# CL-2

**Chloride Electrode Gen.2 for Direct, Indirect and Urine mode**



**English**

## Intended use

The ISE module of the COBAS INTEGRA systems is intended for use in the quantitative determination of sodium, potassium, chloride in serum, plasma and urine, and lithium in serum and plasma using ion-selective electrodes.

This Chloride Electrode, Cat. No. 04581008001, is recommended to be used if a significant proportion of the samples are plasma samples. Serum and urine samples may also be analyzed with this electrode.

## Summary[1]

Electrolytes are involved in most major metabolic functions in the body. Sodium, potassium and chloride are amongst the most important physiological ions and the most often assayed electrolytes. They are supplied primarily through the diet, absorbed in the gastrointestinal tract and excreted by the kidneys.

*Chloride* is the major extracellular anion and serves to regulate the balance of extracellular fluid distribution.

*Serum/plasma:* Similarly to the other ions, common causes of decreased chloride include reduced dietary intake, prolonged vomiting, reduced renal reabsorption as well as some forms of acidosis and alkalosis. Increased chloride values are found in dehydration, kidney failure, some forms of acidosis, high dietary or parenteral chloride intake and salicylate poisoning.

*Urine:* Urinary excretion of chloride normally approximates the dietary intake. Physiological increase of urinary chloride is found with postmenstrual diuresis and a decrease with premenstrual salt and water retention, in parallel with an increase or decrease of urinary sodium levels. Chloride in urine is examined in evaluation of electrolyte composition and in acid-base balance studies.

## Test principle

Ion-selective electrodes, using undiluted (ISE Direct) or automatically diluted (ISE Indirect, ISE in Urine) specimens.

## Note

The slope and test ranges for this electrode differ from the other Chloride Electrode (Cat. No. 03003523001). Therefore in order to use this Chloride Electrode Gen.2 (Cat. No. 04581008001) the installation of special test settings TAS/U is mandatory.

- "ICKA3399" for COBAS INTEGRA 400 plus analyzer
- "98A.99" for COBAS INTEGRA 800 analyzer

## Precautions and warnings

Pay attention to all precautions and warnings listed in Section 1 / Introduction of this Method Manual.

For USA: For prescription use only.

## On-board stability

| | |
|---|---|
| Electrode life span: | 2 weeks or 2000 samples |
| Slope ranges: | -35 to -56 mV/dec direct mode |
| | -38 to -56 mV/dec indirect mode |

## Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable. Serum or plasma, free from hemolysis.

If heparinized plasma is used, ensure that the collection tubes are filled with the correct volume of blood. The tested anticoagulant for chloride determinations is lithium heparin.

*Urine:* Collect 24-hour urine for chloride determinations without addition of preservatives and/or stabilizers. Store refrigerated during collection.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

## Note

Serum separator tubes containing acrylic, ester, styrene, urethane or olefin based gels may be used for sample collection as long as they are used in accordance with the manufacturer's recommended procedures. It is especially important that storage temperature, adequate mixing and clotting times at sufficient g-forces for sufficient time periods are respected. Ensure also correct filling levels and ensure a minimum of 1 cm sample above gel layer. If these precautions are not taken, it is possible to accidentally coat the sample probe with gel (interfering with proper sample level detection), or even to aspirate gel into the ISE system (resulting in a clogged system). Inadequate mixing of plasma tubes can cause interference with micro fibrin clots.

It is strongly recommended to avoid silicone-type gels, due to risk of silicon oil contaminations. Today's global tube suppliers do not employ silicone based gels at all, but it may be that silicone gels are in use by small local suppliers. In addition, tubes that exhibit a layer of clear liquid, which rises to the top of the serum after centrifugation, should not be used for direct sample aspiration, in order to prevent coating the sample probes and interfering with ISE system.

It is possible to clog the sample probes or the ISE tubing with gel or clots if these precautions are not taken.

