cobas® HIV-1/HIV-2 Qualitative

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Roche Molecular Systems, Inc.
Address	4300 Hacienda Drive Pleasanton, CA 94588-2722
Contact	Samantha Logan Phone: (b) (6) Email: samantha.logan@roche.com
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Proprietary Name	**cobas**® HIV-1/HIV-2 Qualitative nucleic acid test for use on the **cobas**® 5800/6800/8800 systems
Common Name	**cobas**® HIV-1/HIV-2 Qualitative
Classification Name	Human immunodeficiency virus (HIV) nucleic acid (NAT) diagnostic and/or supplemental test
Product Code	QST
Predicate Devices	**cobas**® HIV-1/HIV-2 Qualitative nucleic acid test for use on the **cobas**® 5800/6800/8800 systems
Establishment Registration	Roche Molecular Systems, Inc. (2243471)

1. DEVICE DESCRIPTION

cobas® HIV-1/HIV-2 Qualitative is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection. The **cobas**® 5800 system is designed as one integrated instrument. The **cobas**® 6800/8800 systems consist of the sample supply module, the transfer module, the processing module, and the analytic module. Automated data management is performed by the **cobas**® 5800 or **cobas**® 6800/8800 systems software (SW) which assigns test results for all tests as non-reactive, reactive, or invalid. Results can be reviewed directly on the system screen, exported, or printed as a PDF report.

Nucleic acid from patient samples and added armored RNA internal control (IC) molecules (which serve as the sample preparation and amplification/detection process control) is

simultaneously extracted. In addition, the test utilizes three external controls: two positive and one negative control. 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. Unbound substances and impurities, such as denatured protein, cellular debris and potential PCR inhibitors are removed with subsequent wash 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 the HIV-1 and HIV-2 genomes. The HIV-1 gag gene, the HIV-1 LTR region (dual target for HIV-1) and HIV-2 LTR region are amplified by **cobas**® HIV-1/HIV-2 Qualitative.

Selective amplification of IC is achieved by the use of sequence-specific forward and reverse primers which are selected to have no homology with the HIV-1 or HIV-2 genomes. A thermostable deoxyribonucleic acid (DNA) polymerase enzyme is used for both reverse-transcription and PCR amplification. The target and IC 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). Any contaminating amplicons from previous PCR runs are eliminated by the AmpErase enzyme, which is included in the PCR master mix, during the first thermal cycling step. However, newly formed amplicons are not eliminated since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

cobas® HIV-1/HIV-2 Qualitative master mix contains two detection probes specific for the HIV-1 target sequences, one for HIV-2 target sequences and one for the IC. The probes are labeled with target specific fluorescent reporter dyes allowing simultaneous detection of HIV-1 target, HIV-2 target and IC in three different target channels. When not bound to the target sequence, the fluorescent signal of the intact probes 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' exonuclease 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 IC, respectively.

2. INDICATIONS FOR USE

cobas® HIV-1/HIV-2 Qualitative for use on the **cobas**® 5800/6800/8800 systems is an in vitro nucleic acid amplification test for the qualitative detection and differentiation of human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) RNA in human serum and plasma.

The test is intended to be used as an aid in diagnosis of HIV-1/HIV-2 infection. Detection of HIV-1 or HIV-2 nucleic acid is indicative of HIV-1 or HIV-2 infection, respectively. The presence of HIV-1 or HIV-2 nucleic acid in the plasma or serum of individuals without antibodies to HIV-1 or HIV-2 is indicative of acute or primary infection. The **cobas**® HIV-1/HIV-2 Qualitative may also be used as an additional test to confirm the presence of HIV-1 or HIV-2 infection in an individual with specimens reactive for HIV-1 or HIV-2 antibodies or antigens. The assay may also be used as an aid in the diagnosis of infection with HIV-1 and/or HIV-2 in pediatric subjects and pregnant women.

This assay is not intended to be used for monitoring patient status, or for screening donors of blood, plasma, or human cells, tissues, and cellular and tissue-based products (HCT/Ps) for HIV.

3. TECHNOLOGICAL CHARACTERISTICS

The primary technological characteristics and intended use of the **cobas**® HIV-1/HIV-2 Qualitative are substantially equivalent to other legally marketed nucleic acid amplification tests intended for the qualitative detection and differentiation of human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) RNA in human serum and plasma. There are no changes to the assay reagents. New labeling for the assay has been included in this submission. This labeling contains revisions related to the use of the assay on the **cobas**® 5800/6800/8800 systems.

