

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k073055

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Quantitative

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension® Enzymatic Creatinine (ECRE) Flex® Reagent Cartridge (DF270)

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JFY	Class II	21 CFR§ 862.1225 Creatinine test system	75 - Clinical Chemistry

H. Intended Use:

1. Intended use(s):

See Indications for Use below

2. Indication(s) for use:

The ECRE method is an *in vitro* diagnostic test for the quantitative measurement of creatinine in human serum, plasma and urine on the Dimension® clinical chemistry system. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis and as a calculation basis for other urine analytes.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Dimension® Clinical Chemistry System

I. Device Description:

The Dimension® ECRE Flex® reagent cartridge is a prepackaged *in-vitro* diagnostic test method that is specifically designed to be used on the Dade Behring Dimension® Clinical Chemistry System. The reagents contained in the Dimension® ECRE Flex® reagent cartridge are: Reagent 1 contains TAPS buffer, creatinase, sarcosine oxidase and HTIB; Reagent 2 contains TAPS buffer, creatininase, horseradish peroxidase, 4-aminophenazon and potassium hexacyanoferrate (II).

J. Substantial Equivalence Information:

Feature	Dimension® ECRE Flex® reagent cartridge	Roche Creatinine Plus Reagent (K003261)
Intended Use	The ECRE method is an <i>in vitro</i> diagnostic test for the quantitative measurement of creatinine in human serum, plasma, and urine on the Dimension® clinical chemistry system. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for other urine analytes.	Enzymatic <i>in vitro</i> assay for the direct quantitative determination of creatinine in human serum, plasma and urine using Roche clinical chemistry analyzers.
Sample Type	Plasma, serum, and urine.	Human serum, plasma and urine.
Measuring	0.03 -20.00 mg/dL	0.03 – 30 mg/dL

Feature	Dimension® ECRE Flex® reagent cartridge	Roche Creatinine Plus Reagent (K003261)
Range		
Sample Size	6 µL	6 µL
Measurement	Bichromatic end point	Bichromatic end point

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition (2004)

CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures, A Statistical Approach: Approved Guideline (2003)

CLSI EP7-A: Interference Testing in Clinical Chemistry; Approved Guideline (2002)

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (2004)

CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (2002)

L. Test Principle:

The Creatinine Assay is based on an enzymatic reaction. In TAPS buffer creatinine is hydrolyzed by creatininase to creatine, which is then hydrolyzed by creatinase to sarcosine. Sarcosine oxidase hydrolyzes sarcosine to glycine, formaldehyde and peroxide. During the reaction peroxide and a chromogen form a colored end product that is proportional to the amount of creatinine in the sample and is measured at 510 and 700 nm using a bichromatic end point.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility studies were conducted by testing two levels of a commercially available control, serum pool and a urine pool. The samples were run in duplicate, twice a day for twenty days using one lot and one instrument. The results are presented in the table below:

	Mean	Reproducibility		Within-Lab	
Serum	mg/dL	SD	CV%	SD	CV%
Serum pool 1	1.04	0.01	1.1	0.02	2.0
Serum pool 2	1.55	0.01	0.7	0.02	1.5
Control Level 1	.79	0.01	1.3	0.03	3.4
Control Level 2	5.80	0.03	0.5	0.05	0.9
Urine					
Urine pool 1	66.45	1.41	2.1	2.36	3.6
Urine pool 2	203.13	3.38	1.7	4.07	2.0
Control Level 1	73.14	0.91	1.2	1.82	2.5
Control Level 2	164.90	1.97	1.2	4.68	2.8

b. Linearity/assay reportable range:

The reportable range of the assay is 0.3 -20 mg/dL. The urine measuring range goes to 200 mg/dL due to the dilution 1:10 of the sample before it is analyzed. The range is based on linearity, detection limit and method comparison. Linearity across the assay range was confirmed for serum samples by inter diluting a sample spiked (high sample) with anhydrous creatinine with a sample having a low endogenous creatinine to create seven additional samples. The Chem I calibrator was used as the zero sample. A high urine sample was made by spiking it with anhydrous creatinine. Additional samples were made by diluting the high sample with deionized water to create six additional samples. Deionized water was used as the zero sample. Five determinations of each pool were tested and a linear regression analysis was performed by the method of least squares. The instrument generates a flag which states "Above Assay Range" or "Below Assay Range". In addition to this, automatic dilutions are performed by the instrument for results that fall outside the assay range. Automatic dilutions are defined in the method parameters and cannot be changed by an operator. The results are presented below:

