Alinity m

CMV AMP Kit

en
CMV
RE 09N46-095
53-608277/R1

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RE 09N46-095
53-608277/R1

ONLY

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Instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from these instructions.

NAME

Alinity m CMV AMP Kit

INTENDED USE

The Alinity m CMV assay is an in vitro polymerase chain reaction (PCR) assay for use with the automated Alinity m System to quantitate cytomegalovirus (CMV) DNA in human EDTA plasma.

The Alinity m CMV assay is intended for use as an aid in the management of Hematopoietic Stem Cell Transplant and Solid Organ Transplant patients who are undergoing anti-cytomegalovirus therapy. The Alinity m CMV assay can be used to assess virological response to anti-cytomegalovirus therapy.

The results from the Alinity m CMV test must be interpreted within the context of all relevant clinical and laboratory findings. The Alinity m CMV test is not intended as a screening test for the presence of CMV DNA in blood or blood products.

SUMMARY AND EXPLANATION OF THE TEST

Found worldwide, human cytomegalovirus (CMV) is a double-stranded DNA virus of over 230 kb and belongs to the ß-herpesvirus subgroup of the human herpesvirus family.[1-4] The seroprevalence of CMV in the general world population is high with estimated global seroprevalence of approximately 80%.[5,6] Infections of CMV usually manifest as mild or subclinical diseases in immunocompetent individuals and establishes life-long latency within the individual without causing serious health problems.[3,4] However, primary CMV infection or reactivation of latent CMV in immunocompromised individuals, such as solid organ or hematopoietic stem cell transplant patients, advanced AIDS patients, and congenitally infected newborns, can be severe and life-threatening.[4,7-9]

CMV infection in hematopoietic stem cell and solid organ transplant recipients remains a significant cause of morbidity and mortality.[8,10-13] Infection occurs as a result of transmission from the transplanted organ or reactivation of latent infection.[7] CMV is a direct cause of tissue-invasive infections, and an indirect cause of acute and chronic graft rejection or secondary bacterial, fungal, and viral infections. Ultimately CMV infection can reduce allograft success and patient survival.[12-14]

Quantitation of CMV DNA in conjunction with clinical presentation and other laboratory markers provides clinicians with a means to assess CMV DNA levels for patient management.[13-17] Alinity m CMV is intended for use in conjunction with clinical presentation and other laboratory markers to provide clinicians with a means to assess CMV DNA levels in the management of CMV in solid organ transplant patients, hematopoietic stem cell transplant patients, and patients receiving anti-CMV therapy. This assay is not intended to be used in screening blood, blood products, tissue or organ donors for CMV.

The Alinity m CMV amplification reagents include primers and probes that amplify and detect dual targets in the CMV genome. Amplification and detection of the two CMV targets ensures sensitive detection of the viral genome even at low levels. In addition to the CMV primers and probes, the assay utilizes an internal control (IC) primer/probe set for amplification and detection of the IC target sequence, which is not related to CMV. The IC probe is labeled with a different fluorophore than the CMV probes. This allows for simultaneous detection and discrimination of both the CMV and IC amplified products within the same reaction vessel.

The assay tests human EDTA plasma specimens. The assay is standardized to the 1st World Health Organization (WHO) International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques (NIBSC code: 09/162).[17] Results are reported in International Units per milliliter (IU/mL) or Log IU/mL. The assay can quantitate CMV over the range 30 IU/mL (1.48 Log IU/mL) to 100,000,000 IU/mL (8.00 Log IU/mL).

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The Alinity m CMV assay requires 3 separate assay specific kits:

- Alinity m CMV AMP Kit (List No. 09N46-095) consisting of 2 types of multi-well assay trays. The amplification trays (AMP TRAY 1) contain lyophilized, unit-dose PCR amplification/detection reagents and lyophilized, unit-dose IC with proteinase K in separate wells, and the activation trays (ACT TRAY 2) contain liquid unit-dose activation reagent. The intended storage condition for the Alinity m CMV AMP Kit is 2°C to 8°C.
- Alinity m CMV CTRL Kit (List No. 09N46-085) consisting of negative controls, low-positive controls and high-positive controls, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m CMV CTRL Kit is −25°C to −15°C.
- Alinity m CMV CAL Kit (List No. 09N46-075) consisting of 2 calibrator levels, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m CMV CAL Kit is −25°C to −15°C.

The Alinity m CMV assay utilizes real-time polymerase chain reaction (PCR) to amplify and detect CMV genomic DNA sequences that have been extracted from human EDTA plasma specimens. The steps of the Alinity m CMV assay consist of sample preparation, PCR assembly, amplification/detection, and result calculation and reporting. All steps of the Alinity m CMV assay procedure are executed automatically by the Alinity m System. Manual dilutions may be performed for low-volume specimens to meet the minimum volume requirement.

The Alinity m System is designed to be a random access analyzer that can perform the Alinity m CMV assay in parallel with other Alinity m assays on the same instrument.

CMV DNA from human plasma is extracted using the Alinity m Sample Prep Kit 2, Proteinase K, Alinity m Lysis Solution, and Alinity m Diluent Solution. The Alinity m System employs magnetic microparticle technology to facilitate nucleic acid capture, wash, and elution. The resulting purified DNA is then combined with liquid unit-dose Alinity m CMV activation reagent and lyophilized unit-dose Alinity m CMV amplification/detection reagents and transferred into a reaction vessel. Alinity m Vapor Barrier Solution is then added to the reaction vessel which is then transferred to an amplification/detection unit for PCR amplification, and real-time fluorescence detection of CMV.

At the beginning of the Alinity m CMV sample preparation process, a lyophilized unit-dose IC on the AMP Tray is rehydrated by the Alinity m System and delivered into each sample preparation reaction. The IC is then processed through the entire sample preparation and real-time PCR procedure along with the specimens, calibrators, and controls to demonstrate proper sample processing and validity.

The Alinity m CMV amplification/detection reagents consist of enzymes, primers, probes, and activation reagents that enable polymerization, and detection.

A CMV calibration curve is required for determination of CMV DNA concentration. Two levels of calibrators are processed through sample preparation and PCR to generate the calibration curve. The concentration of CMV DNA in specimens and controls is then calculated from the stored calibration curve.

Assay controls are tested at or above an established minimum frequency to help ensure that instrument and reagent performance remains satisfactory. During each control event, a negative control, a low positive control, and a high positive control are processed through sample preparation and PCR procedures that are identical to those used for specimens.

The possibility of nucleic acid contamination on the Alinity m System is minimized because:

- Aerosol barrier pipette tips are used for all pipetting. The pipette tips are discarded after use.
- PCR amplification and detection is carried out automatically in a sealed reaction vessel.
- Disposal of the reaction vessel is performed automatically by the Alinity m System.

For additional information on system and assay technology, refer to the Alinity m System Operations Manual, Section 3.

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REAGENTS

Kit Contents

Alinity m CMV AMP Kit List No. 09N46-095

The Alinity m CMV AMP Kit is comprised of 2 types of multi-well trays: Alinity m CMV AMP TRAY 1 and Alinity m CMV ACT TRAY 2.
Each Alinity m CMV AMP TRAY 1 (individually packed in a foil pouch with a desiccant bag) contains 48 unit-dose lyophilized amplification reagent wells and 48 unit-dose lyophilized IC/ proteinase K (PK) wells. One well of each is used per test.

- Amplification reagent wells consist of synthetic oligonucleotides, DNA Polymerase, excipient, and dNTPs in a buffered solution with a reference dye.
- Internal Control (IC) wells consist of noninfectious linearized DNA with IC sequences, PK, and excipient in buffer solution with carrier DNA.

Each Alinity m CMV ACT TRAY 2 (individually packed in a foil pouch without a desiccant bag) contains 48 unit-dose liquid activation reagent wells. One reagent well is used per test.

- Activation reagent wells consist of magnesium chloride, potassium chloride and tetramethylammonium chloride.
  Preservative: 0.15% ProClin 950.

	Quantity
Σ	192 tests
Alinity m CMV AMP TRAY 1	4 trays / 48 tests each
Alinity m CMV ACT TRAY 2	4 trays / 48 tests each

WARNINGS AND PRECAUTIONS

IV

- **For In Vitro Diagnostic Use**

Safety Precautions

Human specimens should be handled as if infectious using safe laboratory procedures, such as those outlined in Biosafety in Microbiological and Biomedical Laboratories,[18] OSHA Standard on Bloodborne Pathogens,[19] CLSI Document M29-A4,[20] and other appropriate biosafety practices.[21] Therefore, all human sourced materials should be considered infectious.

These precautions include, but are not limited to, the following:

- Wear gloves when handling specimens or reagents.
- Do not pipette by mouth.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in areas where these materials are handled.
- Clean and disinfect spills of specimens by including the use of a tuberculocidal disinfectant such as 1.0% sodium hypochlorite or other suitable disinfectant.[18]

Decontaminate and dispose of all potentially infectious materials in accordance with local, state and federal regulations.[21]

The following warnings and precautions apply to:
Alinity m CMV AMP TRAY 1.

DANGER	Contains Tris hydroxymethyl aminomethane and proteinase K
H315	Causes skin irritation.
H317	May cause an allergic skin reaction.
H319	Causes serious eye irritation.
H334	May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H335	May cause respiratory irritation.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P264	Wash hands thoroughly after handling.
P280	Wear protective gloves / protective clothing / eye protection.
P284	In case of inadequate ventilation wear respiratory protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P304+P340	IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P312	Call a POISON CENTER / doctor if you feel unwell.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P337+P313	If eye irritation persists: Get medical advice/ attention.
P342+P311	If experiencing respiratory symptoms: Call a POISON CENTER / doctor.
P362+P364	Take off contaminated clothing and wash it before reuse.
Storage	
P405	Store locked up.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to:
Alinity m CMV ACT TRAY 2.

DANGER	Contains Tetramethylammonium chloride, and 2-Methyl-4-isothiazolin-3-one
H302	Harmful if swallowed.
H316	Causes mild skin irritation.[a]
H317	May cause an allergic skin reaction.
H370	Causes damage to organs.
H412	Harmful to aquatic life with long lasting effects.
Prevention	
P260	Do not breathe mist / vapors / spray.
P264	Wash hands thoroughly after handling.
P272	Contaminated work clothing should not be allowed out of the workplace.
P273	Avoid release to the environment.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P301+P312	IF SWALLOWED: Call a POISON CENTER / doctor if you feel unwell.
P302+P352	IF ON SKIN: Wash with plenty of water.
P308+P311	IF exposed or concerned: Call a POISON CENTER / doctor.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

[a] Not applicable where regulation EC 1272/2008 (CLP) or OSHA Hazard Communication 29 CFR 1910.1200 (HCS) 2012 have been implemented.

Important information regarding the safe handling, transport, and disposal of this product is contained in the Safety Data Sheet.

Safety Data Sheets are available from your Abbott Representative.

For a detailed discussion of safety precautions during system operation, refer to the Alinity m System Operations Manual, Section 7 and Section 8.

Reagent Shipment

	Shipment Condition
Alinity m CMV AMP Kit	On dry ice

Reagent Storage

In order to minimize damage to foil pouches, it is recommended that the Alinity m CMV AMP TRAY 1 (AMP TRAY 1) and Alinity m CMV ACT TRAY 2 (ACT TRAY 2) are stored in the original kit packaging. Open the foil pouch for the reagent trays just prior to loading onto the instrument. Onboard storage time begins when reagents are loaded on the Alinity m System.

