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SYNCHRON® System(s) Chemistry Information Sheet

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CL Chloride

REF 467935 & 467915
REF A28937 & A28945

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® System(s), UniCel® DxC 600/800 System(s) and SYNCHRON® Systems AQUA CAL 1 and 2, are intended for the quantitative determination of chloride concentration in human serum, plasma, urine or cerebrospinal fluid (CSF).

CLINICAL SIGNIFICANCE

Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

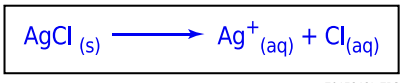
METHODOLOGY

The SYNCHRON® System(s) determines chloride ion concentration by indirect potentiometry utilizing a solid state chloride electrode in conjunction with a glass sodium reference electrode.

To measure chloride ion 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 of chloride ions, calibrating the electrode to concentration values.

CHEMICAL REACTION SCHEME

The solid state chloride electrode consists of a sparingly soluble silver chloride compound.[1] When sample buffer mixture contacts the electrode, changes in electrode potential occur as the chloride ions in the sample shift the following chemical equilibrium:



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A stable electrode potential, referenced to the sodium reference electrode, is reached when a new chemical equilibrium is established, which is in part determined by the solubility product (Ksp) of the silver chloride compound. The silver chloride based electrode responds to silver ion concentration change according to the Nernst equation:

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

Since

$$K_{sp} = [Ag^+][Cl^-]$$

Thus,

$$E = \text{Constant} + (\text{slope})(\log(K_{sp}/[Cl^-]))$$

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The AgCl electrode indirectly responds to chloride ions, and the electrode potential is inversely proportional to the chloride ion concentration in the sample.

For more accurate measurement, the reference reagent containing chloride ions is introduced to the flow cell after the sample cycle, and the same chemical equilibrium shift takes place. The differential potential (voltage) between sample and reference reagent cycles is used for chloride calculation.

SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.[2] Freshly drawn serum, plasma, CSF 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.[3]
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.[3]
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.[4]
4. CSF specimens should be centrifuged and analyzed without delay. Specimens may be refrigerated or frozen for 7 to 10 days for repeat determinations.[5]

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 µL
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 and 2
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, completely warm to room temperature and mix thoroughly by gently inverting bottle at least 20 times to redissolve salts into solution.

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

CALIBRATION

CALIBRATOR REQUIRED

SYNCHRON® Systems AQUA CAL 1 and 2

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

SYNCHRON® Systems AQUA CAL 1 and 2 are stable until the expiration date printed on the calibrator bottles if stored capped in the original containers at +2°C to +8°C. Once opened, calibrators are stable for 30 days stored at room temperature unless the expiration date is exceeded.

Calibrator storage location:

CALIBRATION INFORMATION

1. The system must have valid calibration factors in memory before controls or patient samples can be run.
2. Under typical operating conditions the CL 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.[6]

Table 2.0 Reference intervals

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Literature	Serum or Plasma	98 – 107 mmol/L	98 – 107 mmol/L
	Urine (timed)	110 – 250 mmol/24 hrs	110 – 250 mmol/24 hrs
	CSF	118 – 132 mmol/L	118 – 132 mmol/L
SYNCHRON	Serum or Plasma	101 – 111 mmol/L	101 – 111 mmol/L

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Laboratory			

Refer to References (5, 7, 8) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

1. 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[a]
Lithium Heparin	14 Units/mL	NSI
Sodium Heparin	14 Units/mL	NSI
Potassium Oxalate/Sodium Fluoride	2.0 / 2.5 mg/mL	NSI

a NSI = No Significant Interference (within ±4.0 mmol/L or 4%).

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

Table 4.0 Incompatible Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	AVERAGE PLASMA-SERUM BIAS (mmol/L)[a]
EDTA	1.5 mg/mL	-5.3

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 or CSF samples are cloudy or turbid or if CSF samples are visibly contaminated with blood, it is recommended that they be centrifuged before analysis.

INTERFERENCES

1. The following substances were tested for interference with this methodology:

Table 5.0 Interferences

SUBSTANCE	SOURCE	LEVEL TESTED	INTERFERENCES[a]
Bilirubin (unconjugated)	Bovine	30 mg/dL	NSI[b]
Hemoglobin	RBC hemolysate	500 mg/dL	NSI
Lipemia	Intralipid[c]	500 mg/dL	NSI
Acetylsalicylic Acid	NA[d]	60 mg/dL	NSI
Ammonium Nitrate	NA	40 mmol/L	NSI
Cefotaxime	Cefotaxime sodium salt	500 µg/mL	NSI
Cefoxitin	Cefoxitin sodium salt	200 µg/mL	NSI
Sulfobromophthalein	Sulfobromophthalein sodium salt	2.0 mg/dL	NSI
N-Acetyl Cysteine	NA	2 mmol/L	+3 mmol/L
Bromide	Lithium bromide	1 mmol/L	+8 mmol/L
Iodide	Sodium Iodide	4 mmol/L	+2 mmol/L
L-Dopa	NA	40 µg/mL	-3 mmol/L

