SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: CMV DNA Quanitative Assay

Device Trade Name: Abbott RealTi*m*e CMV

Device Procode: PAB

Applicant's Name and Address: Abbott Molecular, Inc.
1300 E. Touhy Ave.
Des Plaines, IL 60018

Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160044

Date of FDA Notice of Approval: May, 18, 2017

II. INDICATIONS FOR USE

Abbott RealTi*m*e CMV Assay:
The Abbott RealTi*m*e CMV test is an in vitro polymerase chain reaction (PCR) assay for the quantitation of cytomegalovirus (CMV) DNA in human EDTA plasma. The Abbott RealTi*m*e CMV test is intended for use as an aid in the management of Hematopoietic Stem Cell Transplant patients who are undergoing anti-cytomegalovirus therapy. In this population, serial DNA measurement can be used to assess virological response to anti-cytomegalovirus therapy. The results from the RealTi*m*e CMV test must be interpreted within the context of all relevant clinical and laboratory findings. The RealTi*m*e CMV test is not intended as a screening test for the presence of CMV DNA in blood or blood products.

Abbott RealTi*m*e CMV Control Kit:
The Abbott RealTi*m*e CMV controls are used to establish run validity of the Abbott RealTi*m*e CMV assay when used for the quantitation of cytomegalovirus (CMV) DNA in human plasma.

Abbott RealTi*m*e CMV Calibrator Kit:
The Abbott RealTi*m*e CMV calibrators are for calibration of the Abbott RealTi*m*e CMV assay when used for the quantitation of cytomegalovirus (CMV) DNA in human plasma.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Abbott RealTi*m*e CMV labeling.

V. DEVICE DESCRIPTION

The Abbott RealTi*m*e CMV assay uses the Abbott *m*2000*sp* for processing samples and the Abbott *m*2000*rt* instrument for amplification and detection. Specimens for the assay are loaded on the *m*2000*sp* instrument and DNA is isolated using the sample preparation reagents (the Abbott *m*Sample Preparation System$_{DNA}$) on board. Purified specimen nucleic acid and the CMV amplification/detection reagents are combined into a 96-well PCR tray by the *m*2000*sp*, and this tray is manually transferred to the *m*2000*rt* to perform amplification and real time fluorescence detection reaction. Patient results are automatically reported on the *m*2000*rt* workstation. A nucleic acid internal control (IC) is introduced into each specimen at the beginning of the sample preparation process and measured on the *m*2000*rt* to demonstrate that the process was completed correctly for each specimen and control and the samples are free of inhibition.

Sample preparation, extraction and concentration of nucleic acid is accomplished by the Abbott *m*2000*sp*, an automated sample preparation system which utilizes a magnetic microparticle process for the purification of nucleic acid from plasma samples. The *m*Sample Preparation System$_{DNA}$ (4 x 24 Preps) reagents lyse the virion, capture the nucleic acids on magnetic microparticles, and wash the particles to remove unbound sample components. Proteinase K is included in the lysis step for plasma samples to digest proteins associated with the sample. The nucleic acids are eluted from the magnetic microparticles and transferred to the Abbott 96-Deep-Well Plate. The nucleic acids are then ready for amplification. The IC is introduced into the sample preparation procedure and is processed along with the calibrators, controls, and specimens.

During the amplification/detection reaction on the Abbott *m*2000*rt* instrument, the target DNA is amplified by the DNA Polymerase in the presence of deoxynucleotide triphosphates (dNTPs) and magnesium. The amplification reagent contains specific sets of amplification primers for CMV and IC. During PCR amplification, high temperature is used to separate the strands of double-stranded DNA. When the reaction is cooled to a temperature where DNA annealing can again occur, the analyte-specific, single-stranded DNA oligonucleotide primers bind to the analyte DNA. The primers are extended by DNA Polymerase, thereby making an exact copy of a short target stretch of the analyte DNA. The DNA Polymerase is a thermophilic enzyme that has been modified in its active site by a molecule that renders it inactive. When the DNA Polymerase is heated prior to the initiation of PCR, the inhibitory molecule is cleaved from the DNA Polymerase allowing it to regain its activity. In this way, the DNA Polymerase is only active at temperatures where specific DNA-DNA interactions occur. This procedure greatly reduces non-specific PCR artifacts such as primer dimers.

During each round of thermal cycling, amplification products dissociate to single strands at high temperature, allowing primer annealing and extension as the temperature is lowered. Exponential amplification of the target is achieved through repeated cycling between high and

lower temperatures. Amplification of the CMV and IC targets takes place simultaneously in the same reaction.

The Abbott RealTi*m*e CMV assay targets 2 short sequences within the UL34 and UL80.5 genes of the CMV genome. The regions are specific for CMV and are highly conserved based on analysis of published CMV sequences. The IC target sequence is derived from the hydroxypyruvate reductase gene from the pumpkin plant *Cucurbita pepo*, and is provided as a linearized DNA plasmid in a buffer solution with carrier DNA.

During each round of PCR amplification, the fluorescent probes anneal to the amplified target DNA, if present. The probes are labeled with different fluorescent molecules, which allow CMV and IC to be distinguished from each other. The probes are single-stranded, linear DNA oligonucleotides modified with a fluorescent moiety covalently linked to one end of the probe and a quenching moiety to the other end. In the absence of target sequences, the probes adopt a conformation that brings the quencher close enough to the excited fluorophore to absorb its energy before it can be fluorescently emitted. When the probe binds to its complementary sequence in the target, the fluorophore and the quencher are held apart, allowing fluorescent emission and detection. Since this fluorescence occurs during every cycle, the PCR reaction can be read in real-time. The amplification cycle at which fluorescent signal is detected by the Abbott *m*2000*rt* is inversely proportional to the log of the CMV DNA concentration present in the original sample.

Application parameters specific to the Abbott RealTi*m*e CMV assay are contained in an assay specific application file, which is loaded on to an assay disc.

The optional amplification reagent extended use feature allows amplification reagent packs containing prepared master mix to be stored at – 20 ± 5°C, capped and protected from light, for up to 14 days before a second use. The internal control (IC) may be used again within 14 days if the vial remains capped at – 20 ± 5°C until the second use.

The Abbott RealTi*m*e CMV assay is comprised of three kits which are provided separately: Abbott RealTi*m*e CMV Amplification Reagent Kit, Abbott RealTi*m*e CMV Control Kit, and Abbott RealTi*m*e CMV Calibrator Kit.

