K974503

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Diagnostics

510(k) Summary

Roche AMPLICOR® CT/NG Test for Neisseria gonorrhoeae

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K974503

Intended Use:

The AMPLICOR® CT/NG Test for *Neisseria gonorrhoeae* is a qualitative *in vitro* test for the detection of *Neisseria gonorrhoeae* in clinical specimens. The test utilizes polymerase chain reaction (PCR) for the multiplex nucleic acid amplification of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* DNA in endocervical and male urethral swab specimens and in male and female urine specimens from symptomatic and asymptomatic patients, and target-specific probe hybridization capture for the detection of the amplified *Neisseria gonorrhoeae* DNA.

Description of the Device:

The AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* is a multiplex *in vitro* diagnostic test that enables the simultaneous amplification of *Neisseria gonorrhoeae, Chlamydia trachomatis* and an Internal Control sequence in a sample. The Test is designed for use with the Perkin Elmer 2400 or the Perkin Elmer 9600 thermal cycler for nucleic acid amplification of target DNA by polymerase chain reaction, and colorimetric detection using a conventional microwell plate washer and reader. The AMPLICOR CT/NG Test also incorporates an Internal Control for the identification of specimens that contain inhibitory substances to the PCR amplification reaction.

Similarities and Differences to Predicate Device:

The 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 biochemical and immunologic assays for specific identification of *N. gonorrhoeae* on selective culture medium, and tests for specific nucleic acid in patient specimens. Isolation of *N. gonorrhoeae* on selective culture medium with confirmation by acid production from carbohydrates, rapid enzyme tests, serologic assays, and tests for

November 23, 1999
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specific nucleic acid are generally considered to be the international gold standard methods 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 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 culture-based methods identify isolated organisms according to their biochemical or immunologic properties. The clinical performance of the AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* has been shown to be substantially equivalent to culture methods.

The AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* allows the automated multiplex amplification of *Neisseria gonorrhoeae, Chlamydia trachomatis* and an Internal Control that is used to detect the presence of PCR inhibitors. 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 AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* is 5 colony forming units (CFU) per test for each of 15 isolates tested for CTM and urine specimens. The AMPLICOR CT/NG Test for *N. gonorrhoeae* gave positive results for all strains tested at 20, 10, and 5 CFU/test. 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 14 of the 15 strains at 2 CFU/test.

The analytical specificity of the AMPLICOR CT/NG Test for *Neisseria gonorrhoeae* was tested against 132 bacteria, 6 fungi, 1 protozoan and 11 virus isolates that are commonly isolated from the urogenital tract. Isolates were added to CTM and normal human urine at approximately 10^4 copies of genomic DNA per test. CTM and urine samples were processed and tested using the standard AMPLICOR CT/NG Test procedure. Multiple isolates of *Neisseria subflava* and *Neisseria cinerea* obtained from the American Type Culture Collection were tested. Four of the *Neisseria subflava* and one *Neisseria cinerea* isolate gave false positive test results. All of the remaining organisms gave negative results with the AMPLICOR CT/NG Test for *Neisseria gonorrhoeae*.

The precision of the 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.. The results of this study are presented in Tables 1 and 2.

Table 1
AMPLICOR CT/NG Test for Neisseria gonorrhoeae
CTM Reproducibility Study Results

	N. gonorrhoeae Spiked CTM (CFU/test)			
	0	12.5	37.5	62.5
Number of Replicates	72	36	36	36
No. Correct Results (%)*	72 (100)	36 (100)	36 (100)	33 (100)
No. Equivocal A_{450} 0.2-1.999	0	0	0	3
No. Equivocal A_{450} 2.0-3.499	0	14	16	16
Median A_{450}	0.056	4.000	4.000	2.889
Minimum A_{450}	0.044	2.208	2.054	1.634
Maximum A_{450}	0.177	4.000	4.000	4.000

* Specimens with initial equivocal results 0.2-1.999 were considered non-reportable, and were excluded from the calculations of % correct results. Specimens with equivocal results 2.0-3.499 were considered positive in the calculations.

Table 2
AMPLICOR CT/NG Test for Neisseria gonorrhoeae
Urine Reproducibility Study Results

	N. gonorrhoeae Spiked Urine (CFU/test)			
	0	10	30	50
Number of Replicates	72	36	36	36
No. Correct Results (%)*	(100)	27 (90.0)†	(100)	(100)
No. Equivocal A_{450} 0.2-1.999	0	6	7	4
No. Equivocal A_{450} 2.0-3.499	0	12	5	7
Median A_{450}	0.055	2.754	4.000	4.000
Minimum A_{450}	0.047	1.097§	1.535	1.395
Maximum A_{450}	0.106	4.000	4.000	4.000

* Specimens with initial equivocal results 0.2-1.999 were considered non-reportable, and were excluded from the calculations of % correct results. Specimens with equivocal results 2.0-3.499 were considered positive in the calculations.

