K140887

510(k) Summary

MAY 05 2014

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Contact:	Wilk von Gustedt
Date of Preparation:	
Device Trade Name:	**cobas®** CT/NG v2.0 Test **cobas®** CT/NG Test
Common Name:	*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoea* (NG) Test
Type of Test:	Nucleic Acid Amplification Test, DNA, *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoea* (NG), qualitative
Classification Names:	Chlamydia serological reagents Neisseria spp. Direct serological test reagents Instrumentation for clinical multiplex test systems
Regulations:	866.3120 866.3390 862.2570
Product Codes:	MKZ (DNA Probe, Nucleic Acid Amplification, Chlamydia) LSL (DNA Reagents, Neisseria) OOI: Real Time Nucleic Acid Amplification System
Panel:	Microbiology
Predicate Device-Assay:	**cobas®** CT/NG v2.0 Test (K132270, Cleared 12/02/2013) **cobas®** CT/NG Test (K110923, Cleared 1/24/2012)

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1. INTRODUCTION

This Special 510(k) addresses software system changes to the cobas® CT/NG v2.0 Test (K132270) cleared on December 2nd, 2013 and the cobas® CT/NG Test cleared on January 24 2012 (K110923).

The software system related changes to the cobas® CT/NG v2.0 Test (K132270) and the cobas® CT/NG Test tests are limited to the modification of the core software and the related required migration to software system version 2.1. There are no changes to the diagnostic sample processing and data analysis, the Intended Use, the reagents, the technology or the design of the two CT/NG Tests. In the following sections the cobas® CT/NG v2.0 Test (K132270) and the cobas® CT/NG Test (K110923) will also be referred to as the CT/NG Tests.

While this Special 510(k) addresses the migration of the CT/NG Test to this new software architecture, other Tests, e.g. cobas® HPV Test, will also be migrated.

2. DEVICE DESCRIPTION

The **cobas**® CT/NG Tests for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) are based on two major processes: (1) automated sample preparation to obtain nucleic acids, including CT and NG DNA; (2) simultaneous PCR amplification of target DNA sequences using both CT and NG specific complementary primer pairs and real-time detection of cleaved fluorescent-labeled CT and NG specific oligonucleotide detection probes. Internal control, containing CT and NG DNA, is added to all samples during automated sample preparation and is amplified and detected simultaneously with each sample to monitor the entire process.

The Roche Molecular Systems (RMS) **CT/NG Tests** consist of six reagent kits:

- **cobas**® 4800 System Sample Preparation Kit
- **cobas**® 4800 CT/NG v2.0 Amplification/Detection Kit (**cobas**® CT/NG v 2.0 Test)
- **cobas**® **4800** CT/NG Amplification/Detection Kit (**cobas**® CT/NG Test)
- **cobas**® 4800 CT/NG Controls Kit
- **cobas**® 4800 System Wash Buffer Kit
- **cobas**® 4800 System Control Diluent Kit
- **cobas**® 4800 System Liquid Cytology Preparation Kit

Sample Collection Kits to be used for the CT/NG Tests are:

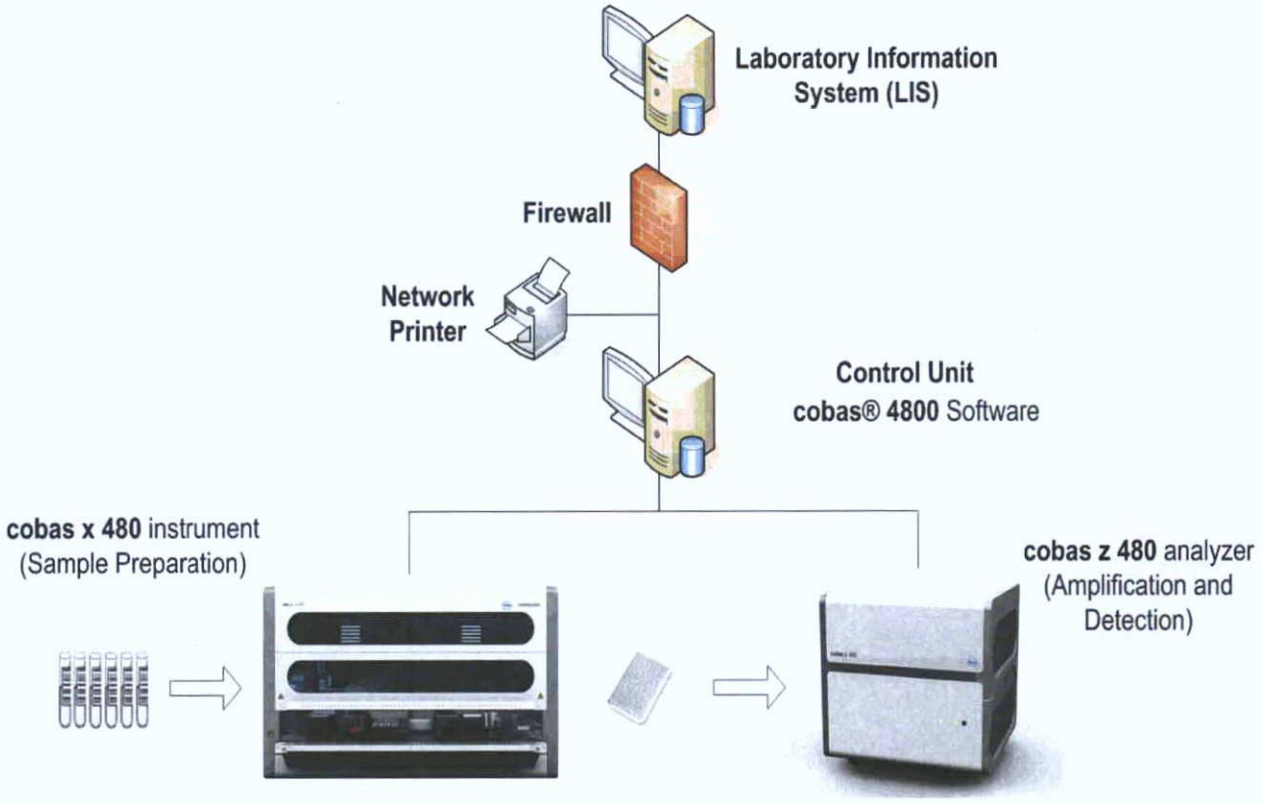
- **cobas**® PCR Female Swab Sample Kit
- **cobas**® PCR Urine Sample Kit
- **PreservCyt® (Hologic, Inc.)** (only for cobas® **CT/NG v2.0 Test)**

The cobas® CT/NG Tests utilize the **cobas**® 4800 System for automated sample preparation and automated amplification and detection. The **cobas**® 4800 system software integrates the sample preparation with nucleic acid amplification and detection to generate test results.

This platform consists of modular hardware components that are linked by a dedicated network. The major hardware components of the **cobas**® 4800 system are shown in Figure 1:

- **cobas x** 480 instrument (for automatic sample preparation)
- **cobas z** 480 analyzer (for automatic amplification and detection using real-time PCR)
- Control Unit with **cobas**® 4800 software
- Assay reagents
- (Optional) Communication through a firewall with a Laboratory Information System (LIS) and/or intranet for LIS and/or telecommunications

Figure 1: cobas® 4800 System Hardware Components



The cobas ® 4800 System is controlled by the cobas 4800 System software and is the primary interface for operators to access the cobas® 4800 system. It allows operators to manage test orders, operate the instruments, report test results, and manage data.