Components of the Abbott RealTi*m*e CMV Amplification Reagent Kit:

- Abbott RealTi*m*e CMV Internal Control
- Abbott RealTi*m*e CMV Amplification Reagent Pack
  - DNA Polymerase
  - CMV Oligonucleotide Reagent
  - Activation Reagent

Components of the Abbott RealTi*m*e CMV Control Kit:

- Negative Control
- Low Positive Control
- High Positive Control

Components of the Abbott RealTi*m*e CMV Calibrator Kit:

- Calibrator A

- Calibrator B

Ancillary Reagents Required:

- *m*Sample Preparation System$_{DNA}$ reagents
  - Abbott *m*Lysis$_{DNA}$
  - Abbott *m*Wash 1$_{DNA}$
  - Abbott *m*Wash 2$_{DNA}$
  - Abbott *m*Elution Buffer$_{DNA}$
  - Abbott *m*Microparticles$_{DNA}$
- Proteinase K

Interpretation of Results:

The Abbott *m*2000*rt* system automatically determines the concentration of CMV DNA for specimens and controls by comparing the results to a calibration curve. CMV DNA concentrations are reported in IU/mL. The interpretation of results is provided in the table below:

Interpretation of Results

Result	Interpretation
Not detected	Target not detected
< 1.70 log IU/mL[a]	Detected[b]
1.70 to 8.19 log IU/mL	[c]
> 8.19 log IU/mL	> ULQ[d]

[a] 50 IU/mL

[b] Below LLOQ (lower limit of quantitation); CMV DNA is not quantifiable.

[c] Calcaluated results are within assay quantitation range. If calculated results are obtained, the interpretation field is left blank.

[d] Above ULOQ (upper limit of quantitation); if log IU/mL results are above the quantitation range of the assay, results are reported as ">8.19 log IU/mL"; if IU/mL results are above the quantitation range of the assay, results are reported as ">156,000,000 IU/mL."

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are currently two FDA approved in vitro diagnostic tests for the quantitation of CMV DNA. The patient's medical history and thorough clinical examination, in addition to serology, PCR or nucleic acid testing (NAT), will provide further information on the status of a CMV infection in the intended use population. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Abbott RealTi*m*e CMV assay was launched March 2011 outside of the United States. The Abbott RealTi*m*e CMV assay is distributed in the following countries:

Austria	Brazil	Costa Rica
Australia	Canada	Denmark
Bahrain	Chile	Egypt
Belarus	China	France
Belgium	Colombia	Germany

Hungary	Norway	Spain
India	Pakistan	Switzerland
Indonesia	Paraguay	Taiwan
Italy	Peru	Thailand
Kazakhstan	Philippines	Tunisia
Libya	Poland	Turkey
Luxembourg	Russia	United Arab
Macedonia	Saudi Arabia	Emerits
Mexico	Singapore	United Kingdom
Morocco	Slovakia	Vietnam
Netherlands	South Africa	
New Zealand	South Korea	

This product has not been withdrawn from the market from any country related to safety or effectiveness, or for any other reasons.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

The primary adverse events from use of the device are caused by an inaccurate measurement result of CMV viral load. Failure of the Abbott RealTi*m*e CMV assay to perform as indicated, or human error in the use of the test or the interpretation of the test result, may result in an incorrect test result that is too low or too high.

An erroneous low test result or a false negative result may lead to inappropriate patient management decisions, a premature discontinuation of antiviral therapy, or may instill a false sense of security in a patient or clinician. Similar assays that differ in LoD or other analytic characteristics may lead to different durations of treatment; theoretically a less sensitive assay could lead to earlier discontinuation of treatment relative to an alternative assay, with perhaps greater risk of relapse. Although clinical practice has evolved to recommend two consecutive “negative” responses as a treatment endpoint, this is based on different tests across different institutions. At the very low viral levels where differences between negative and positive assays appear, there may not be clinical repercussions from a patient ‘discontinued early’ from treatment.

An erroneous high test result, or a false positive result, may contribute to a change in therapy, unnecessary treatment, prolonged duration of therapy, or create anxiety in the patient. This may be mitigated by local practice; as experience with these assays evolves at local institutions, it is likely that low level positive results in the context of otherwise negative results will be recognized and that therapy would be unlikely to be unnecessarily prolonged.

The risk of these adverse events is readily mitigated in clinical practice by serial and/or repeat measurement as well as clinical evaluation, which would likely show symptomatic improvement.

To aid in the management of Hematopoietic Stem Cell Transplant patients who are undergoing anti-CMV drug therapy, the results from the Abbott RealTi*m*e CMV assay must be interpreted in the context of all relevant clinical and laboratory findings.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Limit of Detection (LoD):

The LoD was determined by testing dilutions of the WHO International Standard (IS) (genotype gB1), and strain AD169 (genotype gB2), in pooled CMV negative human plasma. Testing was performed with 4 lots of amplification reagents on 4 *m*2000 Systems. Testing with each lot was performed over 3 days. Each dilution was tested in replicates of 8 per day. The results obtained with the WHO IS are summarized in Table 1. Results for the AD169 strain are summarized in Table 2**.** The results support a claimed LoD of 31.20 IU/mL (1.49 $\log_{10}$ IU/mL) for the Abbott RealTi*m*e CMV assay.

Table 1. LoD Using the WHO IS, Genotype gB1

IU/mL	Number Tested	Number Detected	Percent Detected
46.80	96	96	100
31.20	96	95	99
23.40	96	93	97
15.60	96	91	95
12.48	96	91	95
9.36	96	83	86
7.80	96	86	90
6.24	96	66	69
3.90	96	52	54
1.56	96	24	25

Table 2 LoD Using Strain AD169, Genotype gB2.

IU/mL	Number Tested	Number Detected	Percent Detected
46.80	96	96	100
31.20	95	94	99
23.40	96	88	92
15.60	96	85	89
12.48	96	76	79
9.36	96	79	82
7.80	96	66	69

6.24	96	58	60
3.90	96	40	42
1.56	96	20	21

To confirm the ability of the Abbott RealTi*m*e CMV assay to meet the claimed LoD of 31.20 IU/mL (1.49 $\log_{10}$ IU/mL), the Toledo strain of CMV (genotype gB3) and a cultured clinical specimen of (genotype gB4) were each diluted to 31.20 IU/mL (1.49 $\log_{10}$ IU/mL) and tested with the Abbott RealTi*m*e CMV assay. For each strain, 2 independent dilutions were made in pooled CMV negative EDTA plasma. Two amplification reagent lots were used to test 30 replicates each for a total of 60 replicates per genotype. Testing used 2 *m*2000 Systems and was performed over 3 days with each lot. Results demonstrated that Abbott RealTi*m*e CMV assay can detect 31.20 IU/mL of CMV DNA with strains of genotypes gB3 and gB4. Results are summarized in Table 3. The results support a claimed LoD of 31.20 IU/mL (1.49 log IU/mL) for the Abbott RealTi*m*e CMV assay.

Table 3 LoD Confirmation, Using Genotype gB3 and gB4.

CMV Genotype	IU/mL	Number Tested	Number Detected	Percent Detected
gB3	31.20	60	58	97
gB4	31.20	60	60	100

The claimed LoD of 31.20 IU/mL was also confirmed with anti-viral resistant clinical specimens. Two anti-viral resistant clinical specimens were diluted to 31.20 IU/mL (1.49 $\log_{10}$ IU/mL) and tested with the Abbott RealTi*m*e CMV assay. For each strain, 2 independent dilutions were made in pooled CMV negative EDTA plasma. Two amplification reagent lots were used to test 30 replicates each for a total of 60 replicates per specimen. Testing used 2 *m*2000 Systems and was performed over 3 days with each lot. Results demonstrated that Abbott RealTi*m*e CMV assay can detect 31.20 IU/mL of CMV DNA with anti-viral resistant specimens. Results are summarized in Table 4.

