SYNCHRON CX®3 DELTA System
Chemistry Information Sheet

UREA
Urea

REF 443350

For *In Vitro* Diagnostic Use

ANNUAL REVIEW

Reviewed by:	Date	Reviewed by:	Date

PRINCIPLE

INTENDED USE

BUN reagent, in conjunction with the SYNCHRON CX®3 DELTA System and SYNCHRON CX® Calibrators 1, 2 and 3, is intended for the quantitative determination of urea nitrogen in human serum, plasma or urine.

CLINICAL SIGNIFICANCE

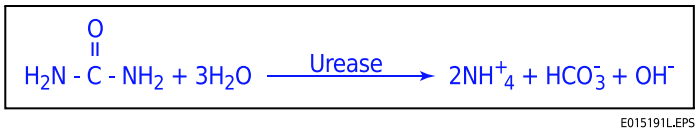
Urea nitrogen measurements are used in the diagnosis and treatment of certain renal and metabolic diseases.

METHODOLOGY

The SYNCHRON CX®3 DELTA System determines urea concentration by means of the Beckman Coulter developed enzymatic conductivity rate method.

A precise volume of sample (10 microliters) is injected into a reaction cup containing a urease solution. The ratio used is one part sample to 100 parts reagent. The reaction converts the non ionic species (urea) to one which is ionic (ammonium carbonate). During the reaction, the timed rate of increase of solution conductivity is directly proportional to the concentration of urea present in the reaction cup.[1,2,3]

CHEMICAL REACTION SCHEME



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SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.[4] Freshly drawn serum, plasma or properly collected urine are the preferred specimens. Acceptable anticoagulants are listed in the PROCEDURAL NOTES section of this chemistry information sheet. Whole blood is not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum or plasma be physically separated from contact with cells within two hours from the time of collection.[5]
2. Separated serum or plasma should not remain at room temperature longer than 8 hours. If assays are not completed within 8 hours, serum or plasma should be stored at +2°C to +8°C. If assays are not completed within 48 hours, or the separated sample is to be stored beyond 48 hours, samples should be frozen at -15°C to -20°C. Frozen samples should be thawed only once. Analyte deterioration may occur in samples that are repeatedly frozen and thawed.[5]
3. It is recommended that urine assays be performed within 2 hours of collection. For timed specimens, the collection container is to be kept in the refrigerator or on ice during the timed period. If a special preservative is required, it should be added to the container before urine collection begins.[6]

Additional specimen storage and stability conditions as designated by this laboratory:

SAMPLE PREPARATION

Urine samples require a 1:10 dilution with saline or ISE Electrolyte Reference reagent prior to analysis.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet for information on unacceptable specimens.

Criteria for sample rejection as designated by this laboratory:

PATIENT PREPARATION

Special instructions for patient preparation as designated by this laboratory:

SPECIMEN HANDLING

Special instructions for specimen handling as designated by this laboratory:

REAGENTS

CONTENTS

Each kit contains the following items:

One BUN Reagent Bottle (500 mL)

VOLUMES PER TEST

Sample Volume	10 µL
ORDAC Sample Volume	5 µL
Total Reagent Volume	1.00 mL
Component Volume	
Urease	0.22 mL
Wash Solution	0.88 mL

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

Jack Bean Urease	120 U/mL

Also non-reactive chemicals necessary for optimal system performance.

⚠ CAUTION

Avoid skin contact with reagent. Use water to wash reagent from skin.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

SYNCHRON CX Wash Solution
SYNCHRON CX® Calibrators 1, 2 and 3
At least two levels of control material. Do not use controls containing diethylamine HCl on Ca ISE configured systems.
Saline

REAGENT PREPARATION

Prior to use, allow the BUN Reagent to equilibrate to room temperature. A +25°C water bath may be used to warm reagent. The Wash Solution, packaged separately, requires reconstitution. Follow directions included in package insert. Allow 24 hours for the reconstituted Wash Solution to outgas prior to use.

ACCEPTABLE REAGENT PERFORMANCE

The acceptability of a reagent is determined by successful calibration and by ensuring that quality control results are within your facility's acceptance criteria.

REAGENT STORAGE AND STABILITY

BUN Reagent stored unopened at +2° C to +8° C is stable until the expiration date indicated on each bottle. BUN Reagent is stable for 30 days when stored at room temperature or until the expiration date, if sooner. The reconstituted Wash Solution is stable for 30 days or until the expiration date, if sooner.

Reagent frozen in transit will lose urease activity and may fail to calibrate. If frozen reagent calibrates, it will not have claimed on-instrument or unopened bottle stability. Frozen reagent should be discarded.

Reagent storage location:

CALIBRATION

CALIBRATOR REQUIRED

SYNCHRON CX® Calibrators 1, 2 and 3

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

1. Unopened calibrators should be stored at +2°C to +8°C until the expiration date printed on the calibrator bottle. Once opened, the calibrators are stable at room temperature for 30 days.
2. Repetitive refrigeration of the aqueous calibrators may facilitate crystal formation. Once removed from refrigerated storage, these calibrators should remain at room temperature.