	Storage Temperature	Maximum Storage Time
Unopened	2°C to 8°C	Until expiration date
Onboard	System Temperature	30 days (not to exceed expiration date)

Reagent Handling

- Do not use reagents that have been damaged.
- Minimize contact with the surface of reagent trays during handling.
- Up to 2 lots of assay trays (AMP TRAY 1 and ACT TRAY 2) can be loaded on each Alinity m Assay Tray Carrier, as long as the AMP TRAY 1 and ACT TRAY 2 from the same AMP kit lot are included together as a set.
- The Alinity m System will track the onboard storage time of AMP TRAY 1 and ACT TRAY 2 while on the instrument. The Alinity m System will not allow the use of AMP TRAY 1 and ACT TRAY 2 if the maximum onboard storage time has been exceeded.
- For a detailed discussion of reagent handling precautions during system operation, refer to the Alinity m System Operations Manual, Section 8.

Indications of Reagent Deterioration

- Deterioration of the reagents may be indicated when a calibration or control error occurs or controls are repeatedly out of the specified ranges.
- Reagents are shipped on dry ice and are stored at 2°C to 8°C upon arrival. If reagents arrive in a condition contrary to this recommendation or are damaged, immediately contact your Abbott Representative.
- For troubleshooting information, refer to the Alinity m System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The Alinity m CMV assay application specification file must be installed on the Alinity m System prior to performing the assay.

For a detailed description of system operating instructions, refer to the Alinity m System Operations Manual, Section 5.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen types listed below can be used with this assay on the Alinity m System. Plasma specimens may be tested for viral load determination. For the Alinity m CMV assay, only use collection tubes as described in the following table for the corresponding specimen type. Alinity m CMV assay performance with other specimen types or collection tubes has not been evaluated.

Specimen Types[a]	Blood Collection Tubes
Plasma	K_2 EDTA K_3 EDTA Plasma Preparation Tube (PPT)[b]

[a] The instrument does not provide the capability to verify specimen types. It is the responsibility of the operator to use the correct specimen types in the assay.

[b] Plasma Preparation Tubes are gel tubes.

Specimen Storage

Specimen	Temperature	Maximum Storage Time	Special Instructions
Whole Blood	2°C to 8°C	5 days	Whole blood may be stored between draw and plasma separation.
	15°C to 30°C	1 day	Whole blood storage plus separated plasma storage at 2°C to 8°C must not exceed a combined total of 120 hours.
Plasma	2°C to 8°C	5 days	Plasma may be stored in primary tubes with or without gel or secondary tubes after separation from blood cells.
	15°C to 30°C	1 day	Whole blood storage plus separated plasma storage at 2°C to 8°C must not exceed a combined total of 120 hours. Plasma may further stay onboard Alinity m System for up to 4 hours prior to processing.
	−70°C or colder	Longer storage	Plasma may be stored frozen in primary gel tubes (PPT) or secondary tubes after separation from blood cells. Plasma from non-gel tubes must be transferred to secondary tubes prior to freezing.[a] Plasma can be subjected to at most 3 freeze-thaw cycles. Defrosted samples may be stored at 2°C to 8°C for up to 6 hours prior to loading on Alinity m System. Plasma may further stay onboard Alinity m System for up to 4 hours prior to processing.

[a] Avoid more than 3 freeze-thaw cycles.

Specimen Shipping

Ship specimens according to the recommended storage temperature and time listed in the **Specimen Storage** section. Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical, diagnostic, or biological specimens.

Preparation for Analysis

Freshly Drawn Whole Blood Specimens:

- Follow the specimen collection tube manufacturer instructions for blood collection and centrifugation. Separate plasma from cells by centrifugation.
- Prior to centrifugation, whole blood may be stored as indicated in the table above.
- After centrifugation, plasma may be stored on the blood cells (in tube with or without gel) or be transferred to a secondary tube prior to being loaded onto the Alinity m System or used for dilution. Refer to the table above for storage times and temperatures.
- If longer storage is required, plasma specimens in primary gel tubes or secondary tubes may be stored frozen at −70°C.

NOTE: Plasma specimens stored on the blood cells cannot be frozen without a gel.

Frozen Plasma Specimens: Primary Gel Tubes

- Thaw specimens at 15°C to 30°C or at 2°C to 8°C. Once thawed, specimens can be stored at 2°C to 8°C for up to 6 hours if not processed immediately.
- Vortex each specimen 3 times for 2 to 3 seconds.
- Centrifuge specimens stored in primary gel tubes at 2000*g* for 5 minutes before loading onto the Alinity m System or before preparing a specimen dilution. If any debris is observed, transfer the supernatant of the specimen into the new tube. Avoid transferring any debris into the new tube.

Frozen Plasma Specimens: Secondary Aliquot Tubes

- Thaw specimens at 15°C to 30°C or at 2°C to 8°C. Once thawed, specimens can be stored at 2°C to 8°C for up to 6 hours if not processed immediately.
- Vortex each specimen 3 times for 2 to 3 seconds. If any debris is observed, transfer the specimen into a new tube. Avoid transferring any debris into the new tube.
- Alternatively, vortex each specimen 3 times for 2 to 3 seconds. If any debris is observed centrifuge specimens at 2000*g* for 5 minutes and transfer the supernatant of the specimen into a new tube. Avoid transferring any debris into the new tube.

All specimen tubes (primary and secondary tubes) must be labeled with specimen ID barcodes or must be identified with a specimen ID and rack and position. Refer to the **Assay Procedure** section of this package insert or the Alinity m System Operations Manual, Section 4, for tube sizes. Avoid touching the inside of the cap when opening tubes.

PROCEDURE

Materials Provided

09N46-095 Alinity m CMV AMP Kit

Materials Required but not Provided

- 09N46-075 Alinity m CMV CAL Kit
- 09N46-085 Alinity m CMV CTRL Kit
- 09N12-001 Alinity m Sample Prep Kit 2
- 09N20-001 Alinity m Lysis Solution
- 09N20-003 Alinity m Diluent Solution
- 09N20-004 Alinity m Vapor Barrier Solution
- 09N50-001 Alinity m Specimen Dilution Kit I[a]
- Alinity m CMV Application Specification File (09N46-05A or higher)
- Vortex mixer
- Centrifuge capable of 2000*g*
- 09N49-001 Alinity m LRV Tube[a]
- Calibrated pipettes capable of delivering 10 to 1000 µL[a]
- Aerosol barrier pipette tips for 10 µL to 1000 µL pipettes[a]
- Plate adapter for 384 well plates (eg, Eppendorf Catalog No. 022638955)
- Centrifuge with swing plate rotor capable of accommodating the plate adapter and capable of ≥ 100*g*

Other Optional Materials

- 09N49-010 Alinity m Transport Tube Pierceable Capped
- 09N49-011 Alinity m Transport Tube
- 09N49-012 Alinity m Pierceable Cap
- 09N49-013 Alinity m Aliquot Tube

[a] These items are used in the **Specimen Dilution Procedure** if dilution is required.

For information on materials required for operation of the instrument, refer to the Alinity m System Operations Manual, Section 1.

For general operating procedures, refer to the Alinity m System Operations Manual, Section 5.

For optimal performance, it is important to perform routine maintenance as described in the Alinity m System Operations Manual, Section 9.

Procedural Precautions

- Read the instructions in this package insert carefully before processing samples.
- Use aerosol barrier pipette tips or disposable pipettes only one time when pipetting specimens. To prevent contamination to the pipette barrel while pipetting, care should be taken to avoid touching the pipette barrel to the inside of the sample tube or container. The use of extended aerosol barrier pipette tips is recommended.
- Work area and instrument platforms must be considered potential sources of contamination.
- Ensure the Alinity m CMV AMP TRAY 1 is tapped prior to loading on the Alinity m System per instructions in the **Assay Procedure** section.
- Ensure the Alinity m CMV ACT TRAY 2 is centrifuged prior to loading on the Alinity m System per instructions in **Assay Procedure** section.
- Monitoring procedures for the presence of amplification product can be found in the Alinity m System Operations Manual, Section 9.
- To reduce the risk of nucleic acid contamination, clean and disinfect spills of specimens by including the use of a tuberculocidal disinfectant such as 1.0% sodium hypochlorite or other suitable disinfectant.
- To prevent contamination, change to new gloves before handling the Alinity m Sample Prep Kit 2, assay trays, system solutions, Integrated Reaction Unit (IRU) sleeves, and pipette tips. Also change to new gloves whenever they are contaminated by a specimen, a calibrator, a control, or a reagent. Always use powder-free gloves.
- The use of the Alinity m CMV CAL Kit and CTRL Kit is integral to the performance of the Alinity m CMV assay. Refer to the **QUALITY CONTROL PROCEDURES** section of this package insert for details. Refer to the Alinity m CMV CAL Kit package insert and/or Alinity m CMV CTRL Kit package insert for preparation and usage.
- The Alinity m CMV calibrator and control reagents are contained in single-use tubes with pierceable caps. Avoid contamination or damage to the caps after removal from their original packaging. Discard tubes after use.

Assay Procedure

Prior to loading on the Alinity m System, hold the AMP TRAY 1 by the edges with the label facing up and tap 3 times on the bench.

Prior to loading on the Alinity m System, the ACT TRAY 2 must be centrifuged as follows:

1. Load the ACT TRAY 2 onto the plate adapter (eg, Eppendorf Catalog No. 022638955).
2. Load the plate adapter (with the ACT TRAY 2) on a swing plate centrifuge capable of accommodating the plate adapter. Spin at 100*g* to 800*g* for 1 to 5 minutes to remove potential bubbles.
3. Immediately following centrifugation, carefully transfer the ACT TRAY 2 to the Alinity m Assay Tray Carriers. Take care to minimize disturbance to the ACT TRAY 2. Load the tray carriers per the Alinity m System Operations Manual, Section 5.
4. If disturbance occurs during the transfer that could potentially introduce bubbles (eg, dropping, bumping, inversion of the ACT TRAY 2), re-centrifuge the ACT TRAY 2.
5. Proceed with the **Reagent and sample inventory management** procedure per the Alinity m System Operations Manual, Section 5.

For a detailed description of how to run an assay, refer to the Alinity m System Operations Manual, Section 5. Prior to testing specimens, check the calibration and control status. If recalibration or control testing is required, refer to the **QUALITY CONTROL PROCEDURES** section. Calibrators and/or controls may be tested separately or with specimens.

From the Create Order screen, select the appropriate assay (CMV). Confirm that the appropriate specimen type is selected (ie, Plasma). The Alinity m System will track the onboard storage time of amplification reagents, calibrators, controls, and specimens while on the instrument. The Alinity m System will not allow the use of amplification reagents, calibrators, controls, or process specimens that have exceeded the allowable onboard storage time.

Specimen tubes need to meet the requirements for minimum and maximum sample volumes and use of caps when loaded on the Alinity m System. Blood collection tubes with separated plasma and specimen aliquot tubes may be placed on the Alinity m Universal Sample Rack (sample rack) onboard the system for up to 4 hours prior to processing.

