



**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT**

I Background Information:

A 510(k) Number

K252481

B Applicant

Roche Molecular Systems, Inc.

C Proprietary and Established Names

cobas CMV

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PAB	Class II	21 CFR 866.3180 - Quantitative Cytomegalovirus Nucleic Acid Tests For Transplant Patient Management	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain clearance of cobas CMV assay on the upgraded cobas 6800/8800 systems.

B Measurand:

Cytomegalovirus (CMV) DNA

C Type of Test:

Quantitative Molecular assay - nucleic acid amplification test

III Intended Use/Indications for Use:

A Intended Use(s):

cobas CMV is an in vitro nucleic acid amplification test for the quantitation of cytomegalovirus (CMV) DNA in human EDTA plasma.

cobas CMV is intended for use as an aid in the management of CMV in solid organ transplant patients and in hematopoietic stem cell transplant patients. In patients receiving anti-CMV therapy, serial DNA measurements can be used to assess viral response to treatment.

The results from cobas CMV must be interpreted within the context of all relevant clinical and laboratory findings.

cobas CMV is not intended for use as a screening test for blood or blood products.

B Indication(s) for Use:

See Intended Use.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

For use on the cobas 5800/6800/8800 systems.

IV Device/System Characteristics:

A Device Description:

The cobas CMV is a quantitative test for use on the cobas 5800 system, cobas 6800 system and cobas 8800 system. The cobas CMV enables the detection and quantitation of CMV DNA in EDTA plasma of infected transplant patients. The viral load is quantified against a non-CMV DNA quantitation standard (DNA-QS), which is introduced into each specimen during sample processing. The DNA-QS also functions to monitor for the entire sample preparation and PCR amplification process. In addition, the test utilizes three external controls: a high titer positive, a low titer positive, and a negative control.

cobas CMV Reagents and Controls

cobas CMV kit

cobas CMV Control kit (Low Positive Control (CMV L(+))C), High Positive Control (CMV H(+))C))

cobas NHP Negative Control kit (Normal Human Plasma Negative Control (NHP-NC))

Reagents for sample preparation (cobas omni reagents)

CMV primers and probes

cobas CMV targets a conserved region of the DNA polymerase gene (UL54). One forward primer and two reverse primers are used for amplification, and detection is effected by a single probe.

Instrument and Software

The cobas 5800 system and cobas 6800/8800 systems provide a fully automated and integrated platform to perform PCR testing (specimen preparation, extraction, amplification and detection).

B Principle of Operation:

Nucleic acid from patient samples and added lambda DNA-QS molecules is simultaneously extracted. In summary, viral nucleic acid is released by addition of proteinase and lysis reagent to the sample. The released nucleic acid binds to the silica surface of the added magnetic glass particles. Selective amplification of target nucleic acid from the sample is achieved by the use of target virus-specific forward and reverse primers which are selected from highly-conserved regions of the CMV DNA polymerase (UL54) gene. Selective amplification of DNA-QS is achieved by the use of sequence-specific forward and reverse primers which are selected to have no homology with the CMV genome. A thermostable DNA polymerase enzyme is used for amplification. The target and DNA-QS sequences are amplified simultaneously utilizing a universal PCR amplification profile with predefined temperature steps and number of cycles.

The cobas CMV master mix contains one detection probe specific for CMV target sequences and one for the DNA-QS. The probes are labeled with target-specific fluorescent reporter dyes allowing simultaneous detection of CMV target and DNA-QS in two different target channels. During the PCR amplification step, hybridization of the probe to the specific single-stranded DNA templates results in cleavage by the 5'-to-3' nuclease activity of the DNA polymerase resulting in separation of the reporter and quencher dyes and the generation of a fluorescent signal. With each PCR cycle, increasing amounts of cleaved probes are generated and the cumulative signal of the reporter dye is concomitantly increased. Real-time detection and discrimination of PCR products is accomplished by measuring the fluorescence of the released reporter dyes for the viral targets and DNA-QS.

Results Interpretation

Results	Interpretation
Target Not Detected	CMV DNA not detected. Report results as "CMV not detected."
< Titer Min	Calculated titer is below the Lower Limit of Quantitation (LLoQ) of the assay. Report results as "CMV detected, less than (Titer Min)." Titer min = 34.5 IU/mL
Titer	Calculated titer is within the Linear Range of the assay – greater than or equal to Titer Min and less than or equal to Titer Max. Report results as "(Titer) of CMV detected".
> Titer Max ^a	Calculated titer is above the Upper Limit of Quantitation (ULoQ) of the assay. Report results as "CMV detected, greater than (Titer Max)." Titer max = 1.0E+07 IU/mL

^a Sample result > Titer Max refers to CMV positive samples detected with concentrations above the upper limit of quantitation (ULoQ). If a quantitative result is desired, the original sample

should be diluted with CMV-negative human EDTA plasma and the test should be repeated. Multiply the reported result by the dilution factor.

C Instrument Description Information:

1. Instrument Name:

cobas 5800/6800/8800 systems

2. Specimen Identification:

The samples are identified by the barcode on the sample tube automatically via the instrument barcode scanner or manually by using the handheld barcode reader or virtual keyboard.

3. Specimen Sampling and Handling:

Specimen processing is fully automated on the cobas 5800/6800/8800 Systems.

4. Calibration:

The user does not perform calibration of the cobas 5800/6800/8800 Systems.

5. Quality Control:

Cobas CMV control kits consist of one NHP Negative Control [(-) C] and two CMV Positive Controls, a low positive control [CMV L (+) C] and a high positive control [CMV H (+) C].