The software is designed according to IVD guidelines and provides the interface between the user and the system. Each instrument has its own internal instrument control software, which is not accessible to the user. The cobas ® 4800 System software will communicate with the instrument software to execute the run.

The user is able to enter specimen test orders either manually (via the integrated work order editor) or automatically (when connected to an LIS system). A software wizard will guide the user through the necessary steps to perform a run (i.e. choose a test, load samples, load reagents and consumables, and handle error conditions).

The cobas ® 4800 System maintains positive identification for each specimen during processing and analysis on the cobas x 480 instrument and the cobas z 480 analyzer through the use of

barcodes on specimen vials. Controls are also identified and tracked via barcodes. Samples are processed on the cobas x 480 and then transferred to a barcoded PCR microwell plate containing master mix reagent. The plate is then transferred to the cobas z 480 analyzer for PCR amplification and detection. The software tracks the transfer time, and will invalidate the run if the plate is not transferred within 90 minutes.

The cobas z 480 analyzer measures the generated raw fluorescence signal and sends the data to the cobas 4800 software. The software processes the raw fluorescence data using data analysis algorithms, determines validity, and outputs the results. When the run is complete, the system allows the user to view, print, export the results, or upload to LIS.

1.1. cobas 4800 System Workflow

The basic workflow on the cobas® 4800 System is outlined below.

Barcoded primary specimen containers (e.g., PreservCyt vials) are opened by the user and placed in a sample rack (alternatively barcoded secondary tubes can be loaded).

1. The user first selects the desired test to be performed. After the test is selected, the cobas 4800 software guides the user in performing the steps required to perform a run using a "wizard" style interface.

2. The sample carriers are loaded onto the cobas x 480 Instrument. As the specimens are loaded, the instrument scans the specimen barcodes and automatically creates a work order list.

3. If the system is connected to an LIS, the test orders are automatically applied to each specimen. If the system is not connected to an LIS, the user manually selects the test orders in the work order list.

4. The user then loads the required consumables and reagents for the test orders, then selects to start the automated sample preparation on the cobas x 480 Instrument.

5. Automated sample preparation on the cobas x 480 consists of automated sample DNA extraction and PCR microwell plate setup. After sample DNA extraction is finished, the

cobas x 480 Instrument prepares the PCR microwell plate by pipetting working master mix into the microwell plate and then adding specimen eluate to the plate.

6. The user removes the plate from the cobas x 480 Instrument and manually seals it with a pressure activated sealing film.

7. The PCR microwell plate is now ready for amplification and detection. The user seals and transfers the plate to the cobas z 480 analyzer.

1.2. Current cobas® 4800 System Software

In the current version of the **cobas**® 4800 system software, the tests are integrated with the main software:

a. Software Release (SR) 1.1 includes the **cobas** CT/NG test,

b. Software Release (SR) 1.2 includes the **cobas** CT/NG v2.0 test

The differences between the previously cleared **cobas**® CT/NG Test (K110923) and the **cobas**® CT/NG v2.0 Test (K132270) are limited to the modification of the sample preparation workflow (see Table 1) which required an update of the **cobas**® 4800 system software to software release 1.2. There are no differences in the reagents or the design between the **cobas**® CT/NG v2.0 Test and the **cobas**® CT/NG Test.

Table 1: High Level Changes to the cobas® CT/NG v2.0 Sample Preparation Workflow

Feature	Result
Magnetic Glass Particle (MGP) Mixing Improvement	Mixes 2 times instead of one (draws the MGP reagent into the pipettor and returns it to the reagent trough) to provide better mixing and more uniform delivery of the MGP before introduction to the deep well plate for DNA capture
New liquid class	Provides more accurate pipetting of eluate, average eluate transfer to microwell plate approximately 15% higher
Longer Elution Time	30 minutes elution instead of 12 minutes to elute more target from the MGP and to concentrate eluate to increase target copies transferred to the PCR reaction

3. INTENDED USE

As mentioned, the intended use for both CT/NG Tests will not change due to the transition to cobas 4800 system release 2.1 software.

Currently the intended use for the **cobas**® CT/NG v2.0 Test (K132270) is defined as follows:

The **cobas**® CT/NG v2.0 Test is an automated, in vitro nucleic acid amplification test for the qualitative detection of *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) DNA in urogenital specimens. The Test utilizes the Polymerase Chain Reaction (PCR) for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* DNA in male and female urine, self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical swab specimens, all collected in cobas PCR Media (Roche Molecular Systems, Inc.), and cervical specimens collected in PreservCyt® solution. This test is intended as an aid in the diagnosis of chlamydial and gonococcal disease in both symptomatic and asymptomatic individuals.

The **cobas**® PCR Female Swab Sample Kit is used to collect and transport endocervical and vaginal swab specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for gynecological specimens. Use this collection kit only with either the **cobas**® CT/NG Test or the **cobas**® CT/NG v2.0 Test.

The **cobas**® PCR Urine Sample Kit is used to collect and transport urine specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens. Use this collection kit only with either the **cobas**® CT/NG Test or the **cobas**® CT/NG v2.0 Test.

Currently the intended use for the **cobas**® CT/NG Test (K110923) is defined as follows:

The **cobas**® CT/NG Test is an in vitro nucleic acid amplification test that utilizes the Polymerase Chain Reaction (PCR) and nucleic acid hybridization for the qualitative detection of Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG) DNA to aid in the diagnosis of chlamydial

and gonococcal disease. The test may be used with vaginal swab specimens self-collected in a clinical setting and male urine from both symptomatic and asymptomatic individuals. Specimens to be tested should be collected in cobas® PCR Media.

The cobas® PCR Female Swab Sample Kit is used to collect and transport self-collected vaginal swab specimens in a clinical setting. The cobas® PCR Media serves as a nucleic acid stabilizing transport and storage medium for gynecological specimens. Use this collection kit only with the cobas® CT/NG Test. NOTE: This collection kit should not be used for collection of alternative gynecological specimens.

The cobas® PCR Urine Sample Kit is used to collect and transport male urine specimens. The cobas® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens. Use this collection kit only with the cobas® CT/NG Test.

Note: *This collection kit should not be used for collection of female urine specimens.*

4. TECHNOLOGICAL CHARACTERISTICS

The primary technological characteristics and intended use of the RMS **cobas**® CT/NG Tests with software system version 2.1 are substantially equivalent to other legally marketed nucleic acid amplification tests intended for the qualitative detection of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG).

As indicated in Table 2, the RMS **cobas**® CT/NG Tests with SW v.2.1 are substantially equivalent to significant characteristics of the identified predicate device, the currently cleared **cobas**® CT/NG Tests (K132270 and K110923). The fundamental scientific technology of the proposed devices is unchanged from the legally marketed device (predicate).

