NOV 19 2004

510(k) SUMMARY

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: K042731.

Submitter Information

Address:	Fujirebio Diagnostics, Inc. 201 Great Valley Parkway Malvern, PA 19355
Contact person:	Kimberly Peterson, (610) 240-3828
Summary preparation date:	September 30, 2004

Name of Device

Trade/Proprietary Name:	ARCHITECT® CA 125 II™ Assay
Common/Usual Name:	CA 125 Assay
Classification Name:	Test, Epithelial Ovarian Tumor-associated Antigen (CA125)

Predicate Device

AxSYM® CA 125™ Assay

Device Description

The ARCHITECT CA 125 II assay is a two-step immunoassay to determine the presence of OC125 reactive determinants in human serum or plasma, using Chemiluminescent Microparticle Immunoassay (CMIA) technology with flexible assay protocols, referred to as Chemiflex™.

In the first step of the ARCHITECT CA 125 II assay, sample and OC125 coated paramagnetic microparticles are combined. CA 125 reactive determinants present in the sample bind to the OC125 coated microparticles. After washing, M11 acridinium-labeled conjugate is added in the second step. Pre-Trigger and Trigger Solutions are then added to the reaction mixture; the resulting chemiluminescent reaction is measured as relative light

units (RLUs). A direct relationship exists between the amount of CA 125 reactive determinants in the sample and the RLUs detected by the ARCHITECT *i* *optical system.

For additional information on system and assay technology, refer to the ARCHITECT *i* System Operations Manual, Section 3.
**i* =immunoassay

Intended Use

Reagent Kit
The ARCHITECT CA 125 II assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of CA 125 reactive determinants in human serum and plasma on the ARCHITECT *i* System. The ARCHITECT CA 125 II assay is to be used as an aid in monitoring response to therapy for patients with epithelial ovarian cancer. Serial testing for patient CA 125 II assay values should be used in conjunction with other clinical methods used for monitoring ovarian cancer.

Calibrator Kit
The ARCHITECT CA 125 II Calibrators are for the calibration of the ARCHITECT *i* System when used for the quantitative determination of OC 125 defined antigen in human serum and plasma. Refer to the ARCHITECT CA 125 II reagent package insert for additional information.

Control Kit
The ARCHITECT CA 125 II Controls are for the verification of the accuracy and precision of the ARCHITECT *i* System when used for the quantitative determination of OC 125 defined antigen in human serum and plasma. Refer to the ARCHITECT CA 125 II reagent package insert for additional information.

Statement of Substantial Equivalence

The ARCHITECT CA 125 II assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of CA 125 reactive determinants in human serum and plasma on the ARCHITECT *i* System. The ARCHITECT CA 125 II assay is to be used as an aid in monitoring response to therapy for patients with epithelial ovarian cancer. Serial testing for patient CA 125 II assay values should be used in conjunction with other clinical methods used for monitoring ovarian cancer.

ARCHITECT CA 125 II Assay kit is substantially equivalent to Abbott Laboratories AxSYM CA 125 assay. Both of the devices are IVD products and are indicated for the quantitative determination of CA 125 assay values (CA 125 reactive determinants) and as aids in monitoring response to therapy for patients with epithelial ovarian cancer.

A comparison of the features of the ARCHITECT CA 125 II Assay device and the AxSYM CA 125 Assay follows.

