

K973707

510(k) Summary

AMPLICOR™ CT/NG Test for *Chlamydia trachomatis*
Roche Molecular Systems, Inc.
1080 U.S. Highway 202
Somerville, New Jersey 08876-1760
(908) 253-7200

Intended Use:

The AMPLICOR CT/NG Test for *Chlamydia trachomatis* is a qualitative *in vitro* test for the detection of *C. trachomatis* plasmid DNA in urine from males and females, in endocervical swab specimens, and in male urethral swab specimens as evidence of symptomatic or asymptomatic infection with *C. trachomatis*. *C. trachomatis* DNA is detected by Polymerase Chain Reaction (PCR) amplification of target DNA and by hybridization capture of amplified target.

Description of the Device:

The AMPLICOR CT/NG Test for *Chlamydia trachomatis* is a multiplex *in vitro* diagnostic test for the detection of *Chlamydia trachomatis* in male and female urogenital specimens. The AMPLICOR CT/NG Test for *Chlamydia trachomatis* also has an Internal Control that identifies specimens that contain substances inhibitory to PCR.

Similarities and Differences to Predicate Device:

The AMPLICOR CT/NG Test for *Chlamydia trachomatis* is substantially equivalent to other commercially available *in vitro* diagnostic devices for the detection of *Chlamydia trachomatis* in urogenital swab and urine specimens. These methods include culture with immunofluorescent staining, ELISA, DFA, and nucleic acid hybridization. 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 *Chlamydia trachomatis* detects DNA from the cryptic plasmid of the *Chlamydia trachomatis* organism while cell culture detects the complete viable inclusion forming unit. The clinical performance of the AMPLICOR *Chlamydia trachomatis* Test has been shown to be substantially equivalent to cell culture methods.

The AMPLICOR CT/NG Test for *Chlamydia trachomatis* is also similar to the AMPLICOR *Chlamydia trachomatis* Test and to the COBAS AMPLICOR *Chlamydia trachomatis* Test performed on the COBAS AMPLICOR Analyzer. Improvements in the AMPLICOR CT/NG Test for *Chlamydia trachomatis* allow the automated multiplex amplification of *Chlamydia trachomatis* and an Internal Control that is used to detect the presence of PCR inhibitors. All of these tests use the same oligonucleotide primers and probe for the detection of *Chlamydia trachomatis* and have similar detection reactions that are based on the absorbance measurement of a chromophore that is produced by the oxidation of 3,3',5,5'-tetramethylbenzidine by hydrogen peroxide in the presence of horseradish peroxidase.

Non-Clinical Performance:

The AMPLICOR CT/NG Test for *Chlamydia trachomatis* was shown to have an analytical sensitivity (limit of detection) of 1 Inclusion Forming Unit (1 IFU) per test for all 15 *Chlamydia* serovars (A, B, Ba, C, D, E, F, G, H, I, J, K, LGV1, LGV2, LGV3).

The analytical specificity of the AMPLICOR CT/NG Test for *C. trachomatis* was tested against 132 bacteria, 6 fungi, 1 protozoon and 11 virus isolates that may be isolated from the urogenital tract. The AMPLICOR CT/NG Test for *C. trachomatis* gave negative results for each isolate present in culture transport media and normal human urine at $\geq 10^4$ copies of genomic DNA per test.

The precision of the AMPLICOR CT/NG Test for *Chlamydia trachomatis* was determined for a panel of CTM specimens containing 0, 1.25, 3.75 and 6.25 *Chlamydia trachomatis* IFU/test and urine specimens containing 0, 1, 3 and 5 *Chlamydia trachomatis* IFU/test. Three independent operators at three different geographical sites tested the panel once a day for three days in duplicate. The AMPLICOR CT/NG Test for *Chlamydia trachomatis* gave 100% qualitatively correct and concordant results across all specimen types, concentrations and sites. The results of this study are presented in Tables 1 and 2.

Table 1
AMPLICOR CT/NG Test for *Chlamydia trachomatis*
CTM Specimen Precision

	<i>C. trachomatis</i> Spiked CTM (IFU/test)			
	0	1.25	3.75	6.25
Number of Replicates	72	36	36	36
% Correct Results	100	100	100	100
Median A ₄₅₀	0.056	4.000	4.000	4.000
Minimum A ₄₅₀	0.049	4.000	4.000	4.000
Maximum A ₄₅₀	0.073	4.000	4.000	4.000

Table 2
AMPLICOR CT/NG Test for *Chlamydia trachomatis*
Urine Specimen Precision

	<i>C. trachomatis</i> Spiked Urine (IFU/test)			
	0	1	3	5
Number of Replicates	72	36	36	36
% Correct Results	100	100	100	100
Median A ₄₅₀	0.057	4.000	4.000	4.000
Minimum A ₄₅₀	0.049	1.491	1.893	2.538
Maximum A ₄₅₀	0.083	4.000	4.000	4.000