Tube Types and Volume Requirements

Tube Type[a]	List No.	Minimum Volume Required	Maximum Volume Allowed	Cap Requirement on Instrument
Blood Collection Tube (Primary Tubes)				
Blood collection tubes	NA	10.0 mm[b] above the gel or blood cells for blood collection tubes with inner diameter of 10.0 mm or greater	5.0 mL, 6.0 mL, and 10.0 mL for non-gel tubes with 10.0-10.6 mm, 10.6-13.2 mm, and >13.2 mm inner diameter, respectively. 4.0 mL, 5.0 mL, and 8.5 mL for gel tubes with 10.0-10.6 mm, 10.6-13.2 mm, and > 13.2 mm inner diameter, respectively	Uncapped

Tube Type[a]	List No.	Minimum Volume Required	Maximum Volume Allowed	Cap Requirement on Instrument
Specimen Aliquot Tube (Secondary Tubes)				
Alinity m Aliquot Tube	09N49-013	0.65 mL	3.5 mL	Capped[c] or uncapped
Alinity m Transport Tube	09N49-011	1.0 mL	7.0 mL	Uncapped
		0.65 mL	3.5 mL	Capped[c]
Alinity m Transport Tube Pierceable Capped	09N49-010	1.0 mL	7.0 mL	Uncapped
		0.65 mL	3.5 mL	Capped
Other aliquot tubes	NA	0.9 mL, 1.4 mL, and 1.5 mL for tubes with 10.0–10.6 mm, 10.6–13.2 mm, and > 13.2 mm inner diameter, respectively.	5.0 mL, 6.0 mL, and 10.0 mL for tubes with 10.0-10.6 mm, 10.6-13.2 mm, and >13.2 mm inner diameter, respectively.	Uncapped

[a] Refer to the Alinity m System Operations Manual, Section 4, for sample tube specifications and requirements and Section 5 for sample rack loading instructions.

[b] Represents requirement for minimum column height of plasma above the gel / blood cells in the primary tube. The minimum volume in milliliters can be calculated using the inner diameter (ID in mm) of the tube using formula: Plasma Minimum Volume = 0.00785 x ID^2

[c] Alinity m Pierceable Cap, List No. 09N49-012, is the only type of cap that can be used when loaded on the Alinity m System.

Prior to loading the specimen tubes on to the Alinity m System:

- Ensure individual specimen tubes are labeled correctly with specimen ID barcodes.
- Inspect specimens for bubbles and foam. Specimens should be free of bubbles and foam. If found, remove them with a new sterile pipette tip for each tube to prevent cross-contamination.

Specimen Dilution Procedure (Optional)

Specimens may be diluted manually for testing on the Alinity m System using the Alinity m Specimen Dilution Kit I per the table below.

Low volume plasma specimens with 220 µL to 649 µL volume available for Alinity m CMV testing can be diluted 1: 2.5.

Specimen Dilution Scenario	Available Plasma Volume	Dilution Factor
Low Volume	220 µL to 649 µL	1:2.5

Refer to the **Specimen Dilution Procedure Scheme** section.

The operator must select the dilution factor in the Specimen tab on the Create Order screen of the Alinity m System software. The system will use the selected dilution factor to automatically calculate and report the result of the neat specimen.

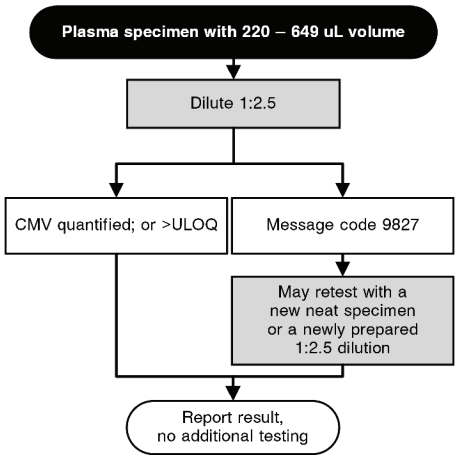
NOTE: Upon dilution, the specimen must be loaded onto the system within 2 hours. The Alinity m Specimen Diluent Tubes are single use and may not be reused.

Plasma specimens are diluted with a dilution factor of 2.5, using the Alinity m Specimen Dilution Kit I as follows:

1. Apply a barcode label for the designated specimen ID to an Alinity m LRV Tube.
2. Open a fresh Alinity m Specimen Diluent Tube and transfer 330 µL of Specimen Diluent into the Alinity m LRV Tube.
3. Add 220 µL of the patient plasma specimen into the Alinity m LRV Tube.
4. Cap the tube, vortex 3 times for 2 to 3 seconds, and tap upright on the bench to bring liquid to the bottom of the tube.
5. Remove the cap from the Alinity m LRV Tube. Inspect the fluid in the tube and remove any bubbles if found.
6. Place the Alinity m LRV Tube in the sample rack.

NOTE: Do not use an Alinity m Specimen Diluent Tube that has crystals or liquid on the outside of the tube because this may be evidence of leakage.

Specimen Dilution Procedure Scheme



QUALITY CONTROL PROCEDURES

Assay Calibration

For instructions on performing an assay calibration, refer to the Alinity m System Operations Manual, Section 6.

Lot-specific concentration values for assay calibrators and controls are available via: Abbott Mail, the Abbott customer portal www.molecular.abbott/portal, and from your Abbott Representative.

When an assay calibration is being performed:

- Lot-specific concentration values can be automatically imported to the Alinity m System via Abbott Mail upon scanning the calibrators (CMV CAL A and CMV CAL B) or controls (CMV NEG CTRL, CMV LOW POS CTRL, and CMV HIGH POS CTRL) tube barcodes.
- Lot-specific concentration values can also be obtained from the Abbott customer portal or provided by your Abbott Representative and imported via a USB drive.

For instructions on creating a test order for calibration and loading calibrators on the instrument, refer to the Alinity m System Operations Manual, Section 5.

A calibration curve is required to quantitate the CMV DNA concentration.

At a minimum, 1 Alinity m CMV CAL A tube and 1 Alinity m CMV CAL B tube from the Alinity m CMV CAL Kit are required for performing an assay calibration on the Alinity m System. The Alinity m System will process 3 replicates from each calibrator tube. The output data of the 2 calibrators will be used to generate a calibration curve (lot-specific CMV concentration versus the threshold cycle [C_t] at which a reactive level of fluorescent signal is detected). The calibration curve slope and intercept are calculated and stored on the instrument.

Once an assay calibration is accepted and stored, all subsequent samples may be tested without further calibration unless any of the following situations occurs:

- An Alinity m CMV AMP Kit with a new lot number is used.
- An Alinity m Sample Prep Kit 2 or Alinity m Lysis Solution with a new lot number is used.
- The assay calibration has expired.
- A new version of the Alinity m CMV Application Specification File is installed.

This assay may require recalibration after maintenance to critical parts or subsystems or after service procedures have been performed. Contact your Abbott Representative for further instructions.

Detection of Inhibition

An IC C_t assay validity parameter is established during a calibration run.

A defined, consistent quantity of IC is introduced into each specimen, calibrator, and control at the beginning of sample preparation and measured on the Alinity m System to demonstrate proper specimen processing and assay validity.

The median IC C_t value from calibrator samples establishes an IC C_t validity range for subsequently processed specimens and controls.

A Message Code is assigned to a specimen or control when its IC C_t value is outside of the IC C_t validity range. When the IC C_t value exceeds the upper limit of the IC C_t validity range, abnormal assay conditions, such as inhibition, are indicated.

Refer to the Alinity m System Operations Manual, Section 10 for an explanation of the corrective actions for Message Codes.

Negative and Positive Controls

An Alinity m CMV Negative CTRL, Low Positive CTRL, and High Positive CTRL are recommended to be tested, at or above the minimum frequency of once every 24 hours, to monitor the performance of the assay and Alinity m System. Valid results for all control levels must be obtained before specimen results are reported. The assay controls are also tested following calibrators and valid results for controls are required to establish a new calibration curve.

Additional controls may be tested in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

A flag is displayed for specimens when a control result is invalid. All of the specimens processed following an invalid assay control must be retested.

If control results are invalid, refer to the Alinity m System Operations Manual, Section 5 for a description of quality control flags, and Section 10 for troubleshooting information.

The presence of CMV must not be detected in the negative control. CMV detected in the negative control is indicative of contamination by other samples or by amplified product. To avoid contamination, clean the Alinity m System and repeat sample processing for controls and specimens following the Procedural Precautions in this package insert. Monitoring procedures for the presence of amplification product can be found in the Alinity m System Operations Manual, Section 9.

If negative controls are persistently reactive, contact your Abbott Representative.

When a set of assay controls are being processed, the lot-specific concentration values of the Alinity m CMV Low Positive CTRL and Alinity m CMV High Positive CTRL can be:

- Automatically imported to the Alinity m System via Abbott Mail upon scanning the barcode labels on control tubes (CMV LOW POS CTRL and CMV HIGH POS CTRL).
- Obtained from the Abbott customer portal or provided by your Abbott Representative and imported to the Alinity m System via a USB drive.

RESULTS

Calculation

Quantitative viral load results are reported for patient specimens with CMV viral concentrations within the assay's quantitation range. The concentration of CMV DNA in a specimen is calculated from the calibration curve by the system software. The Alinity m System reports the results in International Units as IU/mL or Log [IU/mL]. Refer to the Alinity m System Operations Manual for configuration of result units.

For specimens tested with the Specimen Dilution Procedure, the Alinity m System calculates and reports the neat concentration (ie, prior to dilution), by using the dilution factor selected by the user.

Interpretation of Results

Undiluted Specimens

The Alinity m System will report a Result and an Interpretation for each specimen. If applicable, message codes or flags will also be displayed.

Diluted Specimens

For specimens tested with dilution procedure, the Alinity m System reports a Result, an Interpretation (if applicable), and a DIL flag indicating that the specimen has been diluted. The quantitative results represent the CMV DNA concentration in the specimen prior to dilution.

For diluted specimens with analyte concentration below the detection limit, no result is reported, and a message code (9827) is displayed. These specimens cannot be interpreted as target not detected and may be retested with a new neat specimen or a newly prepared dilution (refer to Specimen Dilution Procedure Scheme).

Note: The LLoQ of Alinity m CMV is 30 IU/mL (1.48 Log IU/mL) for specimens tested without dilution. Therefore, the lowest CMV DNA concentration that can be reported for a specimen that is tested diluted is 75 IU/mL (1.88 Log IU/mL).

The ULoQ of Alinity m CMV is 100,000,000 IU/mL (8.00 Log IU/mL) for specimens tested without dilution. Therefore, the CMV DNA concentration of a specimen that is tested diluted and returns a result of >ULoQ is >250,000,000 IU/mL (8.40 Log IU/mL).

Result and Interpretation

Alinity m System Reported		Interpretation
Result	**Interpretation**	**Additional Information**
Not Detected	CMV DNA not detected	
< LLoQ	CMV DNA detected but not quantified	CMV DNA concentration is below the Lower Limit of Quantitation (LLoQ) of the assay.
LLoQ to ≤ULoQ	CMV DNA detected and quantified	CMV DNA concentration is within the linear range of the assay (≥LLoQ to ≤ULoQ).
> ULoQ	CMV DNA detected	CMV DNA concentration is above the Upper Limit of Quantitation (ULoQ) of the assay.

Flags, Results Codes, and Message Codes

Some results may contain information in the Flags and Codes fields. For a description of the flags and result codes that may appear in these fields, refer to the Alinity m System Operations Manual, Section 5.

For a description of message codes refer to the Alinity m System Operations Manual, Section 10.

