CLIA Waiver by Application Approval Determination
Decision Summary

I. Document Number

CW250022

II. Parent Document Number

K253759

III. CLIA Waiver Type

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

IV. Applicant

Roche Molecular Systems, Inc.

V. Proprietary and Established Names

cobas liat CT/NG/MG nucleic acid test

VI. Measurand (analyte)

Chlamydia trachomatis (CT) cryptic plasmid DNA and 23S ribosomal RNA
Neisseria gonorrhoeae (NG) pivNG and NGR9 DNA
Mycoplasma genitalium (MG) mgpC DNA and 23S ribosomal RNA

VII. Sample Type(s)

Male Urine
Female Urine
Vaginal Swab

VIII. Type of Test

Qualitative, real time nucleic acid amplification test (NAAT)

IX. Test System Description

A Overview

cobas liat system

The cobas liat system can automatically perform qualitative in vitro nucleic acid amplification tests. The cobas liat system consists of three main system components: Analyzer, Assay and Accessories. The system components of the cobas liat system are described below.

cobas liat analyzer
The Analyzer is a system component of the cobas liat system and consists of one software subsystem and three hardware units which are the: Infrastructure unit, Thermal, Loading and Motion unit and Detection unit. It is an automated nucleic acid test instrument. In conjunction with an assay tube, the Analyzer performs reagent preparation, target enrichment, inhibitor removal, nucleic acid extraction, polymerase chain reaction (PCR) amplification, real-time detection, and result interpretation to automate thedetection or quantification of nucleic acid targets in a biological sample.

cobas liat Assay Tube
The cobas liat assay tube uses a flexible tube as a sample processing vessel. It contains all requisite PCR reagents pre-packed in tube segments that are separated by breakable seals. When a cobas liat assay tube containing a raw biological sample is inserted into the cobas liat analyzer, multiple sample processing actuators in the cobas liat analyzer compress the cobas liat assay tube to selectively release the reagents, moving the sample from one segment to the next, and controlling reaction conditions. An embedded microprocessor controls and coordinates these actions to perform all required assay processes, including sample preparation, nucleic acid extraction, target concentration enrichment, inhibitor removal, nucleic acid elution, and realtime RT-PCR. All assay steps are performed within the closed and self-contained cobas liat assay tube, minimizing cross-contamination between samples.

The detection module monitors the reaction in real-time, while an on-board computer analyzes the collected data and outputs an interpreted result. The latter is displayed in the assay report on the integrated LCD touch screen of the cobas liat analyzer and in an electronic file. The report can be printed directly through a USB or network-connected printer. The results can also be exported to an external server, middleware or data management system (DMS), or to a Laboratory Information System (LIS).

The test system was cleared under K240197 and CLIA waived under CW240002. The current submission supports modifications made to the test system which include adding a new sample type (i.e. female urine).

B Test System Components

1. The cobas liat CT/NG/MG nucleic acid test requires the following:

- Internal process control (IPC) - Controls for adequate processing of target bacteria through all steps of assay and to monitor for presence of PCR inhibitors
- PCR mastermix (assay specific oligonucleotides and polymerase)
- Co-factor, Liat magnetic particles, Lysis buffer, Wash buffer, and Elution buffer

2. Specimen sample stored in cobas PCR Media

3. cobas liat CT/NG/MG Control Kit - Contains positive and negative control tubes for validating new cobas liat CT/NG/MG assay tube lots

4. cobas liat System

5. Liat Assay Specific Package (LASP)

Accessories:

- cobas liat Cleaning Tool Kit (CTK) - Used to manually clean the lens adjacent to the assay tube cavity. Contains foam pads, a plastic tool, and alcohol swabs

X. Specific Contents for CLIA Waiver

A Demonstrating "Simple":

Please refer to CW240002.

B Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-Safe Mechanisms

1. Risk Analysis:

   Please refer to CW240002.

2. Fail-Safe and Failure Alert Mechanisms:

   Please refer to CW240002.

3. Flex Studies:

   There are no new flex studies performed since the last submission. Please refer to CW240002.