Calibrator storage location:

CALIBRATION INFORMATION

1. The system must have a valid calibration in memory before controls or patient samples can be run.
2. Under typical operating conditions the UREA assay must be calibrated every 24 hours or with each new bottle of BUN reagent or Wash Solution and also with certain parts replacements or maintenance procedures, as defined in the *Maintenance, Diagnostics and Troubleshooting* manual.
3. For detailed calibration instructions, refer to the SYNCHRON CX3 Delta *Operating Instructions* manual.

4. The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will print out with error codes and the system will alert the operator of the failure. An explanation of these error codes can be found in the *Maintenance, Diagnostics and Troubleshooting* manual.

TRACEABILITY

For Traceability information refer to the Calibrator instructions for use.

QUALITY CONTROL

At least two levels of control material, normal and abnormal, should be analyzed daily. In addition, these controls should be run with each new calibration, with each new bottle of reagent, and after specific maintenance or troubleshooting procedures as detailed in the *Maintenance, Diagnostics and Troubleshooting* manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on work load and work flow.

The following controls should be prepared and used in accordance with the package inserts. Discrepant quality control results should be evaluated by your facility.

Table 1.0 Quality Control Material

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

1. If necessary, load the reagent onto the system as directed in Section 6 of the SYNCHRON CX3 Delta *Operating Instructions* manual.
2. After reagent load is completed, calibration is required. Refer to Section 6 of the SYNCHRON CX3 Delta *Operating Instructions* manual for details of the calibration procedure.
3. Program samples and controls for analysis as directed in Section 6 of the SYNCHRON CX3 Delta *Operating Instructions* manual.
4. After loading samples and controls onto the system, follow the protocols for system operation as directed in Section 6 of the SYNCHRON CX3 Delta *Operating Instructions* manual.

CALCULATIONS

The system performs calculations internally, including ORDAC, to produce the final reported result. SYNCHRON CX3 DELTA Systems will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming. For information on timed urine calculations, refer to Appendix Timed Urine Results in the Synchron CX3 Delta *Operating Instructions* manual.

REPORTING RESULTS

REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The reference intervals listed below were taken from literature.[7,8]

Table 2.0 Reference Range

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Literature	Serum or Plasma	15 – 39 mg/dL	2.5 – 6.4 mmol/L
	Urine (timed)	15 – 34 g/24 hrs	0.25 – 0.57 mol/24 hrs

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Laboratory			

Refer to References (9,10,11) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

LIMITATIONS

1. If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method:

   Table 3.0 Acceptable Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	AVERAGE PLASMA-SERUM BIAS (mmol/L)
Ammonium Heparin	29 Units/mL	NSI[a]
EDTA	3.0 mg/mL	NSI
Lithium Heparin	29 Units/mL	NSI
Sodium Heparin	29 Units/mL	NSI

   a NSI = No Significant Interference (within ±1.1 mmol/L or 6%).

2. The following anticoagulants were found to be incompatible with this method:

Table 4.0 Incompatible Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	PLASMA-SERUM BIAS (mmol/L)[a]
Potassium Oxalate/Sodium Fluoride	4.0 / 5.0 mg/mL	- 2.5
Sodium Citrate	6.6 mg/mL	- 2.1

a Bias is based on worst case instead of average. Plus (+) or minus (-) signs in this column signify positive or negative bias.

INTERFERENCES

1. Common chemical substances were tested for possible interference with the SYNCHRON CX3 DELTA urea nitrogen method. Substances which were tested include endogenous metabolites, antibiotics, stimulants, depressants, barbiturates, hypnotics, anticoagulants and preservatives. Those materials which demonstrated any clinically significant interferences are listed below:

Table 5.0 Interferences - Serum/Plasma

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT[a]
n-Acetylcysteine	n-Acetylcysteine	40 mmol/L	≤+1.8 mmol/L
Ampicillin	D-α-aminobenzylpenicillin sodium salt	1000 mg/dL	NSI[b]
		5000 mg/dL	≤+2.1 mmol/L
Arginine	L-Arginine	10 mg/dL	≤+1.8 mmol/L
Histidine	L-α-amino-β-imidazolepropionic acid	1 mg/dL	NSI
		10 mg/dL	≤+1.2 mmol/L
α-Ketoglutarate	α-Ketoglutaric acid	10 mg/dL	NSI
Sodium Fluoride	Sodium fluoride	4 mg/dL	≤-2.4 mmol/L
Hemoglobin	RBC hemolysate	500 mg/dL	NSI
Lipemia	Intralipid[c]	1000 mg/dL	NSI
Bilirubin	Bilirubin	30 mg/dL	NSI

a Plus (+) or minus (-) signs in this column signify positive or negative interference.
b NSI = No Significant Interference (within ±1.1 mmol/L or 6%).
c Intralipid is a registered trademark of KabiVitrum, Inc., Clayton, NC 27250.