a Plus (+) or minus (-) signs in this column signify positive or negative interference.
b NSI = No Significant Interference (within ±4.0 mmol/L or 4%).
c Intralipid is a registered trademark of KabiVitrum, Inc., Clayton, NC 27250.
d NA = Not applicable.

2. Lipemic samples with visual turbidity >3+, or with a Lipemia Serum Index >10, should be ultracentrifuged and the analysis performed on the infranate.
3. Refer to References (9,10,11) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

ANALYTIC RANGE

The SYNCHRON® System(s) method for the determination of this analyte provides the following analytical ranges:

Table 6.0 Analytical Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum/Plasma/CSF	50 – 200 mmol/L	50 – 200 mmol/L
Urine	15 – 300 mmol/L	15 – 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 to 95% confidence. Sensitivity for the chloride determination is 50 mmol/L for serum, plasma or CSF and 15 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 83.36 to 179.93 mmol/L):

Y (SYNCHRON LX Systems)	= 1.018X - 1.92
N	= 99
MEAN (SYNCHRON LX Systems)	= 114.3
MEAN (SYNCHRON CX Systems)	= 114.2
CORRELATION COEFFICIENT (r)	= 0.992

Urine (in the range of 15.6 to 290.4 mmol/L):

Y (SYNCHRON LX Systems)	= 0.986X + 0.15
N	= 125
MEAN (SYNCHRON LX Systems)	= 129.3
MEAN (SYNCHRON CX Systems)	= 130.9
CORRELATION COEFFICIENT (r)	= 0.997

CSF (in the range of 48.77 to 198.93 mmol/L):

Y (SYNCHRON LX Systems)	= 1.038X - 5.27
N	= 71
MEAN (SYNCHRON LX Systems)	= 127.23
MEAN (SYNCHRON CX Systems)	= 126.76
CORRELATION COEFFICIENT (r)	= 0.999

Serum or Plasma (in the range of 53 to 200 mmol/L):

Y (UniCel DxC Systems)	= 1.005X - 0.86
N	= 194
MEAN (UniCel DxC Systems)	= 108.0
MEAN (SYNCHRON LX Systems)	= 108.3
Correlation Coefficient (r)	= 0.997

Urine (in the range of 14.9 to 300 mmol/L):

Y (UniCel DxC Systems)	= 0.982X +0.52
N	= 72
MEAN (UniCel DxC Systems)	= 141.8
MEAN (SYNCHRON LX Systems)	= 143.8
Correlation Coefficient (r)	= 1.000

CSF (in the range of 52.3 to 194.4 mmol/L):

Y (UniCel DxC Systems)	= 0.980X + 0.58
N	= 108
MEAN (UniCel DxC Systems)	= 130.8
MEAN (SYNCHRON LX Systems)	= 133.0
Correlation Coefficient (r)	= 0.993

Refer to References (12) for guidelines on performing equivalency testing.

PRECISION

A properly operating SYNCHRON® 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[a]	
		mmol/L	mmol/L	% CV
Within-run	Serum/Plasma/CSF	2.0	100.0	2.0
	Urine	3.0	100.0	3.0
Total	Serum/Plasma/CSF	3.0	100.0	3.0
	Urine	4.5	100.0	4.5

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 LX System evaluated using the NCCLS Approved Guideline EP5-A appears in the table below.[13] 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[a]	Test Mean Value (mmol/L)	EP5-A Calculated Point Estimates	
						SD	%CV
Within-run	Serum	Control 1	1	80	79.88	0.37	0.5
	Serum	Control 2	1	80	118.44	0.60	0.5
	Urine	Control 1	1	80	82.27	0.50	0.6
	Urine	Control 2	1	80	203.76	1.45	0.7
	CSF	Control	1	80	148.57	0.84	0.6
Total	Serum	Control 1	1	80	79.88	0.78	1.0
	Serum	Control 2	1	80	118.44	1.03	0.9
	Urine	Control 1	1	80	82.27	0.70	0.9
	Urine	Control 2	1	80	203.76	2.62	1.3
	CSF	Control	1	80	148.57	1.46	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® 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 DxC Systems, refer to the appropriate system manual.

SHIPPING DAMAGE

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

REFERENCES

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13. 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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