Table 2: Comparison of the cobas® CT/NG Tests (software version 2.1) with the Predicate Devices

	Submitted Device: RMS cobas® CT/NG v2.0 Test w/ SW v.2.1	**Predicate Device: RMS cobas® CT/NG v2.0 Test (K132270)**	**Submitted Device: RMS cobas® CT/NG Test w/ SW v.2.1**	**Predicate Device: RMS cobas® CT/NG Test (K110923)**
Intended Use	Qualitative *in vitro* diagnostic test for the direct qualitative detection of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* in patient specimens	Same	Qualitative *in vitro* diagnostic test for the direct qualitative detection of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* in patient specimens	Same
Sample Types	Male urine	Same	Male urine	Same
	Female urine			
	Endocervical swabs			
	Clinician-collected vaginal swabs			
	Patient-collected vaginal swabs		Patient-collected vaginal swabs	
Subject Status	Asymptomatic and symptomatic	Same	Asymptomatic and symptomatic	Same
Sample Collection Devices	Urine collection kit Female swab collection kit	Same	Urine collection kit Female swab collection kit	Same
CT Analyte Targets	CT cryptic plasmid DNA CT *ompA* gene	Same	CT cryptic plasmid DNA CT *ompA* gene	Same
NG Analyte Targets	NG genomic DNA	Same	NG genomic DNA	Same
Sample Preparation Procedure	Semi-automated	Same	Semi-automated	Same
Amplification Technology	Real-time PCR	Same	Real-time PCR	Same

	Submitted Device: RMS cobas® CT/NG v2.0 Test w/ SW v.2.1	Predicate Device: RMS cobas® CT/NG v2.0 Test (K132270)	Submitted Device: RMS cobas® CT/NG Test w/ SW v.2.1	Predicate Device: RMS cobas® CT/NG Test (K110923)
Detection Chemistry	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology) using fluorescence resonance energy transfer (FRET)	Same	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology) using fluorescence resonance energy transfer (FRET)	Same
Result Analysis	Based on PCR cycle threshold analysis	Same	Based on PCR cycle threshold analysis	Same

In summary, the intended use, technology, and functionality of the **cobas**® CT/NG v2.0 Test and **cobas**® CT/NG Test with software system version 2.1 are identical to their predicate devices.

5. DESCRIPTION OF THE CHANGE

The cobas® 4800 system is an integrated platform that can automatically perform qualitative in vitro nucleic acid amplification tests.

As mentioned in the current versions of the **cobas**® 4800 system software, the tests are integrated with the main software (Figure 2):

a. Version 1.1 included the cobas HPV and **cobas** CT/NG test,

b. Version 1.2 **cobas** CT/NG v2.0 test

The current 1.1 or 1.2 software architecture (see Figure 2) is not amenable to a "plug and play" model in which different analytical test packages, e.g., CT/NG, HPV, can be added without reprogramming more fundamental core or instrument management systems. For the cobas® 4800 system release 2.1 (SR2.1), the software has been updated to support a modular "plug and play" concept for installing tests on the system.

Test specific setting such as the sample preparation process, the PCR thermal cycling profile, and data analysis algorithms will remain the same for each assay; however its organization will be changed to allow addition or modification of assays without compromising the rest of the system software.

Instead of being written into the system software, the software was modularized such that all test specific items were separated into separate assay specific analysis packages (AP) for each test. (see Figure 2: Software Architecture for version 1.x of the cobas® 4800 Software

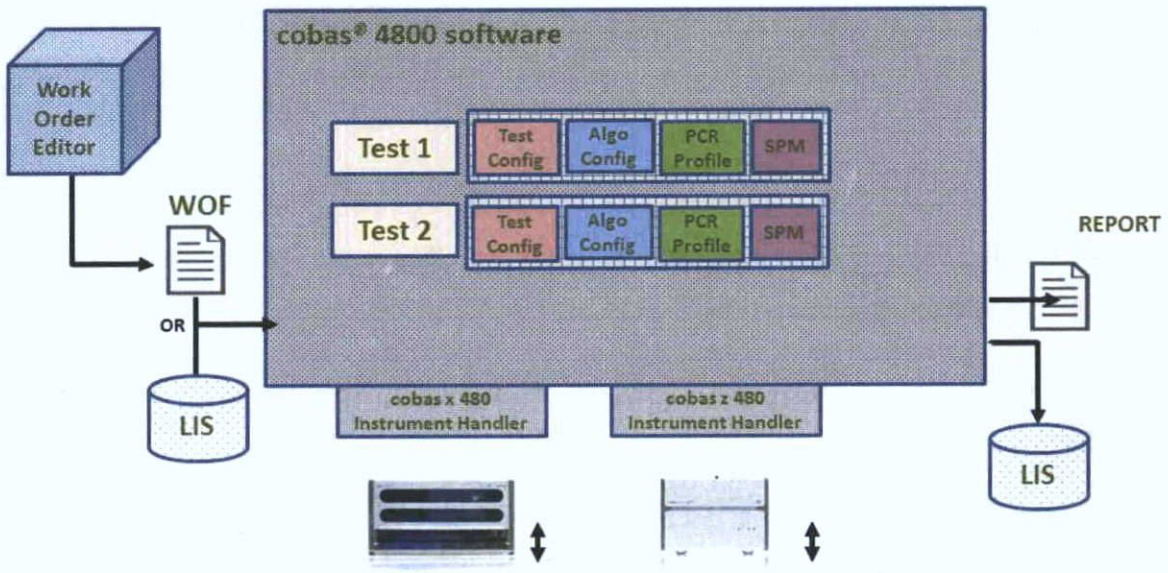


Figure 3). Here cobas ® 4800 Core represents processes common to c4800 instrument function, WP1 –WP4 represent consolidated work flow processes that are shared among particular subsets of assays, for example, a generic calculation engine is used with allows modular use of test specific data analysis settings. Test 1 – Test15 represent individual diagnostic tests.

