

1081857

**510k 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.

Submitter's Name: George M. Plummer  
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P.O. Box 6101  
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**OCT 30 2008**

Date of Preparation: June 26, 2008

Name of Product(s): Dimension SIRO Flex® reagent cartridge

FDA Classification Name(s): Sirolimus Test System(862.3840)  
Clinical Toxicology Calibrator (862.3200)

FDA Guidance Documents: Class II Special Controls Guidance Document: Sirolimus Test Systems

Predicate Device(s): Abbott IMx Sirolimus Microparticle Enzyme Immunoassay and IMx Sirolimus Calibrator (k042411)

**Device Description(s):**

The automated Dimension® SIRO method uses an immunoassay technique in which free and sirolimus-bound antibody-enzyme conjugates are separated using magnetic particles. The assay is performed using a method specific Flex® reagent cartridge. The Flex® cartridge contains a pretreatment reagent, antibody-β-galactosidase conjugate, sirolimus immobilized on chromium dioxide particles, chlorophenol red β-d-galactopyranoside (CPRG) substrate, and diluent to hydrate the tablets.

To perform the SIRO assay, a sample cup (or SSC) containing the whole blood sample to be analyzed and a SIRO Flex® reagent cartridge are placed appropriately on the Dimension® system. The Dimension® system mixes and lyses the whole blood sample. The lysed sample is then mixed with the antibody enzyme conjugate. The sirolimus present in the sample is bound by the sirolimus antibody conjugate reagent. Magnetic particles coated with sirolimus are added to bind free (unbound) antibody-enzyme conjugate. The reaction mixture is then separated magnetically. Following separation, the supernatant containing the sirolimus-antibody-enzyme complex is transferred to another cuvette and mixed with the substrate. β-galactosidase catalyzes the hydrolysis of CPRG (chlorophenol red β-d-galactopyranoside) to produce CPR (chlorophenol red) that absorbs light maximally at 577 nm. The change in absorbance at 577 nm due to the formation of CPR is directly proportional to the amount of sirolimus in the patient's sample and is measured using a bichromatic (577, 700 nm) rate technique.

|                                                             |                     |                                             |
|-------------------------------------------------------------|---------------------|---------------------------------------------|
| Sirolimus + Ab-β-gal                                        | →                   | Sirolimus-Ab-β-gal + Ab-β-gal               |
| Sirolimus-Ab-β-gal + Ab-β-gal + CrO <sub>2</sub> -Sirolimus | Magnetic separation | Sirolimus-Ab-β-gal (transferred to cuvette) |
| CPRG (non-absorbing at 577 nm)                              |                     | CPR (absorbs at 577 nm)                     |

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|--|--|--|
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|--|--|--|

The Dimension® Sirolimus Calibrator (DC306) is an in-vitro diagnostic product intended to be used to calibrate the Dimension® Sirolimus method. It is a frozen liquid product packaged as a single vial for each of five levels. The matrix is human whole blood hemolysate with preservatives. Levels 2, 3, 4, and 5 contain sirolimus drug at target values of 5, 10, 20, and 31.5 ng/mL, respectively. Level 1 is a human whole blood hemolysate that does not contain sirolimus drug.

**Intended Use:**

SIRO Flex® reagent cartridge

The SIRO method is an in vitro diagnostic test for the quantitative measurement of Sirolimus in human whole blood on the Dimension® clinical chemistry system. Measurements of Sirolimus are used as an aid in the management of sirolimus therapy in renal transplant patients.

Sirolimus Calibrator

The Sirolimus calibrator is an in vitro diagnostic product for the calibration of Sirolimus (SIRO) on the Dimension® clinical chemistry system.

**Substantial Equivalence:**

A summary of the performance attributes of the Siemens SIRO Flex® reagent cartridge/SIRO Calibrator and the predicate Abbott IMx Sirolimus Microparticle Enzyme Immunoassay (K042411)/IMx Sirolimus Calibrator is provided in the following charts.

**Table of Similarities**

| <b>Item</b>                          | <b>Abbott Sirolimus</b>                                                                                                                                                                                                                                              | <b>Dimension® SIRO</b>                                                                                                                                                                                                                                                           |
|--------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Intended Use                         | The IMx® Sirolimus assay is an in vitro reagent system for the quantitative determination of sirolimus in human whole blood, as an aid in the management of renal transplant patients receiving therapy with sirolimus                                               | The SIRO method is an in vitro diagnostic test for the quantitative measurement of Sirolimus in human whole blood on the Dimension® clinical chemistry system. Measurements of Sirolimus are used as an aid in the management of sirolimus therapy in renal transplant patients. |
| Assay Technology                     | Enzyme immunoassay (Microparticle)                                                                                                                                                                                                                                   | Enzyme immunoassay (Affinity chrome mediated)                                                                                                                                                                                                                                    |
| Sample Type                          | EDTA whole blood                                                                                                                                                                                                                                                     | EDTA whole blood                                                                                                                                                                                                                                                                 |
| Expected Values (Reference Interval) | Not applicable for immunosuppressive drug assays. Optimal ranges depend upon the patient’s clinical state, individual differences in sensitivity to immunosuppressive and nephrotoxic effects of sirolimus, co-administration of other immunosuppressants, time post | Not applicable for immunosuppressive drug assays. Optimal ranges depend upon the patient’s clinical state, individual differences in sensitivity to immunosuppressive and nephrotoxic effects of sirolimus, co-administration of other immunosuppressants, time post             |

|                   |                                        |                                        |
|-------------------|----------------------------------------|----------------------------------------|
|                   | transplant and of other factors.       | transplant and of other factors.       |
| Calibrator Matrix | human whole blood containing sirolimus | human whole blood containing sirolimus |

