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

I Background Information:

A 510(k) Number

K221007

B Applicant

Roche Molecular Systems, Inc.

C Proprietary and Established Names

cobas HCV

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MZP	Class II	21 CFR 866.3170 - Nucleic Acid-Based Hepatitis C Virus Ribonucleic Acid Tests	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To allow use of the cobas 5800 system with the cobas HCV assay. The cobas HCV assay was originally approved under P150015 for use with the cobas 6800 and cobas 8800.

B Measurand:

Hepatitis C virus (HCV) RNA

C Type of Test:

Nucleic acid amplification test

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
cobas® HCV is an in vitro nucleic acid amplification test for both the detection and quantitation of hepatitis C virus (HCV) RNA, in human EDTA plasma or serum, of HCV antibody positive or HCV-infected individuals. Specimens containing HCV genotypes 1 to 6 are validated for detection and quantitation in the assay.

cobas® HCV is intended for use as an aid in the diagnosis of HCV infection in the following populations: individuals with antibody evidence of HCV with evidence of liver disease, individuals suspected to be actively infected with HCV antibody evidence, and individuals at risk for HCV infection with antibodies to HCV. Detection of HCV RNA indicates that the virus is replicating and therefore is evidence of active infection.

cobas® HCV is intended for use as an aid in the management of HCV-infected patients undergoing anti-viral therapy. The assay can be used to measure HCV RNA levels at baseline, during treatment, at the end of treatment, and at the end of follow up of treatment to determine sustained or non-sustained viral response. The results must be interpreted within the context of all relevant clinical and laboratory findings.

cobas® HCV has not been approved for use as a screening test for the presence of HCV in blood or blood products.

Assay performance characteristics have been established for individuals treated with certain direct-acting antiviral agents (DAA) regimens. No information is available on the assay's predictive value when other DAA combination therapies are used.

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 HCV assay is a quantitative test performed on the cobas 5800 System, cobas 6800 System or cobas 8800 System. The test detects and quantitates HCV RNA in EDTA plasma or serum of infected patients. Dual probes are used to detect and quantify, but not discriminate genotypes 1–6. The viral load is quantified against a non-HCV armored RNA quantitation standard (RNA-QS), which is introduced into each specimen during sample preparation. The RNA-QS also functions as an internal control to assess substantial failures during the sample preparation and PCR amplification processes.

B Principle of Operation:

Nucleic acid from patient samples, external controls and added armored RNA-QS molecules are simultaneously extracted 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. Unbound substances and impurities, such as denatured protein, cellular debris and potential PCR inhibitors are removed with subsequent wash buffer steps and purified nucleic acid is eluted from the magnetic glass particles with elution buffer at elevated temperature.

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 HCV. Selective amplification of RNA-QS is achieved by the use of sequence-specific forward and reverse primers which are selected to have no homology with the HCV genome. A thermostable DNA polymerase enzyme is used for both reverse-transcription and PCR amplification. The target and RNA-QS sequences are amplified simultaneously utilizing a universal PCR amplification profile with predefined temperature steps and number of cycles. The master mix includes deoxyuridine triphosphate (dUTP), instead of deoxythimidine triphosphate (dTTP), which is incorporated into the newly synthesized DNA (amplicon).1-3 Any contaminating amplicon from previous PCR runs are eliminated by the AmpErase enzyme, which is included in the PCR mix, during the first thermal cycling step. However, newly formed amplicon are not eliminated since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

The cobas HCV master mix contains dual detection probes specific for the HCV target sequences and one for the RNA-QS. The probes are labeled with target-specific fluorescent reporter dyes allowing simultaneous detection of HCV target and RNA-QS in two different target channels.

When not bound to the target sequence, the fluorescent signal of the intact probe is suppressed by a quencher dye. During the PCR amplification step, hybridization of the probes to the specific single-stranded DNA template results in cleavage of the probe 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 increases concomitantly. Real-time detection and discrimination of PCR products is accomplished by measuring the fluorescence of the released reporter dyes for the viral targets and RNA-QS.