The stabilities of chloride in the specimens kept in tightly closed tubes are given in the table below:[2]

| | 15-25 °C | 2-8 °C | (-15)-(-25) °C |
|---|---|---|---|
| Chloride | 7 days | 7 days | stable |

## COBAS INTEGRA 400 plus/800 test definition

| Measuring mode | ISE Direct | ISE Indirect | ISE Urine |
|---|---|---|---|
| Specimen | Serum/plasma | Serum/plasma | Urine |
| Typical test range | 60-140 | 60-140 | 20-250 |
| Unit | mmol/L | mmol/L | mmol/L |

The general test range without system flag is 20-250 mmol/L.

## Pipetting parameters

| Measuring mode | ISE Direct | ISE Indirect | ISE Urine |
|---|---|---|---|
| Specimen | 97 | 20 | 20 |
| Diluent ($H_2O$) | – | 100 | 100 |
| Unit | µL | µL | µL |

## Calibration

| | |
|---|---|
| Calibrators | ISE Solutions 1, 2, and 3 |
| | ISE Calibrator Direct |
| | ISE Calibrator Indirect/Urine |
| Calibration replicate | One |
| Calibration interval | Five hours (main calibration) |
| | Every sample (one-point calibration) |

Once opened, ISE Solution 1, 2, and 3 are stable on-board up to 2 weeks.

Once opened, ISE Calibrator Direct and ISE Calibrator Indirect/Urine are stable on-board up to 8 weeks.

## Quality control

| | |
|---|---|
| Serum, plasma | |
| Reference range | Precinorm U, Precinorm U plus, or PreciControl ClinChem Multi 1 |
| Pathological range | Precipath U, Precipath U plus, or PreciControl ClinChem Multi 2 |
| Urine | Quantitative urine controls are recommended for routine quality control. |
| Control interval | 5 hours recommended |
| Control sequence | User defined |
| Control after calibration | Recommended |

For quality control, use control materials as listed above. In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

**Calculation**

Refer to the Section Principle of Measurement in the general description "Ion-Selective Electrode Module".

**Limitations - interference**

*Serum, plasma*

Criterion: Recovery within ± 10 % of initial value.

*Direct mode:*

Hemolysis: No significant interference up to a hemoglobin level of 0.621 mmol/L (10 g/L).

Icterus: No significant interference.

Lipemia: No significant interference.

Drugs: Of the drugs tested in vitro, Ca-dobesilate, phenylbutazone, acetylsalicylic acid and ibuprofen cause artificially high chloride concentrations. In addition to the tested drug panel, salicylic acid was also measured. A salicylic acid concentration of 1.2 mmol/L simulates an increase of the chloride concentration by less than 10 %.
Falsely high chloride values have been reported from patients receiving perchlorate medication. This is due to an interference of perchlorate ions with chloride ISE determinations.

*Indirect mode:*

Hemolysis: No significant interference up to a hemoglobin level of 0.621 mmol/L (10 g/L).

Icterus: No significant interference.

Lipemia: No significant interference.

Drugs: Of the drugs tested in vitro, acetylsalicylic acid and ibuprofen cause artificially high chloride concentrations. In addition to the tested drug panel, salicylic acid was also measured. Including the highest concentration (3 mmol/L), no significant interference was detected.
Falsely high chloride values have been reported from patients receiving perchlorate medication. This is due to an interference of perchlorate ions with chloride ISE determinations.

The following drugs where tested up to the indicated concentration:

*Serum/plasma panel:*

| | |
|---|---|
| Acetylcysteine | 150 mg/L |
| Ampicillin-Na | 1000 mg/L |
| Ascorbic acid | 300 mg/L |
| Ca-dobesilate | 200 mg/L |
| Cyclosporin | 5 mg/L |
| Cefoxitin | 2500 mg/L |
| Heparin | 5000 U/L |
| Intralipid | 10000 mg/L |
| L-Dopa | 20 mg/L |
| Methyldopa | 20 mg/L |
| Metronidazol + 1,5 | 200 mg/L |
| Phenylbutazone | 400 mg/L |
| Doxycyclin | 50 mg/L |
| Acetylsalicylic acid | 1000 mg/L |
| Rifampicin | 60 mg/L |
| Acetaminophen | 200 mg/L |
| Ibuprofen | 500 mg/L |
| Theophilline | 100 mg/L |

*Urine*

Criterion: Recovery within ± 20 % of initial value.

