

For *In Vitro* Diagnostic Use

#### ANNUAL REVIEW

Reviewed by:	Date	Reviewed by:	Date

## PRINCIPLE

### INTENDED USE

ISE Electrolyte Buffer reagent and ISE Electrolyte Reference reagent, when used in conjunction with SYNCHRON LX<sup>®</sup> System(s), UniCel<sup>®</sup> Dx<sub>C</sub> 600/800 System(s) and SYNCHRON<sup>®</sup> Systems AQUA CAL 1, 2 and 3, are intended for the quantitative determination of sodium concentration in human serum, plasma or urine.

### CLINICAL SIGNIFICANCE

Sodium measurements are used in the diagnosis and treatment of aldosteronism (excessive secretion of hormone aldosterone), diabetes insipidus, adrenal hypertension, Addison's disease, dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance.

### METHODOLOGY

The SYNCHRON<sup>®</sup> System(s) determines sodium ion concentration by indirect potentiometry utilizing two glass sodium electrodes (one acts as the reference electrode).

To measure sodium concentrations, a precise volume of sample (40 microliters) is mixed with a buffered solution. The ratio used is one part sample to 33 parts buffer. The high molar strength buffer is used to establish a constant activity coefficient for sodium ions, calibrating the electrode to concentration values.

### CHEMICAL REACTION SCHEME

The sodium electrode is made of lithium-sodium-aluminum-silicate glass. It is essential that the outer layer of the glass electrode is adequately hydrated. When the sample buffer mixture contacts the electrode, sodium ions in the sample undergo an ion exchange process with the sodium ions in the hydrated layer of the electrode. Changes in electrode potential occur as the ion exchange process takes place. These changes in electrode potential are referenced to the reference electrode. The "referenced potential" follows the Nernst equation and allows the calculation of sodium concentration in the sample:

$$E = \text{Constant} + (\text{slope}) (\log[\text{Na}^+])$$

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For more accurate measurement, the reference reagent containing sodium ions is introduced into the flow cell after the sample cycle, and the same ion exchange process takes place. The differential potential (voltage) between sample and reference reagent cycles is used for the calculation.

Under ideal conditions, the electrode imparts a selectivity of 300:1 over potassium and is insensitive to hydrogen ions in solutions buffered from pH 6 to 10.

## SPECIMEN

### TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.<sup>1</sup> Freshly drawn serum, plasma or properly collected urine (random/timed) 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.<sup>2</sup>
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.<sup>2</sup>
3. It is recommended that urine assays be performed within 2 hours of collection. For timed specimens, the collection container should be kept in the refrigerator or on ice during the timed period. No preservative is required.<sup>3</sup>

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

### SAMPLE VOLUME

A filled 0.5 mL sample cup is the optimum volume. For optimum primary sample tube volumes in primary tube samples and minimum volumes, refer to the Primary Tube Sample Template for your system.

### 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:

ISE ELECTROLYTE BUFFER REAGENT:

Two Electrolyte Buffer Reagent Bottles (2 x 2 L)

ISE ELECTROLYTE REFERENCE REAGENT:

Two Electrolyte Reference Reagent Bottles (2 x 2 L)

### VOLUMES PER TEST

Sample Volume	40 $\mu$ L
Reagent Volume	
ISE Electrolyte Buffer	1.27 mL
ISE Electrolyte Reference	3.23 mL
	(not part of sample dilution)

## REACTIVE INGREDIENTS

### REAGENT CONSTITUENTS

#### ISE ELECTROLYTE BUFFER REAGENT:

Tris 230 mmol/L

#### ISE ELECTROLYTE REFERENCE REAGENT:

Sodium 7 mmol/L

Potassium 0.2 mmol/L

Chloride 5 mmol/L

Carbon Dioxide 1.5 mmol/L

Calcium 0.1 mmol/L

Also non-reactive chemicals necessary for optimal system performance.