Table 4. LoD Confirmation Using Anti-Viral Resistant Specimens

Anti-Viral Resistant Specimen	IU/mL	Number Tested	Number Detected	Percent Detected
1	31.20	60	58	97
2	31.20	60	60	100

Traceability to the 1st WHO International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques (NIBSC code:09/162):

The Abbott RealTi*m*e CMV assay is standardized to the 1st WHO International Standard for Human Cytomegalovirus for Nucleic Acid Amplification Techniques (NIBSC code: 09/162). Abbott RealTi*m*e CMV Calibrators trace to the WHO International Standard (IS)

each time a lot is manufactured by means of value assignment using Abbott CMV Primary Calibrators.

Conversion factors were determined by diluting the CMV WHO IS to approximately 5 $\log_{10}$ IU/mL in pooled, normal EDTA plasma and testing against the Abbott CMV Primary Calibrators. The conversion factors were confirmed using the CMV WHO IS diluted to approximately 3.5 $\log_{10}$ IU/mL.

The mathematical relationship between $\log_{10}$ copies/mL and $\log_{10}$ IU/mL is $\log_{10}$ copies/mL + 0.19 = $\log_{10}$ IU/mL. The mathematical relationship between copies/mL and IU/mL is copies/mL × 1.56 = IU/mL.

Limit of Blank and Performance With Negative Specimens:

A total of 100 anti-CMV IgG negative specimens were tested with the Abbott RealTi*m*e CMV assay. Two amplification reagent lots were used to test 50 specimens each. Testing was performed on 2 Abbott RealTi*m*e *m*2000 Systems and each lot was used in 2 independent runs testing 25 specimens. All specimens had reported results of "Not detected". The specificity was 100% (100/100; 95% CI of 96.3 to 100.0 %). The percent of false positives was 0% (0/100). The Limit of Blank (LoB) for the Abbott RealTi*m*e CMV assay is confirmed to be 0 IU/mL.

Linear Range:

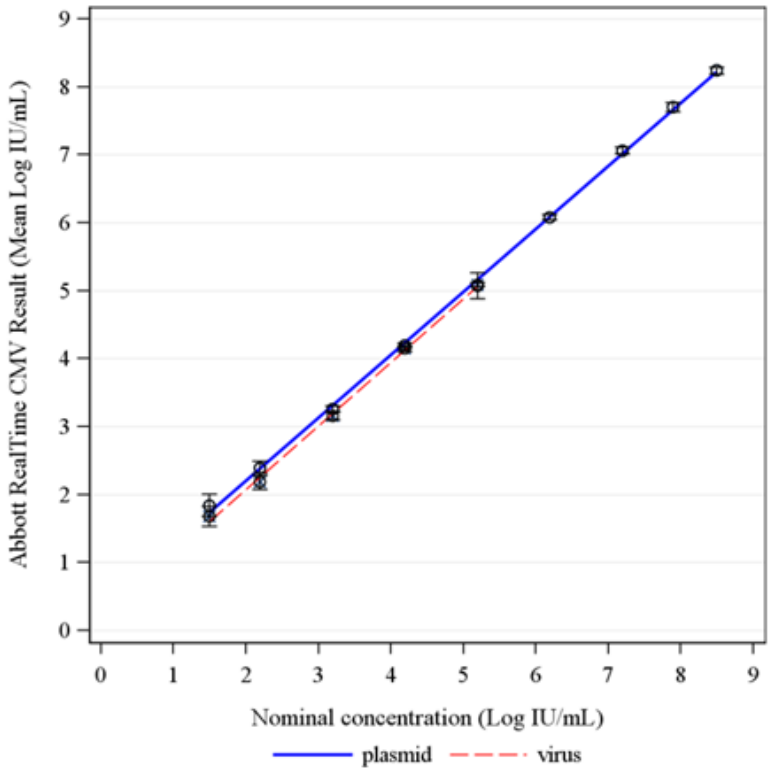
The upper limit of linearity of the Abbott RealTi*m*e CMV assay for plasma specimens is 8.19 $\log_{10}$ IU/mL (156 million IU/mL) and the lower limit of linearity is 1.70 $\log_{10}$ IU/mL (50 IU/mL).

The linear range for genotypes gB1 to gB4 was determined using 2 panels per genotype. The 9-member plasmid panels were prepared by diluting CMV DNA to concentrations ranging from 1.49 to 8.49 $\log_{10}$ IU/mL in pooled CMV negative human plasma. The 5-member virus panels were made using cultured virus strains of genotypes gB1 to gB4 diluted in pooled CMV negative human plasma. The concentrations ranged from 1.49 to 5.19 $\log_{10}$ IU/mL for genotypes gB1, gB2, and gB4 and 1.46 to 5.00 $\log_{10}$ IU/mL for gB3. Testing was performed with a single lot of amplification reagents for 3 days with 4 replicates per day for a total of 12 replicates per panel member.

The deviation from linearity, defined as the difference between values predicted using a linear model vs the best fit polynomial model, was ≤ 0.10 $\log_{10}$ IU/mL for all panel members of genotypes gB1 to gB4.

Figure 1

Abbott RealTi*me* CMV Assay Linearity using CMV genotype gB2 strain AD169.

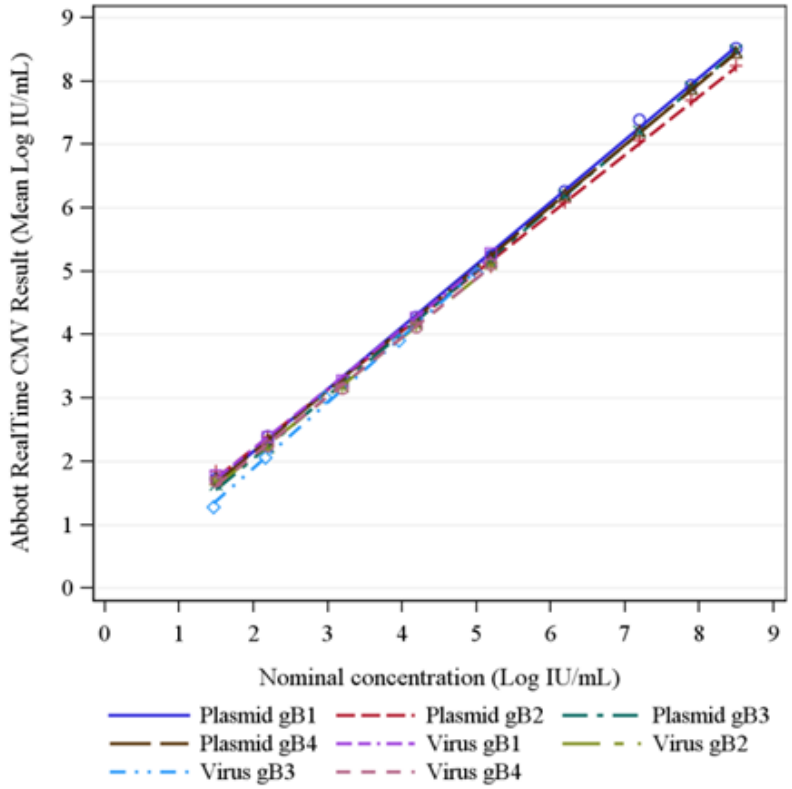


Note: Error Bars represent ± 1 SD of the mean

Sample Size (n)		107
Correlation Coefficient (r)		0.999
Slope		0.93
95% CI for slope		(0.92, 0.93)
Intercept		0.36
95% CI for intercept		(0.31, 0.41)
Target Concentration (Log IU/mL)	Min 1.49	Max 8.49
Abbott Real Time CMV (Log IU/mL)	Min 1.47	Max 8.30