C Instrument Description Information:

1. Instrument Name:

   cobas 5800 System

2. Specimen Identification:

   The cobas 5800 supports multiple types of barcodes. Loaded samples are automatically moved for barcode scanning and processing.

3. Specimen Sampling and Handling:

   Specimen processing is fully automated on the cobas 5800 system.

4. Calibration:

   No instrument calibration is required by the user.

5. Quality Control:

   Refer to cobas HCV assay labeling.

V Substantial Equivalence Information:

A Predicate Device Name(s):
cobas HCV

B Predicate 510(k) Number(s):
P150015

C Comparison with Predicate:

Device & Predicate Device(s):	K221007	P150015
Device Trade Name	cobas HCV	cobas HCV
General Device Characteristic Similarities		
Intended Use/Indications For Use	The cobas HCV is an in vitro nucleic acid amplification test for both the detection and quantitation of hepatitis C virus (HCV) RNA, in human EDTA plasma or serum, of HCV antibody positive or HCV-infected individuals. Specimens containing HCV genotypes 1 to 6 are validated for detection and quantitation in the assay. cobas HCV is intended for use as an aid in the diagnosis of HCV infection in the following populations: individuals with antibody evidence of HCV with evidence of liver disease, individuals suspected to be actively infected with HCV antibody evidence, and individuals at risk for HCV infection with antibodies to HCV. Detection of HCV RNA indicates that the virus is replicating and therefore is evidence of active infection. cobas HCV is intended for use as an aid in the management of	The cobas HCV is an in vitro nucleic acid amplification test for both the detection and quantitation of hepatitis C virus (HCV) RNA, in human EDTA plasma or serum, of HCV antibody positive or HCV-infected individuals. Specimens containing HCV genotypes 1 to 6 are validated for detection and quantitation in the assay. cobas HCV is intended for use as an aid in the diagnosis of HCV infection in the following populations: individuals with antibody evidence of HCV with evidence of liver disease, individuals suspected to be actively infected with HCV antibody evidence, and individuals at risk for HCV infection with antibodies to HCV. Detection of HCV RNA indicates that the virus is replicating and therefore is evidence of active infection. cobas HCV is intended for use as an aid in the management of

	HCV-infected patients undergoing anti-viral therapy. The assay can be used to measure HCV RNA levels at baseline, during treatment, at the end of treatment, and at the end of follow up of treatment to determine sustained or non-sustained viral response. The results must be interpreted within the context of all relevant clinical and laboratory findings. cobas HCV has not been approved for use as a screening test for the presence of HCV in blood or blood products. Assay performance characteristics have been established for individuals treated with certain direct-acting antiviral agents (DAA) regimens. No information is available on the assay's predictive value when other DAA combination therapies are used.	HCV-infected patients undergoing anti-viral therapy. The assay can be used to measure HCV RNA levels at baseline, during treatment, at the end of treatment, and at the end of follow up of treatment to determine sustained or non-sustained viral response. The results must be interpreted within the context of all relevant clinical and laboratory findings. cobas HCV has not been approved for use as a screening test for the presence of HCV in blood or blood products. Assay performance characteristics have been established for individuals treated with certain direct-acting antiviral agents (DAA) regimens. No information is available on the assay's predictive value when other DAA combination therapies are used.
Conditions for Use	For Prescription Use	For Prescription Use
Sample Types	EDTA Plasma and Serum	EDTA Plasma and Serum
Analyte Targets	Hepatitis C RNA genotypes 1-6	Hepatitis C RNA genotypes 1-6
Sample Preparation	Automated RNA extraction & purification	Automated RNA extraction & purification
Amplification Technology	Real Time PCR	Real Time PCR
Detection Chemistry	Dual detection probes labeled with target-specific fluorescent reporter dyes allowing simultaneous detection of HCV target and RNA-QS in two different target channels. Real time detection and discrimination of PCR products is accomplished by measuring the fluorescence of the released reporter dyes.	Dual detection probes labeled with target-specific fluorescent reporter dyes allowing simultaneous detection of HCV target and RNA-QS in two different target channels. Real time detection and discrimination of PCR products is accomplished by measuring the fluorescence of the released reporter dyes.
Assay Controls	RNA-QS functions as an internal control. Three external controls: High Titer Positive, Low Titer Positive, Negative Control	RNA-QS functions as an internal control. Three external controls: High Titer Positive, Low Titer Positive, Negative Control