### **Table of Differences**

| <b>Item</b>            | <b>Abbott Sirolimus</b>    | <b>Dimension® SIRO</b>                                                                             |
|------------------------|----------------------------|----------------------------------------------------------------------------------------------------|
| Sample Pretreatment    | Required                   | Not required                                                                                       |
| Reportable Range       | 0 to 30 ng/mL              | 1.5 to 30 ng/mL                                                                                    |
| Functional Sensitivity | < 2.5 ng/mL                | < 2.0 ng/mL                                                                                        |
| Calibration Interval   | Calibration with each run. | Calibration curve updated for each lot, using five levels every 30 days with the same reagent lot. |
| Sample Volume          | 150 uL                     | 18 uL                                                                                              |

### **Method performance Summary:**

#### **Method Comparison**

A split patient sample (EDTA whole blood) method comparison demonstrated good agreement between the Siemens Dimension® SIRO method and HPLC/MS, the reference method.

| HPLC/MS Sample Range | Dimension® Sample Range | n   | Slope | Intercept  | Correlation Coefficient |
|----------------------|-------------------------|-----|-------|------------|-------------------------|
| 2.8 - 23.7 ng/mL     | 2.4 - 25.6 ng/mL        | 119 | 1.2   | -0.7 ng/mL | 0.95                    |

The model equation for the Linear regression statistics is: [results for Dimension® Siro] = slope x [comparative method results] + intercept.

#### **Reproducibility**

Typical precision observed for the Dimension SIRO method is summarized below:

| <b>Sample</b>            | <b>Mean (ng/mL)</b> | <b>Repeatability</b> |            | <b>Within Lab</b> |            |
|--------------------------|---------------------|----------------------|------------|-------------------|------------|
|                          |                     | <b>SD (ng/mL)</b>    | <b>%CV</b> | <b>SD (ng/mL)</b> | <b>%CV</b> |
| Level 1 Whole Blood Pool | 4.41                | 0.35                 | 8.0        | 0.38              | 8.61       |

|                          |       |      |       |      |       |
|--------------------------|-------|------|-------|------|-------|
| Level 2 Whole Blood Pool | 12.55 | 0.72 | 5.73  | 0.72 | 5.77  |
| Level 3 Whole Blood Pool | 25.35 | 1.69 | 6.67  | 1.79 | 7.07  |
| Level 1 QC               | 2.7   | 0.35 | 12.98 | 0.39 | 14.52 |
| Level 2 QC               | 10.58 | 0.58 | 5.48  | 0.61 | 5.75  |

The reproducibility testing was conducted in accordance with the CLSI Approved Guideline for User Evaluation of Precision Performance of Clinical Chemistry Devices EP5-A2. For each test level, a single test from two independent cups was analyzed twice per day. Testing was conducted with one reagent lot across multiple instruments at one internal and two external locations. The repeatability and within-lab standard deviations were calculated by the analysis of variance method independently for each site. The data above is representative of the results obtained in the reproducibility testing.

**Comments on Substantial Equivalence and Conclusion:**

Both the Abbott IMx Sirolimus (k042411) and the Siemens Dimension® Siro immunoassays are intended for the quantitative determination of sirolimus. The Siemens Dimension® Siro and the predicate Abbott IMx Sirolimus immunoassays are substantially equivalent based on their intended use, performance characteristics, and method comparison to the reference HPLC/MS as described above.

George M. Plummer  
Regulatory Affairs Director  
June 26, 2008



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
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c/o Mr. George M. Plummer  
Director of Regulatory Affairs  
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P.O. Box 6101  
Newark, DE 19714-6101

OCT 30 2008

Re: k081857

Trade/Device Name: Dimension Sirolimus Flex Reagent Cartridge and Dimension  
Sirolimus Calibrator  
Regulation Number: 21 CFR 862.3840  
Regulation Name: Sirolimus Test System  
Regulatory Class: Class II  
Product Code: NRP, DLJ  
Dated: September 24, 2008  
Received: September 25, 2008

Dear Mr. Plummer:

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

## Indication for Use

510(k) Number (if known): K081857

Device Name: Dimension® SIRO Flex® reagent cartridge

### Indication For Use:

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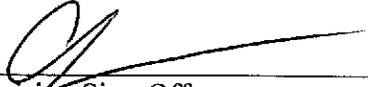
Prescription Use  X   
(21 CFR Part 801 Subpart D)

And/Or

Over the Counter Use        
(21 CFR Part 801 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

  
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Division Sign-Off  
Office of In Vitro Diagnostic Device  
Evaluation and Safety

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## Indication for Use

510(k) Number (if known): K081857

Device Name: Dimension® Sirolimus Calibrator

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The Sirolimus Calibrator is an in vitro diagnostic product for the calibration of Sirolimus (SIRO) on the Dimension® clinical chemistry system.

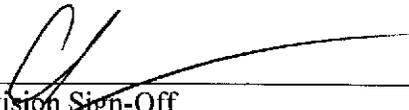
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And/Or

Over the Counter Use \_\_\_\_\_  
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