Figure 2

Abbott RealTi*m*e CMV Assay Linearity by Genotype



The Abbott RealTi*m*e CMV assay was shown to be linear across the range of CMV concentrations tested. See Table 5 for linear equations**.**

Table 5. Linear Equations for CMV Genotypes gB1 to gB4

CMV Genotype	Plasmid Panel	Virus Panel
gB1	y = 0.9821x + 0.1991	y = 0.9485x + 0.3143
gB2	y = 0.9257x + 0.3627	y = 0.9356x + 0.2144
gB3	y = 0.9872x+0.0833	y = 1.0367x - 0.1767
gB4	y = 0.9689x + 0.2178	y = 0.9305x + 0.2382

Lower Limit of Quantitation:

The claimed lower limit of quantitation (LLoQ) for the Abbott RealTi*m*e CMV assay is 50 IU/mL (1.70 $\log_{10}$ IU/mL).

The total analytical error (TAE) was calculated using estimates determined through analysis of data from limit of detection (LoD) and precision studies. These studies included all four genotypes of CMV.

TAE was estimated by 2 different methods: |Bias| + (2 × SD) and SQRT (2) × 2 × SD. The TAE estimates for panel members that had an observed concentration at or near the claimed assay limit of detection (1.49 $\log_{10}$ IU/mL) were evaluated.

For CMV genotypes gB1 to gB4, the TAE analyses demonstrated that the Abbott RealTi*m*e CMV assay can determine CMV DNA concentration of 31.20 IU/mL (1.49 $\log_{10}$ IU/mL) in plasma with an acceptable level of accuracy (TAE ≤ 1.00 $\log_{10}$ IU/mL). The absolute value of the bias plus two SDs (TAE) ≤ 1.00 $\log_{10}$ IU/mL ensures that, for samples with a true value equal to the LLoQ, there is 95% or greater probability that the measured value will be within 1 $\log_{10}$ IU/mL of the true value. The square root of two times two SDs ≤ 1.00 $\log_{10}$ IU/mL ensures that, for samples with a true value equal to the LLoQ, the difference between two measurements of more than 1 $\log_{10}$ IU/mL is statistically significant. Table 6 shows the TAE analyses for the lowest concentration that meets both TAE acceptance criteria for genotypes gB1 to gB4, anti-viral resistant, and clinical strains. Across all strains, the lowest concentration that met TAE acceptance criteria across all CMV genotypes and clinical strains was 46.80 IU/mL (1.67 $\log_{10}$ IU/mL). The results support a claimed LLOQ of 50 IU/mL (1.70 $\log_{10}$ IU/mL).

Table 6. Lower Limit of Quantitation for CMV Genotypes gB1 to gB4, anti-viral resistant, and clinical strains

CMV strain	**Nominal Concentration IU/mL**	**Nominal Concentration $\log_{10}$ IU/mL**	**n**	**Mean ($\log_{10}$ IU/mL)**	**SD ($\log_{10}$ IU/mL)**	**Bias ($\log_{10}$ IU/mL)**	**TAE = |Bias| + (2×SD) ($\log_{10}$ IU/mL)**	**TAE = SQRT(2) ×2×SD ($\log_{10}$ IU/mL)**
gB1	31.20	1.49	95	1.81	0.20	0.32	0.72	0.57
gB2	31.20	1.49	94	1.52	0.28	0.03	0.59	0.79
gB3	31.20	1.49	58	1.60	0.33	0.11	0.77	0.93
gB4	31.20	1.49	60	1.72	0.24	0.23	0.71	0.68
CMV Anti-Viral Resistant Strain 1	46.80	1.67	60	1.79	0.16	0.12	0.44	0.45

Table 6. Lower Limit of Quantitation for CMV Genotypes gB1 to gB4, anti-viral resistant, and clinical strains								
CMV strain	**Nominal Concentration IU/mL**	**Nominal Concentration Log_{10} IU/mL**	**n**	**Mean (Log_{10} IU/mL)**	**SD (Log_{10} IU/mL)**	**Bias (Log_{10} IU/mL)**	**TAE = |Bias| + (2×SD) (Log_{10} IU/mL)**	**TAE = SQRT(2) ×2×SD (Log_{10} IU/mL)**
CMV Anti-Viral Resistant Strain 2	31.20	1.49	60	1.77	0.24	0.28	0.76	0.68
Clinical Strain	31	1.49	78	1.43	0.33	–0.06	0.72	0.93
Clinical Strain	31	1.49	119	1.68	0.24	0.19	0.67	0.68

In addition, the claimed LLoD of 31.20 IU/mL was verified using a CMV anti-viral resistant strain.

Precision – Within Laboratory:

The precision of the Abbott RealTime CMV assay was evaluated with a 10-member panel with CMV DNA concentrations that spanned 12.48 IU/mL to 312,000,000 IU/mL. Four replicates of each panel member were tested per run with 1 run per day on each lot/instrument pair for 5 days, for a total of 15 runs and 60 replicates per panel member. Table 7 presents the precision assay results, between runs, within runs, inter-assay, between lot, and overall.

Table 7: RealTime CMV Precision (Log IU/mL)

				Within-run component		**Between-run component**		**Inter-assay**		**Between-lot/ instrument component**		**Total**	
panel	n	Target Concen-tration (Log IU/mL)	Mean Concen-tration (Log IU/mL)	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	40[b]	1.11[e]	1.23	0.232	18.9	0.055	4.5	0.239	19.4	0.00	0.0	0.239	19.4
2	53[c]	1.41[e]	1.41	0.269	19.1	0.173	12.3	0.320	22.7	0.00	0.0	0.320	22.7
3	60	2.11	1.99	0.134	6.7	0.020	1.0	0.136	6.8	0.024	1.2	0.138	6.9
4	60	3.11	2.92	0.058	2.0	0.067	2.3	0.088	3.0	0.024	0.8	0.092	3.1
5	60	4.11	3.83	0.053	1.4	0.035	0.9	0.063	1.7	0.011	0.3	0.064	1.7
6	60	5.11	4.83	0.046	1.0	0.042	0.9	0.062	1.3	0.065	1.4	0.090	1.9

7	60	6.11	6.07	0.036	0.6	0.017	0.3	0.039	0.6	0.052	0.9	0.065	1.1
8	60	7.19	7.08	0.050	0.7	0.028	0.4	0.057	0.8	0.054	0.8	0.079	1.1
9	59[d]	7.89[d]	7.77	0.036	0.5	0.026	0.3	0.044	0.6	0.079	1.0	0.091	1.2
10	59[d]	8.49[d]	8.26	0.042	0.5	0.020	0.2	0.047	0.6	0.079	0.9	0.091	1.1

[a] Between-run (total inter-assay SD) contains the within-run and between-run components

[b] CMV DNA was not detected in 20 replicates

[c] CMV DNA was not detected in 6 replicates. One replciate was identified as an outlier and was excluded.