Sample	Serum		Urine	
	Theor. ETOH mg/dL	Observed ETOH mg/dL	Theor. ETOH mg/dL	Observed ETOH mg/dL
1	0.00	-0.03	0.00	-0.21
2	0.89	0.97	1.02	.76
3	6.62	6.56	5.12	4.82
4	12.28	12.31	25.60	26.79
5	17.95	17.80	51.21	54.25
6	22.00	23.60	102.41	109.91
7	31.90	30.82	153.62	161.54
8	41.82	40.55	206.00	212.65
9	52.06	50.33		
10	65.00	62.91		
Slope	.9631		1.042	
intercept	.45		.32	
r	.999		.999	

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

This device does not include calibrators or controls. The sponsor recommends using calibrators by Dade Behring Inc. Dimension Chem I Calibrator, Catalog Number DC18B cleared k0611838.

d. *Detection limit:*

The Limit of Blank and Limit of Detection were determined by running a low sample (two different samples) and true blank sample for 4 days, 4 replicates/day, for each sample. The testing was split between two instruments and lots of reagents. The detection limit is 0.3 mg/dL Creatinine

e. *Analytical specificity:*

The Dimension ECRE assay was evaluated for interference according to CLSI EP7-A2. The following substances demonstrated no significant bias (defined as < 10 %).

Substance Tested	Substance concentration	Ethyl Alcohol mg/dL	Bias %
Hemoglobin (hemolysate)	300 mg/dL/ Hemoglobin	1.00	<10
Bilirubin (unconjugated)	23 mg/dL	1.00	<10
Bilirubin (conjugated)	20 mg/dL	1.00	<10

Lipemia (Intralipid)	3000 mg/dL	1.22	<10
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An extensive list of other compounds was evaluated for interference and found to have no significant interference or cross reactivity. A list of these compounds is present in the product labeling.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A split sample method comparison was conducted between the Dimension ECRE and Roche CREA Plus. The assays were performed following CLSI EP9-A2. The correlations are as follows:

Matrix	n	Slope	Intercept	r	Device range (mg/dL)	Predicate range (mg/dL)
Serum	123	1.03	-0.03	1.000	0.64-18.95	0.61-18.58
Urine	42	1.04	-2.29	0.994	14.4-172.5	14.1-163

b. Matrix comparison:

A serum / plasma comparison test was performed for the Dimension® ECRE Flex® assay. Thirty-three serum samples were compared to the following two anticoagulants Sodium and Lithium Heparin. The correlations are as follows:

Matrix	n	Slope	Intercept	r	Device range (mg/dL)
Na Heparin vs. Serum	33	1.03	-0.04	.999	0.5-17.5
Li Heparin vs. Serum	33	1.02	-0.05	0.999	0.5-17.9

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable

b. *Clinical specificity:*

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The creatinine reference range was obtained from the literature. Package insert states that each laboratory should establish its own expected ranges.

Serum/plasma:

Males	0.67-1.17 mg/dL, 59-104 μ mol/L
Females	0.51 -0.95 mg/dL, 45-84 μ mol/L
Combined	0.51-1.17 mg/dL, 45-104 μ mol/L

Random Urine:

Males	40-278 mg/dL, 3536-24575 μ mol/L
Females	29-226 mg/dL, 2564-19978 μ mol/L
Combined	29-278 mg/dL, 2564-24575 μ mol/L

24 Hour Urine Excretion

Males	0.87-2.41 g/day, 8-21 mmol/day
Females	0.67-1.50 g/day, 6-14 mmol/day

Mazzachi BC, Peake MJ, Ehrhardt V, Reference range and method comparison studies for enzymatic and Jaffe creatinine assays in plasma and serum an early morning urine, Clin Lab 2000; 46: 53-55.

Junge W, Wilke B, Haladi A, Klein G, Determination of reference intervals for serum creatinine, creatinine excretion and creatinine clearance with an enzymatic and modified Jaffe method, Clinica Chimica Acta 2004; 344; 137-148.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.