510(k) Summary

COBAS AMPLICOR™ CT/NG Test for Neisseria gonorrhoeae

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Intended Use:

The COBAS AMPLICOR™ CT/NG Test for *Neisseria gonorrhoeae* is a qualitative in vitro diagnostic test for the detection of *Neisseria gonorrhoeae* in clinical specimens. The test is intended for use with the COBAS AMPLICOR Analyzer (K964506). The test utilizes polymerase chain reaction (PCR) for the multiplex nucleic acid amplification of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* DNA and target-specific probe hybridization capture for the detection of the amplified *Neisseria gonorrhoeae* DNA in endocervical swab specimens obtained from asymptomatic and symptomatic female patients, urethral swab specimens obtained from symptomatic male patients and urine specimens obtained from asymptomatic and symptomatic male patients. Testing of male urine specimens may only be performed in conjunction with the use of the Internal Control.

Description of the Device:

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 *Neisseria gonorrhoeae* also has an Internal Control for the identification of specimens that contain PCR inhibitors.

Similarities and Differences to Predicate Device:

The COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* is substantially equivalent to other commercially available *in vitro* diagnostic devices for the detection of *Neisseria gonorrhoeae* in urogenital swab and urine specimens. These methods include direct Giemsa staining of infected tissue, detection of chlamydial inclusion bodies in infected culture cells using fluorescent antibody stain, direct antigen detection using fluorescent antibody stain and nucleic acid probes. Cell culture with fluorescent monoclonal antibody stain is generally considered to be the international gold standard method for detection. A commonality among all of these devices is that the unique biochemical properties of the target organism are all encoded in the DNA of the organism, essentially reducing each device to a test for genetic (i.e., phenotypic or genotypic) characteristics of the organism.

The COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* detects a conserved sequence of 201 nucleotides within the M·*Ngo*PII putative cytosine DNA methyltransferase gene of the *N. gonorrhoeae* bacterial chromosome while cell culture detects the complete viable inclusion forming unit. The clinical performance of the COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* has been shown to be equivalent to cell culture methods.

The COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* allows the automated multiplex amplification of *Neisseria gonorrhea, Chlamydia trachomatis* and an Internal Control. All of these tests use similar detection reactions that are based on the absorbance measurement of a chromophore that is produced by the oxidation of 3,3′,5,5′-tetramethybenzidine by hydrogen peroxide in the presence of horseradish peroxidase.

Non-Clinical Performance:

The analytical sensitivity (limit of detection) of the COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* is 5 colony forming units (CFU) per test for each of 15 isolates tested for culture transport media (CTM) specimens and urine specimens. At 1 CFU/test, the test gave positive results for at least one replicate for all 15 strains, and positive results for all three replicates for 10 of the 15 strains tested.

The analytical specificity of the COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* was tested against 133 bacteria, 6 fungi, 1 protozoon and 11 virus isolates that may be isolated from the urogenital tract. Multiple isolates of some organisms were tested including isolates of Neisseria subflava and Neisseria cinerea obtained from the American Type Culture Collection. All isolates were added to culture transport media and normal human urine at approximately 10^4 copies of genomic DNA per test. The culture transport media and urine specimens were processed and tested using the standard COBAS AMPLICOR CT/NG Test procedure. Two of the *Neisseria subflava* isolates and one *Neisseria cinerea* isolate gave false positive test results. All of the remaining organisms tested including other isolates *Neisseria subflava* and *Neisseria cinerea* gave negative results with the COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae*.

The precision of the COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* was determined for a panel of culture transport media specimens containing 0, 12.5, 37.5 and 62.5 *Neisseria gonorrhoeae* CFU/test; and urine specimens containing 0, 10, 30 and 50 *Neisseria gonorrhoeae* CFU/test. Three independent operators at three different geographical sites tested the panel in duplicate once a day for three days. Two sites gave 100% qualitatively correct results for all specimen types and concentrations. One site had two false positive results from one culture transport media sample and two false negative results from two urine samples. These samples were repeated in duplicate at the site and the correct test results were obtained for each replicate. The results of this study are presented in Tables 1 and 2.

Table 1
COBAS AMPLICOR CT/NG Test for Neisseria gonorrhoeae
CTM Specimen Reproducibility

	***N. gonorrhoeae* Spiked CTM (CFU/test)**			
	0	**12.5**	**37.5**	**62.5**
Number of Replicates	72	36	36	36
% Correct Results	97.2†	100	100	100
Median A_{660}	0.002	3.932	3.984	3.968
Minimum A_{660}	0.000	1.554	2.925	3.266
Maximum A_{660}	0.023‡	4.000	4.000	4.000

† Two samples gave an initial positive test result at one site. Both samples gave negative test results when repeated in duplicate at the site.
‡ Maximum absorbance excluding the two initial positive tests

Table 2
COBAS AMPLICOR CT/NG Test for Neisseria gonorrhoeae
Urine Specimen Reproducibility