[d] One replicate did not generate a result due to instrument error.

[e] The target value for the panel members falls below the claimed LOD, which is 50 IU/mL (1.70 log IU/mL).

Reproducibility (Multi-Site):

Clinical reproducibility and precision were evaluated in a multi-center study that included 3 external sites that used the Abbott RealTi*m*e CMV assay to test an 8 member panel spanning a targeted range from 1.19 to 8.49 $\log_{10}$ IU/mL. The panel was made with CMV positive clinical specimens, cultured strain AD169 or plasmid DNA diluted in pooled plasma. Each panel member was repeated 4 times within the panel. Testing was performed with 3 lots of the Abbott RealTi*m*e CMV Amplification Reagent Kit and Sample Preparation DNA System Kit. Each of the 3 clinical sites tested 2 of the 3 amplification reagent lots and sample preparation reagent lots for 5 non-consecutive days each, resulting in a total of 10 runs at each site. Results are summarized in Table 8.

Table 8. Clinical Reproducibility Precision

				Within-run Component		**Between-run Component**		**Between-lot Component**		**Between-site Component**		**Total[g]**	
Panel Member	**Source**	**n**	**Mean Log_{10} IU/mL**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**
1	Plasmid	120	8.34	0.17	2.0	0.07	0.8	0.16	1.9	0.10	1.1	0.26	3.1
2	Plasmid	120	6.70	0.13	1.9	0.04	0.6	0.08	1.2	0.17	2.5	0.23	3.4
3	Cultured Virus	120	5.29	0.12	2.3	0.04	0.7	0.05	1.0	0.19	3.6	0.23	4.4
4	Cultured Virus	120	3.94	0.14	3.5	0.05	1.4	0.06	1.5	0.19	4.7	0.24	6.2
5	Cultured Virus	119[b]	3.06	0.15	4.9	0.05	1.6	0.04	1.2	0.15	4.9	0.22	7.2

Table 8. Clinical Reproducibility Precision

				Within-run Component		Between-run Component		Between-lot Component		Between-site Component		Total[g]	
Panel Member	**Source**	**n**	**Mean Log_{10} IU/mL**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**
6	Clinical Specimen	119[c]	2.26	0.12	5.4	0.05	2.3	0.03	1.2	0.13	5.8	0.19	8.3
7	Clinical Specimen	119[d]	1.68[f]	0.21	12.8	0.10	6.0	0.04	2.5	0.13	8.0	0.27	16.4
8	Clinical Specimen	101[e]	1.43[f]	0.26	18.5	0.00	0.0	0.06	4.3	0.14	9.5	0.30	21.2

[a] Standard deviations (SD) are in log_{10} IU/mL.
[b] A result was not generated for one replicate due to a missing sample.
[c] One replicate was excluded from the analysis due to technician error.
[d] CMV DNA was not detected in one replicate.
[e] CMV DNA was not detected in 19 replicates.
[f] The mean concentration is below the claimed assay LLoQ (1.70 log_{10} IU/mL).
[g] Total variability includes within-run, between-run, between-lot, and between-site variability.

In addition, operator-to-operator precision of the Abbott RealTi*m*e CMV assay was evaluated by testing the same 8 member panel. One lot of amplification reagents was run on 1 *m*2000*sp* and *m*2000*rt* instrument pair by 3 operators. Each operator completed 1 run per day for 7 days, for a total of 21 runs. Four replicates were tested for each panel member in each run.

Table 9. Operator-to-Operator Precision

				Within-run Component		Between-run Component		Between-operator Component		Total[f]	
Panel Member	**Source**	**n**	**Mean Log_{10} IU/mL**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**
1	Plasmid	84	8.24	0.13	1.6	0.06	0.7	0.12	1.4	0.18	2.2
2	Plasmid	84	6.62	0.14	2.1	0.03	0.5	0.07	1.0	0.16	2.4
3	Cultured Virus	83[b]	5.17	0.12	2.4	0.08	1.6	0.10	1.9	0.18	3.5
4	Cultured Virus	84	3.83	0.11	2.9	0.09	2.4	0.10	2.7	0.18	4.6

Table 9. Operator-to-Operator Precision											
				Within-run Component		**Between-run Component**		**Between-operator Component**		**Total[f]**	
Panel Member	**Source**	**n**	**Mean Log_{10} IU/mL**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**	**SD[a]**	**% CV**
5	Cultured Virus	83[b]	2.96	0.10	3.4	0.10	3.3	0.11	3.7	0.18	6.0
6	Clinical Specimen	84	2.10	0.11	5.4	0.05	2.5	0.11	5.4	0.17	8.0
7	Clinical Specimen	78[c]	1.43[e]	0.33	23.2	0.00	0.0	0.11	7.7	0.35	24.4
8	Clinical Specimen	70[d]	1.28[e]	0.32	24.7	0.05	3.7	0.04	2.8	0.32	25.1

[a]Standard deviations (SD) are in log^{10} IU/mL.
[b] A result was not generated for one replicate due to an instrument error.
[c] CMV DNA was not detected in 6 replicates.
[d] CMV DNA was not detected in 14 replicates.
[e]The mean concentration is below the claimed assay LLoQ (1.70 log^{10} IU/mL).
[f] Total variability includes within-run, between-run, and between-operator variability.

Analytical Specificity – Cross Reactivity:

The following microorganisms (viruses, bacteria and fungi) were evaluated for potential cross-reactivity in the Abbott RealTi*m*e CMV assay. Each microorganism was added to CMV DNA negative plasma samples and plasma samples containing approximately 100 IU/mL and 3,120 IU/mL of CMV DNA. Microorganisms were tested at 10^5 - 10^6 copies/mL, IU/mL, viral particles/mL, cells/mL, $TCID_{50}$/mL, IFU/mL, or CFU/mL. No interference in the performance of the Abbott RealTi*m*e CMV assay was observed in the presence of the potential cross-reactants for all positive and negative samples tested.

