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

A. 510(k) Number:

k070383

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Enzymatic colorimetric, quantitative

E. Applicant:

Diagnostic Chemicals Limited

F. Proprietary and Established Names:

Enzymatic Creatinine Assay

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1225 - Creatinine Test System

2. Classification:

   Class II

3. Product code:

   JFY - enzymatic method, creatinine

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) for use:

   The Diagnostic Chemicals Limited Enzymatic Creatinine Assay is for the quantitative determination of creatinine in serum, plasma and urine. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes. This device is intended for professional use and in vitro diagnostic use only.

3. Special conditions for use statement(s):

   For professional use only

4. Special instrument requirements:

   Bayer Advia 1650 or a spectrophotometer or analyzer capable of accurately measuring absorbance at 545 nm and 37°C.

I. Device Description:

The Diagnostic Chemicals Limited Enzymatic Creatinine Assay is a two reagent system. Both reagents are supplied in liquid ready to use form and contain enzymes with stabilizers and/or buffers.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Roche Diagnostics Corp. Creatinine Plus

2. Predicate 510(k) number(s):

   k003261

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Form	Liquid, ready to use	Liquid, ready to use

Similarities		
Item	Device	Predicate
Sample	Serum, plasma, urine	Serum, plasma, urine
Test Method	Enzymatic colorimetry	Enzymatic colorimetry
Storage	2-8°C	2-8°C

Differences		
Item	Device	Predicate
Measuring range serum/plasma	0.04 – 30 mg/dL	0.03 – 30 mg/dL
Measuring range urine	0.03 – 175 mg/dL	0.3 – 400 mg/dL

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

CLSI Guidance EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods

CLSI Guidance EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach

CLSI Guidance EP9-A2: Method Comparison and Bias Estimation Using Patient Samples

L. Test Principle:

The enzyme creatinine amidohydrolase is used to convert creatinine to creatine. The enzymatic approach to the quantitation of creatine is to use the enzyme creatine amidinohydrolase, which yields sarcosine and urea, the former being measured with further enzyme-linked steps using sarcosine oxidase and peroxidase to produce a colored product.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

    a. *Precision/Reproducibility:*

    Total precision was established by assaying three serum controls and three urine controls in duplicate twice a day for 20 days. The results are summarized below.

EnzymaticCreatinine	N	Mean		Standard Deviation		Coefficient of Variation
		mg/dL	µmol/L	mg/dL	µmol/L	%
Serum 1	80	0.68	60.11	0.017	1.500	2.5 %
Serum 2	80	1.32	115.80	0.032	2.830	2.4 %
Serum 3	80	6.12	540.12	0.166	14.670	2.7 %
Urine 1	80	22.01	1945.68	0.323	28.55	1.5 %
Urine 2	80	44.66	3947.94	0.423	37.390	0.9 %
Urine 3	80	93.31	8248.60	1.269	112.180	1.4 %

Within run precision was established by assaying three serum controls and three urine controls 20 times in a single run. The results are summarized below.

EnzymaticCreatinine	N	Mean		Standard Deviation		Coefficient of Variation
		mg/dL	µmol/L	mg/dL	µmol/L	%
Serum 1	20	0.62	54.81	0.004	0.35	0.6 %
Serum 2	20	1.27	112.27	0.007	0.53	0.5 %
Serum 3	20	5.85	517.14	0.018	1.59	0.3 %
Urine 1	20	22.19	1961.60	0.049	4.15	0.2 %
Urine 2	20	45.12	3988.61	0.083	7.16	0.2 %
Urine 3	20	88.38	7812.79	0.221	19.54	0.2 %

b. *Linearity/assay reportable range:*

Serum linearity was evaluated by measuring 7 serum samples ranging in concentration from 0.00 to 45.39 mg/dL. All samples were run n=4. Linear regression analysis was performed resulting in a slope of 1.051 and a y-intercept of -0.192. The mean recovery of each sample was within ±8% of its assigned value. The reportable range for serum/plasma samples is from 0.04 to 30 mg/dL.

Urine linearity was evaluated by measuring 9 urine samples ranging in concentration from 0.01 to 206.78 mg/dL. All samples were run n=4. Linear regression analysis was performed resulting in a slope of 0.982 and a y-intercept of 2.274. The mean recovery of each sample was within ±5% of its assigned value. The reportable range for urine sample is from 0.03 to 175 mg/dL.

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

Performance testing was performed with an aqueous based commercially

available calibrator traceable to NIST SRM 914A.

d. *Detection limit:*

The lower limit of quantitation for both serum and urine was determined by assaying 40 replicates of multiple sample concentrations. This value was defined as the mean of the lowest sample concentration with a CV of 20% or lower. The lower limit of detection for serum was 0.03 mg/dL and for urine was 0.02 mg/dL.

e. *Analytical specificity:*

Interferences from icterus, lipemia, hemolysis and ascorbic acid were evaluated for this creatinine method on a Bayer ADVIA 1650 analyzer using a significance criterion of >10% variance from control. Interference data for serum and urine was provided. Plasma was expected to be similar to that of serum.

No significant lipemic interference was found at Intralipid levels from 0-1000 mg/dL (0-3000 mg/dL triglycerides) in a 0.75 mg/dL serum sample and a 31.7 mg/dL urine sample.

No significant hemoglobin intereference was found at hemoglobin levels from 0-1000 mg/dL in 0.79 mg/dL serum sample and a 71.7 mg/dL urine sample.

No significant ascorbic acid interference was found at ascorbic acid levels from 0-3000 μg/dL in a 0.76 mg/dL serum sample and a 137.4 mg/dL urine sample.

No significant icteric interference was found at conjugated bilirubin levels from 0-40 mg/dL in a 95.9 mg/dL urine sample.

No significant icteric interference was found at conjugated bilirubin levels from 0-40 mg/dL in a 1.08 mg/dL serum sample.

No significant icteric interference was found at unconjugated bilirubin levels from 0-16 mg/dL in a 0.75 mg/dL serum sample.

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Serum

A comparison was made between this method and a similar enzymatic method using 40 samples ranging from 0.7 to 31.2 mg/dL. The correlation coefficient was 1.0000. Linear regression analysis gave the following equation:

$$y = 1.033x - 0.13$$

<u>Urine</u>

A comparison was made between this method and a similar enzymatic method using 40 samples ranging from 13.5 to 141.7 mg/dL. The correlation coefficient was 0.9995. Linear regression analysis gave the following equation:

$$y = 1.041x + 1.06$$

b. *Matrix comparison:*

A comparison was made between plasma and serum using this 33 samples ranging from 0.61-27.04 mg/dL. The correlation coefficient was 0.9997. Linear regression analysis gave the following equation:

$$y = 1.018x - 0.008$$

3. <u>Clinical studies</u>:

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. <u>Clinical cut-off</u>:

Not applicable

5. <u>Expected values/Reference range</u>:

Serum/Plasma	Male:	$\leq$1.2 mg/dL
	Female:	$\leq$1.0 mg/dL
Urine 1st morning:	Male:	40-280 mg/dL
	Female:	30-230 mg/dL

Heil, W., Koberstein, R., Zawta, B. Reference Ranges for Adults and Children, Roche Diagnostics, Mannheim, 2002.

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.