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

A. 510(k) Number:
   K053289

B. Purpose for Submission:
To add the option for automated swab specimen preparation and control preparation using the software accessory "Roche Scripts for COBAS AMPLICOR™ CT/NG Test for *Neisseria gonorrhoeae*" to direct the Tecan Genesis RSP 150 Workstation.

C. Measurand:
Neisseria gonorrhoeae M.*Ngo* PII DNA sequence

D. Type of Test:
Qualitative determination using Polymerase Chain Reaction (PCR) DNA amplification and colorimetric detection

E. Applicant:
Roche Diagnostics Corporation

F. Proprietary and Established Names:
COBAS AMPLICOR™ CT/NG Test for *Neisseria gonorrhoeae* with optional accessory Roche Scripts for COBAS Amplicor CT/GC Test

G. Regulatory Information:

1. Regulation section:
   866.3390 - Neisseria species, Direct Serological Test Reagents
2. Classification:
   Class II
3. Product code:
   LSL - DNA reagents, Neisseria
4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):
   The COBAS AMPLICOR™ CT/NG Test for *Neisseria gonorrhoeae* is a qualitative in vitro test for the detection of *N. gonorrhoeae* in endocervical swab specimens, and in male urethral swab specimens as evidence of symptomatic or asymptomatic infection with *N. gonorrhoeae*. *N. gonorrhoeae* DNA is detected by Polymerase Chain Reaction (PCR) amplification of target DNA and by hybridization capture of amplified target using the COBAS AMPLICOR™ analyzer.

2. Indication(s) for use:
   This submission is intended to add the option the Roche Scripts for COBAS AMPLICOR™ CT/NG Test to provide software scripts to direct the automated Tecan Genesis RSP 150 Workstation to process swab samples or control material for analysis using the COBAS AMPLICOR™ CT/NG test for *Neisseria gonorrhoeae*.

   The Tecan Genesis Robotic Sample Processor (RSP) 150 Instrument is intended for liquid pipetting and measurement tasks under official laboratory conditions.

   Sample and control preparation can either be accomplished manually or automated using the optional Roche Scripts for COBAS AMPILICOR™ CT/NG Test accessory to direct the Tecan Genesis RSP 150 Workstation. Urine specimens are not indicated for use with the automated sample preparation option.

3. Special conditions for use statement(s):
   Urine specimens are not indicated for use with the automated sample preparation option. Prescription Use only.

4. Special instrument requirements:
   Not applicable

I. **Device Description:**
   The COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* is a multiplex in vitro diagnostic test performed on the COBAS AMPLICOR™ Analyzer. The COBAS AMPLICOR™ Analyzer automates the amplification, the nucleic acid hybridization and the colorimetric detection procedures of the Test. The COBAS AMPLICOR CT/NG Test for *N. gonorrhoeae* also has an Internal Control that identifies specimens that contain substances which are inhibitory to PCR.

   The RSP Genesis 150 Workstation with Gemini software v4.2 is a microprocessor controlled sample diluter and dispenser. It is configured with eight (8) sample processing probes and/or bar code reader. Modular racks will accommodate many types of commonly used tubes and microwell plates. The RSP 150 instrument is capable of handling pipetting volume ranges between 0.5 µL and 5 mL.

   The Roche Scripts v1.0.3 for COBAS AMPLICOR™ CT/NG Test accessory consists of a compact disc (CD) containing scripts to direct the automated Tecan Genesis RSP 150 workstation with Gemini software v4.2 to process swab samples or control material for analysis. The Roche Scripts operate by providing commands in the GEMINI computer language to direct the Tecan in pipetting, dilution, incubation and shaking, and specimen dispersion into up to eight 12-position A rings (the sample rack for the COBAS AMPLICOR Instrument).