	Abbott Laboratories ARCHITECT CA 125 II Assay (Proposed Device)	Abbott Laboratories AxSYM® CA 125™ Assay (Predicate Device) K964020
Device Type	*In vitro* diagnostic	*In vitro* diagnostic
Classification and Product Code	Class II, LTK	Class II, LTK
Principle of Operation	Chemiluminscent Microparticle Immunoassay (CMIA)	Microparticle Enzyme Immunoassay (MEIA)
Product Usage	Clinical and Hospitals laboratories	Clinical and Hospitals laboratories
Intended Use	The ARCHITECT® CA 125 II™ assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of CA 125 reactive determinants in human serum and plasma on the ARCHITECT *i* System. The ARCHITECT CA 125 II assay is to be used as an aid in monitoring response to therapy for patients with epithelial ovarian cancer. Serial testing for patient CA 125 II assay values should be used in conjunction with other clinical methods used for monitoring ovarian cancer.	The AxSYM CA 125 assay is a microparticle enzyme immunoassay (MEIA) for the quantitative measurement of CA 125 assay values in human serum. The AxSYM CA 125 assay is to be used as an aid in monitoring response to therapy for patients with epithelial ovarian cancer. Serial testing for patient CA 125 assay values should be used in conjunction with other clinical methods for monitoring ovarian cancer.
Type of Specimen	Human serum or plasma (EDTA, Lithium Heparin, Sodium Heparin)	Human Serum
Specimen Collection Method	Routine Phlebotomy Techniques	Routine Phlebotomy Techniques
Capture Antibody	OC 125 mouse monoclonal	Anti-CA 125 sheep polyclonal
Conjugate Antibody	M11 mouse monoclonal	OC 125 mouse monoclonal
Standards	6 levels (0 – 1000 U/mL)	6 levels (0 - 600 U/mL) or 2 levels (Master Cals: 0 and 50 U/mL)
Controls	3 levels (Low = 40 U/mL, Medium = 300, High = 650 U/mL)	3 levels (Low = 30 U/mL, Medium = 80 U/mL, High = 200 U/mL)
Interpretation of Results	Standard Curve	Standard Curve

Summary of Performance characteristics

Reproducibility:

Precision was determined as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A. Three defibrinated plasma panel members (1, 2, and 3) were tested, using two lots of reagents, in replicates of two, at two separate times per day, for 20 days on 2 separate instruments. Each reagent lot used a single calibration curve

throughout the study. The total precision was determined by calculating the standard deviation (SD) and percent coefficient of variation (%CV) values for each sample.

The total precision %CV of the ARCHITECT® CA 125 II™ assay was determined to be less than or equal to 10%.

Comparison Study

A total of 280 serum specimens (120 of these serum samples were from Ovarian cancer Patients) were tested using the ARCHITECT CA 125 II assay and the AxSYM CA 125 assay. Passing-Bablok linear regression analysis was performed on all specimens (4.5 – 4085.9 U/mL for the ARCHITECT CA 125 II assay and 2.7 – 3436.1 U/mL for the AxSYM CA 125 assay).

Passing-Bablok linear regression analysis comparing the ARCHITECT CA 125 II assay to the AxSYM CA 125 assay yielded a correlation coefficient of 0.985, a slope of 1.06 (99% confidence interval of 1.03, 1.11), and Y-axis intercept of 4.0 U/mL (99% confidence interval of 2.0, 4.9).

Reference Ranges:

Apparently Healthy Population:
The distribution of CA 125 II assay values determined in 196 normal individual specimens is shown in the table below:

Distribution of ARCHITECT CA 125 II Assay Values

	Number of Subjects	Percent (%) 0-35 U/mL	35.1-65 U/mL	65.1-100 U/mL	>100 U/mL
APPARENTLY HEALTHY					
Females (Pre-Menopausal)	99	89.9	6.1	4.0	0.0
Females (Post-Menopausal)	97	99.0	1.0	0.0	0.0

In this study, 94.4% of the healthy female subjects had CA 125 II assay values at or below 35.0 U/mL. (mean = 16.4, SD = 13.0)

Patient Groups:

The distribution of CA 125 II assay values determined in 615 pf various patient groups individual specimens is shown in the table below:

Distribution of ARCHITECT CA 125 II Assay Values

	Number of Subjects	Percent (%) 0-35 U/mL	35.1-65 U/mL	65.1-100 U/mL	>100 U/mL
MALIGNANT CONDITIONS					
Breast Cancer	50	80.0	20.0	0.0	0.0
Ovarian Cancer	166	49.9	14.3	4.8	32.8
Colorectal Cancer	50	84.0	4.0	10.0	2.0
Endometrial Cancer	25	96.0	4.0	0.0	0.0
Lung Cancer	50	60.0	18.0	10.0	12.0
NON MALIGNANT CONDITIONS					
Ovarian Disease	100	90.0	9.0	1.0	0.0
Urogenital Disease	49	83.7	14.3	2.0	0.0
Hypertension/CHD	100	88.0	11.0	0.0	1.0
Benign Endometrial	25	84.0	8.0	4.0	4.0

Ovarian Cancer Serial Specimens

This analysis is based on 63 patients. There were a total of 306 evaluable observations. The average number of observations per patient is 4.9.