Microorganisms Used for Potential Cross-reactivity Study	
Human Immunodeficiency Virus 1	Human Papillomavirus 18
Human Immunodeficiency Virus 2	Adenovirus
Human T lymphotropic virus type I	Parvovirus B19
Hepatitis A Virus	JC Polyomavirus
Hepatitis B virus	*Neisseria gonorrhoeae*
Hepatitis C Virus	*Chlamydia trachomatis*
Epstein-Barr Virus	*Staphylococcus aureus*

Microorganisms Used for Potential Cross-reactivity Study	
Herpes simplex virus type 1	*Staphylococcus epidermidis*
Herpes simplex virus type 2	*Mycobacterium gordonae*
Human herpesvirus 6	*Mycobacterium smegmatis*
Human herpesvirus 7	*Propionibacterium acnes*
Human herpesvirus 8	*Streptococcus pneumonia*
Varicella-Zoster virus	*Salmonella typhi*
Vaccinia Virus	*Aspergillus niger*
BK Polyomavirus	*Candida albicans*
Human Papillomavirus 16	*Cryptococcus neoformans*

Analytical Specificity - Interfering Substances:

The susceptibility of the Abbott RealTi*m*e CMV assay to interference by elevated levels of potentially interfering substances was evaluated. Ten Anti-CMV IgG negative plasma samples and plasma samples containing approximately 100 IU/mL and 3,120 IU/mL of CMV DNA were spiked with high levels of hemoglobin, bilirubin, protein, lipids, or genomic DNA and tested. No interference in the performance of the Abbott RealTi*m*e CMV assay was observed in the presence of the following endogenous substances for all CMV positive and negative samples tested:

- Hemoglobin 2 g/L
- Bilirubin 342 µM
- Protein 120 g/L
- Lipid 37 mM
- Genomic DNA 350 µg/dL

Forty-four therapeutic drugs were tested in 9 pools, and individually for 13 drugs. CMV DNA negative plasma samples and plasma samples containing approximately 100 IU/mL and 3,120 IU/mL of CMV DNA were spiked with the drugs. No interference in the performance of the Abbott RealTi*m*e CMV assay was observed in the presence of the following drugs and drug pools in excess of peak plasma or serum levels, or in excess of therapeutic dose when peak plasma or serum levels were not available.

Drug Pool	**Drugs Tested**
1	zidovudine, saquinavir, ritonavir, clarithromycin, interferon 2b
2	abacavir sulfate, amprenavir, peginterferon 2a, peginterferon 2b,[a] ribavirin
3	tenofovir disoproxil fumarate, lamivudine, indinavir sulfate, ganciclovir, valganciclovir hydrochloride, acyclovir
4	stavudine, efavirenz, lopinavir, enfuvirtide, ciprofloxacin

Drug Pool	Drugs Tested
5	nevirapine, nelfinavir, azithromycin, valacyclovir
6	adefovir, didanosine, entecavir, cidofovir, mycophenolate mofetil
7	famotidine, cyclosporine
8	prednisone, sirolimus, tacrolimus, azathioprine
9	atenolol, amlodipine besylate, lisinopril, rabeprazole, valsartan

[a] Peginterferon 2b was not tested with the 100 IU/mL sample.

Note: A consideration was made to avoid combining specific drugs within a pool that would not be used together in a clinical setting. For drug interference evaluated using drug pools, effects of individual drug were not assessed with the exception of the 13 drugs that were tested individually.

Drugs Tested Individually

lymphocyte immune globulin
cyclosporine
tacrolimus
mycophenolate mofetil
azathioprine
ganciclovir
valganciclovir
foscarnet
everolimus
adefovir*
didanosine*
entecavir*
cidofovir*

*These drugs were tested individually with CMV positive samples at 100 IU/mL.

The susceptibility of the Abbott RealTi*m*e CMV assay to interference by autoimmune disease states was evaluated. Plasma from 10 patients each with Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), and Anti-nuclear antibodies (ANA) were tested. Each sample was tested unspiked and spiked with CMV virus to approximately 100 IU/mL and 3,120 IU/mL. Results showed that these autoimmune disease states do not interfere with the Abbott RealTi*m*e CMV assay.

Specimen Stability:

The stability of CMV DNA in specimens processed from whole blood and stored under various conditions was evaluated. Whole blood samples from 10 unique donors were spiked with CMV from clinical specimens at a target concentration of 3.49 $\log_{10}$ IU/mL (3.3 $\log_{10}$ copies/mL).

The storage conditions are shown in the following flow diagram. A portion of each whole blood sample was processed to obtain EDTA plasma and tested the same day as the blood was collected for a baseline quantitation (Test 1). The remainder of the spiked whole blood was stored at 30ºC for 25 hours before being processed to plasma. After plasma processing, one aliquot for each of the ten donors was tested the same day as processing (Test 2); the remainder was stored at 30ºC for 25 hours at which time one aliquot from each donor was tested (Test 3). The remaining aliquots of plasma were stored either at 2-8ºC for 137 h (approximately 5.7 days, Test 4) or -70ºC or colder for a total of 1,319 hours (approximately 55 days, Test 5), including 5 rounds of freeze / thaw prior to testing.

The quantitation of CMV in the stored samples was compared to the baseline (Test 1) as an indicator of sample storage stability.

