SEP - 1 2005

510(k) Summary for the
Dimension® Cyclosporine CSAE Flex® reagent cartridge (DF108)

A. 510(k) Number: k052017

B. Analyte: Cyclosporine

C. Type of Test: qualitative or quantitative homogeneous enzyme immunoassay

D. Applicant: Dade Behring Inc., P.O. Box 6101, Newark, DE 19714-6101
(302) 631-9454
Contact: Andrea M. Tasker, Regulatory Affairs and Compliance Manager

E. Proprietary and Established Names: Dimension® Cyclosporine CSAE Flex® reagent cartridge

F. Regulatory Information:

1.Regulation section: 21CFR §862.1235

2. Classification: Class II (Special Controls)

3. Product Code: MKW

4. Panel: Clinical Toxicology Test Systems

G. Intended Use:
1. Intended for Use:
The Cyclosporine CSAE Flex® reagent cartridge is an in vitro diagnostic test intended to quantitatively measure cyclosporine A (CSA) in human whole blood for the Dimension® clinical chemistry system.

2. Indications for Use:
The Cyclosporine CSAE Flex® reagent cartridge is an in vitro diagnostic test intended to quantitatively measure cyclosporine A (CSA) in human whole blood for the Dimension® clinical chemistry system. Measurements of CSA are used as an aid in the management of heart, liver and kidney transplant patients.

3. Special condition for use statement(s): none

4. Special instrument Requirements: Dimension® clinical chemistry system with Heterogeneous Module.

H. Device Description:
The Dimension® CSAE Cyclosporine Flex® reagent cartridge (DF108) is an in vitro diagnostic device that consists of prepackaged reagents in a plastic eight well cartridge for use on the Dade Behring Dimension® clinical chemistry system for the quantitative determination cyclosporine A (CSA) in human whole blood .

I. Substantial Equivalence Information:
1. Predicate Device: Abbott TDx® /TDx FLx® Cyclosporine Monoclonal Whole Blood Assay

2. Predicate K Number(s): P890025

3. Comparison with Predicate:

Item	Device Dimension® CSAE Cyclosporine	Predicate Abbott TDx® /TDx FLx® Cyclosporine Assay
Intended Use	For the measurements of CSA to be used as an aid in the management of heart, liver and kidney transplant patients.	For the measurements of CSA to be used as an aid in the management of heart, liver and kidney transplant patients.
Sample Type	Whole Blood	Whole Blood
Technology	Affinity Particle Mediated Immunoassay	Fluorescence Polarization Immunoassay
Antibody	Mouse monoclonal	Mouse monoclonal
Assay Range	350 -2000ng/mL[a]	25 - 1500 ng/mL

a. The Dimension® CSAE Extended Range Cyclosporine Assay is intended as a high range assay to compliment the low range assay, the Dimension® CSA Cyclosporine Assay, which has an assay range of 25 – 500ng/mL.

J. Standard/Guidance Document Referenced

1. Guidance;

Class II Special Controls Guidance Document: Cyclosporine and Tacrolimus Assays; Guidance for Industry and FDA, Document issued on: September 16, 2002.

2. Standards;

GP22-A	Continuous Quality Improvement Essential Management Approaches
ISO 15223	Medical devices – Symbols to be used with medical device labeling and information to be supplied
EN 1441:1997	Medical Devices - Risk Management
ISO 14971-1	Medical devices: Risk management – Part1: Application of risk analysis
EP9-A2	Method Comparison and Bias Estimation Using Patient Samples
EP7-A	Interference Testing in Clinical Chemistry
EP5-A	Evaluation of Precision Performance of Clinical Chemistry Devices
CEN 13640	Stability testing of In-Vitro Diagnostic Devices

K. Test Principle:

The automated Dimension® CSAE method uses an immunoassay technique in which free and CSA-bound antibody-enzyme species are separated using magnetic particles. The assay is performed using a method specific Flex® reagent cartridge. The calibrators and controls for this assay are sold separately.

L . Performance Characteristics:

1. Reproducibility

Reproducibility testing was done in accordance with the CLSI/NCCLS Approved Guideline for Evaluation of Precision Performance of Clinical Chemistry Devices (EP5-A, Feb.1999). Specimens at each level were analyzed in duplicate, once a day, for 20 days. The within-run (repeatability) and total (within-lab) standard deviations were calculated by analysis of variance (ANOVA) method.

	Mean		Standard Deviation (%CV)	
Material	Units	[SI Units]	Repeatability	Within-lab
Whole Blood pool 1	368.0	[306.2]	12.21 [10.16] (3.32)	19.00 [15.81] (5.16)
Whole Blood pool 2	1123.3	[934.6]	30.65 [25.50] (2.73)	57.24 [47.62] (5.10)
Whole Blood pool3	1750.1	[1456.1]	46.72 [38.87] (2.64)	104.07 [86.59] (5.29)
More Control 1	488.7	[406.6]	13.99 [11.64] (2.86)	28.77 [23.94] (5.89)
More Control 2	866.1	[720.6]	18.61 [15.48] (2.15)	47.71 [39.69] (5.51)
More Control 3	1301.9	[1083.2]	34.41 [28.63] (2.64)	68.89 [57.32] (5.29)

More Diagnostics Cyclosporine Control is a product of More Diagnostics Inc., Los Osos, CA. 93402

2. Method Comparison

A total of 140 specimens were tested with the Dimension® CSAE assay, with the Abbott TDx® /TDx FLx® Cyclosporine Monoclonal Whole Blood Assay and by LC/MS technology. Linear regression was used to calculate a slope, intercept and correlation coefficient. The model equation for regression statistics is: Result of Dimension® system = (Slope x comparative method result) + Intercept.