C Demonstrating "Insignificant Risk of an Erroneous Result" - Accuracy

Two studies were conducted that demonstrated there is an insignificant risk of an erroneous result when using the cobas liat CT/NG/MG nucleic acid test:

i. A prospective clinical study (see below)
ii. Device performance with analyte concentrations near the cutoff (Please refer to CW240002)

Clinical performance of the cobas liat CT/NG/MG nucleic acid test was initially established in CW240002 using vaginal swab and male urine specimens. CT performance in female urine specimens was evaluated using a combination of specimens obtained during the original clinical study and a supplemental study. NG and MG performance in female urine was evaluated using specimens obtained from the original clinical study only.

The original clinical study was a prospective study comparing the results to a Composite Comparator Algorithm (CCA) or Patient Infected Status (PIS) result derived from a combination of FDA-cleared NAATs for the three analytes. In that study, male and female urine and vaginal swabs were collected and tested at 13 geographically diverse intended use clinical sites across the US. There were 48 operators that took part in cobas liat CT/NG/MG testing, of which, 43 represented CLIA-waived operators. Five of the 48 operators had experience in a moderate complexity laboratory. A total of 4852 subjects (2512 females and 2340 males) were enrolled in the study and provided specimens for collection. Of the evaluable subjects, there were 2459 specimens included in the final clinical performance in the original study.

Tables 1 and 2 show the clinical performance of NG and MG in female urine specimens during the original study when compared to CCA.

Table 1: NG Clinical Performance in Female Urine against the CCA Result

Study	Symptom Status	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Original Study	Symptomatic	1111	20	1	1090	0	100% (83.9%-100%)	99.9% (99.5%-100%)
Original Study	Asymptomatic	1347	17	1	1329	0	100% (81.6%-100%)	99.9% (99.6%-100%)
Original Study	Overall	2458	37	2	2419	0	100% (90.6%-100%)	99.9% (99.7%-100%)

Table 2: MG Clinical Performance in Female Urine against the CCA Result

Study	Symptom Status	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Original Study	Symptomatic	1108	101	19	978	10	91.0% (84.2%-95.0%)	98.1% (97.0%-98.8%)
Original Study	Asymptomatic	1343	98	13	1227	5	95.1% (89.1%-97.9%)	99.0% (98.2%-99.4%)
Original Study	Overall	2451	199	32	2205	15	93.0% (88.8%-95.7%)	98.6% (98.0%-99.0%)

A supplemental study was conducted to evaluate the performance of cobas liat CT/NG/MG nucleic acid test for the assessment of detecting CT in female urine specimens. Specimen collection was performed at one external site. Nine operators with minimal or no hands-on laboratory training were used to support CLIA waiver for the device. There were a total of 785 prospective samples from subjects who met the study eligibility criteria. Of these 785 samples, there were a total of 751 samples with evaluable results and included in the final data set. The final evaluation was determined by comparing results from cobas liat CT/NG/MG nucleic acid test to CCA. This supplemental set of data for CT was combined with the female urine data from the original study.

Table 3: CT Clinical Performance in Female Urine against the CCA Result

Study	Symptom Status	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Supplemental Study	Symptomatic	312	17	2	293	0	100% (81.6%-100%)	99.3% (97.6%-99.8%)
Supplemental Study	Asymptomatic	439	15	3	420	1	93.8% (71.7%-98.9%)	99.3% (97.9%-99.8%)

Supplemental Study	Overall	751	32	5	713	1	97.0% (84.7%-99.5%)	99.3% (98.4%-99.7%)
Original Study	Symptomatic	1113	53	2	1054	4	93.0% (83.3%-97.2%)	99.8% (99.3%-99.9%)
Original Study	Asymptomatic	1346	40	3	1302	1	97.6% (87.4%-99.6%)	99.8% (99.3%-99.9%)
Original Study	Overall	2459	93	5	2356	5	94.9% (88.6%-97.8%)	99.8% (99.5%-99.9%)
Combined	Symptomatic	1425	70	4	1347	4	94.6% (86.9%-97.9%)	99.7% (99.2%-99.9%)
Combined	Asymptomatic	1785	55	6	1722	2	96.5% (88.1%-99.0%)	99.7% (99.2%-99.8%)
Combined	Overall	3210	125	10	3069	6	95.4% (90.4%-97.9%)	99.7% (99.4%-99.8%)

D Labeling for Waived Devices

The labeling consists of:

1. Package Insert
2. Quick Reference Instructions
3. Instrument Manual
4. Instructions for the two specimen collection kits (urine and vaginal swabs)

XI. Conclusion

The submitted information in this CLIA waiver application supports a CLIA waiver approval decision.