Results Analysis	PCR cycle threshold analysis.	PCR cycle threshold analysis.
General Device Characteristic Differences		
Insrumentation	cobas 5800 System	Cobas 6800/8800 Systems
Design Concept	Same	Sample loading, sample prep, and PCR amplification/detection in one instrument
Throughput	~144 tests in 8 hours	~384 / 960 tests in 8 hours
Configuration	Single deck rather than separate modules. Same technology but fewer components.	Separate modules (sample supply, transfer, processing, analytic), duplicate components for high throughput.
Consumables	24-well sample prep and amplification/detection plates with same material, geometry, and volume per well. Same disposable pipette tips.	48 and 96-well sample preparation and amplification/detection plates. Disposable pipette tips.
Sample Pipetting	Single two-channel pipettor, smaller but using same technology and volumes	Single four-channel pipettor
Reagent Pipetting	Smaller reagent pipetting head with 2 reagent needles, smaller but same technology	Reagent pipetting head with a single 8 channel pipettor
Process Pipetting	24-well processing plate and single 24-channel process pipettor, smaller but same technology	48-well processing plate and single 48-channel process pipettor
Controls	Default setting the same (positive and negative controls on every plate), but due to smaller plates, options for alternate control frequency can be implemented based on lab requirements and local regulations, e.g., time-based (every 24 hours). Controls will be required at least for each reagent lot change.	Positive control and negative control included on every amplification/detection plate
Reagent Storage	Temperature-controlled (not refrigerated)	On-board refrigerated reagent storage
Sample Prep	Minor changes in timing of reagent pipetting steps due to smaller batches; same incubation times and temps	Sample Setup, Lysis Binding, Washing and Elution
Amplification/ Detection	Same technology but smaller thermal cycler Same temperatures and times for	Real-time PCR using fluorescence spectroscopy

	denaturation, annealing, and elongation steps Same result calculation and interpretation methods	

VI Standards/Guidance Documents Referenced:

CLSI: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline- 2nd Edition, EP17-A2, Wayne, PA: Clinical and Laboratory Standards Institute

CLSI: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition. CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision: See P150015

Reproducibility was assessed with a multi-site study testing a prepared panel ranging from 1.50E+01 IU/mL to 1.00E+08 IU/mL. A dilution series consisting of a clinical specimen and plasmid RNA sample was used to generate the reproducibility panel. HCV positive material was serially diluted in plasma to create a panel of 7 members that includes concentration levels at, below, and above medical decision points. Panel members were tested in 3 replicates/run, 2 runs/day, over 5 days, using 3 cobas 5800 instruments at 3 different sites (1 internal and 2 external) and 3 cobas 6800/8800 instruments at 1 internal site, 2 runs per day per instrument and by using overall three different lots of the cobas HCV kits

Results:

Table 1: Standard Deviation and Coefficient of Variance (%) for cobas HCV on cobas 5800 and cobas 6800/8800. Three Systems at three Sites combined (Absolute and Percentage)

Platform	Panel Member	Standard Deviation (SD) and Percent Coefficient of Variation (CV)											
		Mean observed log10 Titer (IU/mL)	N	Site		Day		Run		Within-Run		Total	
				SD	CV [%]	SD	CV [%]	SD	CV [%]	SD	CV [%]	SD	CV [%]
cobas 5800	PM1	7.80	90	0.18	2.31	0.08	1.00	0.02	0.26	0.05	0.66	0.20	2.61
	PM2	6.65	90	0.14	2.17	0.07	1.03	0.01	0.12	0.04	0.67	0.17	2.50
	PM3	5.79	90	0.15	2.65	0.06	1.11	0.00	0.00	0.06	1.04	0.18	3.05
	PM4	4.07	90	0.11	2.65	0.07	1.77	0.04	1.07	0.06	1.54	0.15	3.70
	PM5	2.01	90	0.15	7.68	0.00	0.00	0.04	1.96	0.16	8.17	0.23	11.38
	PM6	1.50	89	0.09	5.70	0.00	0.00	0.05	3.65	0.23	15.14	0.25	16.59