	***N. gonorrhoeae* Spiked Urine (CFU/test)**			
	0	**10**	**30**	**50**
Number of Replicates	72	36	36	36
% Correct Results	100	88.9†	100	100
Median A_{660}	0.003	3.759‡	3.966	3.967
Minimum A_{660}	0.000	0.820*	0.771	1.518
Maximum A_{660}	0.024	4.000	4.000	4.000

† Two samples tested at one site gave a total of four negative test results.
The specimens gave negative test results when repeated in duplicate at the site.
‡ The median absorbance excluding the four initial negative tests was 3.851
* The minimum absorbance excluding the four initial negative tests

Clinical Performance

The COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* was evaluated in a clinical study conducted at six geographically diverse sites. The clinical performance of the test was evaluated by comparing the results of the 5486 swab and urine specimens to the *Neisseria gonorrhoeae* culture results. Specimens with discrepant results were also tested by an alternate primer (16S rRNA) PCR test. Analyses were also performed including and excluding the use of the Internal Control result. The alternate primer PCR test results were not used to calculate the clinical performance characteristics of the test and are reported for information purposes only.

When the Internal Control result was used in the analysis, specimens with repeatedly negative Internal Control test results were excluded because the results were not interpretable. Of the 5486 specimens collected and tested in the COBAS AMPLICOR CT/NG Test clinical study, 44 were repeatedly inhibitory. Therefore, a total of 5442 specimens were used in the analyses when the Internal Control result was used. Table 3 shows the results from the clinical study.

Table 3
Clinical Performance Of AMPLICOR CT/NG Test for Neisseria gonorrhoeae Including and Excluding the Internal Control[1]

Sex	Specimen	Symptom	TP	TN	FP	FN	No. Inhib.	% Repeatedly Inhibitory	Total	Sensitivity (95% CI)	Specificity (95% CI)	16S+/FP*
Female	CTM	Asymptomatic	49	1026	13	1	12	1.15%	1101	98.0% (89.3-99.9)	98.7% (98.1-99.4)	5/13
			(49)	(1039)	(12)	(1)			(1101)	(98.0%) (89.3-99.9)	(98.9%) (98.2-99.5)	(5/12)
		Symptomatic	69	1032	14	4	18	1.71%	1137	94.5% (86.6-98.5)	98.7% (98.0-99.4)	9/14
			(69)	(1050)	(13)	(5)			(1137)	(93.2%) (84.9-97.8)	(98.8%) (98.1-99.4)	(9/13)
Total for Females			118	2058	27	5	30	1.43%	2238	95.9% (90.8-98.7)	98.7% (98.2-99.2)	14/27
			(118)	(2089)	(25)	(6)			(2238)	(95.2%) (91.4-98.9)	(98.8%) (98.4-99.3)	(14/25)
Male	CTM	Symptomatic	342	862	34	2	2	0.23%	1242	99.4% (97.9-99.9)	96.2% (95.0-97.5)	19/34
			(342)	(865)	(33)	(2)			(1242)	(99.4%) (97.9-99.9)	(96.3%) (95.1-97.6)	(19/33)
	URINE	Asymptomatic	9	703	3	3	1	0.14%	719	75.0% (42.8-94.5)	99.6% (98.8-99.9)	2/3
			(8)	(704)	(3)	(4)			(719)	(66.7%) (34.9-90.1)	(99.6%) (98.8-99.9)	(2/3)
		Symptomatic	336	904	22	14	11	1.18%	1287	96.0% (93.9-98.1)	97.6% (96.6-98.6)	18/22
			(310)	(907)	(21)	(49)			(1287)	(86.4%) (82.8-89.9)	(97.7%) (96.8-98.7)	(17/21)
Total for Males			687	2469	59	19	14	0.56%	3248	97.3% (96.1-98.5)	97.7% (97.1-98.3)	39/59
			(660)	(2476)	(57)	(55)			(3248)	(92.3%) (90.4-94.3)	(97.7%) (97.2-98.3)	(39/57)

[1]Numbers in parenthesis show the performance results when the Internal Control was not used

* Number of apparent false positive COBAS AMPLICOR Test results that were positive by alternate primer pair PCR/Total number of apparent COBAS AMPLICOR false positive results.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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MAY 28 1999

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Re: K974342
Trade Name: Roche COBAS Amplicor CT/NG Test for Neisseria Gonorrhoeae
Regulatory Class: II
Product Code: LSL
Dated: March 08, 1999
Received: March 11, 1999

Dear Dr. Kelly:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). 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.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597, or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

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Director
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Enclosure

{PRIVATE }

510(k) Number (if known): K974342

Device Name: COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae*

Indications For Use:

The COBAS AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* is a qualitative *in vitro* test for the detection of *N. gonorrhoeae* DNA in urine from symptomatic or asymptomatic males, in endocervical swab specimens from symptomatic or asymptomatic females, and in urethral swab specimens from symptomatic males as evidence of 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.

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K974342

PRESCRIPTION USE X

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)