510(k) Summary

K973718

DEC 15 1998

COBAS 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 COBAS 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 using the COBAS AMPLICOR Analyzer.

Description of the Device:

The COBAS AMPLICOR CT/NG Test for *Chlamydia trachomatis* 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 *Chlamydia trachomatis* also has an Internal Control that identifies specimens that contain substances inhibitory to PCR.

Similarities and Differences to Predicate Device:

The COBAS 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 COBAS 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 COBAS AMPLICOR *Chlamydia trachomatis* Test has been shown to be substantially equivalent to cell culture methods.

The COBAS 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 COBAS 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'-tetramethybenzidine by hydrogen peroxide in the presence of horseradish peroxidase.

Non-Clinical Performance:

The COBAS 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 COBAS 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 COBAS 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 COBAS AMPLICOR CT/NG Test for *Chlamydia trachomatis* on the COBAS AMPLICOR Analyzer was determined for a panel of culture transport media 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 COBAS AMPLICOR CT/NG Test for *Chlamydia trachomatis* gave 100% qualitatively correct results across all specimen types, concentrations and sites. The results of this study are presented in Tables 1 and 2.

Table 1
COBAS AMPLICOR CT/NG Test for Chlamydia trachomatis
CTM Specimen Reproducibility

	C. trachomatis Spiked CTM (IFU/test)			
	0	***1.25***	***3.75***	***6.25***
Replicates	72	36	36	36
% Correct Results	100	100	100	100
Mean A_{660}	0.005	3.250	3.153	3.176
Minimum A_{660}	0.000	2.732	2.686	2.681
Maximum A_{660}	0.018	4.000	3.610	3.962

Table 2
COBAS AMPLICOR CT/NG Test for Chlamydia trachomatis
Urine Specimen Reproducibility

	C. trachomatis Spiked CTM (IFU/test)			
	0	***1***	***3***	***5***
Replicates	72	36	36	36
% Correct Qualitative	100	100	100	100
Mean A_{660}	0.004	3.393	3.268	3.270
Minimum A_{660}	0.000	2.691	2.381	2.264
Maximum A_{660}	0.023	4.000	4.000	4.000

Clinical Performance:

The COBAS 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 COBAS Test were tested by DFA for the presence of *C. trachomatis*. The COBAS 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. COBAS testing was repeated for all specimens with initial results in the range of 0.2 to 0.8 A_{660} and when IC results were inhibited (negative).

A total of 8523 specimens collected from 4277 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 was entered into the study for 4201 patients; a urine specimen only was entered into the study from 76 patients. Of the 8523 specimens included in the study, 45 specimens gave initial test results in the Equivocal Range and were excluded from the data analyses. Two specimens that were initially inhibitory gave results in the Equivocal Range upon repeat testing. These specimens are excluded from the analyses when the Internal Control was used but included in the analyses when the Internal Control was not used. In addition, 79 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, 8397 specimens were included in the analyses when the Internal Control result was used and a total of 8478 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 8478 swab and urine specimens to the composite results of the comparative tests (culture, sub-culture and DFA). Alternate PCR testing using oliognucleotide primers targeted for a region of the *C. trachomatis* MOMP gene was performed on COBAS 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 266 COBAS AMPLICOR positive, culture/DFA negative specimens that were classified as false positive results in this study, 185 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 COBAS 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 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 shows the clinical performance of the COBAS 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 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 COBAS AMPLICOR CT/NG Test for Chlamydia trachomatis. The testing of both swab and urine specimens by the COBAS 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 COBAS 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 COBAS AMPLICOR CT/NG Test for *Chlamydia trachomatis*, particularly for low prevalence populations.

The clinical sensitivity and specificity of the COBAS 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, 24.4% of COBAS positive results were from patients with negative cultures and DFA tests. The significance of those results that were COBAS positive, but culture and DFA negative is unknown. A proportion of these COBAS positive specimens (63.8%) were also positive by an alternate target PCR assay; however, the performance of this alternate target assay has not been established

Table 4
Clinical Performance Of COBAS AMPLICOR CT/NG Test for Chlamydia trachomatis 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)	MOMP+/FP
Female	CTM	Asymptomatic	75 (75)	1013 (1017)	17 (16)	4 (4)	2	0.20%	1111 (1112)	94.9% (93.6-96.2) (94.9%) (93.6-96.2)	98.3% (97.6-99.1) (98.5%) (97.7-99.2)	9/17 (10/16)
		Symptomatic	93 (93)	1025 (1031)	21 (21)	4 (4)	6	0.58%	1149 (1149)	95.9% (94.6-97.2) (95.9%) (94.6-97.2)	98.0% (97.1-98.8) (98.0%) (97.2-98.8)	11/21 (11/21)
Female	URINE	Asymptomatic	70 (70)	1011 (1023)	18 (18)	7 (8)	13	1.26%	1119 (1119)	90.9% (84.5-97.3) (89.7%) (83.0-96.5)	98.3% (97.4-99.1) (98.3%) (97.5-99.1)	13/18 (13/18)
		Symptomatic	84 (84)	1018 (1030)	33 (33)	9 (9)	12	1.15%	1156 (1156)	90.3% (84.3-96.3) (90.3%) (84.3-96.3)	96.9% (95.8-97.9) (96.9%) (95.9-97.9)	14/33 (14/33)
Total for Females			322 (322)	4067 (4101)	89 (88)	24 (25)	33	0.73%	4535 (4536)	93.1% (90.4-95.7) (92.8%) (90.1-95.5)	97.9% (97.4-98.3) (97.9%) (97.5-98.3)	47/89 (48/88)
Male	CTM	Asymptomatic	76 (76)	608 (612)	14 (14)	1 (1)	4	0.65%	703 (703)	98.7% (97.1-100) (98.7%) (97.1-100)	97.7% (96.6-98.9) (97.8%) (96.6-98.9)	5/14 (5/14)
		Symptomatic	183 (183)	977 (994)	56 (54)	6 (6)	14	1.40%	1236 (1237)	96.8% (94.3-99.3) (96.8%) (94.3-99.3)	94.6% (93.2-96.0) (94.8%) (93.5-96.2)	32/56 (32/54)
Male	URINE	Asymptomatic	71 (71)	616 (617)	24 (24)	8 (8)	1	0.16%	720 (720)	89.9% (83.2-96.5) (89.9%) (83.2-96.5)	96.3% (94.8-97.7) (96.3%) (94.8-97.7)	14/24 (14/24)
		Symptomatic	173 (168)	976 (1004)	83 (80)	23 (30)	27	2.63%	1282 (1282)	88.3% (83.8-92.8) (84.8%) (79.9-89.8)	92.2% (90.5-93.8) (92.6%) (91.1-94.2)	62/83 (60/80)
Total for Males			503 (498)	3177 (3227)	177 (172)	38 (45)	46	1.41%	3941 (3942)	93.0% (90.8-95.1) (91.7%) (89.4-94.0)	94.7% (94.0-95.5) (94.9%) (94.2-95.7)	113/177 (111/172)