Sample Storage and Processing Conditions

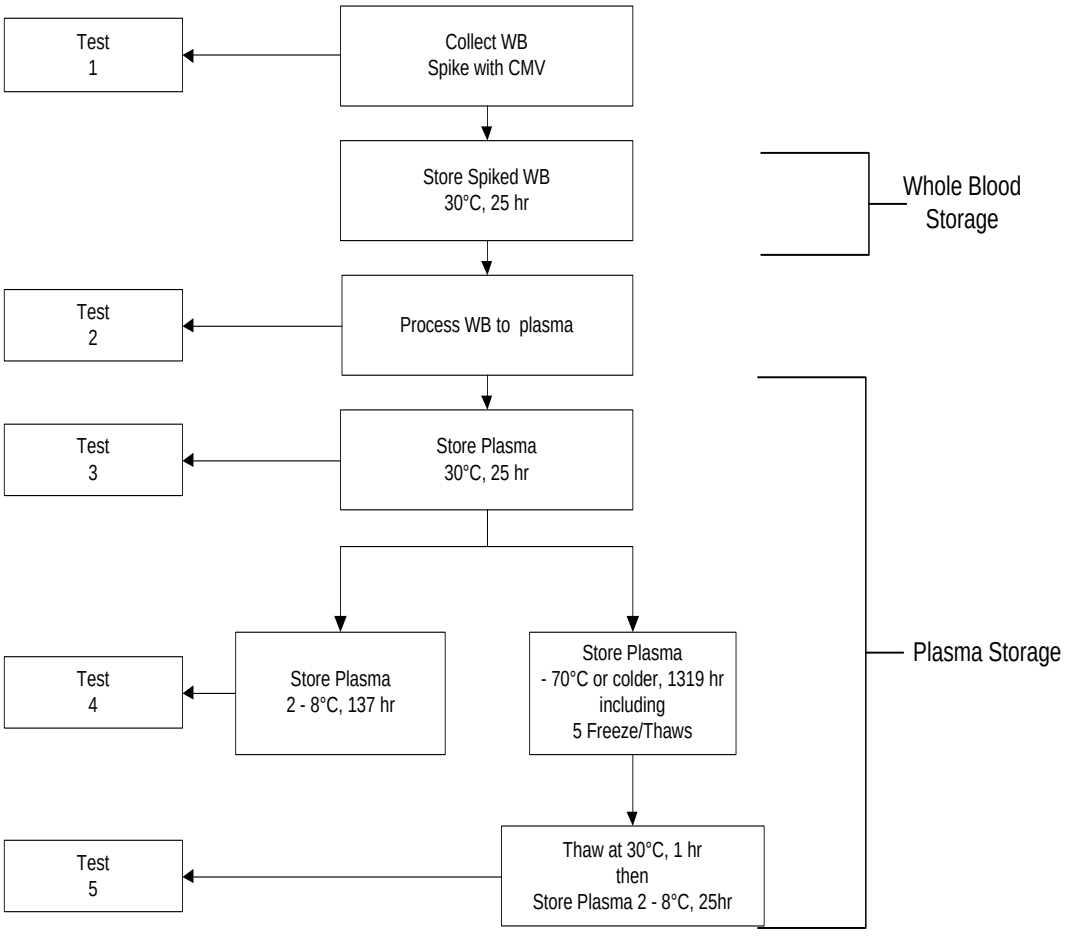


Table 10. Specimen Stability Study Results									
	Baseline Condition (Test 1)			**Storage Condition**					
Condition	**n**	**Mean Log_{10} IU/mL**	**SD**	**n**	**Mean Log_{10} IU/mL**	**SD**	**Mean Difference (Storage-Baseline) Log_{10} IU/mL**	**Pooled SD**	**95% CI Mean Difference**
Test 2	40	3.31	0.078	40	3.27	0.102	-0.04	0.091	(-0.09, -0.00)
Test 3	40	3.31	0.078	40	3.23	0.113	-0.08	0.097	(-0.12, -0.04)
Test 4	40	3.31	0.078	40	3.26	0.102	-0.05	0.091	(-0.09, -0.01)
Test 5	40	3.31	0.078	39	3.28	0.113	-0.03	0.097	(-0.07, 0.01)

The results support the specimen storage claims stated in the assay package insert:
Prior to preparing plasma specimens through centrifugation, freshly drawn whole blood specimens may be held at 2 to 30ºC for up to 24 hours. After centrifugation, remove plasma from cells. Plasma specimens may be stored:

- *At 15 to 30°C for up to 24 hours*
- *At 2 to 8°C for up to 5 days*
- *At – 70°C or colder for longer term*
- *Multiple freeze/thaw cycles should be avoided and should not exceed 3 freeze/thaw cycles. Thaw plasma specimens at 15 to 30°C or at 2 to 8°C. Once thawed, if plasma specimens are not being processed immediately, they can be stored at 2 to 8°C for up to 24 hours.*

Analytical Carryover:

Potential sample carryover in the automated Abbott *m*2000 instrument was determined by testing 218 high concentration CMV positive plasma samples interspersed with 220 negative samples arranged in a checkerboard pattern. The positive samples were spiked with CMV DNA at a target concentration of 15.6 million IU/mL. The carryover rate is defined as the number of CMV negative samples that report a value greater than the assay LoD over the total number of CMV negative samples tested. A total of 5 runs were evaluated. The carryover rate was 0.0% (0/220).

X. SUMMARY OF PRIMARY CLINICAL STUDY:

The clinical utility of the Abbott RealTi*m*e CMV assay was evaluated in a prospective, multicenter trial of subjects undergoing allogenic, hematopoietic stem cell transplantation (HCT).

Study Design

All enrolled study subjects were CMV-seropositive. The Abbott RealTi*m*e CMV assay was used for CMV plasma viral load measurement by the central laboratories in the study. Plasma CMV viral load levels were monitored in subjects according to the following schedule: weekly during days 0 through 100 post-transplant, every other week during days 101 through 180, every 30 days during days 181 through 365. Once a subject commenced CMV-specific antiviral treatment (CMV AVT), plasma viral load testing occurred on a weekly basis until CMV AVT was discontinued; at which point regularly scheduled viral load assessments resumed.

The date and time of initiation and discontinuation of CMV AVT was recorded and CMV viral level in close proximity was used to establish beginning of therapy (BOT) and end of therapy (EOT) viral load levels, respectively. Viral load levels to define baseline were obtained within 0 to + 14 days of transplantation, while BOT viral load levels were collected – 7 to + 2 days of initiation of CMV AVT. EOT was defined as immediately following discontinuation of CMV AVT. If there were multiple viral load measurements within the window, the one closest to the baseline, BOT, or EOT date was chosen.

Data from 93 subjects were analyzed. Of the 93 subjects, 64 were treated with CMV AVT. The remaining 29 subjects received AVT that was not specific for CMV infection (non-CMV AVT). The demographics and ages of the CMV AVT and non-CMV AVT subjects included in the analyses are shown in Table 11 andTable 12, respectively. The mean age for the 93 subjects included in the analysis was 52 years with a range of 21 to 72 years.

Table 11. Summary of Demographics

		CMV AVT Subjects (n=64)	**Non-CMV AVT Subjects (n=29)**	**Total Subjects (n=93)**
	Category	**n (%)**	**n (%)**	**n (%)**
Gender	Female	29 (45.3%)	13 (44.8%)	42 (45.2%)
	Male	35 (54.7%)	16 (55.2%)	51 (54.8%)
Race	Asian	10 (15.6%)	2 (6.9%)	12 (12.9%)
	Black or African American	0 (0.0%)	1 (3.4%)	1 (1.1%)
	White	54 (84.4%)	26 (89.7%)	80 (86.0%)

Ethnicity	Hispanic or Latino	2 (3.1%)	1 (3.4%)	3 (3.2%)
	Not Hispanic or Latino	62 (96.9%)	28 (96.6%)	90 (96.8%)

Table 12. Summary of Age (Years)

		CMV AVT Subjects	**Non-CMV AVT Subjects**	**Total Subjects**
	Category	**(n=64)**	**(n=29)**	**(n=93)**
Age	Mean Years (SD)	53 (12)	51 (13)	52 (13)
	Range (min, max)	(21, 72)	(25, 72)	(21, 72)

The mean number and range of CMV viral load measurements for the 93 subjects included in the analyses are shown in Table 13.

Table 13 Mean and Range of the Number of Viral Load Measurements

Status	**Subjects**	**Mean**	**Range**
CMV AVT	64	25.0	6, 56
Non-CMV AVT	29	23.6	3, 38
All Subjects	93	24.6	3, 56

The mean and duration of the first course of therapy for 63 of the CMV AVT subjects is shown in Table 14. The first course of CMV AVT is defined as the earliest CMV AVT start date and end date for CMV AVT subjects.

Table14. Mean and Range of the Duration of First Course of CMV AVT (Days)

Subjects[a]	**Mean (Days)**	**Range**
63	28.6	1, 123

[a]One subject was excluded; the CMV AVT end date was not provided.

A summary of the CMV specific drugs used for treating the subjects for their first course of CMV AVT are shown in Table 15. Ganciclovir, Valganciclovir Hydrochloride, and

Valganciclovir were the most commonly used CMV AVT drugs for the subjects' first CMV AVT.