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

### MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

SYNCHRON® Systems AQUA CAL 1, 2 and 3

At least two levels of control material

### REAGENT PREPARATION

No preparation is required.

### 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

1. ISE Electrolyte Reference reagent stored unopened at room temperature is stable until the expiration date printed on the bottle label. Once opened, the reagent is stable at room temperature for 30 days, unless the expiration date is exceeded.
2. ISE Electrolyte Buffer reagent stored unopened at room temperature is stable until the expiration date printed on the bottle label. Once opened, the reagent is stable at room temperature for 30 days, unless the expiration date is exceeded.
3. For any electrolyte reagents frozen in transit, warm to room temperature, and mix thoroughly. Mix by gently inverting the bottle at least 20 times to redissolve salts back into solution.

ISE Electrolyte Buffer Reagent and ISE Electrolyte Reference Reagent storage location:

# CALIBRATION

## CALIBRATOR REQUIRED

SYNCHRON® Systems AQUA CAL 1, 2 and 3

## CALIBRATOR PREPARATION

No preparation is required.

## CALIBRATOR STORAGE AND STABILITY

1. If unopened, the 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 NA assay must be calibrated every 24 hours or with each new bottle of reagent and also with certain parts replacement or maintenance procedures, as defined in the SYNCHRON LX *Maintenance Manual and Instrument Log*, or the UniCel DxC 600/800 System *Instructions for Use* (IFU) manual.
3. For detailed calibration instructions, refer to the SYNCHRON LX *Operations Manual*, or the UniCel DxC 600/800 System *Instructions For Use* (IFU) 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 be printed with error codes and the system will alert the operator of the failure. For information on error codes, refer to the SYNCHRON LX *Diagnostics and Troubleshooting Manual*, or the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

## TRACEABILITY

For Traceability information refer to the Calibrator instructions for use.

## QUALITY CONTROL

At least two levels of control material 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 appropriate system manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.

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

**NOTICE**

Do not use controls containing diethylamine HCl.

**Table 1.0 Quality Control Material**

CONTROL NAME	SAMPLE TYPE	STORAGE

## TESTING PROCEDURE(S)

1. If necessary, load the reagent onto the system.
2. After reagent load is completed, calibration is required.
3. Program samples and controls for analysis.
4. After loading samples and controls onto the system, follow the protocols for system operations.

For detailed testing procedures, refer to the SYNCHRON LX *Operations Manual*, or the UniCel DxC 600/800 System *Instructions For Use (IFU)* manual.

## CALCULATIONS

The SYNCHRON® System(s) performs all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

## REPORTING RESULTS

Equivalency between the SYNCHRON LX and UniCel DxC 600/800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

## REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The following reference intervals were taken from literature and a study performed on SYNCHRON Systems.<sup>4</sup>

**Table 2.0 Reference intervals**

RANGE	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Literature	Serum or Plasma	136 – 145 mmol/L	136 – 145 mmol/L
	Urine (timed)	40 – 220 mmol/24 hrs	40 – 220 mmol/24 hrs
SYNCHRON	Serum or Plasma	136 – 144 mmol/L	136 – 144 mmol/L

RANGE	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Laboratory			

Refer to References (5, 6, 7) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

## PROCEDURAL NOTES

### ANTICOAGULANT TEST RESULTS

- If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method based on a study of 20 healthy volunteers:

**Table 3.0 Compatible Anticoagulants**

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	AVERAGE PLASMA-SERUM BIAS (mmol/L)
Ammonium Heparin	14 Units/mL	NSI <sup>a</sup>
Lithium Heparin	14 Units/mL	NSI
Sodium Heparin	14 Units/mL	NSI

a NSI = No Significant Interference (within  $\pm 2.0$  mmol/L or 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) <sup>a</sup>
Potassium Oxalate/Sodium Fluoride	2.0 / 2.5 mg/mL	+3.5

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

### LIMITATIONS

- If urine samples are cloudy or turbid, it is recommended that they be centrifuged before transfer to a sample cup.
- For each sodium measurement, the potassium concentration is used in the calculation of the sodium concentration. If the potassium chemistry is not calibrated, or the potassium value is out of range for the sample type, the sodium value will be suppressed for urine samples. Serum samples will use a nominal value for potassium.