J. **Substantial Equivalence Information:**
   1. Predicate device name(s):
      COBAS AMPLICOR™ CT/NG test for *Neisseria gonorrhoeae*
   2. Predicate 510(k) number(s):
      K974342

3.   Comparison with predicate:

Similarities		
Item	Device COBAS AMPLICOR™ CT/NG for *N. gonorrhoeae* with optional Roche Scripts accessory	Predicate COBAS AMPLICOR™ CT/NG for *N. gonorrhoeae*
Intended Use	The COBAS AMPLICOR™ CT/NG Test for *N. gonorrhoeae* is a qualitative in vitro test for the detection of *N. gonorrhoeae* M .Ngo PII DNA sequence in endocervical swab specimens, and in male urethral swab specimens as evidence of symptomatic or asymptomatic infection with *N. gonorrhoeae*. *N. gonorrhoeae* DNA is detected by Polymerase Chain Reaction (PCR) amplification of target DNA and by hybridization capture of amplified target using the COBAS AMPLICOR™ analyzer.	Same
Test Principle	DNA detection via PCR amplification of target DNA followed by hybridization capture of amplified target using the COBAS AMPLICOR™ Analyzer	Same
Controls provided	Positive control: DNA from *N. gonorrhoeae* Negative control: plasmid DNA from *C. trachomatis* Optional internal control: DNA sequences with primer binding regions identical to *N. gonorrhoeae* target sequence	Same

Differences		
Item	Device	Predicate
Analytical sensitivity - Limit of Detection, Expressed as Colony Forming Units/mL (cfu/mL)	Revised test performance: 250 cfu/mL, equivalent to 3.25 cfu/test, using automated specimen preparation; 400 cfu/mL, equivalent to 5.0 cfu/test, using manual preparation for *N. gonorrhoeae* with swab specimens	Labeled test performance: 400 cfu/mL, equivalent to 5 cfu/test for *N. gonorrhoeae* with swab specimens; 100 cfu/mL, equivalent to 5 cfu/test for urine specimens, manual preparation
Specimen type	Urethral and endocervical swabs only (no urine samples)	Male or female urine specimens; urethral and endocervical swabs
Specimen and Control preparation	Manual or automated using the Roche Scripts to direct the Tecan Genesis RSP 150 workstation	Manual

K. Standard/Guidance Document Referenced (if applicable):
CLSI EP5-A2 "Evaluation of Precision Performance of Quantitative Measurement Methods", (2004). CLSI EP-12A "User Protocol for Evaluation of Qualitative Test Performance", (2002).

L. Test Principle:

DNA detection via PCR amplification of target DNA followed by hybridization capture of amplified target using the COBAS AMPLICOR ™ Analyzer. The PCR-based test system reagents and testing procedures are unchanged.

M. Performance Characteristics (if/when applicable):

The purpose of this submission is to demonstrate equivalency between the automated specimen preparation using Roche Scripts to direct the Tecan Genesis TSP 150, and the manual specimen preparation method. The test system was evaluated at two internal sites and one external site for analytical sensitivity, cross-contamination, precision and analytical specificity; and was subject to a clinical method comparison for 600 samples.

    1. Analytical performance:
        a.   *Precision/Reproducibility:*

The precision was determined for a panel of culture transport media specimens containing samples described in the table below.

Panel Sample	Description
PS1	Spiked M4 media at ~500 IFU/mL CT
PS2	Spiked M4 media at ~300 IFU/mL CT
PS3	Spiked M4 media at ~100 IFU/mL CT
PS4	Spiked M4 media at ~100 IFU/mL CT and ~5000 cfu/mL NG
PS5	Spiked M4 media at ~300 IFU/mL CT and ~3000 cfu/mL NG
PS6	Spiked M4 media at ~500 IFU/ml CT and ~1000 cfu/mL NG
PS7	Spiked M4 media at ~1000 cfu/mL NG
PS8	Spiked M4 media at ~3000 cfu/mL NG
PS9	Spiked M4 media at ~5000 cfu/mL NG
PS10	Spiked M4 media at ~500 IFU/mL CT and ~5000 cfu/mL NG
PS11	M4 media blank

Operators at one internal and one external site tested the panel samples in triplicate, once a day for three days. A third internal site, which did not participate in any other analytical studies, also performed precision studies using the same testing protocol.   Three sets of three aliquots of each of the 11 panel members were prepared for a total of 27 replicates per panel member. Multiple lots of reagents were used for preparation, amplification and detection. The results are presented in the table below.

