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Roche Molecular Systems
a subsidiary of Hoffmann-La Roche

Roche Molecular Systems, Inc.
1080 U.S. Highway 202
Somerville, New Jersey 08876

510(k) Summary

COBAS AMPLICOR™ Analyzer

In accordance with the Safe Medical Devices Act of 1990, a 510(k) summary is provided as outlined in 21 CFR 807.92.

I. Identification of 510(k) Sponsor:

Roche Molecular Systems, Inc.
1080 U.S. Highway 202
Somerville, New Jersey 08876-1760

510(k) submission dated November, 1996

Contact: Alex Wesolowski
Telephone: (908) 253-7540
Facsimile: (908) 253-7547

II. Device Name:

Trade/Proprietary Name - COBAS AMPLICOR™ *Analyzer*

Common or Usual Name - and detection: Automated batch analyzer for nucleic acid amplification

Classification Name - None applicable

III. Identification of legally marketed device to which the 510(k) sponsor claims equivalence:

The primary operational components of the COBAS AMPLICOR analyzer are the pipettor, thermal cycler, wash stations, and the photometric detection system. As independent components, each is categorized as Class I devices under 21 CFR 862 (Table 1). The COBAS AMPLICOR combines these operational functions into a single automated instrument that provides an interpretative qualitative result. The performance of the COBAS AMPLICOR is substantially equivalent to several currently marketed device used independently to perform the same functions.

TABLE 1
Predicate Devices for the COBAS AMPLICOR Analyzer

Predicate Device	*Regulatory Class*	*Classification Number*	*Predicate Product Name*	*Predicate 510(k) Number*
Automated Pipettor	Class 1	862.2750	Matrix Technologies Impact Pipettor	K940390
Thermal cycler (incubator)	Class 1 exempt	862.2750	Perkin-Elmer 9600 Thermal cycler	NA
Incubator	Class 1 exempt	862.2050	Fisher Dry Heat Incubator Model 630D	NA
Automated Microplate Washer	Class 1 exempt	866.2500	Bio-Tek Instruments Automated Microplate Washer Model Model ELP40	NA
Automated Microplate Reader	Class 1	862.2300	Bio-Tek Instruments Auomated EAI Microplate Reader Models Elx800/EL800	K950104

The COBAS AMPLICOR analyzer is designed for exclusive use with COBAS AMPLICOR reagents. The Roche AMPLICOR *Chlamydia trachomatis* Test (microwell plate) and the COBAS AMPLICOR *Chlamydia trachomatis* Test are both intended for the qualitative determination of *Chlamydia trachomatis* plasmid DNA in female endocervical, male urethral, and male urine specimens from symptomatic and asymptomatic patients. The Roche COBAS AMPLICOR *Chlamydia trachomatis* Test performed on the Roche COBAS AMPLICOR analyzer is substantially equivalent to the Roche AMPLICOR *Chlamydia trachomatis* Test (K922906/C, June 15,1993) performed on the Perkin-Elmer 9600 thermal cycler and the Bio-Tek EL800 (K950104) microtiter plate reader.

IV. Description of the Device:

The COBAS AMPLICOR is a flexible, automated bench top batch analyzer that automates the amplification and detection steps of the Polymerase Chain Reaction (PCR) process. The COBAS AMPLICOR combines the operations of automated sample handling, reagents deliver, thermal cycling, controlled temperature incubation, photometric detection and result reporting into a single automated analyzer. The instrument consists of five major sub-components: (1) a thermal cycler module; (2) an automated pipeting station; (3) an incubation station; (4) a wash station; and (5) a photometer. An internal computer controls and monitors the major components includingsystem and run control, input/output, communication, results calculaton, and system diagnostic tests.

Specimens are prepared off-line with AMPLICOR Specimen Preparation reagents before being transferred to amplification tubes (A-tubes) placed on the analyzer. Twelve A-tubes with caps are provided as a molded assembly called an A-ring. The COBAS AMPLICOR automatically performs test specific thermal cycling operations for PCR amplification. Amplified product is automatically transferred to polystyrene specimen cups (D cups) and primer coated magnetic beads are added. Following incubation, unbound material is removed by serial wash steps. Hybridized amplicon is measured by a enzymatically catalyzed color reaction. The intensity of the color is proportional to the amount of infectious organisms present in the specimen and qualitative results are determined based on a specified absorbance cut-off.

The amplification and detection operations can be run in parallel or sequentially depending on the number of samples in the run and user preference. In sequential mode, the analyzer automatically proceeds to sample detection after amplification, and the pipettor transfers amplified products from the A-ring in the thermal cycling segments to the D-cups for hybridization, wash and detection.

In parallel operation, a second set of samples is amplified as the first set is detected. After amplification of the first set of specimens is complete, the system pauses for transfer of the first set of amplified A-rings to the ambient temperature chambers. A second set of A-rings are then added to the thermal cycler for amplification, and the automated pipettor transfers amplified product from each of the first set of A-tubes in the ambient temperature segments to D-cups for hybridization, wash and detection.

