

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

A. 510(k) Number:

k033058

B. Analyte:

Creatinine

C. Type of Test:

Quantitative, Alkaline picrate, colorimetric

D. Applicant:

Diamond Diagnostics / Mission Diagnostics

E. Proprietary and Established Names:

Creatinine Reagent Kit for Beckman Synchron CX[®] & CX[®] Delta Systems

F. Regulatory Information:

1. Regulation section:
21 CFR § 862.1225, Creatinine test system
2. Classification:
Class II
3. Product Code:
CGX, Alkaline picrate, colorimetry, creatinine
4. Panel:
Clinical Chemistry (75)

G. Intended Use:

1. Indication(s) for use:

Creatinine Reagent Kit for Beckman Synchron CX[®] & CX[®] Delta Systems is for the quantitative determination of creatinine in serum, plasma, or urine on the Beckman Synchron CX[®] & CX[®] Delta Systems.

Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring dialysis, and as a calculation basis for measuring other urine analytes.

2. Special condition for use statement(s):

These reagents are intended to serve as a direct replacement to like-named products manufactured by the Original Equipment Manufacturer (OEM).

3. Special instrument requirements:

Beckman Synchron CX[®] & CX[®] Delta analyzers

H. Device Description:

The device consists of two liquid reagents, the Alkaline buffer reagent and the Picric Acid reagent, that are mixed together to form a working reagent. The Alkaline buffer reagent contains 0.188 mol/L sodium hydroxide, sodium borate, sodium phosphate, surfactant, and preservative. The Picric Acid reagent contains 0.05 mol/L picric acid.

I. Substantial Equivalence Information:

1. Predicate device name(s):
Beckman PN 443340
2. Predicate K number(s):
K942676, K864236
3. Comparison with predicate:

This reagent is intended to be able to be used in place of the OEM reagent. The device and its predicate have the same intended use, composition, packaging quantities and dimensions, storage conditions, and shelf life.

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

NCCLS Guidance document EP5A, Evaluation of Precision Performance of Clinical Chemistry Devices

NCCLS Guidance document EP9A2, Method Comparison and Bias Estimation Using Patient Samples

K. Test Principle:

A sample containing creatinine is mixed with the alkaline picric reagent (the working reagent) and the following reaction occurs:

Creatinine + picric acid → creatinine-picrate complex (red)

Absorbance readings are taken at both 520 nm and 560 nm at 25.6 seconds after sample addition. The differential absorbance is directly proportional to the concentration of creatinine in the sample.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Within run precision was measured by assaying the serum and urine controls in triplicate 6 times to lead to N = 18. Total precision included samples run in triplicate

2 to 5 runs per day for 4 days (N = 57 serum, 51 urine). Results are summarized below:

Sample	Mean mg/dL	Mean within Run SD N=3	Total Run SD N=18	Total Mean mg/dL	Total SD – all runs	%CV	N
DCtrol 1	2.0	0.1	0.1	2.1	0.1	5.2	57
DCtrol 2	6.5	0.1	0.2	6.9	0.4	6.1	54
Urine 1 Cntrl	83.5	0.4	0.6	89.5	5.5	6.2	51
Urine 2 Cntrl	213.6	1.1	2.0	220.3	7.9	3.6	51

Additional data were submitted as follows. Data was collected per NCCLS EP5-A. Samples were assayed in duplicates twice a day for 20 days.

	N	Mean mg/dL	Within-run SD	Within-run %CV	Total SD	Total %CV
Serum Control 1	80	1.6	0.07	4.4	0.14	8.4
Serum Control 2	80	6.9	0.10	1.5	0.62	8.9
Urine Control 1	80	89	0.7	0.8	10.9	12.3
Urine Control 2	80	217	2.2	1.0	9.5	4.4

b. Linearity/assay reportable range:

The following useable range was specified by the sponsor:

0.6 – 25 mg/dL for serum or plasma
10 – 400 ml/dL in urine

Users are instructed to dilute samples that exceed the high end of the analytic range with deionized water or saline and reanalyze.

Pooled serum or urine samples were spiked and linearly diluted to cover the reportable range to evaluate % recovery. Expected values were calculated, and the pools were tested using Mission reagents and predicate reagents. Results are summarized below.