Figure 2: Software Architecture for version 1.x of the cobas® 4800 Software

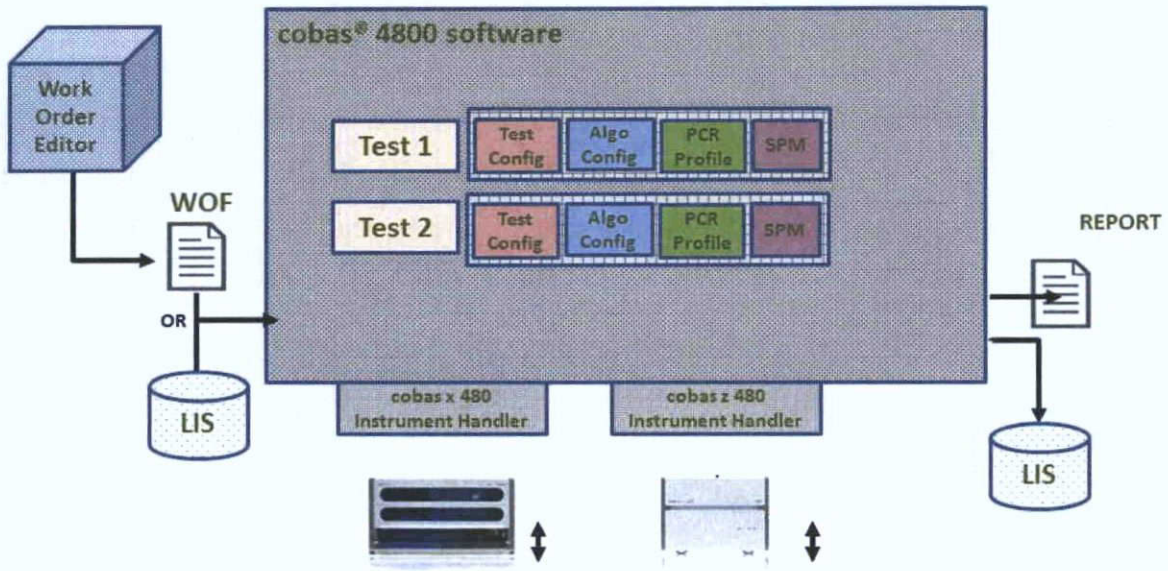
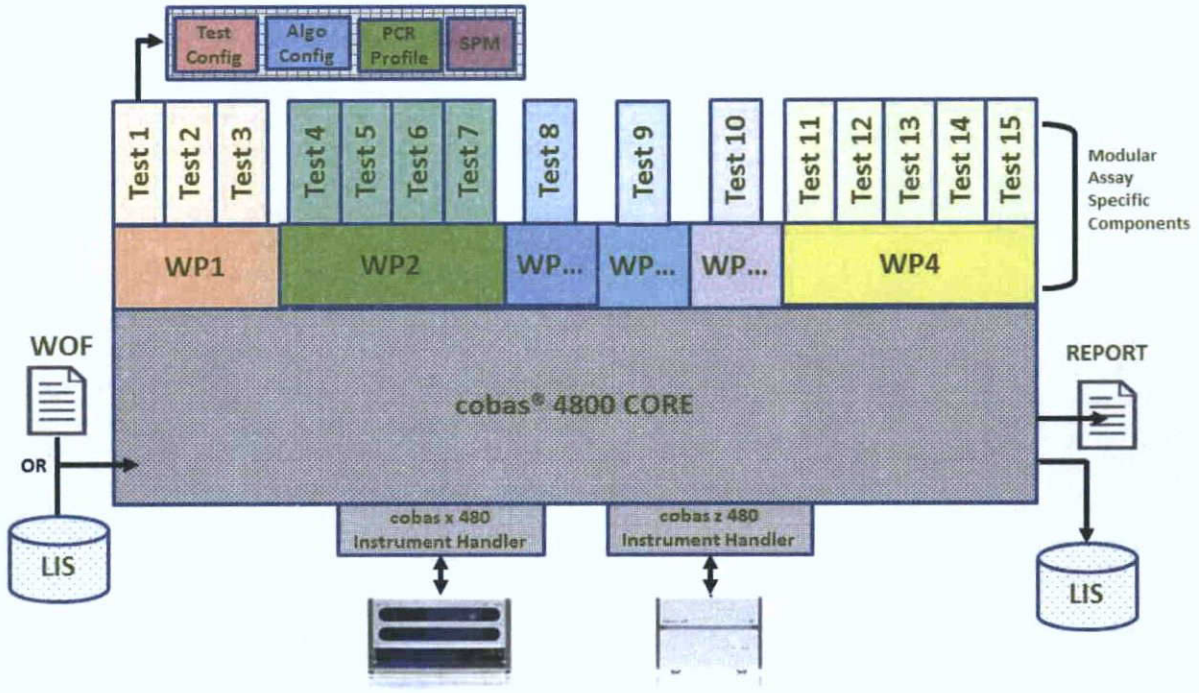


Figure 3: Software Architecture for version 2.1 of the cobas® 4800 Software



As outlined above Roche intends to upgrade the cobas ® 4800 software from its present version, 1.1 for **cobas**® CT/NG Test (K110923) and 1.2 for the **cobas**® CT/NG v2.0 Test (K132270) to software version 2.1. While the primary purpose for this upgrade of the software system is to consolidate existing tests onto one platform and to facilitate menu addition, other changes were also implemented, as shown in Table 3.

Verification, Validation and regression testing for these changes were performed using both CT/NG tests. Testing has shown that these changes do not impact the sample preparation process, PCR cycling profile, or data analysis of the CT/NG tests that were consolidated onto the version 2.1 platform.

The upgrade to 2.1 will involve the changes shown on Table 3.

Table 3: Changes to cobas 4800 Software

	Change	Description
1	Consolidated Platform	Update software architecture to support a "plug and play" environment for adding different assays (platform menu expansion). Migration of existing tests onto a common system software platform.
2	Microsoft Windows 7	Update software to run on Microsoft Windows 7 Operating System since Windows XP is no longer supported by Microsoft
3	Integrated Work Order Editor	Specimen barcodes automatically scanned into the Work Order as they are loaded onto the x480. Removes the redundancy of having the user manually create a work order by scanning specimen barcodes, then loading specimens onto the x480 (where the barcodes are scanned by the x480), and then checking that barcodes on the Work Order and what is loaded on the x480 match.
4	Integrated CT/NG Workflow Selection	The CT/NG or CT/NG Cytology workflow and sample preparation processing is automatically chosen based on specimen types.
5	Tip Tracking and Counting	Allows use of partially filled tip racks and checks for adequate number of tips required for the run. Previously, user had to always load ten full tip racks regardless of run size.
6	Early Specimen Removal	Allows user to unload specimens after they have been transferred to the Deep Well Plate.
7	Flexible Run Sizes	Enables use of multiple master mix size 24 vials during PCR plate setup (to also support 48 and 72 sample run sizes). Previously, only 24 and 96 batch sizes were supported.
8	Result View and Report Layout Improvements	Redesigned result view to support menu expansion and improved the report layout.
9	Recovery Workflow	Allows regeneration of work order from existing run in case of unexpected need to recover a run using remnant eluate prepared by the cobas x 480. Previously, this work order had to be created manually.
10	Generic calculation engine	Consolidation of tests onto a common platform required that the algorithm components be migrated to the generic calculation engine used for SR2.1. The same data analysis algorithms, algorithm parameters, and final results call tables are used.
11	LIS Improvements	Improve LIS connection communication.

These changes are described in further detail below.

1.3. Consolidated Platform

The current version 1.x software architecture (Figure 2 above) is not amenable to a "plug and play" model for test menu addition. New tests cannot be added without reprogramming more fundamental core or instrument management systems.

For cobas® 4800 system software version 2.1, the code has been reorganized to consolidate common functions and to organize the diagnostic test specific functions into separate modules (Figure 2: Software Architecture for version 1.x of the cobas® 4800 Software

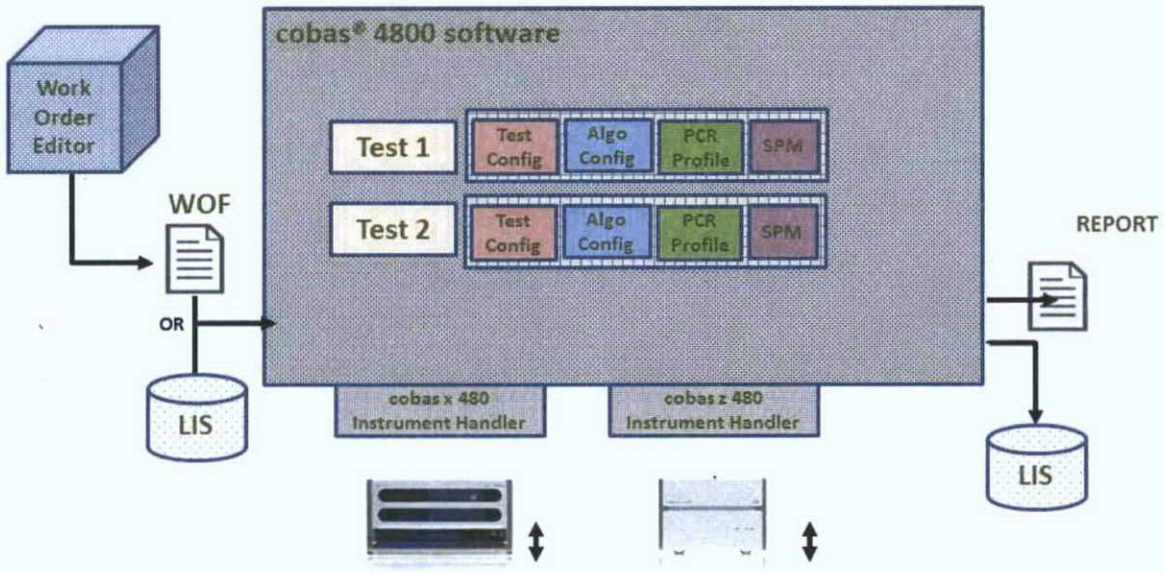


Figure 3 above).

