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

A. 510(k) Number:
k033056

B. Analyte:
Blood urea nitrogen (BUN)

C. Type of Test:
Quantitative, electrochemical

D. Applicant:
Diamond Diagnostics / Mission Diagnostics

E. Proprietary and Established Names:
BUN Reagent for Beckman Synchron CX® & CX® Delta Systems

F. Regulatory Information:
1. Regulation section:
   21 CFR § 862.1770
2. Classification:
   Class II
3. Product Code:
   CDS, Electrode, ion specific, urea nitrogen
4. Panel:
   Clinical Chemistry (75)

G. Intended Use:

1. Indication(s) for use:

The BUN Reagent for Beckman Synchron CX® & CX® Delta Systems is intended for in vitro diagnostic use for the quantitative determination of blood urea nitrogen (BUN) in serum, plasma, and urine on Beckman Synchron CX® & CX® Delta Analyzers.

BUN measurements are useful in the diagnosis and treatment of certain renal and metabolic diseases.

2. Special condition for use statement(s):

This reagent is intended to be used as a direct replacement for like-named products from the original equipment manufacturer (OEM).

3. Special instrument Requirements:

Beckman Synchron CX$^®$ or CX$^®$ Delta Systems

H. Device Description:
This device is a liquid reagent containing 120 U/mL Jack Bean Urease, salts, buffer, and preservative.

I. Substantial Equivalence Information:
1. Predicate device name(s):
   Beckman PN 443350
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:
Urea nitrogen concentration is determined by enzymatic conductivity rate method employing a Conductivity Electrode on the instrument. The conductivity changes as urea (a non-ionic substance) is changed to ammonium carbonate (which is ionic) by the urease reagent. The timed rate of increase of solution conductivity is directly proportional to the concentration of urea 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 = 36 serum), or one day (N = 18 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
DControl 1	14	0.6	0.6	14	0.8	5.9	36
DControl 2	46	0.9	0.9	46	1.5	3.3	36
Urine 1 Cntrl	130	1.2	2.1	130	2.1	1.6	18
Urine 2 Cntrl	223	2.0	2.3	223	2.3	1.0	18

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	13	0.7	5.5	0.7	5.8
Serum Control 2	80	48	1.3	2.7	3.1	6.5
Urine Control 1	80	58	1.2	2.1	1.9	3.3
Urine Control 2	80	63	1.9	2.9	2.6	4.0

> b. *Linearity/assay reportable range:*

The following useable range was specified by the sponsor:

3 – 150 mg/dL for serum, plasma, or urine (only CX Delta for urine).

The CX® Delta Systems Over Range Detection and Correction (ORDAC) function
will accommodate samples with BUN concentrations between 150 - 300 mg/dL.
Users are instructed to dilute these samples that exceed the high end of the analytic
range with saline and reanalyze. (an integrated function of the instrument, K942676,
K864236)

Percent recovery was evaluated on linearly diluted samples. Pooled serum or urine
samples were spiked to values near the upper end of the reportable range and diluted
to cover the entire range. Expected values were calculated and the pools were
measured on the mission reagents and the predicate reagents. Results are summarized
below.

	Reagent	Range of % recovery	Mean Recovery
Serum	Mission	82 – 106	97 %
7.5 – 81 mg/dL	Predicate	94 - 111	105 %
Urine	Mission	85.7 – 103.8	97.6 %
10.5 – 100 mg/dL	Predicate	93.3 - 110	101.2 %

> 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) were tested in triplicate over 13 runs. Results are summarized below.

Mean (mg/dL)	SD	% CV
14.1	0.60	4.3
5.1	0.22	4.4
3.1	0.22	7.3
1.0	0.56	56.2
0.5	0.71	141.4

The sponsor claims a functional sensitivity of 3 mg/dL (as the lowest concentration 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.

Fluoride may inhibit urease activity or increase the reaction conductivity which will suppress the BUN value by 25% when fluoride levels exceed 5 mg/dL of Sodium Fluoride.

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 samples in predetermined ranges were measured in triplicate using

	Range (mg/dL)	N	Mission Reagents			Predicate Reagents		
			Mean (mg/dL)	Within run SD	% CV	Mean (mg/dL)	Within run SD	% CV
Serum	0 - 40	6	22	0.7	3.4	25	0.3	1.2
Serum	0 - 150	9	44	1.8	4.0	51	0.4	0.7
Serum	25 - 300	11	143	1.0	0.7	171	1.6	0.9
Urine	0 - 150	5	77	0.6	0.7	85	0.7	0.8
Urine	0 - 300	11	149	1.2	0.8	168	1.0	0.6

mission reagents and predicate reagents:

Comparisons of spiked serum or urine samples or controls using the Mission reagent and the predicate reagent yielded the following correlations:

Serum:
- Range = 4 – 200 mg/dL, $y = 0.93x – 0.68$, $R^2 = 0.997$
- Range = 4 – 150 mg/dL, $y = 0.90x – 0.32$, $R^2 = 0.997$
- Range = 4 – 100 mg/dL, $y = 0.88x – 0.67$, $R^2 = 0.997$

Urine:
- Range = 7 – 300 mg/dL, $y = 0.87x – 2.89$, $R^2 = 0.992$

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

Sixty-six (66) serum samples were spiked or diluted and tested in triplicate with the Mission reagents and the predicate reagents.
    Range = 4 to 87 mg/dL
    Mission = 0.0892 (Predicate) + 1.22
    $r^2 = 0.997$
    95% CI at 8 mg/dL – 7.7 to 8.9 mg/dL
    95% CI at 20 mg/dL – 18.2 to 19.8 mg/dL

Forty (40) urine samples were spiked or diluted and tested in triplicate with the Mission reagents and the predicate reagents.
    Range = 4 to 100 mg/dL
    Mission = 0.923 (Predicate) + 1.054
    $r^2 = 0.996$
    95% CI at 12 mg/dL – 11.1 to 13.1 mg/dL
    95% CI at 90 mg/dL – 81.7 to 86.5 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 – 6 to 20 mg/dL
Urine – 7 to 16 g/24hrs

The sponsor states that BUN measurements are used in the diagnosis and treatment of certain renal and metabolic diseases. BUN is regulated by the metabolism of proteins and the renal excretion of urea. An increased level of BUN (> 100 mg/dL) is called Azotemia and is associated with such conditions as diminished glomerular filtration, tubular necrosis, nephritis, and high protein diet. A decrease in BUN is associated with pregnancy, low protein intake, starvation, or severe liver disease and in acute tubular necrosis.

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 BUN Reagent for Beckman Synchron CX® & CX® Delta Systems is substantially equivalent to the legally marketed predicate device.