V. Statement of Intended Use:

The COBAS AMPLICOR is an *in vitro* diagnostic device intended for use in the amplification and detection steps of the Polymerase Chain Reaction (PCR) process.

VI. Summary of the technological characteristics of the new device in comparison to those of the predicate:

The COBAS AMPLICOR Analyzer is a flexible, automated, bench top analyzer that automates the amplification and detection steps of the Polymerase Chain Reaction (PCR) process. The principles of operation of the COBAS AMPLICOR are substantially equivalent to manual in-vitro diagnostic PCR testing using general laboratory equipment. The COBAS AMPLICOR Analyzer consists of five major sub-components: (1) a thermal cycler module; (2) an automated pipeting station; (3) an incubation station; (4) a wash station; and (5) a photometer. An internal computer controls and monitors the major components includingsystem and run control, input/output, communication, results calculaton, and system diagnostic tests. The COBAS AMPLICOR Analyzer operating as a system performing automatically various steps such as pipetting, heating and measuring color intensity is substantially equivalent to several currently marketed devices used independently to perform the same functions. The COBAS AMPLICOR is designed to be used in conjunction with AMPLICOR Specimen Preparation Kits (for off-line specimen prepration), AMPLICOR Amplification Kits and COBAS AMPLICOR Detection Kits.

The AMPLICOR Test for *Chlamydia trachomatis* used with the Perkin-Elmer 9600 thermal cycler and Bio-Tek plate reader, and the COBAS AMPLICOR *Chlamydia trachomatis* are both intended for the qualitative determination of *Chlamydia trachomatis* from urogenital swab specimens in specimen transport medium and male urine. The COBAS AMPLICOR *Chlamydia trachomatis* Test is substantially equivalent to the AMPLICOR *Chlamydia trachomatis* Test (K922906/C, June 15,1993) performed on the Perkin-Elmer 9600 thermal cycler and the Bio-Tek EEL800 (K950104) microtiter plate reader.

Similarities and Differences to Comparable Commercial Products

The specimen preparation, amplification and detection methods used in the COBAS AMPLICOR system are similar to that previously described for the microwell plate AMPLICOR Test. The notable similarities and differences are as follows:

Similarities

1. The COBAS AMPLICOR Analyzer provides an automated method for performing the same basic procedures used in manual molecular diagnostic testing. These include, sample handling, reagent preparation, sample incubation, thermal cycling washing and photometric measurement

2. The procedures used specimen preparation, amplification and detection portions of the COBAS AMPLICOR procedure utilize identical reagent formulations as the AMPLICOR microplate assay. Identical reagent formulations include specimen diluent, master mix, free nucleotides, nucleotide primers and probes, TMB chromagen, peroxide substrate, and wash buffers.

3. The COBAS AMPLICOR analyzer performs thermal cycling to tolerances that meet or exceed operational characteristics of conventional general laboratory equipment (e.g. the Perkin Elmer 9600).

4. The COBAS AMPLICOR analyzer measures absorbance using a fixed wavelength photometer with comparable performance to other conventional general laboratory equipment and to automated clinical instrumentation such as the Roche COBAS MIRA.

Differences

1. The COBAS AMPLICOR system automates all sample handling, washing and pipetting steps for test amplification and detection compared to manual requirements with the AMPLICOR microplate assay.

2. PCR amplified products are captured by hybridization to probe-coated paramagnetic microparticles on the COBAS AMPLICOR compared to probe-coated microwell plates in the AMPLICOR test format.

3. The COBAS AMPLICOR method does not require a stop reagent following the substrate incubation as does the AMPLICOR because the automated system precisely times each portion of the hybridization and detection procedures.

4. The optical density of the detection system is measured at 660 nm with the COBAS AMPLICOR system compared to 450 nm in the AMPLICOR system. The stop reagent used in the AMPLICOR microplate assay modifies the oxidation state and thus, the absorbance maximum, of the chromophore.

VI. A brief discussion of the nonclinical and clinical performance data

Non-Clinical Performance

Precision

A multi-operator study was performed to determine the reproducibility of the COBAS AMPLICOR *Chlamydia trachomatis* Test. The study design was based upon the study suggested in the NCCLS document EP5-T2. Three independent operators tested a series of samples once a day for three days. A test run consisted of the amplification and detection of the following samples in triplicate: COBAS AMPLICOR Chlamydia trachomatis Test CT (+) and CT (-) kit controls and specimens that were prepared by spiking AMPLICOR Specimen Transport Medium with infected McCoy cell suspensions to obtain levels of 0, 1, 10 and 50 *C. trachomatis* IFU/PCR. Calculations were performed using the Analysis of Variance model suggested in the NCCLS document to derive estimates of between-day, between-operator, within-operator, and total variance for the Test at each sample concentration. The results of this study are presented in Table 2.