### INTERFERENCES

- The following substances were tested for interference with this methodology:

**Table 5.0 Interferences**

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT <sup>a</sup>
Bilirubin (unconjugated)	Bovine	30 mg/dL	NSI <sup>b</sup>
Hemoglobin	RBC hemolysate	500 mg/dL	NSI
Lipemia	Intralipid <sup>c</sup>	500 mg/dL	NSI
Lithium	Lithium Acetoacetic Acid	20 mmol/L	+5 mmol/L
Benzalkonium chloride	NA <sup>d</sup>	0.5 mg/dL	-2 mmol/L
Methylbenzethonium Chloride	NA	0.2 mg/dL	-2 mmol/L

a Plus (+) or minus (-) signs in this column signify positive or negative interference.

b NSI = No Significant Interference (within  $\pm 2$  mmol/L or 2%).

c Intralipid is a registered trademark of KabiVitrum, Inc., Clayton, NC 27250.

d NA = Not applicable.

- Lipemic samples with visual turbidity >3+, or with a Lipemia Serum Index >10, should be ultracentrifuged and the analysis performed on the infranate.
- Refer to References (8,9,10) for other interferences caused by drugs, disease and preanalytical variables.

## PERFORMANCE CHARACTERISTICS

### ANALYTIC RANGE

The SYNCHRON<sup>®</sup> System(s) method for the determination of this analyte provides the following analytical range:

**Table 6.0 Analytical Range**

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum or Plasma	100 – 200 mmol/L	100 – 200 mmol/L
Urine	10 – 300 mmol/L	10 – 300 mmol/L

Samples with concentrations exceeding the high end of the analytical range should be diluted with deionized water and reanalyzed.

### REPORTABLE RANGE (AS DETERMINED ON SITE):

**Table 7.0 Reportable Range**

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS

### SENSITIVITY

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for NA determination is 100 mmol/L for serum or plasma, and 10 mmol/L for urine.

### EQUIVALENCY

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



**Serum or Plasma (in the range of 100.1 to 190.8 mmol/L):**

Y (SYNCHRON LX Systems)	= 0.979X + 2.20
N	= 236
MEAN (SYNCHRON LX Systems)	= 141.1
MEAN (SYNCHRON CX Systems)	= 141.9
CORRELATION COEFFICIENT (r)	= 0.992

**Urine (in the range of 17.9 to 265.2 mmol/L):**

Y (SYNCHRON LX Systems)	= 1.005X + 0.48
N	= 100
MEAN (SYNCHRON LX Systems)	= 113.9
MEAN (SYNCHRON CX Systems)	= 112.8
CORRELATION COEFFICIENT (r)	= 0.999

**Serum or Plasma (in the range of 104 to 200 mmol/L):**

Y (UniCel DxC Systems)	= 1.012X - 0.07
N	= 149
MEAN (UniCel DxC Systems)	= 141.7
MEAN (SYNCHRON LX Systems)	= 140.7
CORRELATION COEFFICIENT (r)	= 0.997

**Urine (in the range of 18 to 294 mmol/L):**

Y (UniCel DxC Systems)	= 1.017X - 1.57
N	= 110
MEAN (UniCel DxC Systems)	= 125.3
MEAN (SYNCHRON LX Systems)	= 124.8
CORRELATION COEFFICIENT (r)	= 0.999

Refer to References (11) for guidelines on performing equivalency testing.

