

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

k061412

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Quantitative, enzymatic colorimetric

E. Applicant:

Thermo Electron

F. Proprietary and Established Names:

Enzymatic Creatinine Reagent

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1225

2. Classification:

II

3. Product code:

JFY, Enzymatic Method Creatinine

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for use.

2. Indication(s) for use:

The Thermo Electron Enzymatic Creatinine Reagent is intended for *in vitro* quantitative determinations of creatinine in human serum, plasma or urine. Creatinine determinations are used in the diagnosis and treatment of renal impairment, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

3. Special conditions for use statement(s):

Prescription use

4. Special instrument requirements:

Automated clinical chemistry analyzers. Performance characteristics were established on the Roche Hitachi 911 analyzer.

I. Device Description:

The Thermo Electron Enzymatic Creatinine test is a two reagent system for use on automated analyzers. Both reagents contain enzymes with stabilizers and/or buffers. The composition of the two ready-to-use liquid reagents is as follows:

Reagent 1: buffer, creatinine amidinohydrolase, sarcosine oxidase, catalase, ascorbate oxidase, TOPS (N-ethyl-sulfopropyl-m-toluidine).

Reagent 2: buffer, creatinine amidohydrolase, peroxidase and 4-aminoantipyrine.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Diagnostics Creatinine Plus

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

k003261

3. Comparison with predicate:

Similarities and Differences		
Item	New device	Predicate
Method	Enzymatic, colorimetric	Same
Storage	Store at 2-8°C	Same
Measuring Range	0.2 – 30 mg/dL for serum & plasma 2.14 - 150 mg/dL for urine	0.03-30 mg/dL for serum/plasma and 0.3 – 600 mg/dL for urine
Sample type	Serum, plasma, urine	Same

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

CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices - EP05-A2

CLSI - Method Comparison and Bias Estimation Using Patient Samples - EP09-A2

CLSI - Interference Testing in Clinical Chemistry - EP07-A2

L. Test Principle:

The creatinine present in samples is acted upon by creatinine amidohydrolase, creatinine amidinohydrolase, sarcosine oxidase, and peroxidase. In the final reaction sequence, the formation of quinoneimine dye product results in an increase in absorbance at 550 nm which is directly proportional to the creatinine concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Imprecision was evaluated using CLSI Document EP5-A2 as a guideline.

Samples: 3 serum controls and 2 urine controls

Analyzer: Roche Hitachi 911

Reagent lot: one

Calibrator lot: one

Operator: one

Number of runs per day: 2

Number of replicates: 2

Number of days: 20

The results are summarized below:

Sample	Mean mg/dL	Number	Total		Within-run	
			SD	%CV	SD	%CV
Serum 1	0.9	80	0.03	3.7	0.2	2.5
Serum 2	1.6	80	0.04	3.3	0.03	2.8
Serum 3	5.3	80	0.07	1.3	0.04	3.3
Urine 1	67.7	80	1.74	2.6	0.76	1.1
Urine 2	145.3	80	3.3	2.7	0.94	0.6

b. Linearity/assay reportable range:

The claimed measuring range for serum/plasma is 0.2 to 30 mg/dL and for urine is 2.14 to 150 mg/dL.

Linearity studies were performed using CLSI EP6-A as a guideline. Samples were created by diluting a creatinine standard to concentrations within the claimed range. The concentrations tested in the study were 0, 20, 40, 60, 80, 100, 120, 140, 160, 180, and 200 mg/dL creatinine. The sample with a concentration of 200 mg/dL was excluded from the calculations. A slope close to 1 and correlation coefficient of 0.99 resulted. The results demonstrate that with this assay creatinine is linear across the claimed measuring ranges.

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

The calibrator used to calibrate the device for the performance evaluations in this 510(k) was cleared under k022108.

The package insert recommends that an aqueous standard or serum based calibrator with an assigned value traceable to a primary standard (e.g., NIST or IRMM) be used with this reagent.

The reagent is stable until the expiration date when stored at 2 – 8°C.

d. Detection limit:

A blank sample of serum, a serum matrix solution, and 10 serum samples containing low levels of creatinine were assayed on a Roche Hitachi 911 clinical chemistry analyzer. Ten (10) replicate assays were performed on each sample including the blank. This was repeated on two consecutive days. The lowest sample dilution which consistently met with a coefficient of variation percentage (%CV) below 20% for serum samples was 0.2 mg/dL. The lowest sample dilution which consistently met with a coefficient of variation percentage (%CV) below 20% for urine samples was 2.14 mg/dL. The results demonstrate that with this assay the lower end of the measuring range for creatinine is 0.2 mg/dL in serum or plasma and 2.14 mg/dL to 150 mg/dL in urine.

e. Analytical specificity:

Interference studies were performed using CLSI EP7-A as a guideline.

Interfering compounds were evaluated by spiking various concentrations of the interferents into a creatinine sample and comparing the results of the interferent spiked samples with an unspiked creatinine reference sample. Non-interference was defined as a recovery of 90% - 110% of the unspiked reference sample. The highest concentration of each compound that did not interfere is shown below.

<u>Interfering Compound</u>	<u>Maximum Concentration Tested</u>
Hemoglobin	1000 mg/dL
Bilirubin	60 mg/dL
Conjugated Bilirubin	33 mg/dL

<u>Interfering Compound</u>	<u>Maximum Concentration Tested</u>
Lipemia	1490 mg/dL
Ascorbic Acid	82 mg/dL
<u>Creatine</u>	10 mg/dL
B-hydroxybuturate	126 mg/dL
Cephatholin	100 mg/dL
Cefotaxime	100 mg/dL
Acetoacetate	108 mg/dL
Proline	70 mg/dL

f. Assay cut-off:
Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

The method comparison was performed on the Roche Hitachi 911 using CLSI EP9-A2 as a guideline.

Serum

The sponsor compared 107 serum samples ranging from 0.5 to 28.5 mg/dL creatinine to the predicate device. Linear regression produced a slope of 0.951, a y-intercept of -0.1, and a correlation coefficient of 0.999.

Urine

The sponsor compared 107 urine samples ranging from 9.8 to 136.2 mg/dL creatinine to the predicate device. Linear regression produced a slope of 0.992, a y-intercept of -0.4, and a correlation coefficient of 0.999.

b. Matrix comparison:

A method comparison was performed using the Thermo Electron Enzymatic Creatinine method with 64 matched serum-EDTA plasma samples ranging in concentration from 0.49 to 28.48 mg/dL creatinine (in serum). Linear regression produced a slope of 0.953, a y-intercept of -0.022, and a correlation coefficient of 1.00

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 sponsor cites the following reference ranges for serum/plasma from Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Fourth Edition 2006 56:2251-2318:

Adult Male: 0.62 - 1.10 mg/dL

Adult Female: 0.45 – 0.75 mg/dL

The sponsor cites the following reference ranges for urine from Kaplan LA, Pesce AJ, Clinical Chemistry Theory, Analysis and Correlation, CV Mosby Company 1984, 59:1251-1252:

Adult Male: 40 - 278 mg/dL

Adult Female: 29 - 226 mg/dL

Q. Proposed Labeling:

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

R. Conclusion:

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