LIMITATIONS OF THE PROCEDURE

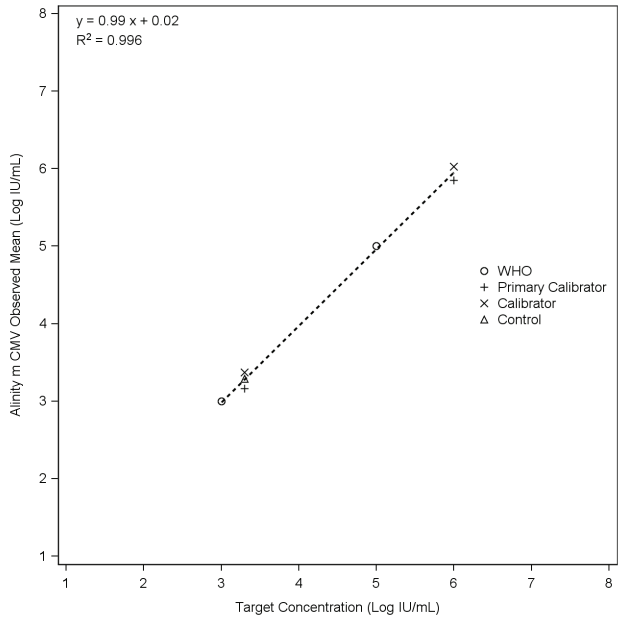
- Optimal performance of this test requires appropriate specimen collection and handling (refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert).
- Human plasma (K_2 EDTA, K_3 EDTA, and PPT) specimens may be used with the Alinity m CMV assay. The use of other plasma tubes has not been evaluated.
- Debris within plasma specimens (eg, fibrin strands) may interfere with sample processing.
- Diluted specimens must be tested within 2 hours after dilution and should not be frozen.
- The instruments and assay procedures reduce the risk of contamination by amplification product. However, nucleic acid contamination from the calibrators, positive controls, or specimens must be controlled by good laboratory practice and careful adherence to the procedures specified in this package insert.
- Test results are to be interpreted by qualified licensed healthcare professionals in conjunction with clinical signs and symptoms and other relevant laboratory results.
- A specimen with a result of "Not Detected" cannot be presumed to be negative for CMV DNA.
- Due to the potential for variability in CMV viral load measurements across different CMV assays, it is recommended that the same device be used for the quantitation of CMV viral load when managing CMV infection in individual patients.
- Testing of drug resistant CMV specimens has not been evaluated in the clinical study.
- Test performance characteristics have been evaluated only for individuals who have undergone solid organ transplant (SOT) and hematopoietic stem cell transplant (HSCT), and have been diagnosed with CMV disease and are undergoing treatment. No information is available on test performance in patients undergoing other types of transplant procedures, neonates or pediatric patients, or AIDS or other immunocompromised patients.
- This test is intended for use as an aid in the management of solid-organ transplant and HSCT patients who have been diagnosed with CMV disease and are undergoing antiviral therapy. In this population, the test can be used to assess virological response to treatment by measuring the baseline CMV DNA level and to assess the effects of antiviral therapy by measuring CMV DNA during the course of antiviral treatment. Patient management decisions should not be made based solely on the results from this test. Other laboratory and clinical factors must also be considered in making clinical decisions.
- Clinicians should take individual patient risk factors as well as current clinical guidelines into account when using CMV viral load results for the management of transplant patients.
- This test is not intended for use as a screening test for the presence of CMV in blood or blood products and has not been evaluated as a diagnostic test to confirm the presence of CMV infection.

SPECIFIC PERFORMANCE CHARACTERISTICS

Traceability to the WHO Standard

Primary calibrators and assay product calibrators with known concentrations were used throughout product development and product manufacturing to establish traceability to the 1st World Health Organization (WHO) International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques (NIBSC code: 09/162). The concentrations tested for the WHO standard were 3.00 Log IU/mL and 5.00 Log IU/mL. The target concentrations tested for the primary calibrators were 3.30 Log IU/mL and 6.00 Log IU/mL. The Alinity m CMV product calibrators and controls were also tested along with the primary calibrators and the WHO standard. All of the panels had observed CMV concentrations similar to the target concentrations, and were linear across the assay's quantitation range, as presented in **Figure 1**.

Figure 1. Traceability to the WHO Standard



Limit of Detection

The limit of detection (LoD) was determined by testing dilutions of the 1st World Health Organization (WHO) International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques, (NIBSC code 09/162, genotype gB1, Merlin) prepared in CMV negative human plasma. Testing for each CMV DNA concentration was performed with 4 lots of amplification reagents across multiple days. The results, representative of the analytical sensitivity performance of Alinity m CMV, are summarized in **Table 1** (Lot 1), **Table 2** (Lot 2), **Table 3** (Lot 3), and **Table 4** (Lot 4).

Probit analysis of the data using the least sensitive lot (Lot 3) determined that the concentration of CMV DNA in plasma detected with 95% probability was 21.52 IU/mL (95% CI: 13.22 to 54.92 IU/mL) (**Table 3**).

Table 1. Alinity m CMV Limit of Detection (LoD) – Lot 1

CMV DNA (IU/mL)	No. of Valid Replicates	No. of Detected	Detection Rate (%)
64.4	30	30	100.0
38.6	30	30	100.0
25.8	30	30	100.0
12.9	30	28	93.3
6.4	30	17	56.7
3.2	30	13	43.3
1.6	30	8	26.7

Table 2. Alinity m CMV Limit of Detection (LoD) – Lot 2

CMV DNA (IU/mL)	No. of Valid Replicates	No. of Detected	Detection Rate (%)
64.4	30	30	100.0
38.6	29	29	100.0
25.8	30	30	100.0
12.9	29	26	89.7
6.4	30	21	70.0
3.2	29	11	37.9
1.6	30	8	26.7

Table 3. Alinity m CMV Limit of Detection (LoD) – Lot 3 (Least Sensitive Lot)

CMV DNA (IU/mL)	No. of Valid Replicates	No. of Detected	Detection Rate (%)
64.4	30	30	100.0
38.6	30	30	100.0
25.8	30	30	100.0
12.9	29	24	82.8
6.4	30	24	80.0
3.2	30	15	50.0
1.6	30	12	40.0

Table 4. Alinity m CMV Limit of Detection (LoD) – Lot 4

CMV DNA (IU/mL)	No. of Valid Replicates	No. of Detected	Detection Rate (%)
64.4	29	29	100.0
38.6	30	30	100.0
25.8	30	30	100.0
12.9	29	28	96.6
6.4	29	16	55.2
3.2	30	14	46.7
1.6	30	7	23.3

The claimed LoD of Alinity m CMV is 30 IU/mL in plasma.

Limit of Detection for Genotypes gB2, gB3, gB4, and Antiviral Resistant Strain

Cultured viruses for CMV genotypes gB2, gB3, gB4, and an antiviral resistant strain were diluted to 4 different concentrations in CMV negative plasma. Testing was performed using one lot of amplification reagents across multiple days. The results, representative of the analytical sensitivity performance of Alinity m CMV for genotypes gB2, gB3, gB4, and the antiviral resistant strain, are summarized in **Table 5**.

Alinity m CMV detected 95% or greater of CMV samples at and above 30 IU/mL (1.48 Log IU/mL). These results demonstrate the ability of Alinity m CMV to detect genotypes gB2, gB3, gB4, and an antiviral resistant strain at the claimed LoD.

Table 5. Alinity m CMV Genotype Limit of Detection (LoD)

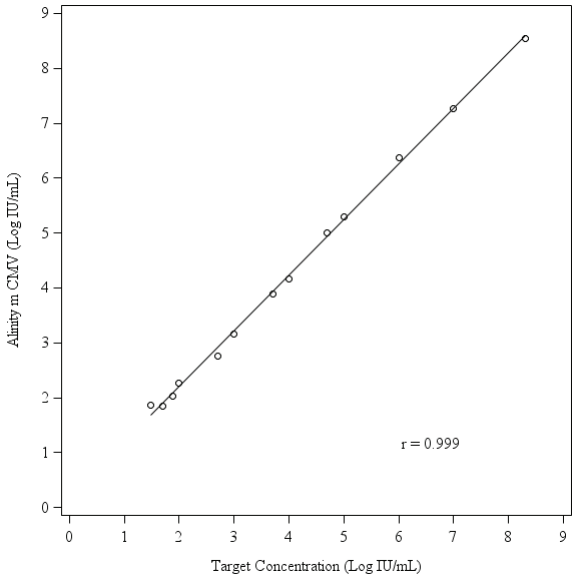
Genotype	CMV DNA IU/mL	No. of Valid Replicates	No. of Detected	Detection Rate (%)
gB2	100	40	40	100.0
	50	40	40	100.0
	30	40	38	95.0
	20	40	39	97.5
gB3	100	39	39	100.0
	50	40	40	100.0
	30	40	40	100.0
	20	39	39	100.0
gB4	100	40	40	100.0
	50	40	40	100.0
	30	40	40	100.0
	20	40	40	100.0
Anti-viral resistant	100	40	40	100.0
	50	40	40	100.0
	30	39	39	100.0
	20	40	40	100.0

Linear Range

The upper limit of quantitation range of Alinity m CMV is the claimed ULoQ (8.00 Log IU/mL) and the lower limit is the claimed LLoQ (1.48 Log IU/mL). Linearity of Alinity m CMV was assessed by testing a dilution series of CMV genotype gB2 in negative plasma consisting of 14 panel levels ranging from 10 IU/mL to 200,000,000 IU/mL (1.00 Log IU/mL to 8.30 Log IU/mL). Panel levels with concentrations from 10 IU/mL to 100,000 IU/mL (1.00 Log IU/mL to 5.00 Log IU/mL) were prepared using cultured virus, while panel levels with concentrations from 500 IU/mL to 200,000,000 IU/mL (2.70 Log IU/mL to 8.30 Log IU/mL) were prepared using plasmid DNA.

Alinity m CMV was linear across the quantitation range from 30 IU/mL to 100,000,000 IU/mL. Representative results for Alinity m CMV linearity performance are shown in **Figure 2**.

Figure 2. Linearity [a]



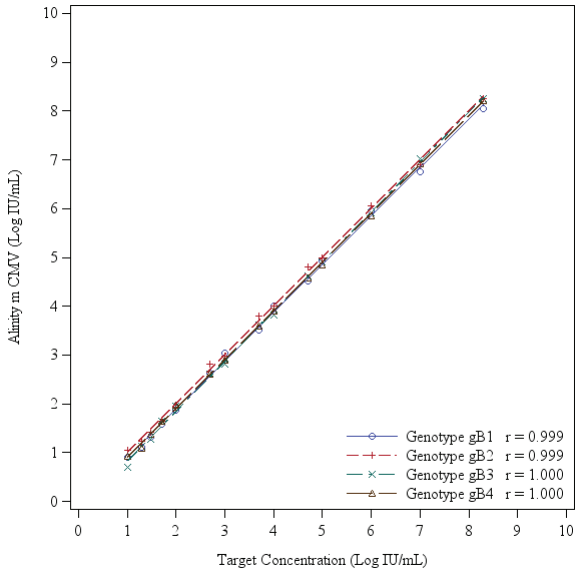
[a] Note: The markers in the plot represent the mean Alinity m CMV concentration (in Log IU/mL) for each panel level.

Linearity Across CMV Genotypes

Linearity of Alinity m CMV for genotypes gB1, gB3, and gB4 was confirmed by testing a dilution series in negative plasma consisting of 14 panel levels ranging from 10 IU/mL to 200,000,000 IU/mL (1.00 Log IU/mL to 8.30 Log IU/mL). For each genotype, panel levels with concentrations from 10 IU/mL to 100,000 IU/mL (1.00 Log IU/mL to 5.00 Log IU/mL) were prepared using cultured virus, while panel levels with concentrations from 500 IU/mL to 200,000,000 IU/mL (2.70 Log IU/mL to 8.30 Log IU/mL) were prepared using plasmid DNA. Alinity m CMV was linear across the quantitation range from 30 IU/mL to 100,000,000 IU/mL for genotypes gB1, gB3, and gB4.

