510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K203771

B Applicant

Abbott Ireland Diagnostics Division

C Proprietary and Established Names

Urea Nitrogen2

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CDQ	Class II	21 CFR 862.1770 - Urea Nitrogen Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Urea Nitrogen

C Type of Test:

Quantitative photometric assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Urea Nitrogen2 assay is used for the quantitation of Urea Nitrogen in human serum, plasma, or urine on the ARCHITECT c System.

The Urea Nitrogen2 assay is to be used as an aid in the diagnosis and treatment of certain renal and metabolic diseases.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Architect c8000 System

IV Device/System Characteristics:

A Device Description:

The Urea Nitrogen2 assay is comprised of a reagent kit that is run on the ARCHITECT c8000 System. The kit has the following reagents:

Reagent 1 (R1)
Active ingredient: β-NADH (1.915 g/L). Preservative: sodium azide.

Reagent 2 (R2)
Active ingredients: α-ketoglutaric acid (13.149 g/L), GLDH (60.000 KU/L), and urease (10.000 KU/L). Preservative: sodium azide.

B Principle of Operation:

The Urea Nitrogen2 assay is a modification of a totally enzymatic procedure as a kinetic assay in which the initial rate of the reaction is linear for a limited period of time. Urea in the sample is hydrolyzed by urease to ammonia and carbon dioxide. The second reaction, catalyzed by glutamate dehydrogenase (GLDH), converts ammonia and α-ketoglutarate to glutamate and water with the concurrent oxidation of reduced nicotinamide adenine dinucleotide (NADH) to nicotinamide adenine dinucleotide (NAD). Two moles of NADH are oxidized for each mole of urea present. The initial rate of decrease in absorbance at 340 nm is proportional to the urea concentration in the sample.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Urea

B Predicate 510(k) Number(s):

K981918

C Comparison with Predicate(s):

Device & Predicate Device(s):	K203771	K981918
Device Trade Name	Urea Nitrogen2	Urea
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Urea Nitrogen2 assay is used for the quantitation of urea nitrogen in human serum, plasma, or urine on the ARCHITECT c System.	Same
Analyte	Urea	Same
Sample Type	Human serum, plasma, urine	Same
Methodology	Urease	Same
Principle of Procedure	Enzymatic	Same
Traceability	NIST SRM 912b	Same
Tube Types	Serum: - Serum tubes - Serum separator tubes Plasma: - Lithium heparin tubes - Lithium heparin separator tubes - Sodium heparin tubes	Same
General Device Characteristic Differences		
Absorbance reading	340 nm	340/380 nm
Calibration	Gravimetrically	Differential Scanning Calorimetry

Assay Range	Serum/Plasma: Analytical Measuring Interval: 2– 125 mg/dL Extended Measuring Interval: 125 – 625 mg/dL Urine: Analytical Measuring Interval: 16 – 1991 mg/dL	Serum/Plasma: Urea Nitrogen is linear from 2 to 125 mg/dL. Urea Nitrogen urine is linear from 2 to 1991 mg/dL.
Lower Limits of Measurement	Serum/Plasma: Limit of Blank: 1 mg/dL Limit of Detection: 2 mg/dL Limit of Quantitation: 2 mg/dL Urine: Limit of Blank: 6 mg/dL Limit of Detection: 11 mg/dL Limit of Quantitation: 16 mg/dL	Serum/Plasma: Limit of Detection: 0.7 mg/dL Limit of Quantitation: 1.4 mg/dL Urine: Limit of Detection: 15.0 mg/dL Limit of Quantitation: 40.0 mg/dL

VI Standards/Guidance Documents Referenced:

- CLSI - EP05-A3: Evaluation of precision of Qualitative Measurement Procedures; Approved Guideline – Third Edition.
- CLSI – EP07: Interference Testing in Clinical Chemistry; Approved Guidance -Third Edition.
- CLSI – EP17-A2: Evaluation of detection Capability for Clinical Laboratory Measurement procedures; Approved Guidance -Second Edition.
- CLSI – EP34: Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking- First Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Testing was performed according to the CLSI EP5-A3 guideline, on 2 levels of control, 3 contrived human serum and 3 human contrived urine panels (A,B,C). Testing was conducted using 3 lots of the Urea Nitrogen2 reagent, 3 lots of Calibrator, 1 lot of commercially available controls, and 3 ARCHITECT c8000 instruments. The samples were tested in 2 replicates, 2 times per day, for 20 days, for a total of 80 measurements per sample per lot. The performance from a representative combination (1 reagent lot, 1 instrument) along with the Within-Laboratory SD and %CV ranges across all lot/instrument combinations is shown for serum and urine samples in the following tables.