† One sample gave negative results in three of six initial replicates at one site The sample was repeat tested in duplicate at the site and correct results were obtained for all replicates % Correct results based on 27 correct results out of 30 tests.

§ Minimum absorbance excluding the three initial negative tests.

Clinical Performance

The 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 5374 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 5374 specimens collected and tested in the AMPLICOR CT/NG Test clinical study, 33 were repeatedly inhibitory. Therefore, a total of 5341 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[2]
Female	CTM	Asymptomatic	49	1032	12	1	6	0.58%	1100	98.0% (89.3-99.9)	98.9% (98.2-99.5)	4/12
			(49)	(1038)	(12)	(1)			(1100)	(98.0%) (89.3-99.9)	(98.9%) (98.2-99.5)	(4/12)
		Symptomatic	69	1034	16	4	15	1.42%	1138	94.5% (86.6-98.5)	98.5% (97.7-99.2)	10/16
			(68)	(1048)	(16)	(6)			(1138)	(91.9%) (85.7-98.1)	(98.5%) (97.8-99.2)	(10/16)
Total for Females			118	2066	28	5	21	1.00%	2238	95.9% (90.8-98.7)	98.7% (98.2-99.2)	14/28
			(117)	(2086)	(28)	(7)			(2238)	(94.4%) (90.3-98.4)	(98.7%) (98.2-99.2)	(14/28)
Male	CTM	Symptomatic	340	858	38	5	2	0.23%	1243	98.6% (96.6-99.5)	95.8%[3] (94.4-97.1)	21/38
			(340)	(860)	(38)	(5)			(1243)	(98.6%) (96.6-99.5)	(95.8%) (94.5-97.1)	(21/38)
	URINE	Asymptomatic	8	672	4	3	2	0.30%	689	72.7% (39.0-94.0)	99.4% (98.5-99.8)	2/4
			(8)	(674)	(4)	(3)			(689)	(72.7%) (39.0-94.0)	(99.4%) (98.5-99.8)	(2/4)
		Symptomatic	308	847	25	16	8	0.92%	1204	95.1%[4] (92.7-97.4)	97.1% (96.0-98.2)	15/25
			(296)	(848)	(24)	(36)			(1204)	(89.2%) (85.8-92.5)	(97.2%) (96.2-98.3)	(14/24)
Total for Males			656	2377	67	24	12	0.50%	3136	96.5% (95.1-97.9)	97.3% (96.6-97.9)	38/67
			(644)	(2382)	(66)	(44)			(3136)	(93.6%) (91.8-95.4)	(97.3%) (96.7-97.9)	(37/66)

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

[2] Number of apparent false positive AMPLICOR test results that were positive by alternate primer pair PCR/Total number of apparent AMPLICOR false positive results.

[3] For site #6, specificity was 89.5% (95% CI 86.0 – 93.0) for CTM specimens. CTM specimens (n = 412) at this site were frozen prior to AMPLICOR CT/NG testing. At all other sites for specimens not frozen prior to AMPLICOR CT/NG testing (n = 733) specificity was 99.1% (95% CI 97.9 – 99.7).

[4] For site #6 sensitivity was 79.6% (95% CI 68.3 – 90.9) for AMPLICOR CT/NG testing frozen urine specimens (n = 161) and 96.2% (95% CI 87.0 – 99.5) for AMPLICOR testing fresh urine specimens (n = 209). At all other sites sensitivity was 98.1% (95% CI 95.1 – 99.5) for both fresh (n = 778) or frozen (n = 56) specimens.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
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DEC - 1 1999

James F. Kelly, Ph.D.
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Re: K974503
Trade Name: AMPLICOR® CT/NG Test for *Neisseria gonorrhoeae*
Regulatory Class: II
Product Code: LSL
Dated: September 23, 1999
Received: September 27, 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 at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html"

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K974503

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

Indications For Use:

The AMPLICOR® CT/NG Test for *Neisseria gonorrhoeae* is a qualitative *in vitro* test for the detection of *Neisseria gonorrhoeae* in clinical specimens. The test utilizes polymerase chain reaction (PCR) for the multiplex nucleic acid amplification of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* DNA in endocervical and male urethral swab specimens and in male and female urine specimens from symptomatic and asymptomatic patients, and target-specific probe hybridization capture for the detection of the amplified *Neisseria gonorrhoeae* DNA.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K974503

Prescription Use X OR Over-The-Counter Use ___
(Per 21 CFR 801.109)

(Optional Format 1-2-96)