**PRECISION**

A properly operating SYNCHRON<sup>®</sup> System(s) 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 8.0 Maximum Performance Limits**

TYPE OF PRECISION	SAMPLE TYPE	1 SD	CHANGEOVER VALUE <sup>a</sup>	% CV
		mmol/L	mmol/L	
Within-run	Serum/Plasma	1.0	100.0	1.0
	Urine	2.0	50.0	4.0

**Table 8.0 Maximum Performance Limits, Continued**

TYPE OF PRECISION	SAMPLE TYPE	1 SD	CHANGEOVER VALUE <sup>a</sup>	% CV
		mmol/L	mmol/L	
Total	Serum/Plasma	1.5	100.0	1.5
	Urine	3.0	50.0	6.0

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 LX System evaluated using the NCCLS Approved Guideline EP5-A appears in the table below.<sup>12</sup> Each laboratory should characterize their own instrument performance for comparison purposes.

**Table 9.0 NCCLS EP5-A Precision Estimate Method**

TYPE OF IMPRECISION	SAMPLE TYPE		No. Systems	No. Data Points <sup>a</sup>	Test Mean Value (mmol/L)	EP5-A Calculated Point Estimates	
						SD	%CV
Within-run	Serum	Control 1	1	80	109.9	0.72	0.7
	Serum	Control 2	1	80	156.2	0.80	0.5
	Urine	Control 1	1	80	84.5	0.55	0.7
	Urine	Control 2	1	80	165.9	1.27	0.8
Total	Serum	Control 1	1	80	109.9	0.98	0.9
	Serum	Control 2	1	80	156.2	1.17	0.8
	Urine	Control 1	1	80	84.5	0.91	1.1
	Urine	Control 2	1	80	165.9	1.61	1.0

a The point estimate is based on the pooled data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer's instructions.

**NOTICE**

These degrees of precision and equivalency were obtained in typical testing procedures on a SYNCHRON LX<sup>®</sup> System and are not intended to represent the performance specifications for this reagent.

**ADDITIONAL INFORMATION**

For more detailed information on SYNCHRON LX Systems or UniCel Dx<sub>C</sub> Systems, refer to the appropriate system manual.

**SHIPPING DAMAGE**

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

## REFERENCES

1. Tietz, N. W., "Specimen Collection and Processing; Sources of Biological Variation", *Textbook of Clinical Chemistry*, 2nd Edition, W. B. Saunders, Philadelphia, PA (1994).
2. National Committee for Clinical Laboratory Standards, *Procedures for the Handling and Processing of Blood Specimens*, Approved Guideline, NCCLS publication H18-A, Villanova, PA (1990).
3. National Committee for Clinical Laboratory Standards, *Routine Urinalysis and Collection, Transportation and Preservation of Urine Specimens*, Tentative Guideline, NCCLS publication GP16-T, Villanova, PA (1992).
4. Tietz, N. W., *Clinical Guide to Laboratory Tests*, 3rd Edition, W. B. Saunders, Philadelphia, PA (1995).
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7. Henry, J. B., *Clinical Diagnosis and Management by Laboratory Methods*, 18th Edition, W. B. Saunders Company, Philadelphia, PA (1991).
8. Young, D. S., *Effects of Drugs on Clinical Laboratory Tests*, 4th Edition, AACC Press, Washington, D. C. (1995).
9. Friedman, R. B., Young, D. S., *Effects of Disease on Clinical Laboratory Tests*, 3rd Edition, AACC Press, Washington, D.C. (1997).
10. Young, D. S., *Effects of Preanalytical Variables on Clinical Laboratory Tests*, 2nd Edition, AACC Press, Washington, D. C. (1997).
11. National Committee for Clinical Laboratory Standards, *Method Comparison and Bias Estimation Using Patient Samples*, Approved Guideline, NCCLS publication EP9-A, Villanova, PA (1995).
12. National Committee for Clinical Laboratory Standards, *Evaluation of Precision Performance of Clinical Chemistry Devices*, Approved Guideline, Vol. 19, No. 2, NCCLS publication EP5-A, Villanova, PA (1999).

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