	PM7	1.28	90	0.16	12.20	0.09	6.94	0.00	0.36	0.27	21.37	0.33	25.57
cobas 6800/ 8800	PM1	7.99	90	0.00	0.00	0.04	0.50	0.01	0.07	0.04	0.49	0.06	0.71
	PM2	6.78	90	0.01	0.09	0.03	0.39	0.02	0.27	0.04	0.65	0.05	0.81
	PM3	5.93	89	0.01	0.24	0.04	0.59	0.02	0.35	0.03	0.58	0.06	0.93
	PM4	4.12	90	0.00	0.00	0.02	0.41	0.00	0.00	0.06	1.51	0.06	1.57
	PM5	2.14	90	0.01	0.64	0.07	3.26	0.00	0.00	0.12	5.66	0.14	6.56
	PM6	1.58	90	0.00	0.00	0.05	3.20	0.00	0.00	0.24	15.21	0.25	15.55
	PM7	1.26	88	0.00	0.00	0.00	0.00	0.00	0.00	0.25	19.80	0.25	19.80

2. Linearity:

Assay linearity was assessed using the predominant genotype (GT1) in plasma. The linearity panels were prepared as serial dilutions designed to cover the entire linear range of the assay. The dilution series consisted of 16 concentration levels spanning the intended linear range. The dilution series were prepared by diluting an arHCV-MS08-pCP1 specimen and an HCV positive clinical specimen in negative pooled EDTA-plasma. The Titer assignment of the study panels has been performed via Calibrator Bracketing Method (CBM). The panels were tested with three different lots of the cobas HCV kits. The dilution series covered a total of 36 replicates per concentration level in negative pooled EDTA plasma which were tested with 3 kit lots and tested on 2 cobas 5800 Systems over the course of 6 days.

Table 2: Linearity Panel Layout

Panel Member	Concentration level description	Concentration aRNA (IU/mL)	Concentration clinical specimen (IU/mL)
PM01	above upper limit of quantification (ULoQ)	2.00E+08	-
PM02	ULoQ	1.00E+08	-
PM03	intermediate level	1.00E+07	-
PM04	intermediate level	1.00E+06	-
PM05	intermediate level	4.00E+05	-
PM06	intermediate level	-	5.00E+04
PM07	intermediate level	1.00E+04	-
PM08	intermediate level	-	1.00E+04
CBMaRNA*	for calibrator bracketing method	5.50E+03	-
CBMclin*	for calibrator bracketing method	-	5.50E+03
PM09	intermediate level	4.00E+03	-
PM10	intermediate level	-	1.00E+03
PM11	intermediate level	1.00E+03	-
PM12	intermediate level	-	1.00E+02
PM13	intermediate level	1.00E+02	-
PM14	intermediate level	-	5.00E+01
PM15	lower limit of quantification (LLoQ)	-	1.50E+01

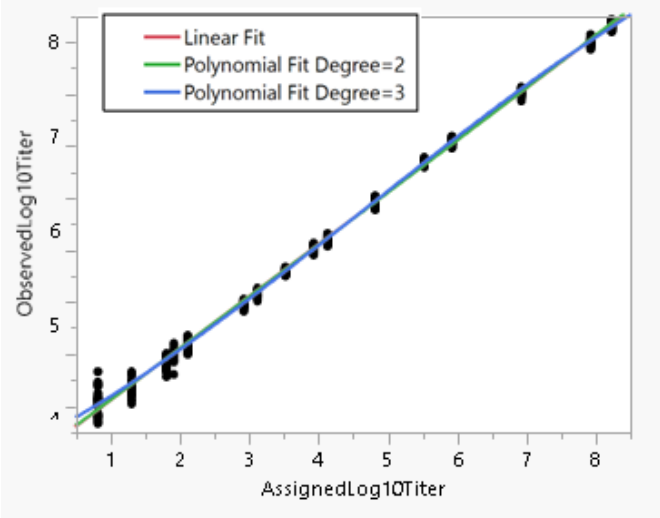
PM16	below LLoQ	-	5.00E+00

* CBMaRNA (5.50E+03 IU/mL) was used for the titer assignment of the aRNA panel members; CBMclin (5.50E+03 IU/mL) was used for the titer assignment of the clinical specimen panel members.