The technical characteristics of **cobas**® HIV-1/HIV-2 Qualitative are compared to the identified predicate device, **cobas**® HIV-1/HIV-2 Qualitative nucleic acid test for use on the **cobas**® 5800/6800/8800 systems (**cobas**® HIV-1/HIV-2 Qualitative) (BP190360) in Table 1. The candidate device utilizes an updated analytical cycler with updated light source (Light Emitting Diode, LED) and Light Detection Digital Camera. Additionally, the **cobas**® 6800 system is updated to include two analytical cyclers compared to the predicate device. The system software has also been updated to version 2.0.

Table 1: Similarities and Differences between cobas® HIV-1/HIV-2 Qualitative and the Predicate Device.

Comparator	Candidate Device: cobas® HIV-1/HIV-2 Qualitative	Predicate Device: cobas® HIV-1/HIV-2 Qualitative (BP190360)
Proprietary Name	**cobas**® HIV-1/HIV-2 Qualitative Nucleic acid test for use on the **cobas**® 5800/6800/8800 systems	Same
Regulation Number	21 CFR 866.3957	Same
Regulation Name	Human immunodeficiency virus (HIV) nucleic acid (NAT) diagnostic and/or supplemental test	Same
Regulatory Class	Class II	Same
Product Code	QST	Same
Intended Use	**cobas**® HIV-1/HIV-2 Qualitative for use on the **cobas**® 5800/6800/8800 systems is an in vitro nucleic acid amplification test for the qualitative detection and differentiation of human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) RNA in human serum and plasma. The test is intended to be used as an aid in diagnosis of HIV-1/HIV-2 infection. Detection of HIV-1 or HIV-2 nucleic acid is indicative of HIV-1 or HIV-2 infection, respectively. The presence of HIV-1 or HIV-2 nucleic acid in the plasma or serum of individuals without antibodies to HIV-1 or HIV-2 is indicative of acute or primary infection. The **cobas**® HIV-1/HIV-2 Qualitative may also be used as an additional test to confirm the presence of HIV-1 or HIV-2 infection in an individual with specimens reactive for HIV-1 or HIV-2 antibodies or antigens. The assay may also be used as an aid in the diagnosis of infection with HIV-1 and/or HIV-2 in pediatric subjects and pregnant women. This assay is not intended to be used for monitoring patient status, or for screening donors of blood, plasma, or human cells, tissues, and cellular and tissue-based products (HCT/Ps) for HIV.	Same
Conditions for use	For prescription use	Same
Sample Types	Human serum and plasma	Same
Subject Status	Individuals suspected of active HIV-1/HIV-2 infection	Same
Analyte Targets	HIV-1 HIV-2	Same
Sample Preparation Procedure	Automated by **cobas**® 5800/6800/8800 systems	Same

Comparator	Candidate Device: **cobas® HIV-1/HIV-2 Qualitative**	Predicate Device: **cobas® HIV-1/HIV-2 Qualitative (BP190360)**
Amplification Technology	Real-time PCR	Same
Detection Chemistry	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology)	Same
Controls used	RNA Internal Control (internal control) **cobas®** HIV-1/HIV-2 Qualitative Control Kit (external positive control) **cobas®** NHP Negative Control Kit (external negative control)	Same
Instrument Platform	**cobas®** 5800/6800/8800 systems	Same
Amplification/Detection	Updated light source (LED) and Light Detection (Digital Camera) Real-time PCR using fluorescence signal detection. Separate detection and thermal cycler units/modules with specific temperatures and times for denaturation, annealing, and elongation steps, result calculation and interpretation methods, and filter specifications	Same (except updated light source (LED) and Light Detection (Digital Camera))
Number of supported assays per run	6 assays/run	3 assays/run
Throughput: **cobas®** 6800 (1 analytical cycler) **cobas®** 6800 (2 analytical cycler) **cobas®** 8800 (4 analytical cycler)	 384 tests in 8 hours 480 tests in 8 hours 960 tests in 8 hours	 384 tests in 8 hours N/A 960 tests in 8 hours
High Level Instrument Software Architecture	Refactored and modularized instrument control (IC) SW module and instrument management (IM) SW module are combined in one SW module. The x800 Data Manager SW module will replace the IG SW Module. x800 ASAP SW will replace the **cobas®** 6800/8800 ASAP and cobas® 5800 ASAP. **cobas®** 5800 system with software version 1.0 (P/N 08707464001), and the **cobas®** 6800/8800 systems with software version 2.0 (P/N 09575154001 and P/N 09575146001)	• Instrument Control (IC) SW • Instrument Management (IM) SW • Instrument Gateway (IG) SW • **cobas®** 6800/8800 Assay-specific analysis packages (ASAP) SW • **cobas®** 6800/8800 systems with software version 1.4 (P/N 05524245001 or P/N 05412722001) • **cobas®** 5800 Assay-specific analysis packages (ASAP) SW • **cobas®** 5800 system with software version 1.0 (P/N 08707464001)