The average age of the subjects at time of diagnosis was 56 years (Exact 95% CI: 52.0 years to 59.4 years). Ninety-three percent of the cohort was post-menopausal at time of diagnosis. Staging was available from the chart for 60 of the 63 women. The majority of the women were stage III (67.7%) while 6.7% and 21.7% were stage I and IV respectively.

Association between Change in Marker Value and Change in Disease State

A 2x2 table was constructed to show the association between a positive change in a patient's CA 125 value and progression of the disease from one observation to the next. A positive change in CA 125 is defined as an increase in the value that is at least 2.5 times greater than the total %CV of the test. For the test assay this value is 10.75%. The following Table (entitled "Distribution of W by V") presents the results for the 243 observation pairs in this study.

Three estimates of Concordance are given for the following Table.

Total Concordance: $C = \frac{85+81}{243} \times 100 = 68.3\%$

Positive Concordance: $C_+ = \frac{85}{11} \times 100 = 76.6\%$

Negative Concordance: $C_{-} = \frac{81}{132} \times 100 = 61.4\%$

Distribution of W by V

	Change in Disease State (W)		
Change in CA 125 (V)	Progression	No Progression	Total
≥ 10.75%	85	51	136
< 10.75%	26	81	107
Total	111	132	243

Per Patient Analysis

The table below (entitled " Per Patient Distribution) demonstrates this distribution for the 63 patients in this study.

Per Patient Distribution

	Change in Disease State (W)		
Change in CA 125 (V)	Progression	No Progression	Total
≥ 10.75%	46	10	56
< 10.75%	1	6	7
Total	47	16	63

Estimates of per-patient concordances can be obtained. Confidence intervals for these estimates can be determined using the binomial distribution. The following table (entitled" Estimate of Per-Patient Positive, Negative and Total Concordance with 95% confidence Intervals) demonstrates the estimates and 95% confidence intervals about each estimate.

Estimate of Per-Patient
Positive, Negative and Total Concordance
With 95% Confidence Intervals

Statistic	Estimate	Lower Bound	Upper Bound
C_{+}	97.9%	88.7%	99.9%
C_{-}	37.5%	15.3%	64.5%
C	82.5%	70.9%	91.0%

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 19 2004

Ms. Kimberly Peterson
Director, Clinical and Regulatory Affairs
Fujirebio Diagnostics, Inc.
201 Great Valley Pkwy
Malvern, PA 19355-1307

Re: k042731
Trade/Device Name: ARCHITECT CA 125 II Reagent Kit
ARCHITECT CA 125 II Calibrator Kit
ARCHITECT CA 125 II Control Kit
Regulation Number: 21 CFR 866.6010
Regulation Name: Carcinoembryonic Antigen (CEA) Immunological Test System
Regulatory Class: Class II
Product Code: LTK, JIT, JJX
Dated: September 30, 2004
Received: October 4, 2004

Dear Ms Peterson:

We have reviewed your Section 510(k) premarket notification of intent to market the devices referenced above and have determined the devices are 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) that do not require approval of a premarket approval application (PMA). You may, therefore, market these devices, 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 devices are classified (see above) into either class II (Special Controls) or class III (PMA), they may be subject to such additional controls. Existing major regulations affecting your devices can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your devices in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your devices comply with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality

labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.
This letter will allow you to begin marketing your devices as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your devices to legally marketed predicate devices results in a classification for your devices and thus, permits your devices to proceed to the market.

If you desire specific advice for your devices on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address
http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,

Robert L. Becker, Jr., M.D., PhD
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K042731

Device Name: ARCHITECT® CA 125 II™ Assay

Indications for Use:

ARCHITECT CA 125 II Reagent Kit

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ARCHITECT CA 125 II Calibrator Kit

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ARCHITECT CA 125 II Control Kit

The ARCHITECT CA 125 II Controls are for the verification of the accuracy and precision of the ARCHITECT *i* System when used for the quantitative determination of OC 125 defined antigen in human serum and plasma. Refer to the ARCHITECT CA 125 II reagent package insert for additional information.

Prescription Use ✓
(Part 21 CFR 801 Subpart D)

AND/OR Over-The-Counter Use _____
(21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Maria M Chan
Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

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