V Substantial Equivalence Information:

A **Predicate Device Name(s):**

cobas CMV

B **Predicate 510(k) Number(s):**

P160041

C **Comparison with Predicate(s):**

Device & Predicate Device(s):	<u>K252481</u>	<u>P160041</u>
Device Trade Name	cobas CMV	Same
General Device Characteristic Similarities		

Intended Use/Indications for Use	<p>cobas CMV is an in vitro nucleic acid amplification test for the quantitation of cytomegalovirus (CMV) DNA in human EDTA plasma.</p> <p>cobas CMV is intended for use as an aid in the management of CMV in solid organ transplant patients and in hematopoietic stem cell transplant patients. In patients receiving anti-CMV therapy, serial DNA measurements can be used to assess viral response to treatment. The results from cobas CMV must be interpreted within the context of all relevant clinical and laboratory findings.</p> <p>cobas CMV is not intended for use as a screening test for blood or blood products.</p>	Same
Conditions for use	For prescription use	Same
Sample Types	Human EDTA plasma	Same
Subject Status	Transplant patient, hematopoietic stem cell transplant patient, patients receiving anti-CMV therapy	Same
Sample Collection Devices	BD Vacutainer PPT Plasma Preparation Tubes for Molecular Diagnostic Test Methods or in sterile tubes using EDTA as the anticoagulant.	Same
Analyte Targets	Cytomegalovirus DNA	Same
Amplification Technology	Real-time PCR	Same
Detection Chemistry	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology)	Same
Result Analysis	PCR Cycle threshold analysis	Same
Controls	<p>DNA Quantitation Standard (DNA-QS) (internal control)</p> <p>cobas CMV Control Kit (external positive control)</p> <p>cobas NHP Negative Control Kit (external negative control)</p>	Same

Traceability/ Standardization	1 st WHO International Standard for Human Cytomegalovirus DNA for Nucleic Acid Amplification Technology Assay	Same
General Device Characteristic Differences		
Control Scheduling	Default setting will remain the same as the predicate device. Additional setting possible for alternate control frequency based on lab requirements and local regulations. Note: - Controls will be required at least for each reagent lot change and every 72 hours. - The new control concept is identical to the one with cobas 5800 system.	Positive control and negative control included on every amplification/detection plate
Instrumentation	cobas 5800 system and cobas 6800/8800 systems 2.0	cobas 5800 system and cobas 6800/8800 systems 1.4

VI Standards/Guidance Documents Referenced:

None.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Refer to P160041.

2. Linearity:

Refer to P160041.

3. Analytical Specificity/Interference:

Refer to P160041.

4. Assay Reportable Range:

Refer to P160041.

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

Refer to P160041.

6. Detection Limit:

Refer to P160041.

7. Assay Cut-Off:

Refer to P160041.

8. Accuracy (Instrument):

Refer to P160041.

9. Carry-Over:

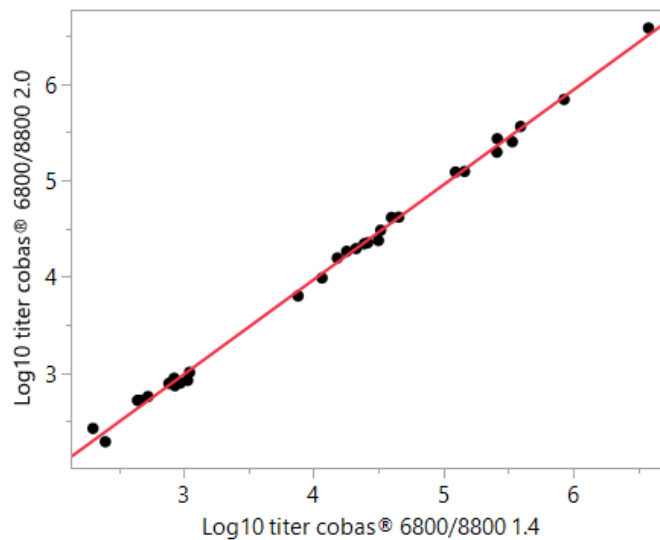
Refer to P160041.

B Comparison Studies:

1. Method Comparison with Predicate Device:

CMV-positive and CMV-negative EDTA plasma specimens collected from the transplant patient population were used to assess the performance equivalency across three cobas CMV kit lots on one cobas 6800/8800 systems 2.0 and one cobas 6800/8800 systems 1.4. Positive samples covered three targeted viral load ranges: $3.45\text{E}+01 - 2\text{E}+03$ IU/mL, $2\text{E}+03 - 2\text{E}+05$ IU/mL and $2\text{E}+05 - 1\text{E}+07$ IU/mL. Figure 1 shows the results of Deming Regression analysis showing the relationship between viral load concentrations measured by cobas 6800/8800 systems 2.0 and cobas 6800/8800 systems 1.4. The Deming regression analysis results have correlation coefficient (r) of 0.999, a slope of 0.984 (95% CI of 0.965 – 1.004%), and intercept of 0.031.

Figure 1. Method Comparison: Deming Regression Analysis



Variable	Mean	Std Dev	Variance Ratio	Correlation
Log10 titer cobas® 6800/8800 1.4	4.101	1.182	1	0.999
Log10 titer cobas® 6800/8800 2.0	4.069	1.163		

2. Matrix Comparison:

N/A

C Clinical Studies:

1. Clinical Sensitivity:

Refer to P160041.

2. Clinical Specificity:

Refer to P160041.

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

N/A

D Clinical Cut-Off:

N/A

E Expected Values/Reference Range:

N/A

F Other Supportive Instrument Performance Characteristics Data:

N/A

VIII Proposed Labeling:

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

IX Conclusion:

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