Serum:

Sample	n	Mean (g/dL)	Within-Run (Repeatability)		Within-Laboratory	
			SD	%CV	SD (Range)	%CV (Range[b])
Control Level 1	80	15	0.3	2.1	0.4 (0.2 – 0.4)	2.4 (1.6 – 2.4)
Control Level 2	80	49	0.5	1.1	0.8 (0.8 – 0.9)	1.7 (1.6 – 1.7)
Panel A	80	4	0.2	4.7	0.2 (0.0 – 0.2)	4.7 (0.0 – 4.7)
Panel B	80	22	0.3	1.1	0.5 (0.3 – 0.6)	2.1 (1.4 – 2.7)
Panel C	80	102	0.8	0.8	1.9 (1.2 – 2.5)	1.8 (1.2 – 2.5)

Urine:

Sample	n	Mean (g/dL)	Within-Run (Repeatability)		Within-Laboratory[a]	
			SD	%CV	SD (Range)	%CV (Range[b])
Control Level 1	80	447	3.7	0.8	7.1 (7.1– 11.7)	1.6 (1.6 – 2.6)
Control Level 2	80	729	5.2	0.7	11.4 (11.2– 15.4)	1.6 (1.6 – 2.1)
Panel A	80	55	2.2	4.1	2.7 (2.7-5.6)	5.0 (5.0 – 10.3)
Panel B	80	715	6.2	0.9	10.2 (10.2-15.1)	1.4 (1.4– 2.1)
Panel C	80	1605	12.6	0.8	22.6 (22.6-27.8)	1.4 (1.4 – 1.8)

[a] Includes within-run, between-run, and between-day variability.
[b] Minimum and maximum SD or %CV across all reagent lot and instrument combinations

2. Linearity:

Linearity studies were conducted by using serum and urine samples. Twelve levels of dilutions spanning the measuring range were prepared by mixing different proportions of samples with high and low level Urea Nitrogen analyte concentrations. Samples were analyzed on one Architect c 8000 instrument in duplicate. The mean result for each sample comprised the observed result and was compared to the expected result. The data was analyzed using linear regression ; the best-fitting model was quadratic.

The results of the regression analysis are shown below and support the claimed analytical measuring interval of the device:

Analyte	Matrix	Slope	Intercept	R^2	Range Conc. Tested (mg/dL)	Claimed analytical measuring interval (mg/dL)
Urea Nitrogen	Serum	1.0352	0	0.996	0-128	2-125
	Urine	1.0058	3	1.000	2-2373	16-1991

Sample Dilution Study:

To support the claimed extended measuring interval (EMI) for serum samples, five human serum samples were prepared to target concentration values of 150, 214, 278, 342 and 405 mg/dL. Samples were tested using the automated and manual dilution labeling instructions on the ARCHITECT c8000 System with one reagent lot for a total of 30 replicates (2 instruments x 3 runs/instrument x 5 replicates/run). The % dilution recovery values for serum ranged from 99.7% to 101.5% for the auto-diluted samples and from 101.6% to 103.5% for the manually diluted samples, when compared to expected values. The total % CV ranged from 1.1% to 1.7% for auto-diluted samples and 0.8% to 1.7% for manually diluted samples. The study results support that serum samples with concentrations above 125 mg/dL may be diluted 1:5 either manually or on-board the analyzer to obtain results up to 625 mg/dL.

Automated or manual sample dilutions have not been evaluated for the Urea Nitrogen2 assay urine application.

3. Analytical Specificity/Interference:

Interference studies were performed based on guidance from the CLSI document EP07 3rd ed. Specimens consisted of human serum and urine representing low and high concentrations of the analyte, with and without the substance tested for interference. Each sample was divided into 2 aliquots: one aliquot for the test sample and one aliquot for the reference sample and tested in 10 replicates on one Architect c8000 analyzer with one reagent lot. Serum samples were tested at urea nitrogen concentrations of approximately 10 and 30 mg/dL, and urine samples were tested at urea nitrogen concentrations of 700 and 1500 mg/dL. The sponsor stated that interference was considered to be non-significant if the difference between the samples with and without interferent was less or equal to ± 10%. The following tables list the highest concentration of each substance at which no significant interference was found.

