DEC 22 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: _____.

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 15-3® Assay
Common/Usual Name:	CA 15-3 Assay
Classification Name:	System, Test, Immunological, Antigen, Tumor

Predicate Device

AxSYM® CA 15-3® Assay

Device Description

The ARCHITECT CA 15-3 assay is a two-step immunoassay to determine the presence of DF3 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, sample, wash buffer and 115D8 coated paramagnetic microparticles are combined. DF3 reactive determinants present in the sample bind to the 115D8 coated microparticles. After washing, DF3 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 DF3 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 15-3 Assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of DF3 defined antigen in human serum and plasma on the ARCHITECT *i* System. The ARCHITECT CA 15-3 assay is to be used as an aid in the management of Stage II and Stage III breast cancer patients. Serial testing for patient CA 15-3 assay values should be used in conjunction with other clinical methods for monitoring breast cancer.
ARCHITECT CA 15-3 Assay kit is substantially equivalent to the AxSYM® CA 15-3® Assay manufactured by Abbott Laboratories. Both of the devices are IVD products and are indicated for the quantitative determination of CA 15-3 assay values (DF3 defined antigen) in human serum and plasma, as an aid in the management of Stage II and Stage III breast cancer patients.
A comparison of the features of the ARCHITECT CA 15-3 Assay device and the AxSYM CA 15-3 Assay follows.

	Abbott Laboratories ARCHITECT CA 15-3 Assay (Proposed Device)	**Abbott Laboratories AxSYM® CA 15-3® Assay (Predicate Device) K963926**
Device Type	*In vitro* diagnostic	*In vitro* diagnostic
Classification and Product Code	Class II, MOI	Class II, MOI
Principle of Operation	Chemiluminscent Microparticle Immunoassay (CMIA)	Microparticle Enzyme Immunoassay (MEIA)
Product Usage	Clinical and Hospital laboratories	Clinical and Hospital laboratories
Intended Use	The ARCHITECT CA 15-3 Assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of DF3 defined antigen in human serum and plasma on the ARCHITECT *i* System. The ARCHITECT CA 15-3 assay is to be used as an aid in the management of Stage II and Stage III breast cancer patients. Serial testing for patient CA 15-3 assay values should be used in conjunction with other clinical methods for monitoring breast cancer.	The AXSYM CA 15-3 Assay is a microparticle enzyme immunoassay (MEIA) for the quantitative measurement of CA 15-3 assay values in human serum and plasma (EDTA) to aid in the management of Stage II and Stage III breast cancer patients. Serial testing for patient CA 15-3 assay values should be used in conjunction with other clinical methods for monitoring breast cancer.
Type of Specimen	Human serum or plasma (EDTA, Lithium Heparin, Sodium Heparin)	Human Serum or plasma (EDTA)
Specimen Collection Method	Routine Phlebotomy Techniques	Routine Phlebotomy Techniques
Analyte Detected	Breast carcinoma-associated mucin antigen encoded by the MUC 1 gene	Breast carcinoma-associated mucin antigen encoded by the MUC 1 gene
Capture Antibody	115D8 mouse monoclonal	115D8 mouse monoclonal
Conjugate Antibody	DF3 mouse monoclonal	DF3 mouse monoclonal
Calibrators	6 levels (0 – 800 U/mL)	6 levels (0 - 250 U/mL)
Controls	2 levels (Low = 40 U/mL, High = 250 U/mL)	2 levels (Low = 35 U/mL, High = 150 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. Five defibrinated plasma based panel members (1, 2, 3, 4 and 5) were tested, in replicates of two, at two separate times per day, for 20 days. Testing was performed on 2 instruments (both instruments are located at FDI) using 2 lots of reagents and a single calibration per instrument. 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 8%.

Comparison Study

A total of 402 serum specimens, of which 250 serum specimens were from patients diagnosed with breast cancer (stage I through stage IV), were tested using the ARCHITECT CA 15-3 assay and the AxSYM CA 15-3 assay. Passing-Bablok linear regression analyses was performed on all specimens with concentration values within the dynamic range of both assays (0.0-1326.5 U/mL*) for the ARCHITECT CA 15-3 assay and (4.9-1621.9 U/mL*) for the AxSYM CA 15-3 Assay.

Passing-Bablok linear regression analysis comparing the ARCHITECT CA 15-3 assay to the AxSYM CA 15-3 assay yielded a correlation coefficient of 0.980, a slope of 0.94 (99% confidence interval of 0.92, 0.97), and Y-axis intercept of –0.3 U/mL (99% confidence interval of –0.9, 0.0).