*Urine mode:*

Drugs: Of the drugs tested in vitro, ascorbic acid, Ca-dobesilate and levodopa cause artificially high chloride concentrations.
Falsely high chloride values have been reported from patients receiving perchlorate medication. This is due to an interference of perchlorate ions with chloride ISE determinations.

The following drugs where tested up to the indicated concentration:

*Urine panel:*

| | |
|---|---|
| Acetaminophen (Paracetamol) | 3000 mg/L |
| Acetylcysteine | 10 mg/L |
| Salicyluric acid | 6000 mg/L |
| Ascorbic acid | 4000 mg/L |
| Ca-dobesilate | 1000 mg/L |
| Na-cefoxitin | 12000 mg/L |
| Gentamycin sulfate | 400 mg/L |
| Ibuprofen | 4000 mg/L |
| L-Dopa | 1000 mg/L |
| Methyldopa | 2000 mg/L |
| Ofloxacine | 900 mg/L |
| Phenazopyridine | 300 mg/L |
| Doxycyclin | 300 mg/L |

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

**Expected values**[1]

| | |
|---|---|
| Serum/plasma (adults) | 98-107 mmol/L (Indirect mode) |
| | 101-110 mmol/L (Direct mode) |
| Urine (24 h) (adults) | 110-250 mmol/L |

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

**Specific performance data**

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

**Precision**

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21, 1 run) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). For intermediate precision (between-run) the second result of threefold determination was taken for calculation. For intermediate precision (total) all results are used for calculation. The following results were obtained:

**Chloride direct**

*Repeatability*

| Specimen | Serum low | Serum high | Plasma low | Plasma high | PNU* | PPU* |
|---|---|---|---|---|---|---|
| N | 21 | 21 | 20 | 21 | 21 | 21 |
| Mean | 92.9 | 127.2 | 89.2 | 125.0 | 86.3 | 119.9 |
| SD | 0.17 | 0.24 | 0.32 | 0.18 | 0.18 | 0.20 |
| CV (%) | 0.19 | 0.19 | 0.36 | 0.15 | 0.21 | 0.17 |
| Min | 92.6 | 126.9 | 88.6 | 124.6 | 85.9 | 119.6 |
| Max | 93.3 | 127.8 | 89.8 | 125.3 | 86.6 | 120.3 |

*PNU = Precinorm U and PPU = Precipath U

*Intermediate precision (between-run)*

| Specimen | Serum low | Serum high | Plasma low | Plasma high | PNU | PPU |
|---|---|---|---|---|---|---|
| N | 21 | 21 | 21 | 21 | 21 | 21 |
| Mean | 94.3 | 126.5 | 91.6 | 126.0 | 87.1 | 120.5 |
| SD | 0.85 | 1.34 | 0.95 | 1.46 | 0.84 | 1.18 |
| CV (%) | 0.9 | 1.1 | 1.0 | 1.2 | 1.0 | 1.0 |
| Min | 93.1 | 123.2 | 90.0 | 122.7 | 85.4 | 118.8 |
| Max | 96.4 | 130.0 | 93.8 | 130.0 | 89.2 | 124.0 |

*Intermediate precision (total)*

| Specimen | Serum | | Plasma | | PNU | PPU |
|---|---|---|---|---|---|---|
| | low | high | low | high | | |
| N | 63 | 63 | 63 | 62 | 63 | 63 |
| Total mean | 94.4 | 126.4 | 91.8 | 125.8 | 87.0 | 120.6 |
| Repeatability SD | 0.20 | 0.20 | 0.20 | 0.90 | 0.5 | 0.3 |
| Repeatability CV (%) | 0.20 | 0.20 | 0.2 | 0.8 | 0.5 | 0.2 |
| Total imprec. SD | 0.9 | 1.3 | 0.9 | 1.8 | 1.0 | 1.1 |
| Total imprec. CV (%) | 0.9 | 1.1 | 1.0 | 1.4 | 1.1 | 0.9 |