- The **cobas**® 4800 Core represents processes common to **cobas**® 4800 instrument function
- Work packages WP1 –WP4 represent consolidated work flow processes that are shared among particular subsets of assays, for example, a common loading sequence is used between HPV and CT/NG

- Test 1 – Test 15 represent individual diagnostic tests and contain the test specific data analysis settings (note, for existing tests such as CT/NG, these test specific settings are the same in version 1.x and cobas 4800 System Release 2.1.

1.4. Microsoft Windows 7

Microsoft no longer supports Windows XP. The software used by the cobas® 4800 system was updated for Windows 7.

1.5. Integrated Work Order Editor

The current version 1.x workflow involves the use of a separate Work Order Editor tool which requires the operator to manually scan individual specimen barcodes and create a Work Order file. Then the operator uses the cobas® 4800 software to select the manually created work order file, and then load the specimens onto the cobas x 480. The cobas x 480 then scans the specimen barcodes and verifies the loaded specimen barcodes against the selected Work Order file. In version 2.1, integration of the Work Order Editor eliminates manual input (which is prone to human error) and, since the Work Order is automatically created from the loaded specimens, eliminates redundant scanning and the possibility of a mismatch between the Work Order and the loaded specimens.

These changes only affect the test ordering step, which precedes any functional assay processing steps. Hence, assay performance is not impacted by this workflow efficiency improvement.

1.6. Integrated CT/NG Workflow Selection

When initiating a run in version 1.x, the user must choose either the "CT/NG" workflow or the "CT/NG Cytology" workflow. In version 2.1, the user simply chooses "CT/NG" and the workflow (sample preparation process) is automatically chosen based upon the specimen types that are loaded.

1.7. Tip Tracking and Counting

Currently, to ensure that there are enough tips for a run, the user must always load 10 completely full tip racks when setting up a run. Tip counting calculates the number of tips needed for the run (based on number of specimens) and informs the user to load at least that many tips. Tip tracking allows the operator to load partially filled tip racks (e.g. remnant unused tips from a rack used in a previous run). Tip counting plus tip tracking allows the system to verify that sufficient tips have been loaded to perform the run. These changes are implemented in the consumables loading

step, which precedes any functional assay processing steps. Hence, assay performance is not impacted by this consumables usage efficiency improvement.

1.8. Early Specimen Removal

Currently, once specimens are loaded onto the cobas x 480, they cannot be accessed for other laboratory usage (e.g. other diagnostic testing) until the cobas x 480 completes the sample preparation process. This new feature provides an option to unload the specimen vials after required test volumes have been transferred to the deep well plate for cobas x 480 processing. Early removal of the specimen vials does not impact assay performance since the sample extraction process on the plate is not affected.

1.9. Flexible Run Sizes

Currently, PCR plate setup only supports run sizes of either up to 24 samples or up to 96 samples. This results in inefficient usage of the master mix reagents, since a run with 25 or more samples requires using the 96 sample size master mix reagents. This change enables the use of multiple sets of 24 size master mix reagents. PCR plate setup now supports up to 24, 48, and 72 samples (using one, two, or three sets of 24 size master mix reagents) and up to 96 samples (using one set of 96 size master mix reagents). The use of multiple sets of master mix reagents does not change the sample preparation processing steps. Hence assay performance is not affected.

1.10. Result View and Report Layout Improvements

The Result View was adapted to accommodate consolidation and addition of assays to the test menu of the cobas® 4800 system. For example, instead using test specific column names (e.g. "CT Result" or "NG Result") with generic result values ("POS" or "NEG"), a generic column name was used ("Result 1") with more descriptive results ("POS CT" or "NEG NG"). Report Layouts were improved by organizing the information into separate test details and test results tables. These changes only re-organize the display/presentation of the results and hence assay performance is not affected.

1.11. Recovery Workflow

In cases where the PCR thermo-cycling process was interrupted or failed, the current Version 1.x software includes an optional workflow to re-run specimens ("PCR Only Run") by manually setting up the PCR microwell plate using remnant eluate (from the deep-well plate) and newly prepared master mix. This process also involved manually creating the "PCR Only" work order, which had to match the original well to well plate layout exactly.

This feature is retained in the version 2.1 software, but has been renamed and improved. To avoid confusion with workflows that involve manual sample preparation followed by automated PCR ("PCR Only"), this rescue workflow has been renamed as "Recovery Run". To facilitate this workflow, creation of the recovery work order is now automatically generated from the run that is being recovered. These changes do not affect any assay functional processing steps. Hence assay performance is not affected.

1.12. Generic Calculation Engine

To consolidate all tests onto the version 2.1 software, algorithm components for each test had to be migrated to a common (generic) calculation engine. The same data analysis algorithms, algorithm parameters, and final results determination tables were retained for each migrated test. Results outputs were verified to be the same before and after migration.

1.13. LIS Improvements

Currently, the version 1.x software merely outputs a results file for LIS processing. After outputting the file, no further actions or acknowledgements are taken by the cobas® 4800 system. The LIS interface has been improved in version 2.1 to acknowledge results upload and receipt by the LIS. It also now monitors and displays the LIS connection status. Initially, the version 2.1 system will support the ASTM protocol and will be updated later to also support the HL7 protocol.

2. DESIGN AND DEVELOPMENT APPROACH

The cobas® 4800 system version 2.1 is an update to an existing system. Specifically, this was a change only to the cobas® 4800 system software, which was updated as described in section 1. The design and development approach was based on this scope.

The scope of the design and development effort focused on the change to the software:

- The cobas x 480 instrument hardware did not change and did not require revalidation. New instrument firmware and Hamilton Phoenix software was introduced to support the Windows 7 operating system. This firmware and software was developed, tested, and released by Hamilton Company. These software components were then incorporated into the cobas 4800 system SR 2.1 configuration and tested as part of the Roche component and system-level verifications.
- The cobas z 480 analyzer hardware component did not change and did not require re-validation.
- The control unit (computer) hardware did not change, however a new Windows 7 OS was introduced and used as part of the configurations used during Roche component and system level verifications.
- The cobas® 4800 consumables did not change and did not require re-validation
- The cobas® 4800 assay specific reagents did not change and did not require re-validation
- The cobas® 4800 software was changed and re-validated at the unit, component, and system level for both the core system and the migrated test analysis packages (AP)

Technical performance verification regression testing was also done for the migrated cobas® CT/NG and cobas® CT/NG v2.0 Tests.

2.1. System Development Environment

The Systems Development team at Roche Molecular Systems (RMS) in Pleasanton, CA coordinated the activities necessary for successful development, verification and validation of the cobas® 4800 system and the cobas® CT/NG and cobas® CT/NG v2.0 analysis packages. These activities included (but were not limited to) overall project management, systems development, verification and validation, and clinical trials.