Representative results for Alinity m CMV linearity performance for genotypes gB1, gB3, and gB4, along with results for genotype gB2 (**Linear Range** section), are shown in **Figure 3**.

Figure 3. Linearity Across CMV Genotypes in Plasma [a]



[a] Note: The markers in the plot represent the mean Alinity m CMV concentration (in Log IU/mL) for each panel level.

The Alinity m CMV assay was demonstrated to be linear across the quantitation range for genotypes gB1, gB2, gB3, and gB4 from 30 IU/mL to 100,000,000 IU/mL.

Precision

Precision of Alinity m CMV was determined by analyzing an 8-member plasma panel. Panel members with targeted concentrations from 1.48 to 2.00 Log IU/mL (30 to 100 IU/mL) were prepared with a positive clinical sample. Panel members targeted from 2.70 to 5.00 Log IU/mL (500 to 100,000 IU/mL) were prepared using cultured virus. Panel members with targeted concentrations greater than 5.00 Log IU/mL were prepared using plasmid DNA. Each panel member was tested in 5 replicates, twice each day for 12 days, on 3 Alinity m Systems operated by 3 operators (one operator per instrument), using 3 AMP kit lots (one lot per instrument), for a total of 360 replicates per panel member.

The results, representative of the precision of Alinity m CMV (**Table 6** and **Table 7**), demonstrated that Alinity m CMV within-laboratory standard deviation (SD) in plasma was less than or equal to 0.25 Log IU/mL for CMV DNA from 2.70 to 8.00 Log IU/mL (500 to 100,000,000 IU/mL), and less than or equal to 0.50 Log IU/mL for CMV DNA from 1.70 Log IU/mL to less than 2.70 Log IU/mL (50 to less than 500 IU/mL). Results below LLoQ are not displayed in the table.

Table 6. Precision

		Mean Concentration	Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory [d]		Between-Instrument Component [e]		Total [f]	
Panel [a]	N [b]	(Log IU/mL)	SD [c]	%CV	SD [c]	%CV	SD [c]	%CV	SD [c]	%CV	SD [c]	%CV	SD [c]	%CV
08	356	8.35	0.08	0.9	0.01	0.2	0.01	0.1	0.08	0.9	0.11	1.3	0.13	1.6
07	355	6.99	0.06	0.8	0.03	0.5	0.02	0.3	0.07	1.0	0.08	1.2	0.11	1.5
06	358	4.99	0.06	1.3	0.04	0.7	0.00	0.0	0.07	1.4	0.04	0.8	0.08	1.7
05	356	3.98	0.06	1.5	0.03	0.9	0.00	0.1	0.07	1.7	0.03	0.6	0.07	1.8
04	356	2.65	0.08	3.0	0.03	1.3	0.02	0.8	0.09	3.3	0.06	2.3	0.11	4.1
03	360	1.92	0.11	5.9	0.00	0.0	0.00	0.0	0.11	5.9	0.05	2.8	0.13	6.5
02	356	1.64	0.17	10.5	0.05	3.1	0.00	0.0	0.18	10.9	0.07	4.1	0.19	11.7

[a] One panel member below LLoQ is not shown in the table.

[b] Number of valid replicates with detectable viral load.

[c] Standard deviations (SD) are in Log IU/mL.

[d] Within-Laboratory includes Within-Run, Between-Run, and Between-Day components.

[e] Alinity m System, AMP Kit lot and Operator are confounded and the confounding effect is represented by Instrument

[f] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument components.

Table 7. Precision

			CV(%) [d]				
Panel [a]	N [b]	Mean Concentration [c] (IU/mL)	Within-Run Component	Between-Run Component	Between-Day Component	Between-Instrument Component [e]	Total [f]
08	356	234362988	17.5	3.2	2.9	25.6	31.7
07	355	9978289	13.6	7.8	4.9	18.7	25.1
06	358	99644	14.6	8.2	0.0	9.6	19.4
05	356	9671	13.7	8.0	0.8	5.9	17.0
04	356	457	18.3	7.7	5.0	14.1	25.1
03	360	86	26.3	0.0	0.0	12.6	29.4
02	356	48	41.1	11.5	0.0	15.6	46.2

[a] One panel member below LLoQ is not shown in the table.

[b] Number of valid replicates with detectable viral load.

[c] Titer data are considered to be log-normally distributed and the mean values for titer data are calculated as $\exp(\text{mean} \times \ln(10) + [\text{SD} \times \ln(10)]^2/2)$.

[d] Titer data are considered to be log-normally distributed and %CV values are calculated as $\text{CV}\ (\%) = \text{sqrt}(10^{\wedge}[\text{SD}^2 \times \ln(10)] - 1) \times 100$.

[e] Alinity m System, AMP Kit lot, and Operator are confounded and the confounding effect is represented by Instrument.

[f] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument components.

Lower Limit of Quantitation

The lower limit of quantitation (LLoQ) is defined as the lowest concentration at which CMV DNA is reliably quantitated within an acceptable total error. Total error was estimated for detected samples from the LoD study by 2 methods:

- Total Analytical Error(TAE)=|bias|+2×SD, and
- Total Error(TE)=SQRT(2)×2×SD.

The results of the calculations are shown in **Table 8**.

Panel members were dilutions of the 1st World Health Organization (WHO) International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques, (NIBSC code 09/162) prepared in CMV negative plasma.

The results of these analyses supports a claimed LLoQ of 30.00 IU/mL (1.48 Log IU/mL) for the Alinity m CMV assay with an acceptable level of accuracy and precision, ie, TAE and TE less than or equal to 1.00 Log IU/mL.

Table 8. Total Error

Target Conc. (Log IU/mL)	Mean Conc (Log IU/mL)	Bias [a] (Log IU/mL)	SD (Log IU/mL)	TAE (Log IU/mL)	TE (Log IU/mL)
1.41	1.39	−0.02	0.27	0.56	0.76
1.59	1.57	−0.02	0.23	0.48	0.65
1.81	1.83	0.02	0.15	0.32	0.42

[a] Mean concentration − target concentration.

Analytical Specificity – Potential Cross-Reactants

The analytical specificity of Alinity m CMV was evaluated with a panel of microorganisms (**Table 9**) in CMV negative plasma, positive plasma containing 125 IU/mL CMV DNA, and positive plasma containing 2,000 IU/mL CMV DNA. Microorganisms were tested at a final concentration of 10^5 Units/mL for viruses and fungi or 10^6 Units/mL for bacteria. No cross-reactivity or interference in the performance of the Alinity m CMV assay was observed in the presence of the tested microorganisms.

Table 9. Microorganisms

Viruses	**Bacteria**
Adenovirus	*Chlamydia trachomatis*
BK polyomavirus	*Enterococcus faecalis*
Epstein Barr Virus (EBV)	*Escherichia coli*
Hepatitis B Virus (HBV)	*Listeria monocytogenes*
Hepatitis C Virus (HCV)	*Mycobacterium gordonae*
Herpesvirus 6B	*Mycobacterium pneumoniae*
Herpesvirus 7	*Mycobacterium smegmatis*
Herpesvirus 8 (Kaposi's sarcoma associated virus)	*Neisseria gonorrhoeae*
Human Immunodeficiency Virus-1 (HIV-1)	*Propionibacterium acnes (PA) (Cutibacterium acnes)*
Human Immunodeficiency Virus-2 (HIV-2)	*Salmonella typhi*
Herpes Simplex Virus -1 (HSV-1)	*Salmonella typhimurium*
Herpes Simplex Virus -2 (HSV-2)	*Staphylococcus aureus (SA)*
Human papilloma virus 16 (HPV-16)	*Staphylococcus epidermidis*
Human papilloma virus 18 (HPV-18)	*Streptococcus pneumoniae*
Human T-lymphocyte virus 1 (HTLV-1)	**Fungi**
JC Polyomavirus	*Aspergillus niger*
Parvo virus B19	*Candida albicans (CA)*
Vaccinia virus (VACV)	*Cryptococcus neoformans*
Varicella-Zoster virus (VZV)	

Analytical Specificity – Potentially Interfering Substances

The effects of endogenous substances, the presence of autoimmune diseases, and the presence of high levels of therapeutic drugs commonly prescribed in transplant patients were evaluated. Potential interference on Alinity m CMV performance in plasma was assessed by testing 8 negative samples, 8 positive samples containing 125 IU/mL CMV DNA, and 8 positive samples containing 2,000 IU/mL CMV DNA.

No interference was observed in the presence of albumin (60 mg/mL), hemoglobin (10 g/L), triglycerides (16.94 mmol/L), conjugated bilirubin (475 µmol/L), unconjugated bilirubin (684 µmol/L), or human genomic DNA (2 µg/mL) that were introduced in the sample.

No interference was observed for specimens collected from patients with the following disease states: systemic lupus erythematosus (SLE), anti-nuclear antibodies (ANA), or rheumatoid arthritis (RA).

No interference was observed in the presence of drug compounds tested in pools or individually as listed in **Table 10**, at a concentration of 3 times the reported C_{max} or higher.

Table 10. Drug Compounds

Pools Tested	**Drug Compounds**
1	Mycophenolic acid
2	Amoxicillin, Clavulanate, Foscarnet, Piperacillin, Tazobactam sodium, Vancomycin
3	Acyclovir, Amlodipine besylate, Atenolol, Azathioprine, Cefotetan, Cidofovir, Cyclosporine, Everolimus, Famotidine, Fluconazole, Ganciclovir, Lisinopril, Mycophenolate mofetil, Prednisone, Rabeprazole, Sirolimus, Sulfamethoxazole, Tacrolimus, Ticarcillin, Trimethoprim, Valacyclovir, Valganciclovir HCl, Valsartan

Carryover

The carryover rate for Alinity m CMV was determined by analyzing 629 valid replicates of CMV negative samples processed from alternating positions with 637 valid replicates of high concentrated CMV positive samples greater than or equal to 1,000,000 IU/mL, across a minimum of 27 runs.

The carryover resulting in a detectable concentration greater than or equal to LoD (LLoQ) was 0.0% (95% CI: 0.0% to 0.6%). The carryover resulting in CMV detection was 0.3% (95% CI: 0.1% to 1.2%).

Alinity m CMV Testing Using Dilution Procedure

The 1:2.5 dilution procedure was evaluated by comparing quantitation of neat samples and samples tested using the Alinity m CMV dilution procedure. Five plasma panel members consisting of CMV concentrations ranging from 225 to 200,000,000 IU/mL were tested. Each panel member was tested, neat or using the dilution procedure, in a minimum of 8 replicates. The differences in mean quantitation (ie, diluted minus neat) ranged from 0.03 to 0.16 Log IU/mL.

Precision of Alinity m CMV Using Dilution Procedure

Precision of Alinity m CMV, using the dilution procedure, was determined by analyzing 3 panel members. Panel members 1 and 2 were prepared by spiking cultured virus in CMV negative plasma, and panel 3 was prepared by spiking plasmid DNA in CMV negative plasma. Each panel member was tested in 5 replicates, twice each day for 12 days, on 3 Alinity m Systems with 3 Specimen Diluent lots and 3 AMP kit lots by 3 operators (1 Specimen Diluent lot, 1 AMP kit lot, and 1 operator per instrument), for a total of 360 replicates.

The results, representative of the precision of Alinity m CMV using dilution procedures, are summarized in **Table 11**.