Table 3: Linearity Results

Panel Member	Nominal Titer [IU/mL]	Assigned Titer [IU/mL]	Assigned log_{10} Titer	Mean Observed log_{10} Titer	Predicted log Titer		Absolute Difference	Meets Acceptance Criterion?
					1st Order	3rd Order		
PM01	2.00E+08	1.66E+08	8.22	8.29	8.31	8.26	-0.05	Yes
PM02	1.00E+08	8.31E+07	7.92	7.99	8.01	8.00	-0.01	Yes
PM03	1.00E+07	8.31E+06	6.92	7.02	7.01	7.07	0.06	Yes
PM04	1.00E+06	8.31E+05	5.92	6.07	6.01	6.07	0.06	Yes
PM05	4.00E+05	3.32E+05	5.52	5.68	5.61	5.65	0.05	Yes
PM06	5.00E+04	6.54E+04	4.82	4.90	4.90	4.92	0.02	Yes
PM07	1.00E+04	8.31E+03	4.12	4.19	4.20	4.18	-0.02	Yes
PM08	1.00E+04	1.31E+04	3.92	3.99	4.01	3.98	-0.03	Yes
PM09	4.00E+03	3.32E+03	3.52	3.58	3.61	3.57	-0.04	Yes
PM10	1.00E+03	1.31E+03	3.12	3.17	3.20	3.15	-0.05	Yes
PM11	1.00E+03	8.31E+02	2.92	2.96	3.01	2.95	-0.05	Yes
PM12	1.00E+02	1.31E+02	2.12	2.15	2.20	2.17	-0.03	Yes
PM13	1.00E+02	8.31E+01	1.92	2.00	2.00	1.99	-0.02	Yes
PM14	5.00E+01	6.54E+01	1.82	1.83	1.90	1.89	-0.01	Yes
PM15	1.50E+01	1.96E+01	1.29	1.38	1.38	1.42	0.04	Yes
PM16	5.00E+00	6.54E+00	0.82	1.09	0.90	1.01	0.11	Yes

Regression Plot:



3. Analytical Specificity/Interference:

See P150015

4. Assay Reportable Range:

   The results of the linearity study and calculation of the Lower and Upper Limits of Quantitation confirm the assay reportable range is consistent across analyzer platforms: 15 IU/mL – 1.00E+08 IU/mL.

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

   See P150015

6. Detection Limit:

   The Limit of Detection (LoD) was assessed with a sample panel prepared with an HCV secondary standard and HCV negative pooled EDTA plasma. The dilution series was prepared with 6 concentration levels - 3 levels below the expected LoD, 1 level near the expected LoD and 2 levels above the expected LoD by diluting the secondary standard in pooled negative EDTA plasma. The panel was tested with 3 kit lots, on 7 days, on 3 cobas 5800 systems and 1 cobas 6800/8800 system over multiple runs, with multiple operators and with multiple replicates per run.

Table 4: Results Summary HCV on the cobas 6800/8800

Concentration HCV (IU/mL)	HCV		
	Number of Valid Replicates	Number of Positives	% Positives
20.0	66	66	100.00%
15.0	66	63	95.45%
10.0	66	57	86.36%
8.0	66	57	86.36%
5.0	66	46	69.70%
2.5	66	27	40.91%
LoD by PROBIT analysis (95% Hit Rate)	**13.70 IU/mL (95% CI: 11.19 – 18.31)**		
LoD by Hit Rate	15 IU/mL		
log10 Probit 95%	1.14 log10 IU/mL		

Table 5: Results Summary on the cobas 5800

Concentration HCV (IU/mL)	HCV		
	Number of Valid Replicates	Number of Positives	% Positives
20.0	66	65	98.48%
15.0	66	63	95.45%
10.0	66	59	89.39%
8.0	66	55	83.33%

