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

A. 510(k) Number:

k161527

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Quantitative, enzymatic colorimetric method

E. Applicant:

Teco Diagnostics, Inc.

F. Proprietary and Established Names:

Teco Creatinine Enzymatic Reagent Kit

G. Regulatory Information:

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

H. Intended Use:

1. Intended Use(s):

   See Indications for Use below

2. Indication(s) for Use:

   Creatinine Enzymatic Reagent Kit is a device which is intended for measurement of creatinine level in human serum, in vitro diagnostic use only. Test results may provide information regarding the status of kidney function and the diagnosis of renal diseases, and also serve as a component of several calculations for determination or estimation of creatinine clearance or glomerular filtration rate (GFR).

3. Special conditions for use statement(s):

   In vitro diagnostic test for prescription use only

4. Special instrument requirements:

   TC-MATRIX instrument

I. Device Description:

Creatinine Enzymatic Reagent Kit contains two reagent – Creatinine R1 and Creatinine R2 reagents. Reagents are provided as ready to use liquids.

Creatinine R1 Reagent contains 25mM Good's buffer (pH 7.4), 25KU/L Creatine amidinohydrolase, 7KU/L Sarcosine oxidase, 4KU/L Ascorbate oxidase and 140mg/L ESPMT (3- (N-Ethyl-3-methylanilino) propanesulfonic acid sodium salt).

Creatinine R2 Reagent contains 100mM Good's buffer (pH 7.3), 250KU/L Creatinine amidohydrolase, 5KU/L Peroxidase and 600mg/L 4-Aminoantipyrine.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Stanbio Creatinine LiquiColor test system

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

   k050283

3. Comparison with predicate:

Items	Teco Creatinine Enzymatic Reagent Kit (Candidate device)	Stanbio Creatinine LiquiColor test system, k050283 (Predicate Device)
Intended Use	For the quantitative determination of creatinine.	Same
Specimen Type	Serum	Serum and urine
Test Methodology	Enzymatic	Same
Wavelength	Primary: 546nm Secondary: 670 nm	546 nm
Measuring Range	0.37 to 5.06 mg/dL	0.04 to 5.1 mg/dL for serum
Storage Conditions	2 to 8 °C	Same

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

- CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.
- CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline- Second Edition
- CLSI EP09-A3- Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Third Edition

- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition.
- CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline-Second Edition
- EP28-A3C, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline-Third Edition

L. Test Principle:

Teco Diagnostic's creatinine enzymatic method employs a two reagent system which eliminates interferences by endogenous creatine and ascorbic acid. Step wise enzymatic reactions are shown below:

- Creatinine + H_2O, in the presence of Creatinine amidohydrolase, produce Creatine
- Creatine + H_2O, in the presence of Creatine amidinohydrolase, produce Sarcosine + Urea
- Sarcosine + H_2O +O_2, in the presence of Sarcosine oxidase, produce Glycine + HCHO +H_2O_2
- $2H_2O_2$ + 4-aminoantipyrine + ESPMT*, in the presence of Peroxidase, produce Quinoneimine Dye + $4H_2O$

*ESPMT: 3-(N-Ethyl-3-methylanilino) propanesulfonic acid sodium salt

Hydrogen peroxide generated from creatinine reacts with 4- aminoantipyrine and ESPMT in the presence of peroxidase to yield a quinoneimine dye. The change in absorbance at 546 nm is proportional to the creatinine concentration in sample. The rate of formation of color is proportional to the creatinine concentration in the sample.

M. Performance Characteristics (if/when applicable):

The following data were collected on the TC-MATRIX instrument.

1. Analytical performance:

   a. Precision/Reproducibility:

   A precision study was performed following a modification to the recommendations in the CLSI EP5-A3 guideline. The precision study was conducted over 20 non-consecutive days with two reagent lots using three serum samples at approximately 0.9 mg/dL, 1.5 mg/dL and 3.0 mg/dL creatinine. The serum samples were prepared by mixing natural patients' serum sample pools. The testing included two runs per testing day, with at least two hours separation between runs, three replicates per sample per run using one instrument. A total of 240 replicates per sample were generated. The calibrator used was the Teco Chemistry Calibrator. The representative results from one lot are shown below. The within-laboratory imprecision estimate includes imprecision from within-run, between run and between reagent lots.