**Chloride indirect**

*Repeatability*

| Specimen | Serum low | Serum high | Plasma low | Plasma high | PNU | PPU |
|---|---|---|---|---|---|---|
| N | 21 | 21 | 21 | 21 | 21 | 21 |
| Mean | 90.3 | 124.1 | 86.4 | 121.9 | 83.1 | 116.0 |
| SD | 0.59 | 0.31 | 0.25 | 0.28 | 0.25 | 0.29 |
| CV (%) | 0.65 | 0.25 | 0.29 | 0.23 | 0.30 | 0.25 |
| Min | 89.7 | 123.5 | 85.9 | 121.3 | 82.7 | 115.5 |
| Max | 92.6 | 124.6 | 86.9 | 122.3 | 83.8 | 116.6 |

*Intermediate precision (between-run)*

| Specimen | Serum low | Serum high | Plasma low | Plasma high | PNU | PPU |
|---|---|---|---|---|---|---|
| N | 21 | 21 | 21 | 21 | 21 | 21 |
| Mean | 92.0 | 122.8 | 88.7 | 121.6 | 85.9 | 116.5 |
| SD | 0.96 | 1.12 | 0.98 | 1.24 | 0.93 | 1.16 |
| CV (%) | 1.0 | 0.9 | 1.1 | 1.0 | 1.1 | 1.0 |
| Min | 89.8 | 120.1 | 86.6 | 118.4 | 83.6 | 114.9 |
| Max | 93.4 | 125.3 | 90.4 | 124.0 | 87.5 | 119.6 |

*Intermediate precision (total)*

| Specimen | Serum | | Plasma | | PNU | PPU |
|---|---|---|---|---|---|---|
| | low | high | low | high | | |
| N | 63 | 63 | 62 | 62 | 63 | 63 |
| Total mean | 92.1 | 122.8 | 88.8 | 121.6 | 86.1 | 116.5 |
| Repeatability SD | 0.30 | 0.30 | 0.2 | 0.2 | 0.6 | 0.3 |
| Repeatability CV (%) | 0.30 | 0.30 | 0.2 | 0.2 | 0.7 | 0.3 |
| Total imprec. SD | 0.9 | 1.2 | 1.0 | 1.2 | 1.0 | 1.1 |
| Total imprec. CV (%) | 1.0 | 1.0 | 1.1 | 1.0 | 1.2 | 0.9 |

**Chloride urine**

*Repeatability*

| Specimen | Liqui-check 1 | Liqui-check 2 | Urine low | Urine high |
|---|---|---|---|---|
| N | 20 | 20 | 21 | 20 |
| Mean | 108.7 | 202.8 | 61.4 | 194.4 |
| SD | 0.32 | 0.78 | 0.31 | 0.97 |
| CV (%) | 0.29 | 0.38 | 0.50 | 0.50 |
| Min | 108.4 | 201.2 | 61.1 | 192.8 |
| Max | 109.5 | 204.1 | 62.2 | 195.9 |

*Intermediate precision (between-run)*

| Specimen | Liqui-check 1 | Liqui-check 2 | Urine low | Urine high |
|---|---|---|---|---|
| N | 21 | 21 | 21 | 21 |
| Mean | 105.5 | 192.8 | 64.9 | 186.4 |
| SD | 1.99 | 4.85 | 1.52 | 8.06 |
| CV (%) | 1.9 | 2.5 | 2.3 | 4.3 |
| Min | 101.7 | 184.9 | 61.6 | 173.6 |
| Max | 108.4 | 205.2 | 67.2 | 206.8 |