5.0	65*	47	72.31%
2.5	66	30	45.45%

LoD by PROBIT analysis (95% Hit Rate)	**14.41 IU/mL (95% CI: 11.55 – 19.99)**
LoD by Hit Rate	15 IU/mL
log10 Probit 95%	1.16 log 10 IU/mL

*one (1) sample was invalid

7. Assay Cut-Off:

   See P150015

8. Carry-Over:

   Sample carryover on the cobas 5800 was evaluated with the cobas HBV assay. Alternating negative and HBV high positive samples were processed and detected with several checkerboard configurations on the cobas 5800 Systems. A high titer HBV plasmid sample used in this study was prepared by diluting in pooled negative EDTA plasma to yield a mean titer of 9.11 $x10^8$ IU/mL.

   Eighty-three runs were performed yielding 1926 valid sample results.

Table 6: Summary of Cross Contamination Study

	Total Positive Results from Negative Samples	Total Samples		Cross Contamination Rate	Acceptance Criteria
		positive samples	negative samples		
Total	**1**	**960**	**966**	**0.104 %** (upper one-sided 95% CI of 0.490%)	**met**

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was conducted using 150 archived, well-characterized HCV positive plasma specimens and 30 HCV negative individual plasma specimens. Some of the individual positive specimens were diluted to achieve the desired number of samples at specified concentrations: ~50 HCV specimens between 1.5 E+01 to 3E+03 IU/mL, ~50 specimens between 3E+03 to 5E+05 IU/mL and ~50 specimens between 5E+05 to 1E+08 IU/mL. Each specimen was tested on the cobas 5800 System at three different sites (1 internal and 2 external) and on a cobas 6800/8800 System at one site (internal) using three reagent lots.

   Results:

   For the 30 samples with target not detected (TND) results by cobas 6800/8800, one sample (1/30) by cobas 5800 test at one site was positive (with concentration <1.5E+01, out of the linear range). At the other two sites the NPA=100% (30/30).

   All of the positive samples were within the linear range of 1.5E+1 IU/mL to 1E+8 IU/mL by cobas 6800/8800 (150/150 =100%) and by cobas 5800 (450/450=100%). Among the three

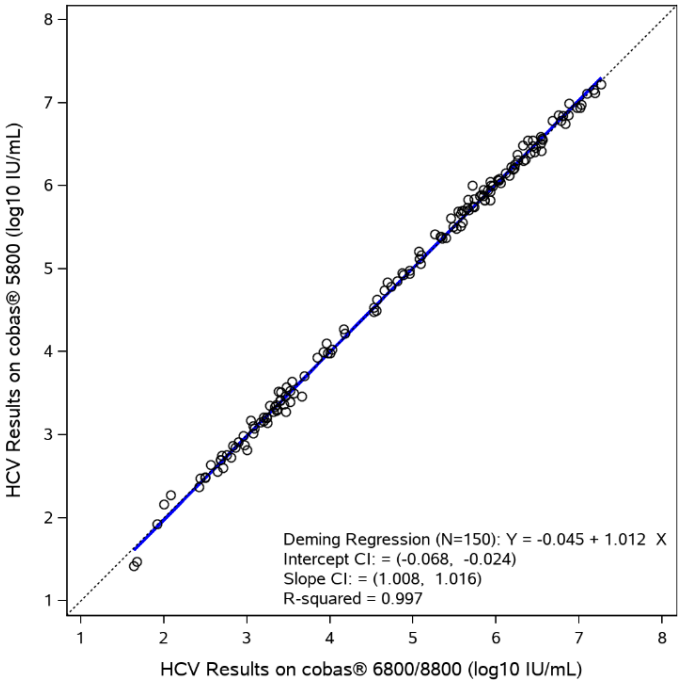
categories (low, medium, and high viral loads) within the linear range, the test results between the two systems were highly concordant.

Table 7 summarizes the parameter estimates (slope and intercept) of Deming regression between cobas 5800 and cobas 6800/8800 by site.