TABLE 2
COBAS AMPLICOR Chlamydia trachomatis Test Precision
Analysis of Variance Test Results

	SAMPLE					
	Chlamydia trachomatis Spiked STM (IFU/PCR)				Kit Controls	
	0	1	10	50	Negative	Positive
Total Replicates	27	27	27	27	27	27
Mean Absorbance	0.004	3.856	3.685	3.639	0.004	3.831
Minimum	0.000	3.646	3.220	3.220	0.000	3.279
Maximum	0.017	4.000	4.000	4.000	0.011	4.000
Between Day Variance	0.0000	0.0000	0.0040	0.0037	0.0000	0.0022
Standard Deviation	0.0013	0.0000	0.0632	0.0610	0.0000	0.0468
CV (%)	32.0	0.0	1.7	1.7	0.0	1.2
Between Operator Variance	0.0000	0.0145	0.0271	0.0230	0.0000	0.0587
Standard Deviation	0.0029	0.1206	0.1647	0.1517	0.0027	0.2422
CV (%)	72.4	3.1	4.5	4.2	69.7	6.3
Within Operator Variance	0.0000	0.0059	0.0162	0.0125	0.0000	0.0109
Standard Deviation	0.0035	0.0767	0.1274	0.1118	0.0026	0.1045
CV (%)	87.0	2.0	3.5	3.1	67.4	2.7
Total Variance	0.0000	0.0204	0.0474	0.0392	0.0000	0.0718
Standard Deviation	0.0047	0.1429	0.2176	0.1980	0.0037	0.2679
CV (%)	117.6	3.7	5.9	5.4	97.0	7.0

Clinical Performance

The clinical data reported here were obtained using the AMPLICOR Chlamydia trachomatis Test. The AMPLICOR microwell assay and the COBAS AMPLICOR Chlamydia trachomatis Test procedures are highly conserved and differ only in the method of detection. The COBAS AMPLICOR utilizes a magnetic microparticle based solid support compared to microwell plates and the automated analyzer enables the elimination of a endpoint hydrolysis Stop reagent that changes the absorbance maximum of the chromophore. The COBAS AMPLICOR and AMPLICOR Tests use the exact same specimen preparation, detection and amplification reagents, including identical amplification primer (CP24 and CP27) and detection probe (CP35) sequences. Therefore, the equivalent clinical performance is expected from the microwell and automated COBAS Tests.

Clinical Results - COBAS AMPLICOR

To ensure that equivalent clinical performance of the COBAS AMPLICOR *Chlamydia trachomatis* Test and the AMPLICOR *Chlamydia Trachomatis* Test are obtained, a comparison of the two test procedures was performed in which 639 clinical specimens were tested. The specimens included 266 endocervical swabs, 93 male urethral swabs, and 280 male urine specimens. Table 3 shows the comparative clinical performance obtained when these specimens were tested by the two test procedures. The results for each specimen type were evaluated for statistical difference in comparative clinical performance using McNemar's Test. For each of the three specimen types tested, the McNemar's Test found a value of $P > 0.4$. This finding provides strong evidence that there are no differences in the positive and negative results obtained when testing these specimens by either the COBAS AMPLICOR *Chlamydia Trachomatis* Test or the AMPLICOR *Chlamydia Trachomatis* Test.

Table 3
Comparative Clinical Performance of the COBAS AMPLICOR Chlamydia Trachomatis Test versus the AMPLICOR Chlamydia Trachomatis Test

		AMPLICOR MWP					
		Cervical		Male Urethral		Male Urine	
		Pos	Neg	Pos	Neg	Pos	Neg
COBAS	Pos	34	1*	16	1†	63	4‡
AMPLICOR	Neg	1**	230	0	76	5‡‡	208

* Sample was culture positive
** Sample was culture negative/MOMP negative
† Sample was culture negative/MOMP negative
‡ Two samples were culture positive/MOMP positive; one was culture negative/MOMP positive
‡‡ Two samples were culture positive/MOMP positive; three samples were culture negative/MOMP positive

VIII. Conclusions

The COBAS AMPLICOR is an automated bench-top analyzer for the *in vitro* diagnostic analysis of clinical laboratory specimens using PCR based nucleotide amplification methods. The instrument gives substantially equivalent analytical performance to other general laboratory equipment for thermal cycling and photometric detection of colormetric clinical assays. Based on the clinical performance data, substantially equivalent results were obtained for the qualitative COBAS AMPLICOR *Chlamydia trachomatis* Test on the COBAS AMPLICOR and the Roche AMPLICOR *Chlamydia trachomatis* Test (microwell plate) performed using the Perkin-Elmer 9600 thermal cycler and a conventional photometric microwell plate reader.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 21 1997

Alex Wesolowski
Director, Regulatory and Clinical Affairs
Roche Molecular Systems, Inc.
1080 U.S. Highway 202
Branchburg, New Jersey 08876-1760

Re: K964506
COBAS AMPLICOR™ Analyzer
Regulatory Class: I
Product Code: JJF
Dated: March 24, 1997
Received: March 25, 1997

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 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 Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP 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/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) _____

Device Name: COBAS AMPLICOR™ Analyzer

Indications for Use:

The COBAS AMPLICOR Analyzer is an *in vitro* diagnostic device intended for use in clinical laboratories for the automation of the AMPLICOR™ Polymerase Chain Reaction test procedures.

(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)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K964506