Comparator	Candidate Device: **cobas® HIV-1/HIV-2 Qualitative**	Predicate Device: **cobas® HIV-1/HIV-2 Qualitative (BP190360)**
Control Scheduling	Default setting will remain the same as **cobas®** HIV-1/2 Qualitative 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

4. NON-CLINICAL PERFORMANCE EVALUATION

The update of the analytic cycler with a different LED Source and light detection may potentially affect the Assay performance. To confirm System Performance Equivalency between the new **cobas®** 6800/8800 Systems 2.0 and the current on-market **cobas®** 6800/8800 Systems 1.4, three system equivalency studies have been performed testing performance with the **cobas®** MPX as representative assay. Other analytical studies were completed as part of BP190360. There are no changes to the assay reagents.

4.1. cobas® 6800/8800 Systems 2.0 Equivalency Study – Reproducibility

Reproducibility of the new **cobas®** 6800/8800 systems 2.0 was assessed by testing co-formulated panels with HIV-1, HBV, and HCV, and single-formulated HIV-2, diluted in pooled negative EDTA-plasma at 1.5×LoD and 3×LoD concentration levels. An HIV/HBV/HCV negative EDTA-Plasma panel member was also tested.

Testing was conducted over five days using three **cobas®** 6800/8800 Systems 2.0 Instruments and three operators at one internal site, two runs per day and instrument and using three different Kit lots of cobas® MPX. Three replicates per panel member were tested in two runs performed per day. A total of 90 replicates per concentration level and target were distributed.

The detection rate for panel members with target concentration level at 1.5× LoD and 3×LoD on the new **cobas®** 6800/8800 Systems 2.0 was demonstrated to be greater than 95%. Additionally, all the negative samples tested negative, and the detection rate for the negative/blank panel

member was demonstrated to be less than the acceptance criteria of 5% on **cobas**® 6800/8800 Systems 2.0. Based on these results, the study met all the acceptance criteria.

4.2. cobas® 6800/8800 Systems 2.0 Equivalency Study – Diagnostic specificity

601 individual pre-screened, non-reactive individual plasma specimens were selected for this study to demonstrate performance equivalency in regard to specificity. The study was conducted using the 601 negative EDTA plasma specimens (one replicate per specimen per system configuration) with three test specific reagent lots on three new **cobas**® 6800/8800 Systems 2.0 and two **cobas**® 6800/8800 Systems 1.4. Testing was conducted over the course of three days. of which 599 specimens were valid and tested negative.

The Negative Percent Agreement (NPA) between both the new **cobas**® 6800/8800 Systems 2.0 and the current on-market cobas® 6800/8800 Systems 1.4 with a lower bound of the one-sided 95% confidence interval is 99.55%. The results met the acceptance criteria.

4.3. cobas® 6800/8800 Systems 2.0 Equivalency Study – Correlation

155 individually spiked single donor specimen for each target (HIV-1 Group M, HIV-2, HBV, HCV) as well as 155 individual HIV/HBV/HCV negative single donor specimens were used to assess the performance equivalency between the updated and original systems. The individual HIV-1 Group M, and HIV-2, HBV, HCV positive and individual negative specimens were distributed across three **cobas**® MPX kit lots, and tested on three **cobas**® 6800/8800 Systems 2.0. Testing was performed at one site (internal) over the course of four days

Test results showed that for HIV-1, HIV-2, HBV, and HCV specimens the positive percent agreement (PPA) was 100%. The lower bound of the one-sided 95% confidence interval (CI) for PPA was 98.28%. For the negative specimen the negative percent agreement (NPA) was 100%. The lower bound of the one-sided 95% CI for NPA was 98.28%. The overall percent agreement was 100%. These results met the acceptance criteria.

5. CLINICAL PERFORMANCE EVALUATION

Completed as part of BP190360. There are no changes to the assay reagents.

6. CONCLUSIONS

As the **cobas**® HIV-1/HIV-2 Qualitative assay reagents and intended use population have not changed, additional clinical studies were not performed. Non-clinical studies were used to evaluate the performance of the updated **cobas**® HIV-1/HIV-2 Qualitative Assay on the **cobas**® 5800/6800/8800 systems. The conclusions drawn from the nonclinical tests that demonstrate that the device is as safe, as effective, and performs as well as the predicate. These studies support a conclusion of substantial equivalence between the updated **cobas**® HIV-1/HIV-2 Qualitative Assay on the **cobas**® 5800/6800/8800 systems and the current on-market **cobas**® 5800/6800/8800.