System components were developed and tested by Roche Molecular Systems (Pleasanton, CA), Roche Diagnostics Ltd. (Rotkreuz, Switzerland), and Hamilton Bonaduz AG (Bonaduz, Switzerland):

- Roche Molecular Systems (Pleasanton, CA) was responsible for development and design of the Sample Preparation Method (SPM) which is incorporated into cobas® 4800 System Software.
- Roche Diagnostics Ltd. (Rotkreuz, Switzerland) was responsible for design of the cobas® 4800 System Software, the associated computer Control Unit, and for design and manufacture of cobas z 480 analyzer and associated consumables.
- Hamilton Bonaduz AG (Bonaduz, Switzerland) was responsible for design and manufacture of the cobas x 480 instrument and associated consumables.

All versions of cobas® 4800 software and all components of cobas z 480 analyzer software were developed and controlled at Roche Diagnostics Ltd. (Rotkreuz, Switzerland). The cobas x 480 Instrument Control software (Hamilton Microlab STAR IVD Software) was developed by Hamilton Bonaduz AG (Bonaduz, Switzerland) as part of the Phoenix Software System.

3. DEVICE RISK ASSESSMENT

Risk assessment was performed throughout the development of the cobas® 4800 system, starting with assessment of Customer Requirements, and continuing through verification and validation of the final product.

The following general methodology was used for risk assessment:

- Identify and analyze hazards
- Mitigate the risk associated with each identified hazard
- Verify the effectiveness of each risk mitigation

Analysis of each identified hazard included the manner in which the risk associated with that hazard would be mitigated. Risk mitigation was either by hardware control, software control, or by user-controlled processes specified in product inserts and product labeling, the Operators Manual, and training.

The FMEA process was conducted in a series of team meetings, in which the project team decided whether each identified risk was acceptable and whether the mitigation of an identified risk introduced the possibility of new risks. All potential hazards were initially ranked, based on severity (impact and magnitude of risk), occurrence (potential frequency of failure), and potential for detection of the failure or hazard. The hazards that were identified included risks to patients, risks to users and operators, risks to service and maintenance people, and risks to the environment.

The level of risk associated with each identified hazard was classified as either Green, Yellow, or Red for the intended use of the cobas® 4800 system, as described in **Table** 4.

Table 4: Classification of Risk Levels

Risk Level	Range of Risk (Determined from Risk Table)
Green	The respective feature corresponds to the realized state of the art of comparable products and, if applicable, to respective product standards. Thus the residual risk is acceptable.
Yellow	It has to be investigated whether all planned measures of risk reduction have been implemented and the level of safety obtained corresponds to the realized state of the art of comparable products and, if applicable, to respective product standards. Rationale for risk acceptance has to be documented in the Risk Management Report.
Red	A (residual) risk in this range is not acceptable unless medical value was evaluated against risks. Furthermore, resulting risk needs to be approved by Senior Area Management.

A summary of the risk categories before and after mitigation are given in **Table** 5 and Table 6 for cobas® 4800 System Release 2.1: Core and the CT/NG Tests respectively (risks for CT/NG and CT/NG v2.0 are shared and identical).

Table 5: cobas® 4800 System Release 2.1: Core Risks Before and After Mitigation

	Risk Level		
	Green	Yellow	Red
Before Mitigation	21	39	5
After Mitigation	43	22	0

Table 6: cobas® 4800 System Release 2.1: CT/NG and CT/NG v2.0 Risks Before and After Mitigation

	Risk Level		
	Green	Yellow	Red
Before Mitigation	31	23	3
After Mitigation	36	21	0

Final risk assessments were performed for the cobas® 4800 system and CT/NG tests after hazard analysis and risk mitigations were completed. These final risk assessments identified no intolerable risks. The overall level of risk associated with each instrument, software or component was determined to be acceptable for its intended use in the cobas® 4800 system.

4. REQUIREMENTS SPECIFICATIONS

4.1. Overview of Requirements Management

Requirements for the cobas® 4800 system were created and managed according to guidelines outlined in "Customer and Product Requirements Management" [RMS SOP 90.01.18].

Customer Requirements for the cobas® 4800 system are based on customer feedback and represent expectations of the customers. The system-related customer expectations plus the business needs for the cobas® 4800 system were formalized into a list of requirements.

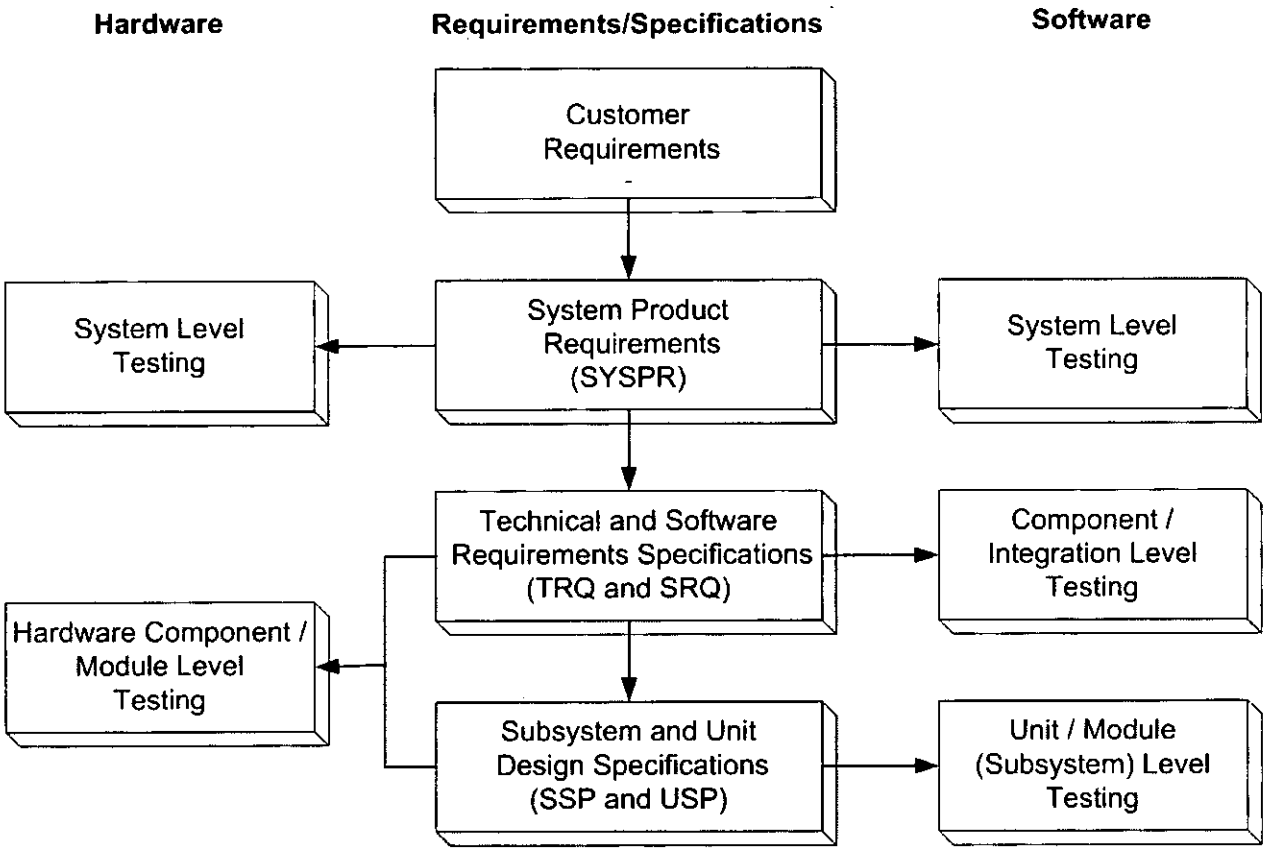
System Product Requirements were primarily derived from and traced to the Customer Requirements. Additional System Product Requirements were derived from sources such as hazard assessments, regulatory requirements, safety requirements, and Roche internal needs. Requirements and specifications for the cobas® 4800 system were created and maintained in accordance with the project requirements management plan (DH-309-020). The requirements management plan describes requirements management activities and responsibilities for the cobas® 4800 system.