Table 15. Summary of Drugs Used for First CMV AVT

Drug Name	Total Number of Subjects with CMV AVT	Number of Subjects Receiving the Drug	Percentage of Subjects Receiving the Drug (%)
Ganciclovir	64	31	48.4 (31/64)
Ganciclovir Sodium	64	2	3.1 (2/64)
Valganciclovir Hydrochloride	64	29	45.3 (29/64)
Valganciclovir	64	17	26.6 (17/64)
Foscarnet Sodium	64	3	4.7 (3/64)
Foscarnet	64	2	3.1 (2/64)
Immunoglobulin Cytomegalovirus	64	3	4.7 (3/64)

Comparison of viral loads at BOT versus baseline and peak versus EOT are shown in Table 16 for CMV AVT subjects. 62 CMV AVT subjects were included in this analysis. Measurements for 58 CMV AVT subjects fell within the time window for baseline and BOT. Measurements for 61 CMV AVT subjects fell within the time window for EOT. The mean difference in viral load between the BOT and baseline for 58 subjects for whom results were available at both time points was 2.62 $\log_{10}$ IU/mL with a 95% confidence interval of 2.16 to 3.08. The p-value is less than 0.0001 which shows the mean difference is significantly different than zero. The mean difference in viral load between peak and EOT for the 61 subjects for whom results were available at both time points was 2.14 $\log_{10}$ IU/mL, with a 95% confidence interval of 1.81 to 2.47. The p-value is less than 0.0001 which shows the mean difference is significantly different than zero.

Table 16. Comparison of CMV Viral Load Between Different Time Points (Baseline vs BOT, Peak vs EOT) for the First Course of CMV AVT

	n[a]	Mean Difference (SD)	95% Confidence Interval	p-value
Difference in VL Between BOT and Baseline ($\log_{10}$ IU/mL)	58[b]	2.62 (1.733)	2.16, 3.08	< 0.0001[d]
Difference in VL Between Peak and EOT ($\log_{10}$ IU/mL)	61[c]	2.14 (1.293)	1.81, 2.47	< 0.0001[e]

[a] A total of 2 subjects were excluded from the original 64 CMV AVT subjects. One subject was excluded because no CMV AVT end date was provided; 1 subject was excluded because there was no viral load measurement during the first course of CMV AVT.

[b] The viral load measurements of 2 subjects fell outside of the time window of BOT; the viral load measurements of 2 subjects fell outside of the time window of baseline.
[c] The viral load measurement of 1 subject fell outside of the time window of EOT.
[d] p-value comparing VL at BOT vs VL at baseline (using paired t-test).
[e] p-value comparing VL at peak vs VL at EOT (using paired t-test).

Viral loads for CMV AVT subjects during the first course of CMV AVT versus viral loads for non-CMV AVT subjects during 1 year post-transplant were also analyzed and are shown in Table 17.

This analysis demonstrates that, during the first course of CMV AVT, the CMV viral loads at BOT and peak are statistically significantly higher than the highest CMV viral loads for subjects with non-CMV AVT.

Table 17. Viral Load Analysis for the First Course of CMV AVT vs non-CMV AVT Populations

	n[a]	**Mean (SD)**	**Range**	**p-value**
VL at BOT (log_{10} IU/mL) for CMV AVT Subjects	60[b]	3.48 (1.205)	0, 5.93	0.0001[c]
VL at Peak (log_{10} IU/mL) for CMV AVT Subjects	62	3.66 (1.138)	0, 5.93	< 0.001[d]
VL at Peak (log_{10} IU/mL) for non-CMV AVT Subjects	29	2.46 (0.976)	0, 4.04	

[a] A total of 2 subjects were excluded from the original 64 CMV AVT subjects. One subject was excluded because no CMV AVT end date was provided; 1 subject was excluded because there was no viral load measurement during the first course of CMV AVT.
[b] The viral load measurements of 2 subjects fell outside of the time window of BOT.
[c] p-value comparing VL at BOT for first CMV AVT subjects vs VL at peak for non-CMV AVT subjects using a t-test.
[d] p-value comparing VL at peak for first CMV AVT subjects vs VL at peak for non-CMV AVT subjects using a t-test.

Safety and Effectiveness Results

1. Safety Results

   There were no adverse effects of the device reported while the study was conducted.

2. Effectiveness Results

   The results of the clinical study support the use of the Abbott RealTi*m*e CMV assay as an aid in the management of HCT patients who are undergoing anti-cytomegalovirus antiviral therapy (see Tables 16 and 17). In this population, serial DNA measurement can be used to assess virological response to anti-cytomegalovirus antiviral therapy.

3. Subgroup Analyses

   Not applicable.

4. Pediatric Extrapolation

   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 4 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Microbiology Devices Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

- The effectiveness of the Abbott RealTi*m*e CMV assay has been demonstrated when used for the quantitation of cytomegalovirus (CMV) DNA in human plasma for the management of Hematopoietic Stem Cell Transplant patients who are undergoing anti-cytomegalovirus antiviral therapy.
- There are no issues with endogenous interferents at physiological levels or with commonly administered medications.
- Whole blood can be stored at 2 to 30ºC for up to 24 hours. After centrifugation and removal from cells, EDTA plasma may be stored:
  - At 15 to 30°C for up to 24 hours
  - At 2 to 8°C for up to 5 days
  - At – 70°C or colder for longer term
  - No more than 3freeze/thaw cycles

B. Safety Conclusions

Based on the results of the analytical and clinical laboratory studies, the Abbott RealTi*m*e CMV assay, when used according to the provided directions and in

conjunction with other laboratory results and clinical information, should be safe and pose minimal risk to the patient due to false test results.

C. Benefit-Risk Determination

The benefits outweigh the risks at the level of performance observed in the pivotal clinical study. Complementary analytical studies strengthen this conclusion. When used for the proposed intended use, benefits to both the clinician and patient include confirmation that CMV viral load is responding to treatment as anticipated, and an approximation of the time that therapy can be discontinued.

The risk from a falsely high result is the misinterpretation that a patient is not responding to treatment. This is mitigated by the known likelihood that most patients respond to treatment, understanding of the time course of response, and monitoring of the patient's clinical symptoms. The risks of false negative results may be greater, and the need for the sponsor to monitor MDR and literature suggesting the emergence or recognition of CMV viral mutations is essential. This risk is mitigated, however, by the recognition in transplant centers that CMV disease can occur absent detectable viremia.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for the management of HCT patients who are undergoing anti-cytomegalovirus antiviral therapy, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The results of the nonclinical and clinical laboratory studies support the use of the Abbott RealTi*m*e CMV assay as an aid in the management of HCT patients who are undergoing anti-cytomegalovirus antiviral therapy. In this population, serial DNA measurement can be used to assess virological response to anti-cytomegalovirus antiviral therapy.

XIII. CDRH DECISION

CDRH issued an approval order on May 18, 2017.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.
Hazards to Health from Use of the Device: See Indications, in the device labeling.
Post-approval Requirements and Restrictions: See approval order.