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: K070822

Submitter Information

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

Contact person: Diana L. Dickson
(610) 240-3917
dicksond@fdi.com

Summary preparation date: September 28, 2007

Name of Device

Trade/Proprietary Name: ARCHITECT Sirolimus Assay
ARCHITECT Sirolimus Calibrators

Common/Usual Name: Sirolimus Test Systems
Calibrator

Regulation Number: 21 CFR 862.3640
21 CFR 862.3200

Regulatory Class: Class II

Product Code: NRP
DLJ

Predicate Device

ABBOTT IMx® Sirolimus Microparticle Enzyme Immunoassay (K042411)

Device Description

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

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, heated,
and centrifuged. The supernatant is decanted into a Transplant Pretreatment Tube, which is placed onto the ARCHITECT i System.

Sample, assay diluent, and anti-sirolimus coated paramagnetic microparticles are combined to create a reaction mixture. Sirolimus present in the sample binds to the anti-sirolimus coated microparticles. After a delay, sirolimus acridinium-labeled conjugate is added to the reaction mixture. The sirolimus acridinium-labeled conjugate competes for the available binding sites on the anti-sirolimus coated paramagnetic 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 sirolimus in the sample and the RLUs detected by the ARCHITECT i System optics.

**Reportable Range**
The reportable range for the ARCHITECT Sirolimus assay is 2 ng/mL (minimum reportable value based on Functional Sensitivity) to 30 ng/mL.

**Intended Use**

**Reagent Kit**
The ARCHITECT Sirolimus assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of sirolimus in human whole blood on the ARCHITECT i System. The ARCHITECT Sirolimus assay is to be used as an aid in the management of renal transplant patients receiving sirolimus therapy.

**Calibrator Kit**
The ARCHITECT Sirolimus Calibrators are for the calibration of the ARCHITECT i System when used for the quantitative determination of sirolimus in human whole blood.

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

The ARCHITECT Sirolimus assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of sirolimus in human whole blood on the ARCHITECT i System. The ARCHITECT Sirolimus assay is to be used as an aid in the management of renal transplant patients receiving sirolimus therapy.

The ARCHITECT Sirolimus assay is substantially equivalent to the IMx Sirolimus assay. Both of the devices are IVD products and are indicated for the quantitative determination of sirolimus in human whole blood and used as an aid in the management of renal transplant patients receiving sirolimus therapy.

A study was performed using human whole blood specimens from renal transplant patients receiving sirolimus therapy, where regression analysis was performed using the Passing-Bablok\textsuperscript{1} method. Data from the study are summarized in the following table.

<table>
<thead>
<tr>
<th>ARCHITECT Sirolimus vs. IMx Sirolimus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Observations</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>168</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Confidence Interval

Specimen Range (ARCHITECT): 2.1 ng/mL – 29.7 ng/mL
Specimen Range (IMx): 1.8 ng/mL – 29.6 ng/mL

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

<table>
<thead>
<tr>
<th>ARCHITECT Sirolimus vs. LC/MS/MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Observations</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>167</td>
</tr>
</tbody>
</table>

Specimen Range (ARCHITECT): 2.1 ng/mL – 29.7 ng/mL
Specimen Range (LC/MS/MS): 1.65 ng/mL – 29.1 ng/mL

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

### Similarities

<table>
<thead>
<tr>
<th>Device Type</th>
<th>ARCHITECT Sirolimus (Proposed Device)</th>
<th>IMx Sirolimus (Predicate Device) K042411</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification and Product Code</td>
<td>In vitro diagnostic</td>
<td>Class II, NRP</td>
</tr>
<tr>
<td>Product Usage</td>
<td>Clinical and Hospital laboratories</td>
<td>Clinical and Hospital laboratories</td>
</tr>
<tr>
<td>Intended Use</td>
<td>Quantitative determination of sirolimus in human whole blood as an aid in the management of renal transplant patients receiving sirolimus therapy.</td>
<td>Quantitative determination of sirolimus in human whole blood as an aid in the management of renal transplant patients receiving sirolimus therapy.</td>
</tr>
<tr>
<td>Type of Specimen</td>
<td>Human Whole Blood</td>
<td>Human Whole Blood</td>
</tr>
<tr>
<td>Specimen Collection Method</td>
<td>EDTA Whole Blood Collection Tubes</td>
<td>EDTA Whole Blood Collection Tubes</td>
</tr>
<tr>
<td>Specimen Pretreatment Step</td>
<td>Manual extraction of sirolimus in human whole blood</td>
<td>Manual extraction of sirolimus in human whole blood</td>
</tr>
<tr>
<td>Calibrators</td>
<td>6 Levels (0 – 30 ng/mL)</td>
<td>6 Levels (0 – 30 ng/mL)</td>
</tr>
<tr>
<td>Calibrator Matrix</td>
<td>Processed human whole blood</td>
<td>Processed human whole blood</td>
</tr>
<tr>
<td>Antibody</td>
<td>Mouse monoclonal (anti – sirolimus)</td>
<td>Mouse monoclonal (anti – sirolimus)</td>
</tr>
<tr>
<td>Interpretation of Results</td>
<td>Calibrator Curve An indirect relationship exists between the amount of sirolimus in the sample and the light detected by the instrument system</td>
<td>Calibrator Curve An indirect relationship exists between the amount of sirolimus in the sample and the light detected by the instrument system</td>
</tr>
</tbody>
</table>