Serum:

Substance	Highest concentration tested at which no interference was observed
Endogenous	

Substance	Highest concentration tested at which no interference was observed
Conjugated Bilirubin	60 mg/dL
Unconjugated Bilirubin	60 mg/dL
Hemoglobin	2000 mg/dL
Triglycerides	1500 mg/dL
Total Protein	10 g/dL
Exogenous	
3-methyl-(triazen-1-yl)imidazole-4-carboxamide (MTIC)	0.6 mg/L
4-methylamino-antipyrine	3.3 g/dL
5-amino-4-imidazolecarboxamide (AIC)	3 g/L
Acetaminophen	160 mg/L
Acetylcysteine	150 mg/L
Acetylsalicylic acid	30 mg/L
Ampicillin-Na	80 mg/L
Ascorbic acid	60 mg/L
Biotin	4250 ng/mL
Ca-dobesilate	60 mg/L
Cefoxitin	6287 mg/L
Cyclosporine	2 mg/L
Dipyrone (metamizole)	45 mg/dL
Doxycycline	20 mg/L
Ibuprofen	220 mg/L
Levodopa	8 mg/L
Methyldopa	25 mg/L
Metronidazole	130 mg/L
Phenylbutazone	330 mg/L
Rifampicin	50 mg/L
Sodium Heparin	4 U/mL
Sulfa pyridine	300 mg/L
Sulfasalazine	300 mg/L
Temozolomide	20 mg/L
Theophylline	60 mg/L

The sponsor included the following limitations in the product labeling to identify interference with cefoxitin and total protein at the concentrations below:

Potentially Interfering Substance	Interferent Level	Analyte Level	% Interference (95% CI)
Cefoxitin	6600 mg/L	10 mg/dL	10% (6%, 14%)

Potentially Interfering Substance	Interferent Level	Analyte Level	%Interference (95% CI)
Total Protein	11 g/dL	10 mg/dL	11% (9%, 14%)

Urine:

Substance	Highest concentration tested at which no significant interference was observed
Endogenous	
Ascorbate	200 mg/dL
Glucose	1000 mg/dL
Protein	50 mg/dL
Exogenous	
Acetaminophen	160 mg/L
Acetic Acid (8.5N)	6.25 mL/dL
Acetylcysteine	15 mg/dL
Boric Acid	250 mg/dL
Hydrochloric Acid (6N)	2.5 mL/dL
Nitric Acid (6N)	5.0 mL/dL
Sodium Carbonate	1.25 g/dL
Sodium Fluoride	400 mg/dL
Sodium Oxalate	60 mg/dL
Biotin	4250 ng/mL
Ibuprofen	22 mg/dL

4. Assay Reportable Range:
   Based on the limit of quantitation (LoQ), precision, accuracy, and linearity, the ranges over which results can be reported are provided below according to the definitions from CLSI EP34, 1st ed.

Serum/Plasma Analytical Measuring Interval (AMI)	2-125 mg/dL
Serum/Plasma Extended Measuring Interval (EMI)	125-625 mg/dL
Urine Analytical Measuring Interval (AMI)	16-1991 mg/dL

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Traceability: The Urea Nitrogen2 assay is traceable to NIST SRM 912b.
   (NIST SRM: National Institute of Standards & Technology Standard Reference Material)

6. Detection Limit:
   The limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) studies were performed in accordance with CLSI EP17-A2.

Limit of Blank (LoB):
The LoB was determined by testing zero-analyte serum and urine samples, 10 replicates, 3 lots of reagent on 2 instruments over three days for a total of 60 measurements per lot. The 95th percentile of the zero-analyte sample concentrations was calculated. Using the parametric approach, LoB was derived from the 95^{th} percentile of a normal distribution from $n \geq 60$ replicates of zero-analyte samples.

Limit of Detection (LoD):
The LoD was determined by testing 12 low analyte samples and 12 low analyte urine samples, in 10 replicates per day using 3 lots of reagent on 2 instruments for three days for a total of 60 measurements per lot. The data was analyzed to calculate the LoD using a parametric analysis. The LoD represents the lowest concentration at which the analyte can be detected with 95% probability based on $n \geq 60$ replicates of low-analyte level samples.