Table 6.0 Interferences - Urine

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT[a]
n-Acetylcysteine	n-Acetylcysteine	60 mmol/L	NSI[b]
Ampicillin	Ampicillin sodium salt	5 g/dL	NSI
		10 g/dL	≤-13 mmol/L
Arginine	L-Arginine	20 mg/dL	NSI
Histidine	L-α-amino-β-imidazolepropionic acid	20 mg/dL	NSI

Table 6.0 Interferences - Urine, Continued

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT[a]
α-Ketoglutarate	α-Ketoglutarate	20 mg/dL	NSI
Sodium Fluoride	Sodium fluoride	10 mg/dL	NSI

a Plus (+) or minus (-) signs in this column signify positive or negative interference.
b NSI = No Significant Interference (within ± 2.0 mmol/L or 10%)

2. Lipemic samples >3+ should be ultra-centrifuged and the analysis performed on the infranate.
3. If urine samples are cloudy or turbid, it is recommended that they be centrifuged before transfer to a sample cup.
4. Refer to References (12,13,14) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

ANALYTIC RANGE

The SYNCHRON CX®3 DELTA System method for the determination of this analyte provides the following analytical ranges:

Table 7.0 Analytical Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum/Plasma/Urine	0 – 321.6 mg/dL	0 – 53.6 mmol/L
Serum, Plasma or Urine (ORDAC)	321.6 – 643.2 mg/dL	53.6 – 107.2 mmol/L

Printed or displayed UREA values obtained in the non auto-ORDAC mode between 53.8 mmol/L and 56.1 mmol/L must be diluted with normal saline and reanalyzed. Printed or displayed UREA values obtained in the ORDAC mode between 107.3 mmol/L and 114.1 mmol/L must also be diluted and reanalyzed.

REPORTABLE RANGE (AS DETERMINED ON SITE):

Table 8.0 Reportable Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS

EQUIVALENCY

Equivalency was assessed by Deming regression analysis of patient samples to accepted clinical methods.

Serum or Plasma:

Y (SYNCHRON CX3 DELTA)	= 1.031X - 0.26
N	= 95
MEAN (SYNCHRON CX3 DELTA)	= 14.07
MEAN (SYNCHRON CX3)	= 13.90
CORRELATION COEFFICIENT (r)	= 0.9994

Diluted Urine:

Y (SYNCHRON CX3 DELTA)	= 1.068X - 18.73
N	= 100
MEAN (SYNCHRON CX3 DELTA)	= 190.06
MEAN (COBAS FARA - GLDH)[a]	= 195.40
CORRELATION COEFFICIENT (r)	= 0.9943

a COBAS FARA is a registered trademark of Roche Analytical Instruments, Inc.

Refer to References (15) for guidelines on performing equivalency testing.

PRECISION

A properly operating SYNCHRON CX®3 DELTA System should exhibit imprecision values less than or equal to the maximum performance limits in the table below. Maximum performance limits were derived by an examination of the imprecision of various methods, proficiency test summaries, and literature sources.

Table 9.0 Maximum Performance Limits

TYPE OF PRECISION	SAMPLE TYPE	1 SD		CHANGEOVER VALUE[a]		% CV
		mmol/L	mg/dL	mmol/L	mg/dL	
Within-run	Serum/Plasma	3.0	0.5	100	16.7	3.0
Total	Serum/Plasma	4.5	0.8	100	16.7	4.5
Within-run	Urine	6.0	1.0	120	20.0	5.0
Total	Urine	9.0	1.5	120	20.0	7.5
Within-run	Serum/Plasma (ORDAC)	NA	NA	NA	NA	5.0
Total	Serum/Plasma (ORDAC)	NA	NA	NA	NA	7.5

a When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test % CV to the guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

Comparative performance data for the SYNCHRON CX®3 DELTA System evaluated using the NCCLS Proposed Guideline EP5-T2 appears in the table below.[16] Each laboratory should characterize their own instrument performance for comparison purposes.

Table 10.0 NCCLS EP5-T2 Precision Estimate Method

TYPE OF IMPRECISION	SAMPLE TYPE		No. Systems	No. Data Points[a]	Test Mean Value (mmol/L)	EP5-T2 Calculated Point Estimates	
						SD	%CV
Within-run	Serum	Control 1	1	80	2.0	14	7.0
	Serum	Control 2	1	80	11.3	0.20	1.7
	Serum	Control 3	1	80	20.3	0.19	0.9
	Urine	Control	1	80	190.9	1.42	0.7

Table 10.0 NCCLS EP5-T2 Precision Estimate Method, Continued

TYPE OF IMPRECISION	SAMPLE TYPE		No. Systems	No. Data Points[a]	Test Mean Value (mmol/L)	EP5-T2 Calculated Point Estimates	
						SD	%CV
Total	Serum	Control 1	1	80	2.0	0.18	8.9
	Serum	Control 2	1	80	11.3	0.20	1.8
	Serum	Control 3	1	80	20.3	0.20	1.0
	Urine	Control	1	80	190.9	4.71	2.5

a The serum/plasma and urine point estimate is based on the pooled data from 1 system, each run for 20 days, 2 runs per day, 2 observations per run on instruments operated and maintained according to the manufacturer's instructions.

ADDITIONAL INFORMATION

SHIPPING DAMAGE

If damaged product is received, notify your Beckman Coulter Clinical Support Center.

REFERENCES

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