Reference Ranges:

Apparently Healthy Population:
The distribution of CA 15-3 assay values determined in 396 normal individual specimens is shown in the table below:

Distribution of ARCHITECT CA 15-3 Assay Values

		Percent (%)			
	Number of Subjects	0-31.3 U/mL	31.4-60 U/mL	60.1-120 U/mL	>120 U/mL
Apparently Healthy					
Females (Pre Menopausal)	99	99.0	1.0	0.0	0.0
Females (Post Menopausal)	100	99.0	0.0	1.0	0.0
Males	197	98.5	1.5	0.0	0.0

In this study, 99.0% of the healthy female subjects had CA 15-3 assay values at or below 31.3 U/mL. (mean = 13.0, SD = 7.0)

Patient Groups:

The distribution of CA 15-3 assay values determined in 569 specimens from various diseases is shown in the table below:

Distribution of ARCHITECT CA 15-3 Assay Values					
		Percent (%)			
	Number of Subjects	0-31.3 U/mL	31.4-60 U/mL	60.1-120 U/mL	>120 U/mL
Malignant Conditions					
Ovarian Cancer	120	76.7	13.3	4.2	5.8
Colorectal Cancer	50	96.0	4.0	0.0	0.0
Lung Cancer	50	78.0	14.0	4.0	4.0
NonMalignant Conditions					
Breast Disease	100	97.0	3.0	0.0	0.0
Ovarian Disease	100	99.0	1.0	0.0	0.0
Urogenital Disease	49	84.0	16.0	0.0	0.0
Pregnancy	50	100.0	0.0	0.0	0.0
Hypertension/CHD	100	94.0	6.0	0.0	0.0

Breast Cancer Serial Specimens

This analysis is based on 74 evaluable patient's samples. There were a total of 377 evaluable observations. The average number of observations per patient is 5.1.

The average age of the women in this cohort at time of diagnosis was 48 years (Exact 95% CI: 45.3 years to 48.9 years). Forty-seven percent of the women were post-menopausal at time of diagnosis. Stage was available from the charts for 61 women. Sixty-four percent of the cohort was evenly split between stage II and stage III with 23% of the woman having stage IV disease.

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 CA15-3 value and progression of the disease from one observation to the next. A positive change in CA15-3 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 9.575%. The following Table (entitled "Distribution of W by V") presents the results for the 303 observation pairs in this study.

Three estimates of Concordance are given for the following Table.

Total Concordance: $C = \frac{50+153}{303} \times 100 = 66.9\%$

Positive Concordance: $C_+ = \frac{50}{66} \times 100 = 75.7\%$

Negative Concordance: $C_- = \frac{153}{237} \times 100 = 64.5\%$

Distribution of W by V

	Change in Disease State (W)		
Change in CA15-3 (V)	Progression	No Progression	Total
≥9.575%	50	84	134
<9.575%	16	153	169
Total	66	237	303

Per Patient Analysis:
The table below (entitled " Per Patient Distribution) demonstrates this distribution for the 74 patients in this study.

Per Patient Distribution

	Change in Disease State (W)		
Change in CA15-3 (V)	Progression	No Progression	Total
≥9.575%	36	27	63
<9.575%	1	10	11
Total	37	37	74

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_+	97.3%	85.8%	99.3%
C_-	27.0%	13.8%	44.1%
C	61.3%	50.1%	73.2%

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 22 2004

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

Re: k042732
Trade/Device Name: ARCHITECT® CA 15-3® Assay
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-associated antigen immunological test system
Regulatory Class: Class II
Product Code: MOI, 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 device referenced above and 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) that do not require approval of a premarket approval application (PMA). 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 (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device 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 device complies 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 Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. 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., MD, Ph.D
Director
Division of Immunology and Hematology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known):

Device Name: ARCHITECT® CA 15-3® Assay

Indications for Use:

ARCHITECT CA 15-3 Reagent Kit
The ARCHITECT CA 15-3 assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of DF3 defined antigen in human serum and plasma on the ARCHITECT *i* System. The ARCHITECT CA 15-3 assay is to be used as an aid in the management of Stage II and III breast cancer patients. Serial testing for patient CA 15-3 assay values should be used in conjunction with other clinical methods for monitoring breast cancer.

ARCHITECT CA 15-3 Calibrator Kit
The ARCHITECT CA 15-3 Calibrators are for the calibration of the ARCHITECT *i* System when used for the quantitative determination of DF3 defined antigen in human serum and plasma. Refer to the ARCHITECT CA 15-3 reagent package insert for additional information.

ARCHITECT CA 15-3 Control Kit
The ARCHITECT CA 15-3 Controls are for the verification of the accuracy and precision of the ARCHITECT *i* System when used for the quantitative determination of DF3 defined antigen in human serum and plasma. Refer to the ARCHITECT CA 15-3 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)

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K042732