Limit of Quantification (LoQ):
The LoQ was determined by testing five samples in replicates of 10 using 3 lots of reagent on 2 instruments over three days for a total of 60 measurements. The LoQ was considered acceptable if it was ≤ 3 mg/dL for the serum/plasma application. The sponsor defined the LoQ as the lowest analyte concentration where the %CV was ≤ 20%.

The detection limit results are summarized as follows:

	Serum	**Urine**
LoB	1 mg/dL	6 mg/dL
LoD	2 mg/dL	11 mg/dL
LoQ	2 mg/dL	16 mg/dL
Analytical Measuring Interval	2- 125 mg/dL	16-1991 mg/dL

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was conducted by testing 124 serum samples and 121 urine samples (n=121/124) on the candidate and predicate devices. Two of the serum samples and 4 of the urine samples were contrived. For the candidate device, samples were tested internally using 3 lots of reagents and 1 lot each of calibrator and controls across 2 ARCHITECT c8000 instruments. For the predicate device, samples were tested internally using 1 lot each of reagents, calibrator, and controls across 2 ARCHITECT c8000 instruments. Each sample was tested in a minimum of 2 replicates using both methods and testing occurred over a minimum of 3 calendar days.

A Passing-Bablok evaluation was performed by comparing the first replicate result from the candidate device versus the mean result from the predicate device.

The results are summarized below:

Urea Nitrogen2 vs Urea on the ARCHITECT c8000 System						
Sample type	**n**	**Units**	**Correlation Coefficient**	**Intercept**	**Slope**	**Concentration Range tested (predicate device)**
Serum	124	mg/dL	1.00	0.74	1.02	4-123
Urine	121	mg/dL	1.00	8.95	1.03	41-1754

2. Matrix Comparison:

A matrix comparison study was performed to evaluate the suitability of specific blood collection tube types for use with the Urea Nitrogen2 assay. Donor matched specimens were drawn into tubes of below listed anticoagulant. A total of 64 samples were tested using 1 lot of the Urea Nitrogen2 reagent, 1 lot of the Consolidated Chemistry Calibrator, 1 lot of commercially available controls, and 1 instrument. The first replica result of the test tube type was used for comparison to the mean of the 3 replicas for the control tube type (serum). The results are summarized as follows, and support the claimed use of lithium heparin plasma, lithium heparin (separator tube) plasma, serum (separator tube), and sodium heparin plasma with the Urea Nitrogen2 assay:

The results are shown below:

Collection Tube	N	Min	Max	r	Intercept (95% CI)	Slope (95% CI)
Plasma (Lithium heparin)	64	7	100	1.00	0.00 (0.00, 0.00)	1.00 (1.00, 1.00)
Plasma (Sodium heparin)	64	7	100	1.00	0.28 (0.00, 0.48)	0.98 (0.96, 1.00)
Plasma (Lithium heparin, separator tube)	64	7	100	1.00	0.00 (0.00, 0.14)	1.00 (0.99, 1.00)
Serum (separator tube)	64	7	100	1.00	0.00 (0.00, 0.00)	1.00 (1.00, 1.00)

The study results support the sponsor's claim that serum separator tube (serum) and Lithium heparin (plasma), Lithium heparin separator (plasma), and Sodium heparin (plasma) are acceptable sample types to be used with this assay.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

The following reference ranges, cited from the scientific literature, were included in the labeling.

Serum/Plasma:

Age	**Range, mg/dL**
Pediatrics	
0 - <14 days	2.8-23.0
15 days - <1 year	3.4-16.8
1 - <10 years	9.0-22.1
10 - <19 years, female	7.3-19.0
10 - <19 years, male	7.3-21.0
Adults	6-20
Adults >60 years	8-23

Urine 24 hour reference range: 12-20 g/day

Pediatric Source: Colantonio DA, Kyriakopoulou L, Chan MK, et al. Closing the gaps in pediatric laboratory reference intervals: a CALIPER database of 40 biochemical markers in a healthy and multiethnic population of children. Clin Chem 2012;58:854-868.

Adult source for serum and urine : Rifai N, Horvath AR, Wittwer C, editors. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. St. Louis, MO: Elsevier; 2018:499.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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