Summary of Result for Precision: COBAS AMPLICOR™ CT/NG for
N. gonorrhoeae

	Automated			Manual		
	Total	Correct	%	Total	Correct	%
PS1	59	59	100.0	59	59	100.0
PS2	59	58	98.3	60	60	100.0
PS3	59	58	98.3	59	58	98.3
PS4	60	60	100.0	60	60	100.0
PS5	60	60	100.0	60	59	98.3
PS6	60	60	100.0	60	60	100.0
PS7	60	59	98.3	60	60	100.0
PS8	60	58	96.7	60	60	100.0
PS9	60	60	100.0	60	60	100.0
PS10	60	60	100.0	60	60	100.0
PS11	59	58	98.3	59	58	98.3
Total	656	650	**99.1**	657	654	**99.5**

The overall percentage of correct results was determined as 99.1% (650/656) for the automated method, and 99.5% (654/657) for the manual method, which are determined as equivalent.

b.   *Linearity/reportable range:*
Not applicable

c.   *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The recommended Positive, Negative and Internal Control material were tested a sufficient number of times with acceptable results on all testing days.

d.   *Detection limit:*
The Limit of Detection of the COBAS AMPLICOR™ CT/NG for *N. gonorrhoeae* on the COBAS AMPLICOR™ Analyzer was determined using M4 culture transport media specimens containing 1×10^8 IFU/mL of *Neisseria gonorrhoeae* culture (ATCC strain 19242). The panel contained the following dilutions, which bracket the current labeled limit of detection (in bold):

NG: 50, 100, 200, 250, **400**, 500 cfu/mL (0.62, 1.25, 2.5, 3.12, **5.00**, 6.25 cfu/test)

Three operators at two separate internal sites and one external site tested the panel once a day for two days in duplicate, for a total of 24 replicates per dilution for each sample processing/testing combination. The Limit of Detection (LOD), the lowest dilution at which ≥ 95% of replicates (23/24 or 24/24) yielded positive results, for COBAS AMPLICOR™ CT/NG for *N. gonorrhoeae* is 250 cfu/mL (3.25 cfu/test) for the automated preparation and 400 cfu/mL (5.0 cfu/test) for the manual specimen preparation.

The 250 cfu/mL result for the automated method differs from the current labeled LOD of 400 cfu/mL for the manual method.

The results of study are presented in the table below.

Summary of analytical sensitivity for COBAS AMPLICOR™ CT/NG Test for *N. gonorrhoeae* with automated and manual specimen preparation

Sample cfu/mL	Dilution	N	Automated		N	Manual	
			Positive	%		Positive	%
NG –1 0.62	50	24	10	41.7	19	1	5.3
NG – 2 1.25	100	24	13	54.2	23	12	52.2
NG – 3 2.5	200	24	21	87.5	24	5	20.8
NG –4 3.12	250	24	23	95.8	23	10	43.5
NG—5 5	400	24	24	100.0	24	23	95.8
NG—6 6.25	500	24	23	95.8	24	24	100.0

e. *Analytical specificity:*

The analytical specificity was tested using the automated sample preparation directed by the Roche Scripts compared to the manual method by examining spiked samples with varying concentrations of the test analytes. The same method and concentrations used in the Precision panel testing were utilized for analytical specificity. Data from the three sites were pooled and the percentage of false positives and negatives were calculated. The following table shows the agreement of the specificity results between the automated and the manual methods.

Specificity results for COBAS AMPLICOR CT/NG test for *N. gonorrhoeae*

		COBAS AMPLICOR CT/NG test for *N. gonorrhoeae*					
	N	Automated		N	Manual		
Positive Samples		False negatives	%		False negatives		%
PS4	60	0	0.0	60		0	0.0
PS5	60	0	0.0	60		1	1.7
PS6	60	0	0.0	60		0	0.0
PS7	60	1	1.7	60		0	0.0
PS8	60	2	3.3	60		0	0.0
PS9	60	0	0.0	60		0	0.0
PS10	60	0	0.0	60		0	0.0
Overall	**420**	**3**	**0.7**	**420**		**1**	**0.2**

Negative Samples		False positives				False positives		
PS1	59		1	1.7	59		0	0.0
PS2	59		1	1.7	60		0	0.0
PS3	59		1	1.7	59		1	1.7
PS11	59		1	1.7	59		1	1.7
Overall	**236**		**4**	**1.7**	**237**		**2**	**0.8**