Clinical Performance:

The AMPLICOR CT/NG Test for *Chlamydia trachomatis* was evaluated in a clinical study conducted at six geographically diverse sites. Swab (endocervical and urethral for females, urethral for males) and urine specimens were obtained from all patients entered into the study. Swab specimens were placed in culture transport media (CTM) used at each site. All swab specimens were tested by standard culture with cyclohexamide treated McCoy cells stained with fluorescein-labeled monoclonal antibody for *C. trachomatis*. Swab specimens that were culture negative but positive by the AMPLICOR Test were tested by DFA for the presence of *C. trachomatis*. The AMPLICOR CT/NG Test for *Chlamydia trachomatis* was

performed on all endocervical swab and urine specimens obtained from female patients, and all urethral swabs and urine specimens from male patients. AMPLICOR testing was repeated for all specimens with initial results in the range of 0.2 to 0.8 A₄₅₀ and when IC results were inhibited (negative).

A total of 8521 specimens collected from 4298 patients met the criteria for inclusion in the clinical study (patient was not on antibiotics, a valid culture result was obtained, specimen met storage requirements etc.). Both a swab and urine specimen were entered into the study for 4206 patients; a urine specimen only was entered into the study from 101 patients. A swab specimen only was entered into the study from 36 patients. Of the 8521 specimens included in the study, 143 specimens gave initial test results in the Equivocal Range and were excluded from the data analyses. In addition, 69 specimens were repeatedly inhibitory and were excluded from the data analyses which include the use of the Internal Control because the results were not interpretable. Therefore, 8309 specimens were included in the analyses when the Internal Control result was used and a total of 8378 specimens were included in the analyses when the Internal Control results were not used.

The clinical performance of the test was evaluated by comparing the results of the 8378 swab and urine specimens to the composite results of the comparative tests (culture, sub-culture and DFA). Alternate PCR testing using oligonucleotide primers targeted for a region of the *C. trachomatis* MOMP gene was performed on AMPLICOR positive, culture/DFA negative specimens. The MOMP test results were not used to calculate the clinical performance characteristics of the test and are reported for information purposes only. Of the 242 AMPLICOR positive, culture/DFA negative specimens that were classified as false positive results in this study, 153 were positive for *C. trachomatis* when that specimen or the matching urine or swab specimen from that patient was tested by the MOMP assay. These data suggest that many specimens considered as false positive in the Clinical Data Performance Tables did contain *C. trachomatis* DNA.

The results from the clinical study are shown in Tables 3 and 4. Table 3 shows the clinical performance of the AMPLICOR CT/NG Test for *Chlamydia trachomatis* in comparison to the endocervical culture/DFA results for female patients and to the urethral culture/DFA results for male patients. In this Table, True Positive (TP) represents the number of concordant positive culture or DFA and AMPLICOR Test results. True Negative (TN) represents the number of concordant negative culture and AMPLICOR results. False Negative (FN) represents the number of culture positive, AMPLICOR negative results. False Positive (FP) represents the number of culture and DFA negative, AMPLICOR positive results.

Table 4 shows the clinical performance of the AMPLICOR CT/NG Test for *Chlamydia trachomatis* for testing both swab and urine specimens from female patients, combined and separately for each specimen type, in comparison to the patient infected status. Female patient infected status was determined by endocervical or urethral culture/DFA positive test results. The data in Table 4 show that there is better concordance with culture/DFA positive patients when both swab and urine specimens are tested by the AMPLICOR CT/NG Test for *Chlamydia trachomatis*. The testing of both swab and urine specimens by the AMPLICOR CT/NG Test for *Chlamydia trachomatis* resulted in fewer unverified positive test results and higher assay sensitivity as compared to single specimen (swab or urine) testing only.

A summary of the test results obtained in the clinical study performed for the AMPLICOR CT/NG Test for *Chlamydia trachomatis* is contained in Tables 5 and 6. Table 5 summarizes the combinations of test results obtained for female patients; Table 6 summarizes the combinations of test results obtained for male patients. These tables show that patients with a positive result in both a urine and a swab specimen had a lower rate of unverified positivity (false positives relative to culture and DFA) than single positive specimen results. Testing of both specimen types may be useful for increasing the confidence in a positive result using the AMPLICOR CT/NG Test for *Chlamydia trachomatis*, particularly for low prevalence populations.

