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**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**

AUG - 1 2007

Address: Fujirebio Diagnostics, Inc.  
201 Great Valley Parkway  
Malvern, PA 19355

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Summary preparation date: March 23, 2007

**Name of Device**

Trade/Proprietary Name: ARCHITECT Tacrolimus Assay  
ARCHITECT Tacrolimus Calibrators

Common/Usual Name: Tacrolimus Test Systems  
Calibrator

Regulation Number: 21 CFR 862.1678  
21 CFR 862.3200

Regulatory Class: Class II

Product Code: MLM  
DLJ

**Predicate Device**

ABBOTT IMx® Tacrolimus II Microparticle Enzyme Immunoassay (P97000)<sup>1</sup>

**Device Description**

The ARCHITECT Tacrolimus assay is a delayed one-step immunoassay for the quantitative determination of tacrolimus in human whole blood using CMIA technology with flexible assay protocols, referred to as Chemiflex.

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<sup>1</sup> note: tacrolimus test systems have been reclassified into Class II since the predicate was approved

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Prior to the initiation of the automated ARCHITECT sequence, a manual pretreatment step is performed in which the whole blood sample is extracted with a precipitation reagent and centrifuged. The supernatant is decanted into a Transplant Pretreatment Tube, which is placed onto the ARCHITECT *i* System.

Sample, assay diluent, and anti-tacrolimus coated paramagnetic microparticles are combined to create a reaction mixture. Tacrolimus present in the sample binds to the anti-tacrolimus coated microparticles. After a delay, tacrolimus acridinium-labeled conjugate is added to the reaction mixture. The tacrolimus on the acridinium-labeled conjugate competes for the available binding sites on the microparticles. Following an incubation, the microparticles are washed, and pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs).

An indirect relationship exists between the amount of tacrolimus in the sample and the RLUs detected by the ARCHITECT *i* System optics.

### **Intended Use**

#### **Reagent Kit**

The ARCHITECT Tacrolimus assay is a chemiluminescent Microparticle immunoassay (CMIA) for the quantitative determination of tacrolimus in human whole blood on the ARCHITECT *i* System. The ARCHITECT Tacrolimus assay is to be used as an aid in the management of liver and kidney allograft patients receiving tacrolimus therapy.

#### **Calibrator Kit**

The ARCHITECT Tacrolimus Calibrators are for the calibration of the ARCHITECT *i* System when used for the quantitative determination of tacrolimus in human whole blood.

#### **Whole Blood Precipitation Reagent**

The ARCHITECT Tacrolimus Whole Blood Precipitation Reagent is for the extraction of sirolimus from samples (human whole blood patient specimens, controls, and ARCHITECT Tacrolimus Calibrators) to be tested on the ARCHITECT *i* System.

**Statement of Substantial Equivalence**

The ARCHITECT Tacrolimus assay is a chemiluminescent Microparticle immunoassay (CMIA) for the quantitative determination of tacrolimus in human whole blood on the ARCHITECT / System. The ARCHITECT Tacrolimus assay is to be used as an aid in the management of liver and kidney allograft patients receiving tacrolimus therapy.

The ARCHITECT Tacrolimus assay is substantially equivalent to the IMx Tacrolimus II assay. Both of the devices are IVD products and are indicated for the quantitative determination of tacrolimus in human whole blood and used as an aid in the management of liver and kidney allograft patients receiving tacrolimus therapy.

A study was performed using human whole blood specimens from renal and liver transplant patients receiving tacrolimus therapy, where regression analysis was performed using the Passing-Bablok<sup>2</sup> method. Data from the study are summarized in the following table.

<b>ARCHITECT Tacrolimus vs. IMx Tacrolimus II</b>			
<b>Number of Observations</b>	<b>Intercept (95% CI)<sup>a</sup></b>	<b>Slope (95% CI)</b>	<b>Correlation Coefficient</b>
124	0.37 (0.00 to 0.68)	0.81 (0.75 to 0.88)	0.90

<sup>a</sup> Confidence Interval

Specimen Range (ARCHITECT): 2.2 ng/mL to 14.8 ng/mL

Specimen Range (IMx): 2.1 ng/mL to 15.9 ng/mL

Additional testing of the above sample was completed with LC/MS/MS, where regression analysis was performed using the Passing-Bablok<sup>1</sup> method. Data from the study are summarized in the following table.