4.2. cobas® 4800 System Product Requirements and Decomposition to Lower Level Requirements/Design Specifications — Overview

Requirements and specifications for hardware and software were derived from the cobas® 4800 System Product Requirements. Hardware requirements were designated as Technical Requirements (TRQ), while software requirements were designated as either Software Requirements Specifications (either SRS or SRQ) or as Technical Requirements (TRQ).

Design Specifications for the cobas® 4800 system were created from the Technical Requirements (TRQ) and Software Requirements Specifications (SRS or SRQ). Detailed Design Specifications were created from the corresponding Design Specification for some subsystems or units, depending on the level of detail contained in that Design Specification. An overview of the relationship between the different documentation levels is provided in Figure 4.

Figure 4: Relationship between Requirements, Specifications and Verification Testing



5. TRACEABILITY ANALYSIS

5.1. Methodology for Traceability Analysis

Traceability between requirements, identified hazards, and verification and validation testing has been established using several trace matrices. Gap analysis was performed on each trace matrix to ensure that each higher-level requirement or specification traces to the next lower level requirement or specification, and that each requirement or specification also traces to some verification or validation activity. Identified hazards that are mitigated by implementation of certain requirements are also traced from the risk to the mitigating requirement. The traceability matrices are updated and maintained throughout the development lifecycle of the cobas® 4800 system to ensure traceability between requirements and design, requirements and testing, and between requirements and risk analysis and the related mitigation

The overall requirements and the traceability for the core system are summarized in cobas® 4800 System Release 2.1: Traceability Management File Index (DH-309-030). Traceability for the CT/NG and CT/NG v2.0 tests are summarized in cobas® 4800 System Release 2.1: CT/NG Traceability Management File Index (DH-252-313).

5.2. Verification and Validation Testing

Verification and validation testing was conducted as part of the development of the cobas® 4800 core system version 2.1 and for each of the cobas® CT/NG and cobas® CT/NG v2.0 Analysis Packages (APs).

In general, verification testing was performed at the system level, component level, and unit level to ensure the core system and the CT/NG APs function as expected and are safe for commercial IVD use. A general description of the methodologies used for testing is given below and an overview is provided in Figure 4:

- System Level Testing: The process of testing the integrated hardware/software system and reagents to verify that the system meets its Product Requirements. This type of testing also provides assurance that the system is ready for end-user operation.
- Component / Integration Level Testing: The process of testing software components together to evaluate their interactions before the entire system configuration has been integrated.
- Unit / Module Level Testing: The process of testing an individual software component. This testing is performed independent of the use of the component with other components or in an integrated system.

An overview of the type of testing performed for requirements and specifications is given in Figure 4 above.

5.1. SYSTEM LEVEL VERIFICATION AND VALIDATION TESTING

System level testing was performed at Roche Molecular Systems (RMS) in Pleasanton, California. Testing was carried out on the cobas® 4800 System Core Software Release 2.1 and the cobas® CT/NG and CT/NG v2.0 Analysis Packages. Verification and validation was performed across multiple testing campaigns and is summarized in Table 7.

Table 7: System Level Verification and Validation Testing

Testing Coverage	Testing Scope	Document Reference
cobas® 4800 System Core Software Release 2.1	Initial release of SR2.1 system configuration Includes all new features and changes described in Section 3.1 of this submission	DH-309-016A: cobas® 4800 System Release 2.1: Core System Verification Plan DH-309-016B: cobas® 4800 System Release 2.1: Core System Verification Report
	Regression testing of cobas® 4800 System Release 2.1 after implementation of Channel Shift anomaly correction	DH-309-072A: cobas 4800 System Release 2.1 Channel Shift System Verification Plan DH-309-072B: cobas 4800 System Release 2.1 Channel Shift System Verification Report
cobas® CT/NG Analysis Package	Initial release of CT/NG Analysis Package running under Software Release 2.1 Includes all features, methods, and parameters to run cobas® CT/NG Test	DH-252-315A: cobas 4800 System Release 2.1: CT/NG System Verification Plan DH-252-315B: cobas 4800 System Release 2.1: CT/NG System Verification Summary Report
cobas® CT/NG v2.0 Analysis Package	Initial release of CT/NG v2.0 Analysis Package running under Software Release 2.1 Includes all features, methods, and parameters to run cobas® CT/NG v2.0 Test	DH-252-385A: cobas 4800 System Release 2.1: CT/NG v2.0: System Verification Plan DH-252-385B: cobas 4800 System Release 2.1: CT/NG v2.0: System Verification Report

The scope of the system level test campaigns was to verify that system product requirements were successfully implemented and to verify that observed anomalies were either corrected or accepted as known issues, with no adverse impact on use of the system. Testing of product requirements mitigating risks was also conducted. If a particular product requirement passed testing, then the risk was deemed successfully mitigated. System level risk mitigation testing was captured within the plans and reports completed for each testing campaign.

All planned system level testing for the cobas® 4800 System Core Software Release 2.1 and the cobas® CT/NG and CT/NG v2.0 Analysis Packages was completed successfully.

5.2. COMPONENT AND UNIT LEVEL VERIFICATION AND VALIDATION TESTING

Component and unit level testing of the cobas® 4800 System Core Software Release 2.1 and the cobas® CT/NG and CT/NG v2.0 Analysis Packages was performed at Roche Diagnostics Ltd. (RDI, Rotkreuz, Switzerland).

Sample preparation method (SPM) component testing for the cobas® CT/NG and CT/NG v2.0 Analysis Packages was performed at Roche Molecular System (Pleasanton, California). The SPM consists of the instrument script that defines the sample preparation process (i.e., extraction, purification, and preparation of target nucleic acid) that is performed on the cobas x 480 instrument.

Component and unit level verification was performed across multiple testing campaigns at both Roche sites. Relevant component and unit level verification reports are listed in Table 8 below. All planned component level and unit level testing for the cobas® 4800 System Core Software Release 2.1 and the cobas® CT/NG and CT/NG v2.0 Analysis Packages was completed successfully.