The false negative rate and false positive rate for automated sample preparation are within 95% of false negative and false positive rate for manual sample preparation. The analytical specificity automated results are equivalent to the manual method results.

f. *Assay cut-off:*
    Not applicable

g. *Cross-Contamination Testing*
    This study evaluated the potential for cross contamination / carryover of the COBAS AMPLICOR™ CT/NG for *N. gonorrhoeae* assay with automated sample preparation directed by the Roche Scripts; in comparison to manual sample preparation. This test was designed to observe the effects of potential aerosolization / splash over the entire A-ring. Positive specimens or M4 media blanks were prepared as samples.

    Positive samples were prepared from stock cultures of *Chlamydia trachomatis* (ATCC strain Vr 885, Serovar D) at 1.44×10^7 IFU/mL and *Neisseria gonorrhoeae* (ATCC 19242) at 1.0×10^8 IFU/mL diluted in M4 media. High concentration of ~ 10,000 IFU/mL of *C. trachomatis* alone and ~10,000 IFU/mL of both *C. trachomatis* and *N. gonorrhoeae* combined were utilized. An additional set of rings was prepared and run containing all blanks in the sample positions. Data from rings containing all blanks were not included in the calculations. Testing was performed on three instruments using 8 rings once a day over five days. The overall false positive rate was 0.4% (1/270) with automated specimen preparation and 0.8% (2/263) with manual preparation, Seven blank samples returned an inhibitory result. The difference in the false positivity rates are not statistically significant at the 95% confidence level, and the results are equivalent.

2. Comparison studies:

    a. *Method comparison with predicate device:*
        This method comparison study was designed to demonstrate the equivalency between the automated specimen preparation technique directed by the Roche Scripts and the manual specimen preparation method for 600 samples. The acceptance criteria were based on a concordance of the initial test results; inhibitory or equivocal results were not repeated.

        The two methods should agree in their performance where at least 90% positive

agreement as well as 90% negative agreement is observed for the individual patient groups. The following table shows the agreement of the Roche Scripts directing the automated method versus the manual method comparison, without discrepant resolution, assuming that the manual result is the true result.

Method Comparison for COBAS AMPLICOR CT/NG test for *N. gonorrhoeae*

		Number Tested	Agreement	Confidence Interval	
Overall Agreement	Concordance	567 / 597	95.0%	92.9% - 96.6%	
	% positive	83 / 89	93.3%	85.9% - 97.5%	
	% negative	483 / 494	97.8%	96.1% - 98.9%	
Endocervical	Concordance	156 / 164	95.1%	90.6% - 97.9%	
	% positive	17 / 17	100.0%	80.5% - 100.0%	
	% negative	139 / 144	96.5%	92.1% - 98.9%	
Urethral	Concordance	408 / 430	94.9%	92.4% - 96.8%	
	% positive	66 / 72	91.7%	82.7% - 96.9%	
	% negative	341 / 347	98.3%	96.3% - 99.4%	
No interferent	Concordance	442 / 464	95.3%	92.9% - 97.0%	
	% positive	73 / 78	93.6%	85.7% - 97.9%	
	% negative	368 /375	98.1%	96.2% - 99.2%	
Interferent	Concordance	57 / 62	91.9%	82.2% - 97.3%	
	% positive	6 /6	100.0%	54.6% - 100.0%	
	% negative	51 / 53	96.2%	87.0% - 99.5%	

This table summarizes the combinations of concordance of test results for overall agreement as well as for the specific subgroups. Testing of both methods shows that the overall agreement concordance is 95.0%, and the % positive and % negative agreement for all subgroups are > 90.0%, which is acceptable.

b. *Matrix comparison:*
   Not applicable

3. Clinical studies:

a. *Clinical Sensitivity:*
   Not applicable

b. *Clinical specificity:*
   Not applicable

c. *Other clinical supportive data (when a. and b. are not applicable):*

4. Clinical cut-off:
   The cutoffs for the *N. gonorrhoeae* specimen results and the Internal Control (IC) specimen results were determined in the previous submission for COBAS AMPLICOR™ CT/NG for *N. gonorrhoeae* (K974342).