<b>ARCHITECT Tacrolimus vs. LC/MS/MS</b>			
<b>Number of Observations</b>	<b>Intercept (95% CI)</b>	<b>Slope (95% CI)</b>	<b>Correlation Coefficient</b>
125	0.22 (0.02 to 0.48)	1.07 (1.01 to 1.12)	0.92

Specimen Range (ARCHITECT): 2.1 ng/mL to 14.8 ng/mL

Specimen Range (LC/MS/MS): 1.78 ng/mL to 19.20 ng/mL

<sup>2</sup> Passing H, Bablok W. A new biometrical procedure for testing the equality of measurements from two different analytical methods. *J Clin Chem Clin Biochem* 1983; 21(11)709-20.

A comparison of the features of the ARCHITECT Tacrolimus assay and the IMx Tacrolimus II assay are as follows:

<b>Similarities</b>		
	<b>ARCHITECT Tacrolimus (Proposed Device)</b>	<b>IMx Tacrolimus II (Predicate Device) P970007<sup>1</sup></b>
<b>Device Type</b>	<i>In vitro</i> diagnostic	<i>In vitro</i> diagnostic
<b>Classification and Product Code</b>	Class II, MLM	Class II, MLM
<b>Product Usage</b>	Clinical and Hospital laboratories	Clinical and Hospital laboratories
<b>Intended Use</b>	Quantitative determination of tacrolimus in human whole blood as an aid in the management of liver and kidney allograft patients receiving tacrolimus therapy.	Quantitative determination of tacrolimus in human whole blood as an aid in the management of liver and kidney allograft patients receiving tacrolimus therapy.
<b>Type of Specimen</b>	Human Whole Blood	Human Whole Blood
<b>Specimen Collection Method</b>	EDTA Whole Blood Collection Tubes	EDTA Whole Blood Collection Tubes
<b>Specimen Pretreatment Step</b>	Manual extraction of tacrolimus in human whole blood	Manual extraction of tacrolimus in human whole blood
<b>Calibrators</b>	6 Levels (0 – 30 ng/mL)	6 Levels (0 – 30 ng/mL)
<b>Calibrator Matrix</b>	Processed human whole blood	Processed human whole blood
<b>Antibody</b>	Mouse monoclonal (anti – tacrolimus)	Mouse monoclonal (anti – tacrolimus)
<b>Interpretation of Results</b>	Calibrator Curve An indirect relationship exists between the amount of tacrolimus in the sample and the light detected by the instrument system	Calibrator Curve An indirect relationship exists between the amount of tacrolimus in the sample and the light detected by the instrument system

<b>Differences</b>		
	<b>ARCHITECT Tacrolimus (Proposed Device)</b>	<b>IMx Tacrolimus II (Predicate Device) P970007<sup>1</sup></b>
<b>Instrument System</b>	ARCHITECT System	IMx System
<b>Principle of Operation</b>	Chemiluminescent Microparticle Immunoassay (CMIA)	Microparticle Enzyme Immunoassay (MEIA)
<b>Conjugate</b>	Tacrolimus-Acrinium Conjugate in citrate buffer with protein stabilizers	Tacrolimus-alkaline phosphatase in TRIS buffer with protein stabilizers
<b>Microparticles</b>	Anti-tacrolimus (mouse, monoclonal) coated paramagnetic microparticles in EDTA buffer	Anti-tacrolimus (mouse monoclonal) coated polystyrene latex microparticles in TRIS buffer
<b>Precipitation Reagent</b>	Zinc sulfate solution in methanol and ethylene glycol.	Zinc sulfate solution in methanol and Ethylene glycol

<sup>1</sup> note: tacrolimus test systems have been reclassified into Class II since the predicate was approved

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## **Performance Characteristics**

### **Precision:**

A study was performed with the ARCHITECT Tacrolimus assay based on guidance from the Clinical and Laboratory Standards Institute, document (CLSI, formerly NCCLS) Protocol EP5-A2. Abbott Immunosuppressent-MCC (levels 1, 2, and 3) and five whole blood panels were assayed, using two lots of reagents, on two instruments, in replicates of two at two separate times per day for 20 days. Each reagent lot used a single calibration curve throughout the study.