Comparative Method	Slope	Intercept ng/mL[umol/L]	Correlation Coefficient	n
Abbott TDx®				
All	1.13	-67.2	0.980	140
Heart	0.996	2.52	0.982	35
Liver	1.11	-61.7	0.970	40
Kidney	1.09	-32.3	0.973	60
LCMS				
All	1.09	17.1	0.986	140
Heart	0.93	93.7	0.983	35
Liver	1.00	59.9	0.980	40
Kidney	1.10	15.2	0.990	60

TDx® is the registered trademark of Abbott Diagnostics, Abbott Park, IL 60064

3. Linearity

Standard solutions were prepared by sequential mixing to create a set of eight equally spaced sample pools starting with a high and low pool of known analyte concentration. Theoretical concentrations were computed for all intermediate pools based on the initial concentrations of the high and low pools. The analysis of cyclosporine on the Dimension® RxL by the Dimension® CSAE method shows a deviation from the estimated line of less than 15 ng/mL [12.5 nmol/L] with 95% confidence at the analytical concentration of 794.5 ng/mL [662.1 nmol/L]. The lower limit of the linearity claim is 350.0 ng/mL [291.7 nmol/L].

4. Interference Testing

Interference testing was performed according to the CLSI/NCCLS Protocol EP-7A. A summary of the substances that do not interfere with the Dimension® Cyclosporine methods when present in whole blood at the concentrations indicated. Inaccuracies (biases) due to these substances are less than 10% at a CSA level equivalent to 800 ng/mL [665.6 nmol/L] can be found in the package insert.

5. Analytical Specificity

Six major metabolites were evaluated for cross-reactivity in the presence of 500 ng/mL [416 nmol/L] cyclosporine. The percent cross-reactivity was calculated as follows:

$$\% \text{ cross reactivity} = \frac{\text{measured CSA} - \text{control CSA (500 ng/mL) [41.6 nmol/L]}}{\frac{100}{\text{metabolite added}}} \times$$

Cyclosporine Metabolite	**Metabolite Level Tested ng/mL [nmol/L]**	**Cross-Reactivity %**
AM1 (M17)	1000 [821]	4.7
AM1c (M18)	1000 [821]	2.1
AM1c9 (M26)	1000 [810]	3.9
AM4N (M21)	1000 [842]	3.1
AM9 (M1)	1000 [821]	2.4
AM19 (M8)	1000 [810]	3.0

6. Recovery

Known amounts of CSA were added to human whole blood samples with concentrations of 610.0, 1232.2, and 1861.8 ng/mL [507.5, 1025.2, 1861.8 nmol/L]. CSA concentrations on these samples were then measured and the calculated percent recovery ranged from 94.3% to 103.1% with a mean recovery of 101.0%.

$$\text{Percent Recovery} = \frac{\text{Value obtained - Baseline}}{\text{Amount Added}} \times 100$$

7. Functional Sensitivity

The functional sensitivity of the CSAE method was demonstrated to be less than 350ng/mL. The functional sensitivity is defined as the lowest concentration at which the intra-assay coefficient of variation is not greater than 20%.

Final: August 30, 2005

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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Ms. Andrea Tasker
Regulatory Affairs and Compliance Manager
Dade Behring, Inc.
Glascow Business Community
Bldg. 500 Mail Box 514
P.O. Box 6101
Newark, DE 19714-6101

Re: k052017

Trade/Device Name: Dimension® Cyclosporine Extended Range Assay (CSAE) Flex® reagent cartridge
Regulation Number: 21 CFR 862.1235
Regulation Name: Cyclosporine test system
Regulatory Class: Class II
Product Code: MKW
Dated: August 23, 2005
Received: August 23, 2005

Dear Ms. Tasker:

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);

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/industry/support/index.html.

Sincerely yours,

Carol C. Benson

Carol C. Benson, M.A.
Acting 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 Statement

510(k) Number (if known): K052017

Device Name:

Dimension® CSAE Cyclosporine Extended Range Flex® reagent cartridge

Indications for Use:

The CSAE Flex® reagent cartridge is an in vitro diagnostic test intended to quantitatively measure cyclosporine A (CSA) in human whole blood for the Dimension® clinical chemistry system. Measurements of CSA are used as an aid in the management of heart, liver and kidney transplant patients.

Andrea M. Tasker
Regulatory Affairs and Compliance Manager
June 29, 2005

Prescription Use X **AND/OR** **Over-the-counter Use** _____
(Per 21 CFR 801 Subpart D) **(21 CFR 801 Subpart C)**

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

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

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K052017