

   NA

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Reproducibility: A system reproducibility study was conducted to demonstrate precision performance of the ARCHITECT CMV IgG assay on the ARCHITECT i2000SR System across multiple sites and lots of reagents, calibrators, and controls.

Procedure

The study was performed based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP05-A3. The testing was performed using 3 lots of ARCHITECT CMV IgG Reagents, 2 lots of ARCHITECT CMV IgG Calibrators, and 1 lot of ARCHITECT CMV IgG Controls at each of the 3 external clinical testing sites. The reagent, calibrator, and control lots were paired as shown in the table below:

Table 16. Reproducibility of the ARCHITECT CMV IgG Assay

Sample	n	Mean (AU/mL)	Repeatability		Within-Laboratory[a]		Reproducibility[b]	
			SD	%CV	SD	%CV	SD	%CV
Negative Control	359	0.0	0.02	NA[c]	0.03	NA[c]	0.05	NA[c]
Positive Control 1	360	27.3	0.80	2.9	1.00	3.7	1.24	4.5

Sample	n	Mean (AU/mL)	Repeatability		Within-Laboratory[a]		Reproducibility[b]	
			SD	%CV	SD	%CV	SD	%CV
Panel 1	360	0.3	0.04	NA[c]	0.05	NA[c]	0.12	NA[c]
Panel 2	360	3.1	0.13	NA[c]	0.16	NA[c]	0.30	NA[c]
Panel 3	360	6.5	0.23	NA[c]	0.27	NA[c]	0.49	NA[c]
Panel 4	359	17.2	0.58	3.4	0.69	4.0	0.84	4.8
Panel 5	360	36.7	1.11	3.0	1.40	3.8	1.55	4.2
Panel 6	360	188.9	4.15	2.2	5.62	3.0	7.45	3.9

[a]Includes repeatability, between-run, and between-day variability.
[b]Includes repeatability, between-run, between-day, between-site, between-lot, and the site-lot interaction variability.
[c] Not applicable

D Clinical Cut-Off:

Not applicable

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.