5. Expected values/Reference range:

Interpretive Criteria for COBAS AMPLICOR™ CT/NG for *N. gonorrhoeae*

NG Specimen result		IC Results		Interpretation
A_{660}	COBAS Flag	A_{660}	COBAS FLAG	
< 0.2	Negative	≥ 0.2	Positive	*N. gonorrhoeae* not detected
< 0.2	Negative	< 0.2	Negative	Inhibitory specimen
≥ 2.0	Positive	Any	Any	*N. gonorrhoeae* DNA detected
≥ 0.2, <2.0	GZ 0.2 – 2.0	Any	Any	Equivocal (inconclusive)

GZ = Grey Zone

N. Instrument Name:
Tecan Genesis RSP-RC 150 Workstation Instrument, with Roche Scripts v1.0.3 accessory

O. System Descriptions:
1. Modes of Operation:
The Genesis RSP 150 Workstation is a multiple task liquid handling system that combines a system of microprocessor-controlled liquid handling and other components to one instrument. The User controls the system via a personal computer, equipped with the Genesis Instrument Software, Gemini Software v4.2, and the Roche Scripts. Genesis RSP is designed to handle liquid volumes ranging between 0.5 µL and 5 µL depending on the installed configuration.

The liquid system is the central component of Genesis pipetting function. It transmits the precise movement of the diluter pistons to the tips through the system liquid. The system liquid is delivered to the system in a container and is aspirated and distributed in the whole system via tubes, valves and connectors. The distribution of the system liquid is effected by the movement of the diluter pistons in several strokes. Disposable tips with filter shall be used where no carry over is tolerable.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types in submission K963268:

Yes __X_ or No _____

3. Specimen Identification:
The Positive Identification (PosID2) reads Barcodes on Carriers, Racks and Containers on both, the primary, e.g. sample tube, as well as the secondary side, e.g. microplates by means of a scanner. With its gripper, it pulls carriers towards the rear of the instrument for barcode identification on tubes and microplates, and then, pushes the carrier back into operating position. To use the PosID2, all carriers, racks and containers (sample tubes,

microplates, reagent bottles, troughs) must be labeled with barcodes. Exact positioning of these labels is required for optimal function.

4. Specimen Sampling and Handling:
   To minimize the potential for well-to-well carryover, the Roche Scripts direct the liquid handling arms of the Tecan RSP 150 to discard the pipet tip immediately after any pipetting step involving contact with a sample- or control containing well. Design features intended to minimize the potential for cross-contamination via aerosolization and splashing are listed below:
   - Use of disposable pipet tips with aerosol barrier filters
   - Low disposable tip eject option: tips are ejected into a narrow slit box to reduce aerosolization during the ejection step
   - Use of a deep well plate for extraction steps

   The Gemini 4.2 software and the Tecan Genesis RSP 150 have liquid class settings which control the accuracy of the aspiration and dispense functions of the liquid handling arm. These liquid classes have several sub-options which are configured to the liquid being handled. The sub-options include:
   - LAG, STAG, TAG (air gap settings at specific places within the pipet tip)
   - Rate / speed of aspiration and dispense settings
   - Position of pipet tip in well to optimize liquid aspiration
   - Mixing characteristics

5. Calibration:
   Liquid class handling settings are determined for each liquid by performing volumetric test cases. The documentation for the test cases is provided in the submission.

6. Quality Control:
   An on-line interactive Troubleshooting guide normally detects problems and offers immediate advice for corrective actions pertaining to operations, communication, positioning, and identification errors. Daily, weekly, and periodic preventative maintenance schedules are provided in the Tecan User Manual.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:
   The sponsor acknowledges that the analytical studies cited in the risk assessment as controls for the Tecan functions are more properly identified as verification activities. Roche audited Tecan, and confirmed that Tecan validated the Gemini v4.2 software.

   The Roche Scripts CD's are standalone software designed to run on Off-the-Shelf (OTS) Tecan equipment. Roche Scripts are installed at the user site in read-only mode, and cannot be altered by the User.

Q. Proposed Labeling:
   The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

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