*Intermediate precision (total)*

| Specimen | Liqui-check 1 | Liqui-check 2 | Urine low | Urine high |
|---|---|---|---|---|
| N | 62 | 63 | 63 | 63 |
| Total mean | 105.5 | 192.8 | 65.1 | 186.5 |
| Repeatability SD | 0.4 | 0.7 | 1.1 | 1.1 |
| Repeatability CV (%) | 0.4 | 0.4 | 1.7 | 0.6 |
| Total imprec. SD | 2.0 | 5.0 | 1.8 | 8.2 |
| Total imprec. CV (%) | 1.9 | 2.6 | 2.8 | 4.4 |

**Method comparison**

**Chloride direct**

Chloride values for human plasma samples obtained on a COBAS INTEGRA 800 analyzer (y) were compared to those determined on a Coulometer (x).

| | | |
|---|---|---|
| Sample size | (n) | 57 |
| Corr. coefficient | (r) | 0.999 |
| Passing/Bablok[3] | | y = 0.972x + 3.21 mmol/L |

The sample concentrations were between 52.0 and 151.0 mmol/L.

Chloride values for human plasma samples obtained on a COBAS INTEGRA 800 analyzer (y) were compared to those determined on a Roche/Hitachi 912 analyzer (x).

| | | |
|---|---|---|
| Sample size | (n) | 57 |
| Corr. coefficient | (r) | 0.999 |
| Passing/Bablok[3] | | y = 0.931x + 8.82 mmol/L |

The sample concentrations were between 49.2 and 153.9 mmol/L.

**Chloride indirect**

Chloride values for human plasma samples obtained on a COBAS INTEGRA 800 analyzer (y) were compared to those determined on a Coulometer (x).

| | | |
|---|---|---|
| Sample size | (n) | 56 |
| Corr. coefficient | (r) | 0.999 |
| Passing/Bablok[3] | | y = 0.945x + 4.17 mmol/L |

The sample concentrations were between 52.0 and 151.0 mmol/L.

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**Chloride Electrode Gen.2 for Direct, Indirect and Urine mode**



Chloride values for human plasma samples obtained on a COBAS INTEGRA 800 analyzer (y) were compared to those determined on a Roche/Hitachi 912 analyzer (x).

| | | |
|---|---|---|
| Sample size | (n) | 56 |
| Corr. coefficient | (r) | 0.999 |
| Passing/Bablok[3] | | y = 0.903x + 9.79 mmol/L |

The sample concentrations were between 49.2 and 153.9 mmol/L.

**Chloride urine**

Chloride values for urine samples obtained on a COBAS INTEGRA 800 analyzer (y) were compared to those determined on a Coulometer (x).

| | | |
|---|---|---|
| Sample size | (n) | 51 |
| Corr. coefficient | (r) | 0.997 |
| Passing/Bablok[3] | | y = 0.978x + 5.72 mmol/L |

The sample concentrations were between 23.7 and 224.3 mmol/L.

Chloride values for urine samples obtained on a COBAS INTEGRA 800 analyzer (y) were compared to those determined on a Roche/Hitachi 912 analyzer (x).

| | | |
|---|---|---|
| Sample size | (n) | 51 |
| Corr. coefficient | (r) | 0.994 |
| Passing/Bablok[3] | | y = 0.956x + 10.89 mmol/L |

The sample concentrations were between 20.9 and 231.3 mmol/L.

**References**

1 Tietz NW, Pruden EL, Siggaard-Andersen O. Electrolytes. In: Burtis CA, Ashwood ER, eds. Tietz Textbook of Clinical Chemistry. 2nd ed. Philadelphia: WB Saunders Co 1994;1354-1374.

2 Young DS. Storage of specimen. In: Effects of Preanalytical Variables on Clinical Laboratory Tests. 1st ed. Washington: AACC Press 1993;4:269-278.

3 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

**Symbols**

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard.

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume after reconstitution or mixing |
| GTIN | Global Trade Item Number |

**FOR US CUSTOMERS ONLY: LIMITED WARRANTY**

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