JUL 24 '97

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SUMMARY OF SAFETY AND EFFECTIVENESS K970695

This summary of safety and effectiveness information is being submitted in accordance with the requirements of The Safe Medical Devices Act of 1990 (SMDA 1990) and 21 CFR Part 807.92.

Date of Summary Preparation: July 24, 1997

Company Name:
Chiron Diagnostics Corporation
1401 Harbor Bay Parkway
Alameda, CA 94502

Company Contact:
Nancy Hornbaker
Regulatory Affairs
Chiron Diagnostics
Chiron Corporation
4560 Horton Street
Emeryville, CA 94608

Telephone Number: 510.923.2758
Fax: 510.923.3344

Device Name:
ACS:180 BR
Automated Chemiluminescence System

Common or Usual Name: Automated Tumor Associated Antigen

Classification: Class II device

Predicate Device:
Biomira TRUQUANT® BR™ RIA
PMA P950011

Intended Use and Indications for Use:

Chiron Diagnostics ACS:180 BR is an *in vitro* diagnostic test for the quantitative serial determination of cancer antigen CA 27.29 in human serum. The test is intended for use as an aid in the management of breast cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment.

Summary and Explanation of the Test:

Automatic dilution is available on the ACS:180® for the ACS:180 BR assay. Any sample initially reading with a value higher than the assay range will be rescheduled by the instrument for an automatic dilution. The ACS:180 has the capacity to aspirate as low as 5 µl of sample using the sample probe. Given the sample volume of 25 µl for ACS:180 BR, the maximum dilution that is possible is a 1:5. The instrument will aspirate 5 µl of sample and add 20 µl of diluent to maintain the 25 µl sample size. Instrument operation will then proceed as usual.

Principle of the Assay:

The Chiron Diagnostics ACS:180 BR assay is a competitive, chemiluminescent assay intended for use on the Chiron Diagnostics Automated Chemiluminescent System (ACS). One reagent, designated Lite Reagent, is composed of a mouse monoclonal antibody specific for CA 27.29, labeled with acridinium ester. The Solid Phase is composed of purified breast cancer antigen covalently coupled to paramagnetic particles (PMP). The patient serum sample is incubated with both reagents simultaneously for 7.5 minutes.

An inverse relationship exists between the concentration of CA 27.29 in a sample and the relative light units (RLU) detected by the ACS:180 system.

Specific Performance Characteristics:

Analytical Sensitivity	<3.5 U/mL
Clinical Trial Results	Prospective Clinical Trial
Sensitivity to Change in Disease Status	73%
Specificity to Change in Disease Status	71%
Positive Predictive Value to Change in Disease Status	77%
Negative Predictive Value to Change in Disease Status	67%

A total of 314 healthy volunteer donors were tested at three laboratories to determine the normal range of the assay and to determine the upper limit of normal (ULN). Following good laboratory practice, each laboratory should determine its own normal range and ULN.

Upper Limit of Normal (ULN)	38.6 U/mL

Specificity of the Assay

The specificity of the assay was determined by testing serum samples from patients with active malignancies other than breast and serum from patients with other diseases and conditions. Results from the clinical study are presented below.

Patients with non breast malignancies frequently have raised levels of the CA 27.29 antigen as indicated by their specificities. CA 27.29 is normally expressed by most epithelial tissues and over-expressed by many epithelial cancers. It is not a breast specific antigen.

Specificity of the ACS180:BR in Patients with Malignancies other than Breast

Malignancy	N	Specificity
Colon	43	74.4%
Liver	20	45.0%
Lung	47	57.5%
Ovary	50	44.0%
Pancreas	45	53.3%
Prostate	34	82.4%
Stomach	29	93.1%
Uterus	30	86.7%

Specificity of the ACS:180 BR in Patients with Other Diseases And Conditions

Condition	N	Specificity
Benign Breast Disease		
Breast Adenoma	61	95.08%
Fibrocystic Breasts	68	98.53%
Cirrhosis	25	76.00%
Endometriosis	24	91.67%
Lactating Woman	37	89.19%
Mild Chronic Hepatitis	28	85.71%
Ovarian Cyst	50	94.00%
Pregnancy	49	97.96%
Renal Impairment	20	85.00%
Severe Chronic Hepatitis	20	95.00%

Potentially Interfering Substances

There are no known cross-reactants for CA 27.29 as measured by the ACS:180 BR assay.

The potential interference of chemotherapeutic agents, therapeutic drugs, and tumor marker antigens was tested by adding these substances to five serum pools containing CA 27.29 ranging from 20.0 to 445.8 U/mL. The level of CA 27.29 in each of these pools was then determined using the ACS:180 BR assay and normalized to the level without the respective drugs or antigens.

Substance	Mean % Recovery	Substance	Mean % Recovery
Acetaminophen (10X)	96.3	Granisetron HCl (10X)	99.9
Cimetidine (40X)	100.9	Lorazepam (10X)	98.0
Ciprofloxacin (10X)	100.1	Megestrol acetate (5X)	105.2
Codeine (10X)	96.9	Methotrexate (10X)	105.8
Cyclophosphamide (1X)	96.2	Morphine (10X)	95.6
Dexamethasone (10X)	100.2	Ondansetron (10X)	93.3
Diphenhydramine HCl (10X)	101.8	Paclitaxel (2X)	101.7
Doxorubicin (10X)	95.9	Prochlorperazine (10X)	96.4
Etopside (2X)	99.5	Tamoxifen (10X)	96.6
5-Fluorouracil (10X)	104.2	Vinorelbine tartrate (10X)	104.9

Antigen	Mean % Recovery
Carcinoembryonic antigen (CEA)	103.8
Ovarian Cancer antigen (CA125)	105.9
GI Cancer antigen (CA 19.9)	103.6

Correlation with Predicate Device

The performance of the ACS: 180 BR assay was compared with that of the predicate device in a study of 203 specimens. These specimens had CA 27.29 levels that spanned the range from 7 to 994 U/mL. The results of the linear regression analysis indicated that the two methods were correlated. The correlation coefficient (r) was 0.96; the slope was 1.05 and y-intercept was 6 U/mL.

The CA 27.29 results from a subset of this population, 103 women with histologically confirmed breast cancer, were also highly correlated ($r = 0.96$). In this analysis, the slope was 1.04 and the y-intercept was 8 U/mL.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Ms. Nancy Hornbaker
Regulatory Affairs
Chiron Diagnostics
Chiron Corporation
4560 Horton Street
Emeryville, California 94608

AUG - 8 1997

Re: K970695/S1
Trade Name: ACS:180 BR
Regulatory Class: II
Product Code: MOI
Dated: June 13, 1997
Received: June 16, 1997

Dear Ms. Hornbaker:

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 current Good Manufacturing Practice requirement, 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

501(k) Number (if known): K970695

Device Name: ACS: 180 BR

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Peter E. Madison

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K970695

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-the-Counter Use _____
Prt 21 CFR 801.109

(Optional Format 1-2-96)