Table 11. Precision using Dilution Procedure

		Mean Concentration	Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory [c]		Between-Instrument Component [d]		Total [e]	
Panel	N [a]	(Log IU/mL)	SD [b]	%CV	SD [b]	%CV	SD [b]	%CV	SD [b]	%CV	SD [b]	%CV	SD [b]	%CV
01	353	3.68	0.06	1.7	0.02	0.5	0.07	1.9	0.09	2.6	0.00	0.0	0.09	2.6
02	358	5.01	0.05	1.0	0.03	0.5	0.02	0.5	0.06	1.2	0.03	0.5	0.07	1.4
03	355	8.32	0.07	0.9	0.02	0.2	0.05	0.6	0.09	1.1	0.12	1.4	0.15	1.8

[a] Number of valid replicates with detectable viral load.

[b] Standard deviations (SD) are in Log IU/mL.

[c] Within-Laboratory includes Within-Run, Between-Run, and Between-Day components.

[d] Alinity m System, AMP Kit lot and Operator are confounded and the confounding effect is represented by Instrument

[e] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument components.

Confirmation of the LLoQ Using Dilution Procedure

LLoQ for Alinity m CMV using the dilution procedure was confirmed by testing 2 panel members with targeted concentrations of 30 IU/mL and 36 IU/mL (1.48 Log IU/mL and 1.56 Log IU/mL) after dilution in Specimen Diluent. Panel members were dilutions of the 1st World Health Organization (WHO) International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques, (NIBSC code 09/162) prepared in CMV negative plasma.

A minimum of 14 replicates per day of each panel level were tested using the dilution procedure in 3 runs across 3 days (one run per day). The study was performed using 1 Alinity m CMV AMP Kit lot, 1 Specimen Diluent lot, and 1 Alinity m System. Total error was estimated by TAE and TE, as shown in **Table 12**. The accuracy and precision at 30 and 36 IU/mL were confirmed for Alinity m CMV testing using the 1:2.5 dilution procedure.

Table 12. Total Error Using Dilution Procedure

Panel Member	Dilution Factor	Target Conc. in Specimen Diluent (Log IU/mL)	Target Conc. Neat (Log IU/mL)	Mean Conc [a] (Log IU/mL)	Bias [b] (Log IU/mL)	SD (Log IU/mL)	TAE (Log IU/mL)	TE (Log IU/mL)
1	2.5	1.48	1.88	1.82	−0.06	0.24	0.54	0.68
2	2.5	1.56	1.95	1.93	−0.02	0.25	0.52	0.70

[a] Reported concentration for neat samples.

[b] Mean Concentration − Target Concentration for neat samples

Clinical Reproducibility

Reproducibility performance of Alinity m CMV was evaluated by testing a 9-member reproducibility panel, including 8 positive panel members and 1 negative panel member. The positive panel members were prepared using a CMV positive clinical specimen, cultured virus, or plasmid DNA diluted in negative human plasma. The concentration levels targeted for the reproducibility panels spanned the quantitation range of the assay. A total of 3 Alinity m CMV AMP Kit lots and 3 Alinity m CMV CAL Kit lots were used. Three clinical sites each tested 2 Alinity m CMV AMP Kit lots and 1 Alinity m CMV CAL Kit lot, on 5 non-consecutive days for each lot. Five replicates of each panel member were tested on each of 5 days. Each of the 3 clinical sites used different lots of Alinity m CMV CAL Kit, Alinity m CMV CTRL Kit, and Alinity m Sample Prep Kit 2. The reproducibility results are summarized in **Table 13** and **Table 14** (for the positive panel members greater than LLoQ), and **Table 15** (negative panel member) below. Results below LLoQ are not displayed in the table for positive panel members.

Table 13. Reproducibility for Positive Panel Members

		Mean Concentration	Within-Run/Day Component		Between-Run/Day Component		Within-Laboratory [d]		Between-Lot Component		Between-Site/Instrument Component		Total [e]	
Panel [a]	N [b]	(Log IU/mL)	SD [c]	%CV	SD [c]	%CV	SD [c]	%CV	SD [c]	%CV	SD [c]	%CV	SD [c]	%CV
1	150	8.18	0.06	0.8	0.03	0.3	0.07	0.9	0.07	0.9	0.14	1.7	0.17	2.1
2	150	7.00	0.08	1.2	0.01	0.2	0.08	1.2	0.02	0.3	0.10	1.4	0.13	1.9
3	150	4.75	0.09	2.0	0.02	0.5	0.10	2.0	0.06	1.2	0.10	2.1	0.15	3.1
4	150	4.06	0.05	1.3	0.02	0.6	0.06	1.4	0.06	1.4	0.10	2.4	0.13	3.1
5	150	3.08	0.09	2.8	0.02	0.5	0.09	2.9	0.06	2.0	0.07	2.4	0.13	4.2
6	150	2.04	0.14	7.1	0.00	0.0	0.14	7.1	0.13	6.4	0.00	0.0	0.19	9.5

[a] Two panel members below LLoQ are not shown in the table.

[b] Number of valid replicates with detectable viral load.

[c] Standard deviations (SD) are in Log IU/mL.

[d] Within-Laboratory includes Within-Run/Day and Between-Run/Day Components

[e] Total includes Within-Run/Day, Between-Run/Day, Between-Lot and Between-Site/Instr Components.

Table 14. Reproducibility for Positive Panel Members

			CV(%) [d]				
Panel [a]	N [b]	Mean Concentration [c] (IU/mL)	Within-Run/Day Component	Between-Run/Day Component	Between-Lot Component	Between-Site/Instrument Component	Total [e]
1	150	163024323	14.8	6.4	16.3	32.0	40.2
2	150	10447432	18.7	2.8	5.0	23.4	30.9
3	150	60099	21.6	5.1	13.1	23.1	35.2
4	150	11912	12.3	5.4	12.9	23.1	30.0
5	150	1250	20.1	3.8	13.9	17.0	30.4
6	150	121	34.2	0.0	30.7	0.0	47.1

[a] Two panel members below LLoQ are not shown in the table.

[b] Number of valid replicates with detectable viral load.

[c] Titer data are considered to be log-normally distributed and the mean values for titer data are calculated as $\exp(\text{mean} \times \ln(10) + [\text{SD} \times \ln(10)]^2/2)$.

[d] Titer data are considered to be log-normally distributed and %CV values are calculated as $\text{CV}\ (\%) = \text{sqrt}(10^{[\text{SD}^2 \times \ln(10)]} - 1) \times 100$.

[e] Total includes Within-Run/Day, Between-Run/Day, Between Reagent Lot, and Between-Site/Instrument components.

Table 15. Reproducibility for Negative Panel Member

Expected CMV DNA Concentration	Numbers of Replicates		Negative Rate (%)	95% Confidence Interval
	Valid	Negative		
Negative	150	150	100.0(150/150)	(97.5, 100.0)

Clinical Performance

Alinity m CMV results were compared to those of an FDA-approved CMV nucleic acid test in a representative study. A total of 283 clinical EDTA plasma specimens from hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) subjects were tested, including 202 positive and 81 negative specimens. The 202 positive specimens were residual specimens, tested as individual specimens or pooled consecutive longitudinal specimens from a total of 170 subjects. Of these 202 positive specimens, 91 HSCT specimens were pooled consecutive longitudinal specimens from 59 subjects and one specimen was used from each of 111 SOT subjects. The transplanted organ types for the 111 SOT subjects included kidney (35 subjects), liver (23 subjects), lung (14 subjects), heart (9 subjects), kidney and pancreas (7 subjects), kidney and heart (2 subjects), kidney and liver (2 subjects), kidney and lung (1 subject), HSCT and liver (3 subjects), and type not available (15 subjects). The Alinity m CMV assay testing was performed at 4 clinical testing sites with 3 Alinity m CMV reagent kit lots.

Of the 283 clinical specimens, 267 had evaluable results from both Alinity m CMV and the comparator and were included in the analysis for agreement. Out of the 267 specimens, 139 specimens were from 139 SOT subjects and the remaining 128 specimens were from 101 HSCT subjects. Demographic characteristics of the SOT subjects are shown in **Table 16**. Specimens from 101 HSCT subjects were obtained from the following study: "A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial to Evaluate the Protective Efficacy and Safety of a Therapeutic Vaccine, ASP0113, in Cytomegalovirus (CMV)-Seropositive Recipients Undergoing Allogeneic, Hematopoietic Cell Transplant (HCT)."[22]

Table 16. Summary of Demographic Characteristics of the SOT Subjects

Demographic Characteristics	Statistics (N=139)	Demographic Characteristics	Statistics (N=139)
Age (years)		**Race**	**N (%)**
Mean	55	African American	30 (21.6%)
Median	58	Asian	1 (0.7%)
SD	14	Caucasian	65 (46.8%)
Range	20-78	Other	18 (12.9%)
Gender	**N (%)**	Unknown	25 (18.0%)
Female	64 (46.0%)	**Ethnicity**	**N (%)**
Male	75 (54.0%)	Hispanic or Latino	12 (8.6%)
		Not Hispanic or Latino	69 (49.6%)
		Unknown	58 (41.7%)

The agreement of Alinity m CMV and comparator results are shown in **Table 17** (HSCT specimens), **Table 19** (SOT specimens), and **Table 21** (HSCT and SOT specimens combined). The evaluation of percent agreement and associated two-sided score 95% CI using different clinical thresholds are shown in **Table 18** (HSCT specimens), **Table 20** (SOT specimens), and **Table 22** (HSCT and SOT specimens combined).

Table 17. HSCT Specimens - Agreement Between Alinity m CMV and Comparator

	Comparator Test (IU/mL)					
Alinity m CMV (IU/mL)	**Target Not Detected**	**<LLoQ [a]**	**LLoQ [a] to 500**	**500 to 2000**	**>2000**	**Total**
Target Not Detected	42	0	0	0	0	42
<LLoQ [a]	0	2	0	0	0	2
LLoQ [a] to 500	1	3	30	1	0	35
500 to 2000	0	0	14	15	0	29
>2000	0	0	0	6	14	20
Total	43	5	44	22	14	128

[a] LLoQ used here is the higher LLoQ between Alinity m CMV and comparator.

Table 18. HSCT Specimens - Percent Agreement and Associated Two-Sided Score 95% Confidence Intervals (CIs)

Threshold	**Percent Agreement < Threshold 95% Score CI (n/N)**	**Percent Agreement ≥ Threshold 95% Score CI (n/N)**
Target Not Detected	97.7 (87.9,99.6) (42/43)	100.0 (95.7,100.0) (85/85)
LLoQ [a]	91.7 (80.4,96.7) (44/48)	100.0 (95.4,100.0) (80/80)
500	84.8 (76.1,90.7) (78/92)	97.2 (85.8,99.5) (35/36)
2000	94.7 (89.0,97.6) (108/114)	100.0 (78.5,100.0) (14/14)

[a] LLoQ used here is the higher LLoQ between Alinity m CMV and comparator.

Table 19. SOT Specimens - Agreement Between Alinity m CMV and Comparator

	Comparator Test (IU/mL)					
Alinity m CMV (IU/mL)	**Target Not Detected**	**<LLoQ [a]**	**LLoQ [a] to 500**	**500 to 2000**	**>2000**	**Total**
Target Not Detected	32	0	0	0	0	32
<LLoQ [a]	2	3	2	0	0	7
LLoQ [a] to 500	0	3	44	0	0	47
500 to 2000	0	0	5	10	1	16
>2000	0	0	0	5	32	37
Total	34	6	51	15	33	139

[a] LLoQ used here is the higher LLoQ between Alinity m CMV and comparator.