### Differences

<table>
<thead>
<tr>
<th>Instrument System</th>
<th>ARCHITECT Sirolimus (Proposed Device)</th>
<th>IMx Sirolimus (Predicate Device) K042411</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principle of Operation</td>
<td>Chemiluminescent Microparticle Immunoassay (CMIA)</td>
<td>Microparticle Enzyme Immunoassay (MEIA)</td>
</tr>
<tr>
<td>Conjugate</td>
<td>Sirolimus-Acridinium Conjugate in citrate buffer</td>
<td>Sirolimus-alkaline phosphatase in TRIS buffer with protein stabilizers</td>
</tr>
<tr>
<td>Microparticles</td>
<td>Anti-sirolimus (mouse, monoclonal) coated paramagnetic microparticles in MES buffer</td>
<td>Anti-sirolimus (mouse monoclonal) coated polystyrene latex microparticles in TRIS buffer</td>
</tr>
<tr>
<td>Precipitation Reagent</td>
<td>Zinc sulfate solution in DMSO and Ethylene glycol</td>
<td>Zinc sulfate solution in methanol and Ethylene glycol</td>
</tr>
</tbody>
</table>
Performance Characteristics

Precision:

A study was performed with the ARCHITECT Sirolimus 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 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 Sirolimus assay was determined to be less than or equal to 10%.

Linearity:

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

The ARCHITECT Sirolimus 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 sirolimus to achieve approximate concentrations from 0.1 to 5.3 ng/mL and tested in replicates of 10, twice a day, for five days. At the upper 95% confidence limit, the lowest ARCHITECT Sirolimus assay value exhibiting a 20% CV was calculated to be 0.7 ng/mL, which is below the reportable range of the ARCHITECT Sirolimus assay.

Analytical Sensitivity:

The limit of detection for the ARCHITECT Sirolimus assay, defined as the concentration at two standard deviations above the ARCHITECT Sirolimus Calibrator A (0.0 ng/mL) was calculated to be 0.3 ng/mL, which is below the reportable range of the ARCHITECT Sirolimus assay at 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 106%.
Specificity:

Aliquots of whole blood specimens were augmented with sirolimus, 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.

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Amount Added (ng/mL)</th>
<th>Mean Excess Concentration Detected (ng/mL, n=5)</th>
<th>% Cross Reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>F2 (41-0-demethyl-hydroxyl-sirolimus)</td>
<td>10</td>
<td>0.87</td>
<td>8.7</td>
</tr>
<tr>
<td>F3 (41-0-demethyl-hydroxyl-sirolimus; 7-0-demethyl sirolimus)</td>
<td>3</td>
<td>0.12</td>
<td>7.6</td>
</tr>
<tr>
<td>F4 (11-hydroxy-sirolimus)</td>
<td>10</td>
<td>3.7</td>
<td>36.8</td>
</tr>
<tr>
<td>F5 (41-0-demethyl-sirolimus)</td>
<td>10</td>
<td>2.0</td>
<td>20.3</td>
</tr>
</tbody>
</table>
DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 28 2007

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

Re: k070822
   Trade/Device Name: ARCHITECT Sirolimus Assay
   Regulation Number: 21 CFR 862.3840
   Regulation Name: Sirolimus test system
   Regulatory Class: Class II
   Product Code: NRP, JIT
   Dated: September 14, 2007
   Received: September 17, 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).
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.
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): K070822

Device Name: ARCHITECT Sirolimus

Indications For Use:

Reagent Kit
The ARCHITECT Sirolimus assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of sirolimus in human whole blood on the ARCHITECT i System. The ARCHITECT Sirolimus assay is to be used as an aid in the management of renal transplant patients receiving sirolimus therapy.

Calibrator Kit
The ARCHITECT Sirolimus Calibrators are for the calibration of the ARCHITECT i System when used for the quantitative determination of sirolimus in human whole blood.

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

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

Page 1 of 1