Table 8: Component and Unit Level Verification and Validation Testing

Testing Coverage	Testing Scope	Document Reference
cobas® 4800 System Core Software Release 2.1	Technical level verification of software components for Core Software Release 2.1 (includes core software, workflow packages) Technical level verification of hardware & software components for Control Unit and associated Image software	10533184 DV1 000: c4800 Platform 2.1 Software Version 2.1.0 Design Verification and Validation Report (DVVR) Platform*
	Technical level verification of Common Sample Preparation Method component	DH-309-048B: cobas 4800 System Release 2.1: Common Sample Preparation Method Test Summary Report
	Unit level verification of software units for Core Software Release 2.1	10386174 VER 001: Unit Verification Plan/Report Core and Common Workflow RC4
cobas® CT/NG Analysis Package	Technical verification of CT/NG Test Definition software component	10537755 DV1 000: cobas® 4800 SR2.1 CT/NG DVVR*
	CT/NG Sample Preparation Method component	DH-252-307B: CT/NG Sample Prep Method Test Report*
	Unit level verification of software units for CT/NG Analysis Package	10386174 VER 000: Unit Verification Plan/Report WP1 and CTNG
cobas® CT/NG v2.0 Analysis Package	Technical verification of CT/NG v2.0 Test Definition software component	10537755 DV1 100: cobas® 4800 SR2.1 CT/NG v2.0 DVVR*
	CT/NG v2.0 Sample Preparation Method component	DH-252-387B: cobas® 4800 System Release 2.1: CT/NG v2.0 Sample Preparation Method Test Summary Report*
	Unit level verification of software units for CT/NG v2.0 Analysis Package	10386174 VER 000: Unit Verification Plan/Report WP1 and CTNG

* Provided in attachments section for this submission

5.3. CT/NG TEST TECHNICAL PERFORMANCE VERIFICATION

Limit of Detection (LOD) regression testing was used to verify that the migration of the cobas CT/NG Test (running on cobas 4800 SR1.1) and the cobas CT/NG v2.0 Test (running on cobas 4800 SR 1.2) to cobas 4800 SR2.1 did not affect the performance of the tests.

A total of 10 runs, generating up to 90 replicates for each of six levels, were tested with each software version. The 95% confidence intervals of the Limit of Detection by Probit analysis for both test were overlapping for the different software versions, indicating equivalent levels of sensitivity for CT and NG when using the cobas CT/NG Tests with SR2.1. Results are summarized in Table 9 and Table 10.

Table 9: Probit LOD and Confidence Intervals for CT and NG with SR1.2 and SR2.1

	SR1.2			SR2.1		
	LOD based on Probit Analysis	Lower 95% CI	Upper 95% CI	LOD based on Probit Analysis	Lower 95% CI	Upper 95% CI
CT (EB/mL)	16.5	13.2	22.8	16.5	13.1	23.4
NG (CFU/mL)	0.08	0.07	0.11	0.10	0.08	0.13

Table 10: Probit LOD and Confidence Intervals for CT and NG with SR1.1 and SR2.1

	SR1.1			SR2.1		
	LOD based on Probit Analysis	Lower 95% CI	Upper 95% CI	LOD based on Probit Analysis	Lower 95% CI	Upper 95% CI
CT (EB/mL)	24.7	20.4	36.6	22.4	19.3	32.1
NG (CFU/mL)	0.17	0.13	0.24	0.13	0.11	0.18

5.4. UNRESOLVED ANOMALIES

Anomaly risk assessment was performed to evaluate all formally logged anomalies and identify the appropriate mitigation measure as necessary. Anomalies that were identified and corrected before starting formal testing of the final system configuration were not included in the process.

Unresolved anomalies identified with each configuration of the cobas® 4800 system were deemed acceptable and did not present risk to user, process or product function.

The cobas® 4800 System and CT/NG Known Issues Lists will be provided to users of the system and they include detailed descriptions and workarounds for handling known issues which may be encountered.

5.5. USER DEFINED WORKFLOW

Customers recognize the capability of the cobas z 480 to perform general amplification and detection work in a non-IVD environment. In order to more fully utilize their equipment, some customers have requested the ability to perform both IVD and research workflows on the cobas®

4800 platform. To meet this request, the User Defined WorkFlow (UDF) concept was developed based on an evaluation of the potential patient safety risks. The UDF is an optional feature to the cobas® 4800 system and is installed only upon user order. The cobas® CT/NG Tests, as well as other IVD applications, are independent of this feature being available. Compatibility of the UDF software with the migration to 2.1 was verified and testing concluded that the integrity of the cobas® 4800 IVD workflows and results was not affected.

5.6. UDF NON-INTERFERENCE WITH IVD

Testing was performed with the UDF software v2.0.0 co-installed with the cobas® 4800 system release 2.1. The main purpose of the test case was to verify and validate the UDF non-interference with the cobas® 4800 IVD system. The conclusion from testing is that the UDF software does not interfere with the co-installed cobas® 4800 IVD system. Whether or not the UDF is co-installed, the cobas® 4800 IVD system meets its intended use requirements for running the HPV and CT/NG Tests.

6. CONCLUSION

A comparison of the intended use, technological characteristics, and the results of Regression testing and non-clinical analytical performance studies demonstrate that the cobas® CT/NG v2.0 Test and the cobas® CT/NG Test with software system release 2.1 are substantially equivalent to their predicate devices.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

ROCHE MOLECULAR SYSTEMS, INC.
WILK VON GUSTEDT
REGULATORY AFFAIRS SPECIALIST
4300 HACIENDA DRIVE
PLEASANTON CA 94588

May 5, 2014

Re: K140887
Trade/Device Name: cobas CT/NG v2.0 test
Regulation Number: 21 CFR 866.3390
Regulation Name: Neisseria spp. direct serological test reagent
Regulatory Class: II
Product Code: LSL, MKZ, OOI
Dated: April 4, 2014
Received: April 7, 2014

Dear Mr. Von Gustedt:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809) please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Tamara V. Feldblyum -S for

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K140887

Device Name
Roche cobas® CT/NG Test

Indications for Use *(Describe)*
The cobas® CT/NG Test is an in vitro nucleic acid amplification test that utilizes the Polymerase Chain Reaction (PCR) and nucleic acid hybridization for the qualitative detection of Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG) DNA to aid in the diagnosis of chlamydial and gonococcal disease. The test may be used with vaginal swab specimens self-collected in a clinical setting and male urine from both symptomatic and asymptomatic individuals. Specimens to be tested should be collected in cobas® PCR Media.

Ancillary Collection Kits:
The cobas® PCR Female Swab Sample Kit is used to collect and transport self-collected vaginal swab specimens in a clinical setting. The cobas® PCR Media serves as a nucleic acid stabilizing transport and storage medium for gynecological specimens. Use this collection kit only with the cobas® CT/NG Test. NOTE: This collection kit should not be used for collection of alternative gynecological specimens.

The cobas® PCR Urine Sample Kit is used to collect and transport male urine specimens. The cobas® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens. Use this collection kit only with the cobas® CT/NG Test. NOTE: This collection kit should not be used for collection of female urine specimens.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Tamara V. Feldblyum -S
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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K140887

Device Name
Roche cobas® CT/NG v2.0 Test

Indications for Use *(Describe)*
The cobas® CT/NG v2.0 Test is an automated, in vitro nucleic acid amplification test for the qualitative detection of Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG) DNA in urogenital specimens. The Test utilizes the Polymerase Chain Reaction (PCR) for the detection of Chlamydia trachomatis and Neisseria gonorrhoeae DNA in male and female urine, self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical swab specimens, all collected in cobas® PCR Media (Roche Molecular Systems, Inc.), and cervical specimens collected in PreservCyt® solution. This test is intended as an aid in the diagnosis of chlamydial and gonococcal disease in both symptomatic and asymptomatic individuals.

Ancillary Collection Kits
The cobas® PCR Female Swab Sample Kit is used to collect and transport endocervical and vaginal swab specimens. The cobas® PCR Media serves as a nucleic acid stabilizing transport and storage medium for gynecological specimens. Use this collection kit only with either the cobas® CT/NG Test or the cobas® CT/NG v2.0 Test.
The cobas® PCR Urine Sample Kit is used to collect and transport urine specimens.

The cobas® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens. Use this collection kit only with either the cobas® CT/NG Test or the cobas® CT/NG v2.0 Test.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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