The total precision %CV of the ARCHITECT Tacrolimus assay was determined to be less than or equal to 10%.

### **Linearity:**

A dilution linearity study was performed by diluting high concentration tacrolimus whole blood specimens with the ARCHITECT Tacrolimus Calibrator A. The concentration of Tacrolimus was determined for each dilution of sample and the mean percent (%) recovery was calculated.

The ARCHITECT Tacrolimus assay was determined to have a mean recovery within 10% of the expected result for diluted samples.

### **Functional Sensitivity:**

Whole blood specimens were spiked with tacrolimus to achieve approximate concentrations from 0.2 to 4.4 ng/mL and tested in replicates of 10, twice a day, for five days. At the upper 95% confidence limit, the lowest ARCHITECT Tacrolimus assay value exhibiting a 20% CV was calculated to be 0.8 ng/mL.

### **Analytical Sensitivity:**

The limit of detection for the ARCHITECT Tacrolimus assay, defined as the concentration at two standard deviations above the ARCHITECT Tacrolimus Calibrator A (0.0 ng/mL) was calculated to be 0.3 ng/mL at the 95% confidence (based on one study with n=24 runs, 10 replicates calibrator A and 4 replicates calibrator B per run).

### **Interference:**

Whole blood specimens were supplemented with various drugs and potentially interfering compounds (triglycerides, hematocrit, bilirubin, total protein, cholesterol, uric acid, HAMA, and rheumatoid factor [RF]). The average recovery observed during the study ranged from 95 to 105%.

Specificity:

Aliquots of whole blood specimens were augmented with tacrolimus, targeting values ranging from 5 to 22 ng/mL. These five specimens were spiked with cross-reactant solution. Data from this study are summarized in the following table.

<b>Metabolite</b>	<b>Amount Added (ng/mL)</b>	<b>Mean Excess Concentration Detected (ng/mL, n=5)</b>	<b>% Cross Reactivity<sup>a</sup></b>
M-I (13-O-demethyl-tacrolimus)	10	<1.5	NA <sup>b</sup>
M-II (31-O-demethyl-tacrolimus)	10	9.4	94
M-III (15-O-demethyl-tacrolimus)	10	4.5	45
M-IV (12 hydroxytacrolimus)	10	<1.5	NA <sup>b</sup>



Fujirebio Diagnostics, Inc  
Ms. Diana Dickson  
201 Great Valley Parkway  
Malvern, PA 19355

AUG - 1 2007

Re: k070820  
Trade/Device Name: ARCHITECT Tacrolimus Assay  
Regulation Number: 21 CFR 862.1687  
Regulation Name: Tacrolimus test system (special controls)  
Regulatory Class: Class II  
Product Code: MLM, JIT  
Dated: July 18, 2007  
Received: July 19, 2007

Dear Ms. Dickson:

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).

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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) 276-0490. 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 (240) 276-3150 or at its Internet address at <http://www.fda.gov/cdrh/industry/support/index.html>.

Sincerely yours,

  
Jean M. Cooper, M.S., D.V.M.

Director  
Division of Chemistry and Toxicology  
Office of *In Vitro* Diagnostic Device  
Evaluation and Safety  
Center for Devices and  
Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known): K070820

Device Name: ARCHITECT Tacrolimus

Indications For Use:

### Reagent Kit

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Prescription Use

AND/OR

Over-The-Counter Use

(Part 21 CFR 801 Subpart D)

(21 CFR 807 Subpart C)

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

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

  
Division Sign-Off

Office of In Vitro Diagnostic Device  
Evaluation and Safety

510(k) K070820

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