Sample	Mean (mg/dL)	Repeatability		Within – Laboratory	
		SD	%CV	SD	%CV
Patient pool 1	0.89	0.008353	0.93	0.01761	1.98
Patient pool 2	1.52	0.01323	0.87	0.03316	2.18
Patient pool 3	3.09	0.02800	0.90	0.03361	1.08

b. Linearity/assay reportable range:

A linearity study was performed following the recommendations in the CLSI EP6-A guideline. A set of eleven equally spaced creatinine level samples were prepared by mixing a low serum sample with a high serum sample. The expected creatinine concentration levels used in the study are 0.37, 0.94, 1.50, 2.06, 2.71, 3.31, 3.83, 4.38, 4.90, 5.49, and 6.12 mg/dL. Each sample was tested in duplicate. The results showed that the deviation from linearity did not exceed 5%. The results of the regression analysis are summarized below:

$Y = 0.9992x + 0.0007$, $r^2 = 0.9983$

The study result supports the linearity of the Teco Creatinine Enzymatic Reagent Kit assay from 0.37mg/dL to 5.06 mg/dL of creatinine.

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

Reagent stability – Both reagents are stable until expiration dates found on their labels when stored at 2-8 °C. Once opened the creatinine reagents are stable for 60 days when stored at 2-8 °C.

Traceability and stability of control and calibration materials:

Calibration Material – The sponsor recommends in the labeling using the Teco Chemistry Calibrator. This calibrator is traceable to NIST reference material SRM 967.

Quality Control Materials – The sponsor recommends in the labeling using quality control samples (two levels – low and high) at least once a day and after each calibration and every time a new bottle of reagent is used. The values on control materials are traceable to the reference material, NIST SRM 967.

d. Detection limit:

A limit of blank study was performed following the recommendations in the CLSI Guideline EP17-A2. The study was conducted using four blank samples and two lots of reagents. These samples were measured in replicates of five over three days (15 replicates per sample) with a total of 60 measurements per reagent lot. The data were assessed using the nonparametric analysis option described in the guideline. The claim was based on the lot with the higher estimate.

A limit of detection study was performed using four diluted serum samples prepared by diluting serum pool 100x, 50x, 33x and 25x with saline. The samples were tested

using two reagent lots. Each sample was tested 15 times over three days for a total of 60 measurements per reagent lot. The data were assessed using the parametric analysis option described in the guideline. The claim was based on the lot with the higher estimate.

A limit of quantitation study was performed using four low concentration serum samples prepared using serum pools and two reagent lots. Each sample was assayed 15 times over three days per reagent lot. The %CV and SD were calculated, and LoQ was defined as the concentration with a %CV of less than 20%. The claim was based on the lot with the higher estimate.

The LoB, LoD and LoQ are claimed as 0.00 mg/dL, 0.01 mg/dL and 0.10 mg/dL, respectively.

The claimed measuring range is 0.37 - 5.06 mg/dL for serum creatinine with the candidate device.

e. *Analytical specificity:*

An interference study was performed by evaluating potential interfering substances spiked into serum containing creatinine at either 1.5 mg/dL or 5.0 mg/dL. The recommendations in the CLSI EP7A2 guideline were followed for the interference testing. Each interferent was tested at two levels except for acetaminophen which was tested at only one concentration of 1.963 mg/dL. Each test and control sample was tested in triplicate. The sponsor defines interference as bias exceeding 10%. The following substances had no significant interference (less than 10% interference) when tested on the Teco Creatinine Enzymatic Reagent Kit at the concentrations listed below.

Substance	Concentration of Substance
Acetaminophen	20 mg/dL
Bilirubin (unconj)	20 mg/dL
Bilirubin (conjugated)	16.7 mg/dL
Hemoglobin	500 mg/dL
Triglycerides	2500 mg/dL
Ascorbic acid	20 mg/dL
Creatine	6.0 mg/dL
Glucose	1000 mg/dL
Nitrofurantoin	400 µg/dL
Uric acid	25 mg/dL
Dopamine	90 µg/dL
Methyl dopa	100 µg/dL
L-Dopa	60 µg/dL
Calcium dobesilate	1.0 mg/dL

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A comparison study was performed using 97 unaltered serum samples from patients and one altered serum sample (diluted patient serum sample). The specimens were run on the predicate and the candidate device in singlicate. The analyte concentration ranged from 0.45 mg/dL to 5.06 mg/dL. The linear regression analysis result is shown below:

$Y = 1.004x + 0.0379$, $R^2 = 0.9986$

b. Matrix comparison:

Not applicable. Serum is the only matrix claimed for use with the candidate device.

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 reference ranges provided in the labeling for normal males and females are derived from the literature (Larsen K. Clin. Chem. Acta 41: 209 (1972)) and were verified using the candidate device following the recommendations in the CLSI EP28-A3C guideline.

Males, 0.9 – 1.5 mg/dL

Females, 0.7 – 1.4 mg/dL

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.