

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

A. 510(k) Number:

k062105

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Quantitative, Enzymatic

E. Applicant:

Diazyme Laboratories

F. Proprietary and Established Names:

Diazyme Creatinine Liquid Reagents Assay and Diazyme Creatinine Control

G. Regulatory Information:

1. Regulation section:

21CFR §862.1225 Creatinine test system

21CFR §862.1660 Single Analyte Controls (Assayed and Unassayed)

2. Classification:

Class II (reagent) and Class I, reserved (controls)

3. Product code:

JFY, JJX

4. Panel:

75 (Chemistry)

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

Diazyme Creatinine Liquid Reagents Assay, in conjunction with Diazyme Creatinine Calibrator, is intended for the quantitative determination of creatinine in serum 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. For *in vitro* diagnostic use only.

Diazyme Creatinine Control is an assayed QC material for use in quantitative *in vitro* diagnostic determination of creatinine in human serum and urine. It is intended as a reference sample for monitoring the Diazyme Creatinine Liquid Reagents Assay for gross systematic errors. For *in vitro* diagnostic use only.

3. Special conditions for use statement(s):

For Prescription use only

4. Special instrument requirements:

Performance of the assay was established on the Hitachi 917 analyzer.

I. Device Description:

The Diazyme Creatinine assay has two reagents, R1 and R2, and one calibrator included in the kit. R1 contains 60 mL of the following ingredients: Creatinase and Sarcosine Oxidase. R2 contains 20 mL of the following ingredients: Creatininase, 4-AA, and peroxidase. The calibrator contains 2 mL of 5 mg/dL creatinine in 0.9% saline. All reagents and calibrator come in liquid form, ready to use.

The Diazyme Creatinine control is an assayed QC material containing approximately 2.5 mg/dL of creatinine in 0.9% saline. It comes in a 2mL vial in a ready to use liquid form.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Creatinine Plus assay
Dade Behring Dimension Vista Protein Control

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

k003261, k063206

3. Comparison with predicate:

Similarities and differences between the Diazyme Creatinine and the predicate device

Item	Diazyme Creatinine assay (New device)	Roche Creatinine Plus assay (Predicate device)
Indications for use	The Diazyme Creatinine assay is intended to measure the creatinine levels in serum 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.	Direct quantitative determination of creatinine in human serum, plasma, and urine using Roche clinical chemistry analyzers.
Methodology	Enzymatic colorimetric	Colorimetric
Reagent storage temperature	2-8°C	2-8°C
Sample types	Serum and Urine	Serum/Plasma, and urine
Sensitivity/Detection limits	Serum and urine: 0.14 mg/dL	Serum: 0.03 mg/dL Urine: 0.3 mg/dL
Measuring range	Serum: 0.14- 13.51 mg/dL Urine: 0.14- 141 mg/dL	Serum: 0.03-30 mg/dL Urine: 0.3-400 mg/dL
Expected range	Serum: Male:0.67–1.17 mg/dL (59-104µmol/L) Female: 0.51–0.95 mg/dL (45-84µmol/L) *Urine: Male: 40–278mg/dL (3540-24600 µmol/L) Female: 29–226 mg/dL (2550-20000 µmol/L) * First morning urine	Serum: Male:0.67–1.17 mg/dL(59-104µmol/L) Female: 0.51–0.95 mg/dL(45-84µmol/L) *Urine: Male: 40–278mg/dL (3540-24600 µmol/L) Female: 29–226 mg/dL (2550-20000 µmol/L) * First morning urine

Item	Diazyme Creatinine Control	Dade Dimension Vista Protein Control (Predicate device)
Form	Liquid form	Liquid form
Analyte specific constituent	Creatinine	C3, C4, Homocysteine, IGA, IGG, IGM and prealbumin constituents
Traceability	Traceable to purified Creatinine- NIST SRM 914a standard	Traceable to purified S-adenosyl homocysteine standard
Levels	One level	3 levels (L, M, H)

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

1. CLSI Guideline, EP5-A Evaluation of Precision Performance of Clinical Chemistry Device; Approved Guideline
2. CLSI Guideline, EP6-A Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline
3. CLSI Guideline, EP7-A Interference Testing in Clinical Chemistry; Approved Guideline
4. CLSI Guideline, EP9-A2 Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline, Second Edition.

L. Test Principle:

Creatinine in serum or urine sample is hydrolyzed to creatine, which is then hydrolyzed to sarcosine and urea. Sarcosine is oxidized to formaldehyde, glycine, and hydrogen peroxide. Finally, a peroxidase-catalyzed reaction produces a dye that can be measured by the instrument. The intensity of the dye, when read at 546 nm, is proportional to the amount of creatinine in the patient sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

i.) Precision studies for serum samples were evaluated according to CLSI EP5-A guideline. For within-run precision and total precision studies, four serum specimens were tested on the Hitachi 917 twice daily, in duplicates, over 20 days. The results are presented in the tables below:

Serum Within-Run Precision:

	Level 1	Level 2	Level 3	Level 4
N	80	80	80	80
Mean (mg/dL)	0.74	1.38	4.04	10.21
SD (mg/dL)	0.015	0.015	0.029	0.015
CV (%)	2.1	1.1	0.7	0.1

Serum Total Precision:

	Level 1	Level 2	Level 3	Level 4
N	80	80	80	80
Mean (mg/dL)	0.74	1.38	4.04	10.21
SD (mg/dL)	0.022	0.0259	0.058	0.14
CV (%)	3.0	1.9	1.4	1.4

ii.) Precision studies for urine samples were evaluated with a modified CLSI EP10 protocol. For within-run precision, 21 replicates of commercial urine controls were tested on the Hitachi 917. For total precision, 2 runs of each commercial urine control were performed consecutively for 5 days. The samples were diluted ten-fold with 0.9% saline and tested for Creatinine values. The results are presented in the tables below:

Urine Within-Run Precision:

	Level 1	Level 2	Level 3
N	21	21	21
Mean (mg/dL)	29.09	87.1	196.7
SD (mg/dL)	0.1	0.27	0.90
CV (%)	0.36	0.31	0.46

Urine Total Precision:

	Level 1	Level 2	Level 3
N	20	20	20
Mean (mg/dL)	29.86	87.7	195
SD (mg/dL)	0.79	0.67	1.19
CV (%)	2.64	0.76	0.60

b. Linearity/assay reportable range:

i.) Serum samples: Eleven levels of serum sample pools were prepared by mixing a low sample and a high sample and were then tested on the Hitachi 917 analyzer. Sample pools range from 0.12 to 14 mg/dL. Results showed the measured value and expected value differed by $\leq 10\%$ error. The studies supported the sponsor claimed linearity range of 0.14 to 13.51 mg/dL for serum samples.

ii.) Urine samples: The same procedure as for serum was performed to evaluate assay linearity with the urine sample matrix. Sample pools ranged from 0 to 148 mg/dL. In addition, a urine linearity study with samples that encompass the lower end of the linear range of the assay was performed (sample pools range from 0.14 to 15.3 mg/dL). The studies support the sponsor's claimed linearity range of 0.14 to 141 mg/dL for urine samples.

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

Traceability

The Diazyme Creatinine Control is traceable to NIST SRM 914a Creatinine standard reference material. The value was assigned by performing multiple

determinations using the Hitachi 917 analyzer and the Diazyme Creatinine Liquid Reagents Assay.

Stability

The long term (shelf life) stability of the Diazyme Creatinine Liquid Reagents Assay and Diazyme Creatinine Control were tested on a Hitachi 917 analyzer using a real time study extending at least one month beyond the selected expiration date. Testing was done at intervals of 0, 3, 6, 9 months and is still ongoing. The Diazyme Creatinine Liquid Reagents and controls are stored at refrigerated (2-8°C) and the expiration is at least 12 months.

The opened vial (in use) stability of the Diazyme Creatinine Liquid Reagents Assay and Diazyme Creatinine Control were tested on a Hitachi 917 analyzer with different intervals using accelerated studies. The real time on-board stability studies were done at day 0, 5, 10, 15, 20, 25, 30, and 35. The on-board stability of the reagents is at least 30 days. The control is stable for at least 1 month when stored at 2-8°C.

d. Detection limit:

The lower limit of the assay range was determined by measuring a Limit of Blank (LOB). The LOB of the Diazyme Creatinine assay was determined by assaying the Diazyme Creatinine zero calibrator in 12 replicates on the Hitachi 917 instrument. The LOB was defined as mean + 3SD. The sponsor claimed that the lower limit of the assay is 0.14 mg/dL.

e. Analytical specificity:

Studies were performed to assess common or known substances that could interfere with the method. The interfering substances were evaluated in serum and urine pools that had different creatinine concentrations. The sponsor defined interference as samples for which the analyte recovery varies from the base recovery by more than $\pm 10\%$. The summary of the results of the recovery studies is provided in the table below:

	Serum	Urine
Interference substances	Highest Level Tested with No Interference	Highest Level Tested with No Interference
Triglycerides	1000 mg/dL	1000 mg/dL
Ascorbic Acid	10 mmol/L	10 mmol/L
Bilirubin	40 mg/dL	40 mg/dL
Bilirubin conjugated	30 mg/dL	40 mg/dL
Hemoglobin	500 mg/dL	1000 mg/dL

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

i.) 55 serum samples were used for the method comparison study. In order to include the full measuring range in the study, 5 serum samples were diluted or spiked with prepared creatinine stock solutions. All samples were tested with the Diazyme Creatinine Liquid reagents assay and the Roche Creatinine Plus assay (predicate device) on the Hitachi 917 analyzer. Samples tested range from 0.2 mg/dL to 13.51 mg/dL. The regression equation was $Y = 0.9467X + 0.0643$ and $r^2 = 0.9981$. (Y= Diazyme Creatinine and X= Roche Creatinine Plus assay)

ii.) 42 urine samples were used for the method comparison study. In order to include the full measuring range in the study, 5 urine samples were diluted or spiked with prepared creatinine stock solutions. All samples were tested with the Diazyme Creatinine Liquid reagents assay and the Roche Creatinine Plus assay (predicate device) on the Hitachi 917 analyzer. Samples tested range from 0.14 mg/dL to 141 mg/dL. The regression equation was $Y = 1.005 X - 0.2979$ and $r^2 = 0.9969$. (Y= Diazyme Creatinine and X= Roche Creatinine Plus assay)

b. Matrix comparison:

See method comparison above.

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):

None

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The following literature reference values are provided:

Serum: Male: 0.67–1.17 mg/dL (59-104 μ mol/L) Female: 0.51–0.95 mg/dL(45-84 μ mol/L)

*Urine: Male: 40–278mg/dL (3540-24600 μ mol/L) Female: 29–226 mg/dL (2550-20000 μ mol/L)

* First morning urine

Mazzachi, BC, Peake MJ, Ehrhardt V. Reference Range and Method Comparison Studies for Enzymatic and Jaffe' Creatinine Assays in Plasma and Serum and Early Morning Urine. Clin Lab 2000; 46; 53-55

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.