The clinical sensitivity and specificity of the AMPLICOR CT/NG Test for *Chlamydia trachomatis* has not been reliably determined for detecting those patients with clinically active infection that can be transmitted to partners or cause Chlamydia-related sequelae. In the clinical study described here, 23.1% of AMPLICOR positive results were from patients with negative cultures and DFA tests. The significance of AMPLICOR positive, but culture and DFA negative test results is unknown. A proportion of these AMPLICOR positive specimens (63.2%) were also positive by an alternate target PCR assay; however, the performance of this alternate target assay has not been established.

Table 3
Clinical Performance Of AMPLICOR CT/NG Test for *Chlamydia trachomatis*
Including and Excluding the Internal Control¹

Sex	Specimen	Symptom	TP	TN	FP	FN	No. Inhib.	% Repeat. Inhibitory	Total	Sensitivity (95% CI)	Specificity (95% CI)	MOMP+/FP	
Female	CTM	Asymptomatic	76 (76)	1019 (1019)	14 (14)	4 (4)	0	0.00%	1113 (1113)	95.0% (87.7-98.6%) (95.0%) (87.7-98.6%)	98.6% (97.9-99.3%) (98.6%) (97.9-99.3%)	10/14 (10/14)	
		Symptomatic	94 (94)	1026 (1031)	15 (15)	1 (1)	5	0.48%	1141 (1141)	98.9% (94.3-100.0%) (98.9%) (94.3-100.0%)	98.6% (97.8-99.3%) (98.6%) (97.8-99.3%)	10/15 (10/15)	
	URINE	Asymptomatic	68 (67)	1004 (1018)	14 (14)	8 (10)	15	1.46%	1109 (1109)	89.5% (82.6-96.4%) (87.0%) (79.5-94.5%)	98.6% (97.9-99.3%) (98.6%) (97.9-99.3%)	10/14 (10/14)	
		Symptomatic	82 (82)	1021 (1032)	24 (23)	7 (7)	10	0.96%	1144 (1144)	92.1% (86.5-97.7%) (92.1%) (86.5-97.7%)	97.7% (96.8-98.6%) (97.8%) (96.9-98.7%)	14/24 (13/23)	
	Total for Females			320 (319)	4070 (4100)	67 (66)	20 (22)	30	0.73%	4507 (4507)	94.1% (91.6-96.6%) (93.5%) (90.9-96.2%)	98.4% (98.0-98.8%) (98.4%) (98.0-98.8%)	44/67 (43/66)
	Male	CTM	Asymptomatic	75 (75)	598 (604)	14 (14)	1 (1)	6	0.99%	694 (694)	98.7% (92.9-100.0%) (98.7%) (92.9-1-100.0%)	97.7% (96.5-98.9%) (97.7%) (96.6-98.9%)	4/14 (4/14)
Symptomatic			181 (180)	974 (986)	49 (49)	7 (8)	12	1.21%	1223 (1223)	96.3% (93.6-99.0%) (95.7%) (92.9-98.6%)	95.2% (93.9-96.5%) (95.3%) (94.0-96.6%)	31/49 (31/49)	
URINE		Asymptomatic	69 (69)	603 (603)	27 (27)	6 (6)	0	0.00%	705 (705)	92.0% (85.9-98.1%) (92.0%) (85.9-98.1%)	95.7% (94.1-97.3%) (95.7%) (94.1-97.3%)	14/27 (14/27)	
		Symptomatic	162 (160)	958 (981)	85 (83)	23 (25)	21	2.10%	1249 (1249)	87.6% (82.8-92.3%) (86.5%) (81.6-91.4%)	91.9% (90.2-93.5%) (92.2%) (90.6-93.8%)	60/85 (58/83)	
Total for Males			487 (484)	3133 (3174)	175 (173)	37 (40)	39	1.22%	3871 (3871)	92.9% (90.7-95.1%) (92.4%) (90.1-94.6%)	94.7% (93.9-95.5%) (94.8%) (94.1-95.6%)	109/175 (107/173)	

¹ Test results without the Internal Control shown in parentheses.

True Positive (TP) represents the number of concordant positive culture or DFA and COBAS Test results.
 True Negative (TN) represents the number of concordant negative culture and COBAS results.
 False Negative (FN) represents the number of culture positive, COBAS negative results.
 False Positive (FP) represents the number of culture and DFA negative, COBAS positive results.