Table 20. SOT Specimens - Percent Agreement and Associated Two-Sided Score 95% Confidence Intervals (CIs)

Threshold	**Percent Agreement < Threshold 95% Score CI (n/N)**	**Percent Agreement ≥ Threshold 95% Score CI (n/N)**
Target Not Detected	94.1 (80.9,98.4) (32/34)	100.0 (96.5,100.0) (105/105)
LLoQ [a]	92.5 (80.1,97.4) (37/40)	98.0 (92.9,99.4) (97/99)
500	94.5 (87.8,97.6) (86/91)	100.0 (92.6,100.0) (48/48)
2000	95.3 (89.4,98.0) (101/106)	97.0 (84.7,99.5) (32/33)

[a] LLoQ used here is the higher LLoQ between Alinity m CMV and comparator.

Table 21. HSCT and SOT Specimens Combined - Agreement Between Alinity m CMV and Comparator

	Comparator Test (IU/mL)					
Alinity m CMV (IU/mL)	**Target Not Detected**	**<LLoQ [a]**	**LLoQ [a] to 500**	**500 to 2000**	**>2000**	**Total**
Target Not Detected	74	0	0	0	0	74
<LLoQ [a]	2	5	2	0	0	9
LLoQ [a] to 500	1	6	74	1	0	82
500 to 2000	0	0	19	25	1	45
>2000	0	0	0	11	46	57
Total	77	11	95	37	47	267

[a] LLoQ used here is the higher LLoQ between Alinity m CMV and comparator.

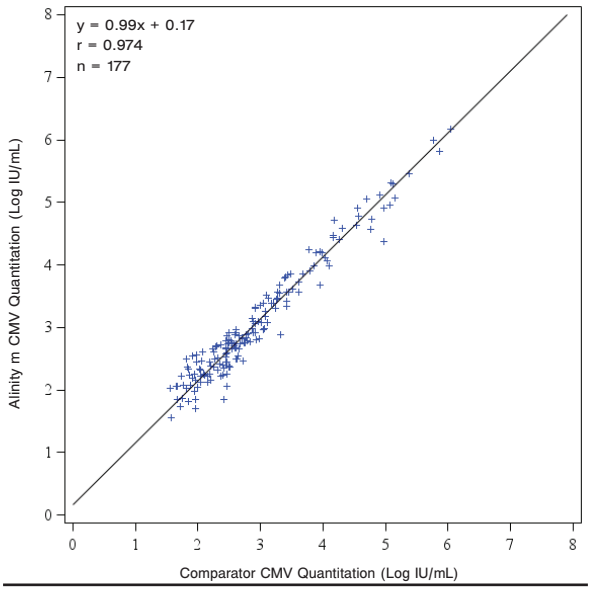
Table 22. HSCT and SOT Specimens Combined - Percent Agreement and Associated Two-Sided Score 95% Confidence Intervals (CIs)

Threshold	Percent Agreement < Threshold 95% Score CI (n/N)	Percent Agreement ≥ Threshold 95% Score CI (n/N)
Target Not Detected	96.1 (89.2,98.7) (74/77)	100.0 (98.0,100.0) (190/190)
LLoQ [a]	92.0 (84.5,96.1) (81/88)	98.9 (96.0,99.7) (177/179)
500	89.6 (84.4,93.3) (164/183)	98.8 (93.6,99.8) (83/84)
2000	95.0 (91.3,97.2) (209/220)	97.9 (88.9,99.6) (46/47)

[a] LLoQ used here is the higher LLoQ between Alinity m CMV and comparator.

Regression analysis included a total of 177 positive specimens with results that fell within the common quantitation range of Alinity m CMV and the comparator. **Figure 4** shows the results of the Deming regression analysis with a slope of 0.99, intercept of 0.17, and correlation coefficient of 0.974. The mean bias between Alinity m CMV and the comparator (Alinity m CMV minus comparator) was 0.14 Log IU/mL with a 95% CI of (0.11, 0.18).

Figure 4. Deming Regression Analysis



Systematic difference at 3 selected viral load levels between Alinity m CMV and the comparator is shown in **Table 23**.

Table 23. Systematic Difference at Selected Viral Load Levels

Viral Load Level (per comparator)	Systematic Difference
2.70 Log IU/mL	0.15 Log IU/mL
3.30 Log IU/mL	0.14 Log IU/mL
4.00 Log IU/mL	0.13 Log IU/mL

A total of 75 negative specimens from HSCT and SOT subjects had evaluable results with both Alinity m CMV and the comparator. The results for the negative clinical specimens (Alinity m CMV versus comparator) is shown in **Table 24**.

Table 24. Results of Negative Clinical Specimens (Alinity m CMV versus Comparator)

	Comparator Test			
Alinity	Target not Detected	<LLoQ [a]	≥LLoQ [a]	Total
Target Not Detected	74	0	0	74
<LLoQ [a]	1	0	0	1
≥LLoQ [a]	0	0	0	0
Total	75	0	0	75

[a] LLoQ used here is the higher LLoQ between Alinity m CMV and comparator.

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KEY TO SYMBOLS

RE	Reference Number
IV	In Vitro Diagnostic Medical Device
LOT	Lot Number
	In Vitro Test
Fo i i i	For In Vitro Diagnostic Use
AMP TRAY	AMP TRAY
ACT TRAY	ACT TRAY
IT	Unit
ONLY	For Prescription Use Only
	Systemic Health Effects
	Warning
	Consult Instructions for Use
	Temperature Limitation
Σ	Sufficient for
	Use By
	Manufacturer

TECHNICAL ASSISTANCE

For technical assistance, call Abbott Technical Services at 1-800-553-7042 (within the US) or +49-6122-580 (outside the US), or visit the Abbott website at www.molecular.abbott.

Abbott Molecular Inc. is the legal manufacturer of the Alinity m CMV AMP Kit.

Abbott Molecular In .

Iai IL 60018 USA

53-608277/R1
May 2022

Abbott

Alinity m

CMV Application Specification File

en

IVD

REF 09N46-05A

53-608274/R1

Created March 2021

For detailed instructions or assay related information please refer to the corresponding Alinity m CMV AMP Kit (List No. 09N46-095) package insert.

INTENDED USE

The Alinity m CMV application specification is intended for use with the Alinity m CMV assay on the automated Alinity m System to allow for processing of assay calibrator, control, and patient samples.

Assay Specific Information	
Application Name	**Version**
CMV-PL-05A	1.00

Specimen Type	
Host Code	**Screen (Manual Order)**
PLAS	Plasma

Manual Dilution
1:2.5

Host Configuration	
Assay Name	**Assay Number**
CMV-PL	1052

The following are important facts to know about this application specification:

- **For In Vitro Diagnostic Use**
- The installation of the application specification file is to be performed by Abbott Molecular Field Service.
- Upon installation by an Abbott Field Service Representative, the Alinity m CMV application specification can be used for processing assay results. The Abbott Field Service Representative will ensure the application is properly installed and ready for processing assay results.
- Prior to processing results, refer to section 2 (Configure screen, Assay tab) of the Alinity m System Operations Manual for options for configuring your application specification. Refer to section 5 of the Alinity m System Operations Manual for ordering tests (Specimen and control orders) and reviewing results (Results screen).
- This application specification contains unique information for communicating with middleware or laboratory information systems. The unique identifier for the assay in this application specification is listed in the host configuration section of this package insert. Use this number when working with your middleware or laboratory information system provider.
- In the event that you experience error conditions during processing this application specification, refer to the Alinity m System Operations Manual for the corrective action associated with the specific message code identified.

KEY TO SYMBOLS USED

REF	Reference Number
IVD	In Vitro Diagnostic Medical Device
	Manufacturer

TECHNICAL ASSISTANCE

For technical assistance, call Abbott Molecular Technical Services at 1-800-553-7042 (within the US) or +49-6122-580 (outside the US), or visit the Abbott Molecular website at www.molecular.abbott/portal.

Abbott Molecular Inc. is the legal manufacturer of the Alinity m CMV Application Specification File.

Abbott Molecular Inc.
1300 East Touhy Avenue
Des Plaines, IL 60018 USA

53-608274/R1

(01)00884999049956(240)09N46-05A(8012)1.00

Abbott

Alinity m

CMV CAL Kit

en

REF 09N46-075
53-608275/R1

Created March 2021

℞ ONLY

REF 09N46-075

53-608275/R1

CUSTOMER SERVICE: 1-800-553-7042
CUSTOMER SERVICE INTERNATIONAL:
CALL YOUR ABBOTT REPRESENTATIVE

Instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from these instructions.

NAME

Alinity m CMV CAL Kit

INTENDED USE

The Alinity m CMV calibrators are for calibration for the Alinity m CMV assay on the automated Alinity m System when used for the quantitative determination of CMV DNA. The calibrators are intended to be used with the Alinity m CMV assay; refer to the assay package insert for additional information.

REAGENTS

Kit Contents

Alinity m CMV CAL A (List No. 9N46A) contains less than 0.01% noninfectious linearized CMV DNA plasmid in a buffer solution with carrier DNA.
Preservatives: Sodium azide and 0.087% ProClin® 950.
Alinity m CMV CAL B (List No. 9N46B) contains less than 0.01% noninfectious linearized CMV DNA plasmid in a buffer solution with carrier DNA.
Preservatives: Sodium azide and 0.087% ProClin 950.

Calibrator	Quantity
Alinity m CMV CAL A	4 tubes x 1.75 mL
Alinity m CMV CAL B	4 tubes x 1.75 mL

STANDARDIZATION

Concentrations were standardized against the 1st World Health Organization (WHO) International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques (NIBSC code: 09/162).

WARNINGS AND PRECAUTIONS

IVD

- **For In Vitro Diagnostic Use**

Safety Precautions

The following warnings and precautions apply to:
Alinity m CMV CAL A and Alinity m CMV CAL B.

WARNING	Contains 2-Methyl-4-isothiazolin-3-one and Sodium azide.
H317	May cause an allergic skin reaction.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P261	Avoid breathing mist / vapours / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

Important information regarding the safe handling, transport, and disposal of this product is contained in the Safety Data Sheet. Safety Data Sheets are available from your Abbott Representative.

For a detailed discussion of safety precautions during system operation, refer to the Alinity m System Operations Manual, Section 7 and Section 8.

Reagent Shipment

	Shipment Condition
Alinity m CMV CAL Kit	On dry ice

Reagent Storage

	Storage Temperature	Maximum Storage Time
Unopened	–25°C to –15°C	Until expiration date
Onboard	System Temperature	Discard after 4 hours

Reagent Handling

- Alinity m CMV calibrator reagents are contained in single-use tubes with pierceable caps. Avoid any contamination or damage to the caps after removal from the tube's original packaging. The Alinity m System will track onboard storage of the Alinity m assay calibrators. Onboard storage time begins when calibrator tubes are loaded on the Alinity m System. The Alinity m System will not allow the use of Alinity m assay calibrators that have exceeded the maximum onboard storage time.
- For a detailed discussion of handling calibrators during system operations, refer to the Alinity m System Operations Manual, Section 5.

Indications of Reagent Deterioration

- Deterioration of the reagents may be indicated when a calibration or control error occurs or controls are repeatedly out of the specified ranges.
- Reagents are shipped on dry ice and are stored at –25°C to –15°C upon arrival. If you receive reagents that are in a condition contrary to this recommendation, or that are damaged, immediately contact your Abbott Representative.
- For troubleshooting information, refer to the Alinity m System Operations Manual, Section 10.