Table 7: Parameter estimates from Deming regression analysis by site

Site	Parameter	Number of Pairs within Linear Range	Parameter Estimate	Standard Error	95% CI	r^2
1	Intercept	150	-0.044	0.029	(-0.102, 0.014)	0.996
	Slope		1.011	0.006	(1.000, 1.022)	
2	Intercept	150	-0.055	0.037	(-0.127, 0.018)	0.996
	Slope		1.014	0.007	(1.000, 1.028)	
3	Intercept	150	-0.031	0.032	(-0.094, 0.032)	0.996
	Slope		1.010	0.006	(0.998, 1.023)	

The figure below shows the scatter plot of the average of $\log_{10}$-tranformed viral load concentration across 3 sites from the cobas 5800 versus $\log_{10}$-tranformed viral load concentration from the cobas 6800/8800 with fitted lines created by Deming regression for all sites combined using bootstrap method.



Using Deming regression analysis, an estimate of the systematic bias between the $\log_{10}$-transformed viral load concentration of the two systems (cobas 5800 and cobas 6800/8800) was calculated at medical decision levels for each site. Jackknife method was used to estimate the 95% CI of systematic bias.

Table 8 presents the estimated systematic bias between the two systems at the medical decision points by site. The biases are very close to zero in all cases, ranging from -0.035 to 0.040 and are all below the SDs observed in the reproducibility study for cobas 6800/8800 (range from 0.098 to 0.244).

Table 8: Systematic bias at medical decision point by site

Site	Medical Decision Point (IU/mL)	Number of Pairs within Linear Range	Medical Decision Point in log_{10} (IU/mL)	Predicted Value at Medical Decision Point in log_{10} (IU/mL)[1]	Bias in log_{10} (IU/mL)	95% CI of Bias
1	25	150	1.398	1.369	-0.029	(-0.072, 0.015)
	800,000	150	5.903	5.924	0.021	(0.004, 0.038)
	6,000,000	150	6.778	6.808	0.030	(0.007, 0.053)
2	25	150	1.398	1.363	-0.035	(-0.089, 0.019)
	800,000	150	5.903	5.931	0.028	(0.009, 0.046)
	6,000,000	150	6.778	6.818	0.040	(0.013, 0.067)
3	25	150	1.398	1.382	-0.016	(-0.064, 0.031)
	800,000	150	5.903	5.934	0.031	(0.013, 0.048)
	6,000,000	150	6.778	6.818	0.040	(0.015, 0.065)

[1] Estimated from the linear equation established by Deming regression method.

A Bland-Altman (BA) plot between the results of the two systems (cobas 5800 and cobas 6800/8800 instrument) with allowable total difference (ATD) zone were created for each site and for all sites combined.

Table 9 shows the percentage of samples falling within the ATD zone at low, medium and high viral load ranges and over the entire range along with the one-sided 95% CIs for all sites combined. Over the entire range, 100% of the samples fell within the ATD zone and the lower bound of the one-sided 95% CI was 100%.

Table 9: Percentage of samples within the ATD zone and ±0.5 log10-range - all sites combined

Viral Load Range Category	Viral Load Range (IU/mL)	Percentage of Samples within ATD Zone (95% One-Sided CI)	Percentage of Samples with difference within ±0.5 log_{10} (95% One-Sided CI)
Low	1.5E+1 - 3.0E+3	100.00% (47/47) (94.56%)	100.00% (47/47) (94.56%)
Medium	3.0E+3 - 5.0E+5	100.00% (46/46) (94.45%)	100.00% (46/46) (94.45%)
High	5.0E+5 - 1.0E+8	100.00% (57/57) (95.47%)	100.00% (57/57) (95.47%)
Overall		100.00% (150/150) (98.23%)	100.00% (150/150) (98.23%)

2. Matrix Comparison:

See P150015

C Clinical Studies:

1. Clinical Sensitivity:

   See P150015

2. Clinical Specificity:

   See P150015

D Expected Values/Reference Range:

See P150015

E Reagent Stability:

Studies were conducted to determine the On-Board and Open Kit stability for the cobas HCV assay when used on the cobas 5800 System. The results of the studies demonstrate the cobas HCV reagent kit cassette for use on the cobas 5800 System are stable for up to 90 days at 2 –8°C once opened and remain stable for up to 36 days at 25°C (On Board Stability), and can be used up to 40 times.

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.