Table 4
Performance of AMPLICOR CT/NG Test for *Chlamydia trachomatis* vs Female Patient Status
Including and Excluding the Internal Control¹

Sex	Specimen	Symptom	Total	% Inhibitory	No. Inhib.	Sensitivity (95% CI)	Specificity (95% CI)	MOMP+/FP
Female	CTM + URINE	Asymp	1123 (1121)	0.00%	0	93.1% (87.8-98.4) (93.1%) (87.8-98.4)	98.0% (97.1-98.8) (98.0%) (97.1-98.8)	16/21 (16/21)
		Symptomatic	1172 (1170)	0.19%	2	94.3% (89.9-98.7) (95.2%) (89.1-98.4)	97.7% (96.7-98.6) (97.7%) (96.7-98.6)	14/25 (14/25)
	CTM	Asymp	1113 (1113)	0.00%	0	87.4% (80.4-94.3) (87.4%) (80.4-94.3)	98.6% (97.9-99.3) (98.6%) (97.9-99.3)	11/14 (11/14)
		Symptomatic	1141 (1141)	0.48%	5	94.0% (89.3-98.7) (94.0%) (89.3-98.7)	98.6% (97.8-99.3) (98.6%) (97.8-99.3)	11/15 (11/15)
	Total CTM		2254 (2254)	0.24%	5	90.9% (86.8-95.0) (90.9%) (86.8-95.0)	98.6% (98.1-99.1) (98.6%) (98.1-99.1)	22/29 (22/29)
	URINE	Asymp	1109 (1109)	1.46%	15	84.3% (76.5-92.2) (82.1%) (74.0-90.3)	98.8% (98.1-99.5) (98.8%) (98.2-99.5)	10/12 (10/12)
		Symptomatic	1144 (1144)	0.96%	10	89.5% (83.3-95.6) (88.4%) (82.0-94.9)	98.0% (97.1-98.8) (98.0%) (97.2-98.8)	14/21 (14/21)
	Total Urine		2253 (2253)	1.21	25	87.1% (82.2-92.0) (85.5%) (80.3-90.6)	98.4% (97.8-98.9) (98.4%) (97.9-98.9)	24/33 (24/33)

Table 5
AMPLICOR CT/NG Test for *Chlamydia trachomatis*
Test Result Summary - Female Patients¹

No. Patients	Culture Status	Endocervical And Urethral Culture Results			DFA Results	AMPLICOR Results by Specimen Type	
		Endocervical Only	Urethral Only	Both Positive		Swab	Urine
138	Positive	79	0	59	N/A	Pos	Pos
11	Positive	8	0	3	N/A	Pos	Neg
8	Positive	3	4	1	N/A	Neg	Pos
9	Positive		8	1	N/A	Neg	Neg
1	Positive		1		Pos	Pos	Pos
5	Negative				Pos	Pos	Pos
2	Negative				Pos	Pos	Neg
16	Negative				Neg	Pos	Pos
11	Negative				Neg	Pos	Neg
15	Negative				Neg	Neg	Pos
1968	Negative				N/A	Neg	Neg

¹ Results from 110 patients without matched CTM and urine results are excluded from the table

Table 6
AMPLICOR CT/NG Test for *Chlamydia trachomatis*
Test Result Summary - Male Patients¹

No. Patients	Urethral Culture Status	DFA Results	AMPLICOR Results By Specimen Type	
			Swab	Urine
208	Positive	N/A	Pos	Pos
13	Positive	N/A	Pos	Neg
6	Positive	N/A	Neg	Neg
14	Negative	Pos	Pos	Pos
5	Negative	Pos	Pos	Neg
1	Negative	Pos	Neg	Pos
44	Negative	Neg	Pos	Pos
18	Negative	Neg	Pos	Neg
55	Negative	Neg	Neg	Pos
1461	Negative	N/A	Neg	Neg

¹ Results from 194 patients without matched CTM and urine results are excluded from the table



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG - 4 1999

Mr. Alex Wesolowski
Senior Director
Regulatory and Clinical Affairs
Roche Molecular Systems, Inc.
1080 U.S. Highway 202
Somerville, New Jersey 08876-3771

Re: K973707
Trade Name: AMPLICOR™ CT/NG Test for *Chlamydia trachomatis*
Regulatory Class: I
Product Code: MKZ
Dated: May 12, 1999
Received: May 14, 1999

Dear Mr. Wesolowski:

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.

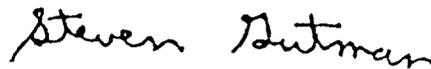
Page 2

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 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): K973707

Device Name: AMPLICOR CT/NG Test for Chlamydia trachomatis

Indications For Use:

The AMPLICOR CT/NG Test for *Chlamydia trachomatis* is a qualitative *in vitro* test for the detection of *Chlamydia trachomatis* plasmid DNA in urine from males and females, in endocervical swab specimens from symptomatic or asymptomatic females, and in urethral swab specimens as evidence of symptomatic or asymptomatic infection with *Chlamydia trachomatis*. *Chlamydia trachomatis* DNA is detected by Polymerase Chain Reaction (PCR) amplification of target DNA and by hybridization capture of amplified target and by hybridization capture of the amplified target.



(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K973707

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓
(Per 21 CFR 801.109)

OR

Over-The Counter Use _____

(Optional Format 1-2-96)