PROCEDURE

Materials Provided

09N46-075 Alinity m CMV CAL Kit

Instructions for Use

For instructions on performing an assay calibration, refer to the Alinity m System Operations Manual, Section 6.

Lot-specific concentration values for assay calibrators are available via: Abbott Mail, the Abbott Molecular customer portal www.molecular.abbott/portal, and from your Abbott Representative.

When an assay calibration is performed:

- Lot-specific concentration values can be automatically imported to the Alinity m System via Abbott Mail upon scanning the calibrator tube barcodes (CMV CAL A and CMV CAL B).
- Lot-specific concentration values can also be obtained from the Abbott Molecular customer portal or provided by your Abbott Representative and imported to the Alinity m System via an USB drive. For instructions on creating a test order and loading calibrators on the instrument, refer to the Alinity m System Operations Manual, Section 5.

One Alinity m CMV CAL A tube and one Alinity m CMV CAL B tube from the Alinity m CMV CAL Kit are required for performing an assay calibration on the Alinity m System. The Alinity m System will process 3 replicates from each calibrator tube. The output data of the two calibrators will be used to generate a calibration curve. The calibrator tubes are intended for single-use only.

Abbott

- Thaw assay calibrators at 15°C to 30°C or at 2°C to 8°C.
- Once thawed, assay calibrators can be stored at 2°C to 8°C for up to 24 hours before use.
- This product may be used immediately after removal from 2°C to 8°C storage.
- Prior to loading on the Alinity m System, vortex each assay calibrator 3 times for 2 to 3 seconds. Ensure that the contents of each tube are at the bottom after vortexing by tapping the tubes on the bench to bring liquid to the bottom of the tube.
- Load the assay calibrators on to the Alinity m Universal Sample Rack.

QUALITY CONTROL PROCEDURES

Refer to the **QUALITY CONTROL PROCEDURES** section of the Alinity m CMV AMP Kit package insert.

KEY TO SYMBOLS

REF	Reference Number
IVD	In Vitro Diagnostic Medical Device
LOT	Lot Number
In Vitro Test	In Vitro Test
For In Vitro Diagnostic Use	For In Vitro Diagnostic Use
CAL A	Calibrator A
CAL B	Calibrator B
Rx ONLY	For Prescription Use Only
	Warning
	Consult Instructions for Use
	Temperature Limitation
	Use By
	Manufacturer

TECHNICAL ASSISTANCE

For technical assistance, call Abbott Molecular Technical Services at 1-800-553-7042 (within the US) or +49-6122-580 (outside the US), or visit the Abbott Molecular website at www.molecular.abbott/portal.

Abbott Molecular Inc. is the legal manufacturer of the Alinity m CMV CAL Kit.

Abbott Molecular Inc.
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Des Plaines, IL 60018 USA

53-608275/R1
March 2021

Alinity m

CMV CTRL Kit

en

REF 09N46-085

53-608276/R1

Rx ONLY

Created May 2021

REF 09N46-085

53-608276/R1

CUSTOMER SERVICE: 1-800-553-7042
CUSTOMER SERVICE INTERNATIONAL: CALL YOUR ABBOTT REPRESENTATIVE

Instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from these instructions.

NAME

Alinity m CMV CTRL Kit

INTENDED USE

The Alinity m CMV controls are for validity determination of the quantitative Alinity m CMV assay on the automated Alinity m System. These controls are intended to be used with the Alinity m CMV assay; refer to the assay package insert for additional information.

REAGENTS

Kit Contents

Alinity m CMV Negative CTRL (List No. 9N46Z) contains a buffer solution with carrier DNA.
Preservatives: Sodium azide and 0.087% ProClin® 950.
Alinity m CMV Low Positive CTRL (List No. 9N46W) contains inactivated CMV in human plasma. Human plasma was tested and found to be nonreactive for HBsAg, HIV-1 RNA, HCV RNA, HBV DNA, anti-HIV-1/ HIV-2, anti-HCV, HIV-1 antigen and Syphilis.
Preservatives: 0.1% ProClin 300 and 0.087% ProClin 950.
Alinity m CMV High Positive CTRL (List No. 9N46X) contains less than 0.01% noninfectious linearized CMV DNA plasmid in a buffer solution with carrier DNA.
Preservatives: Sodium azide and 0.087% ProClin 950.

Control	Quantity
Alinity m CMV Negative CTRL	12 tubes x 0.75 mL
Alinity m CMV Low Positive CTRL	12 tubes x 0.75 mL
Alinity m CMV High Positive CTRL	12 tubes x 0.75mL

STANDARDIZATION

Concentrations were standardized against the 1st World Health Organization (WHO) International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques (NIBSC code: 09/162).

WARNINGS AND PRECAUTIONS

IVD

- **For In Vitro Diagnostic Use**

Safety Precautions

The following warnings and precautions apply to:
Alinity m CMV Low Positive CTRL.

CAUTION: This preparation contains human-sourced and/or potentially infectious components. Refer to the **REAGENTS** section of this package insert. Components sourced from human blood have been tested and found to be non-reactive by appropriate FDA-licensed, approved, or cleared tests for antibody to HCV, antibody to HIV-1, antibody to HIV-2, HBsAg, HIV-1 antigen and Syphilis. The material is also tested and found to be negative by appropriate FDA-licensed, approved, or cleared PCR methods for HIV-1 RNA, HCV RNA, and HBV DNA. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. These reagents and human specimens should be handled as if infectious using safe laboratory procedures, such as those outlined in Biosafety in Microbiological and Biomedical Laboratories,[1] OSHA Standard on Bloodborne Pathogens,[2] CLSI Document M29-A4,[3] and other appropriate biosafety practices.[4] Therefore all human sourced materials should be considered infectious.

These precautions include, but are not limited to, the following:

- Wear gloves when handling specimens or reagents.
- Do not pipette by mouth.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in areas where these materials are handled.
- Clean and disinfect spills of specimens by including the use of a tuberculocidal disinfectant such as 1.0% sodium hypochlorite or other suitable disinfectant.[1]

Decontaminate and dispose of all potentially infectious materials in accordance with local, state and federal regulations.[4]

WARNING	Contains 2-Methyl-4-isothiazolin-3-one Reaction mass of: 5-chloro-2-methyl-4-isothiazolin-3-one (EC no. 247-500-7) and 2-methyl-2H-isothiazol-3-one (EC no. 220-239-6)(3:1); reaction mass of: 5-chloro-2-methyl-4-isothiazolin-3-one (EC no. 247-500-7) and 2-methyl-4-isothiazolin-3-one (EC no. 220-239-6)(3:1).
H317	May cause an allergic skin reaction.
H402[a]	Harmful to aquatic life.
H412	Harmful to aquatic life with long lasting effects.
Prevention	
P261	Avoid breathing mist / vapours / spray.
P272	Contaminated work clothing should not be allowed outof the workplace.
P273	Avoid release into environment.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to:
Alinity m CMV Negative CTRL and Alinity m CMV High Positive CTRL.

WARNING	Contains 2-Methyl-4-isothiazolin-3-one and Sodium azide.
H317	May cause an allergic skin reaction.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P261	Avoid breathing mist / vapours / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.

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Disposal	
P501	Dispose of contents / container in accordance with local regulations.

[a] Not applicable where regulation EU 1272/2008 (CLP) has been implemented.

Important information regarding the safe handling, transport and disposal of this product is contained in the Safety Data Sheet. Safety Data Sheets are available from your Abbott Representative.
For a detailed discussion of safety precautions during system operation, refer to the Alinity m System Operations Manual, Section 7 and Section 8.

Reagent Shipment

	Shipment Condition
Alinity m CMV CTRL Kit	On dry ice

Reagent Storage

	Storage Temperature	Maximum Storage Time
Unopened	–25°C to –15°C	Until expiration date
Onboard	System Temperature	Discard after 4 hours

Reagent Handling

- Alinity m CMV control reagents are contained in single-use tubes with pierceable caps. Avoid any contamination or damage to the caps after removal from the tube's original packaging. The Alinity m System will track onboard storage of the Alinty m assay controls. Onboard storage time begins when control tubes are loaded on the Alinity m System. The Alinity m System will not allow the use of Alinity m assay controls that have exceeded the maximum onboard storage time.
- For a detailed discussion of handling controls during system operations, refer to the Alinity m System Operations Manual, Section 5.

Indications of Reagent Deterioration

- Deterioration of the reagents may be indicated when a calibration or control error occurs or controls are repeatedly out of the specified ranges.
- Reagents are shipped on dry ice and are stored at –25°C to –15°C upon arrival. If you receive reagents that are in a condition contrary to this recommendation, or that are damaged, immediately contact your Abbott Representative.
- For troubleshooting information, refer to the Alinity m System Operations Manual, Section 10.

PROCEDURE

Materials Provided

09N46-085 Alinity m CMV CTRL Kit

Instructions for Use

Lot-specific concentration values for assay positive controls are available via: Abbott Mail, the Abbott Molecular customer portal www.molecular.abbott/portal, and from your Abbott Representative.

When a control test order is created:

- Lot-specific concentration values can be automatically imported to the Alinity m System via Abbott Mail upon scanning the control tube barcodes (CMV NEG CTRL, CMV LOW POS CTRL, and CMV HIGH POS CTRL).
- Lot-specific concentration values can also be obtained from the Abbott Molecular customer portal or provided by your Abbott Representative and imported to the Alinity m System via an USB drive.

For instructions on creating a test order and loading controls on the instrument, refer to the Alinity m System Operations Manual, Section 5.

The Alinity m CMV Negative CTRL, Alinity m CMV Low Positive CTRL, and Alinity m CMV High Positive CTRL tubes are intended for single use only.

- Thaw assay controls at 15°C to 30°C or at 2°C to 8°C.
- Once thawed, assay controls can be stored at 2°C to 8°Cfor up to 24 hours.
- This product may be used immediately after removal from 2°C to 8°C storage.
- Prior to loading on the Alinity m System, vortex each assay control 3 times for 2 to 3 seconds. Ensure that the contents of each tube are at the bottom after vortexing by tapping the tubes on the bench to bring liquid to the bottom of the tube.
- Load the assay controls on to the Alinity m Universal Sample Rack.

QUALITY CONTROL PROCEDURES

Refer to the **QUALITY CONTROL PROCEDURES** section of the Alinity m CMV AMP Kit package insert.

BIBLIOGRAPHY

1. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 6th ed. Washington, DC: US Government Printing Office; December 2020. [Also available online. Type> www.cdc.gov, search>BMBL>look up sections III and IV.]
2. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, *Bloodborne pathogens*.
3. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition*. CLSI Document M29-A4. Wayne, PA: CLSI; 2014.
4. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva, Switzerland: World Health Organization; 2004.

KEY TO SYMBOLS

REF	Reference Number
IVD	In Vitro Diagnostic Medical Device
LOT	Lot Number
In Vitro Test	In Vitro Test
For In Vitro Diagnostic Use	For In Vitro Diagnostic Use
CTRL –	Negative Control
CTRL +	Low Positive Control
CTRL ++	High Positive Control
Rx ONLY	For Prescription Use Only
	Warning
	Caution
	Consult Instructions for Use
	Temperature Limitation
	Use By
	Manufacturer

TECHNICAL ASSISTANCE

For technical assistance, call Abbott Molecular Technical Services at 1-800-553-7042 (within the US) or +49-6122-580 (outside the US), or visit the Abbott Molecular website at www.molecular.abbott/portal.

Abbott Molecular Inc. is the legal manufacturer of the Alinity m CMV CTRL Kit.

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