	Reagent	Range of % recovery	Mean Recovery
Serum 0.2 - .04 mg/dL	Mission	85.7 – 105.3	98.5 %
	Predicate	93.4 – 114.3	104.2 %
Urine 10 – 400 mg/dL	Mission	87 – 102.1	96 %
	Predicate	83 – 102.9	96.2 %

c. Traceability (controls, calibrators, or method):

Not applicable in this submission. The OEM recommends proper control materials as part of the system.

d. Detection limit:

Diluted serum samples (low concentration samples) were tested in 4 times per run over 5 runs. Results are summarized below.

Mean (mg/dL)	SD	% CV
0.57	0.07	12.9
0.18	0.04	25.4
0.08	0.04	51.3
0.04	0.05	136.9
0.11	0.11	94.9

The sponsor claims a functional sensitivity of 0.6 mg/dL (the lowest sample tested with a CV less than 20%).

e. Analytical specificity:

Serum, plasma, and urine are the samples of choice. Whole blood samples are not recommended. The sponsor refers the user to literature references for other interferences caused by drugs and diseases. Lipemic samples $>+3$ should be ultracentrifuged and the analysis performed on the supernatant fraction.

The following anticoagulants or chemical additives are compatible with this method:

Anticoagulants	Acceptable level
Sodium Citrate*	3.5 mg/mL
EDTA	4.0 mg/mL
Ammonium Heparin	45 U/mL
Lithium Heparin	45 U/mL
Sodium Heparin	45 U/mL
Lithium Iodoacetate	1.5 mg/mL

* specimens collected with liquid sodium citrate will exhibit a decrease in value due to dilution.

f. Assay cut-off:
Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Serum and Urine controls were assayed six times in triplicate using both the Mission and predicate reagents (N = 18):

	Mission Reagent				Predicate Reagent			
	Mean (mg/dL)	Within run SD	Total SD	% CV	Mean (mg/dL)	Within run SD	Total SD	% CV
DControl 1	2.0	0.1	0.1	5.0	2.4	0.0	0.1	3.3
DControl 2	6.5	0.1	0.2	3.1	7.1	0.1	0.1	1.8
Urine 1	83.5	1.1	2.0	0.9	87.9	0.9	1.1	1.3
Urine 2	214	1.1	2.0	0.9	216	1.3	2.6	1.2

Serum comparison using spiked serum samples of the Mission reagent and the predicate reagent yielded the following correlation:

$$\text{Range} = 0.9 - 10 \text{ mg/dL}, y = 1.01x - 0.01, R^2 = 0.998$$

Additional data were submitted. Tests were performed per NCCLS EP9-A2 and analyzed by least squares regression.

Seventy-one (71) serum samples were spiked or diluted and tested in triplicate with the Mission reagents and the predicate reagents.

Range = 0.2 to 11.8 mg/dL

Mission = 1.000 (Predicate) + 0.003

$r^2 = 0.998$

95% CI at 0.6 mg/dL – 0.55 to 0.65 mg/dL

95% CI at 1.2 mg/dL – 1.14 to 1.26 mg/dL

Forty-five (45) urine samples were spiked or diluted and tested in triplicate with the Mission reagents and the predicate reagents.

Range = 10 to 400 mg/dL

Mission = 0.988 (Predicate) + 0.634

$r^2 = 0.999$

95% CI at 10 mg/dL – 8.9 to 12.0 mg/dL

95% CI at 200 mg/dL – 195 to 201 mg/dL

b. Matrix comparison:

Not applicable. Performance data was submitted for all matrices.

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:

Serum or Plasma – 0.6 to 1.2 mg/dL

Urine (timed) – 600 to 2000 mg/24hrs

The sponsor states that these values are intended as a reference, and that no adjustments have been made for age, sex, or dietary differences. Each laboratory should establish a reference range based on their patient population.

M. Conclusion:

I recommend that the Mission Diagnostic Creatinine Reagent Kit for Beckman Synchron CX[®] & CX[®] Delta Systems is substantially equivalent to the legally marketed predicate device.