[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 5
Performance of COBAS AMPLICOR CT/NG Test for Chlamydia trachomatis vs Patient Status[1]
Female Patients
Including and Excluding the Internal Control[2]

Specimen	Symptom	Total	% Inhibitory	No. Inhib.	Sensitivity	Specificity (95% CI)	MOMP+/FP
CTM + URINE	Asymp	1126 (1227)	0.00%	0	90.8% (84.7-96.9) 90.8% (84.7-96.9)	97.4% (96.4-98.4) (97.7%) (96.9-98.6)	18/27 (18/26)
	Symptomatic	1169 (1169)	0.10%	1	95.2% (94.0-96.4) (95.2%) (94.0-96.4)	96.4% (95.3-97.5) (96.4%) (95.3-97.5)	15/38 (15/38)
CTM	Asymp	1111 (1112)	0.20%	2	87.2% (80.2-94.3) (87.2%) (80.2-94.3)	98.3% (97.6-99.1) (98.4%) (97.7-99.2)	11/17 (12/16)
	Symptomatic	1149 (1149)	0.58%	6	91.3% (85.8-96.7) (91.3%) (85.8-96.7)	98.1% (97.2-98.9) (98.1%) (97.3-98.9)	16/20 (12/20)
Totals - CTM		2260 (2261)	0.39%	8	(89.4%) (85.0-93.8) (89.4%) (85.0-93.8)	98.2% (97.6-98.8) (98.3%) (97.7-98.8))	27/37 (24/36)
URINE	Asymp	1119 (1119)	1.26%	13	85.7% (78.2-93.2) (84.7%) (77.1-92.4)	98.4% (97.7-99.2) (98.5%) (97.7-99.2)	13/16 (13/16)
	Symptomatic	1156 (1156)	1.15%	12	87.9% (81.4-94.3) (87.9%) (81.4-94.3)	97.1% (96.1-98.1) (97.2%) (96.2-98.2)	14/30 (14/30)
Totals - Urine		2275 (2275)	1.21	25	86.9% (82.0-91.8) (86.4%) (81.5-91.4)	97.8% (97.1-98.4) (97.8%) (97.2-98.4))	27/36 (27/36)

[1]Culture and DFA results in this table include endocervical and urethral results
[2]Test results without the Internal Control shown in parentheses.

Table 6
COBAS AMPLICOR CT/NG Test for Chlamydia trachomatis
Test Result Summary - Female Patients[1]

No. Patients	Culture Status	Endocervical And Urethral Culture Results			DFA Results	COBAS AMPLICOR Results by Specimen Type	
		Endocervical Only	Urethral Only	Both Positive		Swab	Urine
146	+	85	2	59	N/A	+	+
11	+	8	0	3	N/A	+	-
7	+	2	4	1	N/A	-	+
11	+	1	8	2	N/A	-	-
6	-				+	+	+
2	-				+	+	-
1	-				+	-	-
18	-				-	+	+
18	-				-	+	-
26	-				-	-	+
1965	-				N/A	-	-

[1] Results from 85 patients without matched CTM and urine results are excluded from the table

Table 7
COBAS AMPLICOR CT/NG Test for Chlamydia trachomatis
Test Result Summary - Male Patients[1]

No. Patients	Urethral Culture Status	DFA Results	COBAS AMPLICOR Results By Specimen Type	
			Swab	Urine
215	+	N/A	+	+
20	+	N/A	+	-
4	+	N/A	-	-
16	-	+	+	+
3	-	+	+	-
48	-	-	+	+
17	-	-	+	-
51	-	-	-	+
2	-	-	Inhib	Inhib
1503	-	N/A	-	-

[1] Results from 140 patients without matched CTM and urine results are excluded from the table

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 15 1998

Alex Wesolowski
Sr. Director, Regulatory and Clinical Affairs
Roche Molecular Systems, Inc.
1080 U.S. Highway 202
Somerville, NJ 08876-3771

Re: K973718
Trade Name: Roche COBAS Amplicor CT/NG Test for *Chlamydia trachomatis*
Regulatory Class: I
Product Code: MKZ
Dated: September 18, 1998
Received: September 22, 1998

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.

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): K973718

Device Name: COBAS Amplicor CT/NG Test for C. trachomatis

Indications For Use:

The COBAS 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 using the COBAS AMPLICOR Analyzer.

(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 K973718

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

(Optional Format 1-2-96)