i-STAT CHEM8+ Cartridge

Intended for use with the i-STAT Alinity Instrument

NAME

i-STAT CHEM8+ Cartridge – REF 09P31-25

INTENDED USE

The i-STAT CHEM8+ cartridge with the i-STAT Alinity System is intended for use in the *in vitro* quantification of sodium, potassium, chloride, ionized calcium, glucose, blood urea nitrogen, creatinine, hematocrit, and total carbon dioxide in arterial or venous whole blood.

Analyte	Intended Use
Sodium (Na)	Sodium measurements are used for monitoring electrolyte imbalances.
Potassium (K)	Potassium measurements are used in the diagnosis and monitoring of diseases and clinical conditions that manifest high and low potassium levels.
Chloride (Cl)	Chloride measurements are primarily used in the diagnosis, monitoring, and treatment of electrolyte and metabolic disorders including, but not limited to, cystic fibrosis, diabetic acidosis, and hydration disorders.
Ionized Calcium (iCa)	Ionized calcium measurements are used in the diagnosis, monitoring, and treatment of conditions including, but not limited to, parathyroid disease, a variety of bone diseases, chronic renal disease, tetany, and disturbances related to surgical and intensive care.
Glucose (Glu)	Glucose measurements are used in the diagnosis, monitoring, and treatment of carbohydrate metabolism disorders including, but not limited to, diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.
Blood Urea Nitrogen (BUN/Urea)	Blood urea nitrogen measurements are used for the diagnosis, monitoring, and treatment of certain renal and metabolic diseases.
Creatinine (Crea)	Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.
Hematocrit (Hct)	Hematocrit measurements can aid in the determination and monitoring of normal or abnormal total red cell volume status including, but not limited to, conditions such as anemia, erythrocytosis, and blood loss related to trauma and surgery.
Total Carbon Dioxide (TCO_2)	Carbon dioxide is used in the diagnosis, monitoring, and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.

SUMMARY AND EXPLANATION/CLINICAL SIGNIFICANCE

Measured:

Sodium (Na)

Tests for sodium in the blood are important in the diagnosis and treatment of patients suffering from hypertension, renal failure or impairment, cardiac distress, disorientation, dehydration, nausea and diarrhea. Some causes of increased values for sodium include dehydration, diabetes insipidus, salt poisoning, skin losses, hyperaldosteronism and CNS disorders. Some causes for decreased values for sodium include dilutional hyponatremia (cirrhosis), depletional hyponatremia and syndrome of inappropriate ADH.

Potassium (K)

Tests for potassium in the blood are important in the diagnosis and treatment of patients suffering from hypertension, renal failure or impairment, cardiac distress, disorientation, dehydration, nausea and diarrhea. Some causes of increased values for potassium include renal glomerular disease, adrenocortical insufficiency, diabetic ketoacidosis (DKA), sepsis and in vitro hemolysis. Some causes of decreased values for potassium include renal tubular disease, hyperaldosteronism, treatment of DKA, hyperinsulinism, metabolic alkalosis and diuretic therapy.

Chloride (Cl)

Tests for chloride in the blood are important in the diagnosis and treatment of patients suffering from hypertension, renal failure or impairment, cardiac distress, disorientation, dehydration, nausea and diarrhea. Some causes of increased values for chloride include prolonged diarrhea, renal tubular disease, hyperparathyroidism and dehydration. Some causes for decreased values for chloride include prolonged vomiting, burns, salt-losing renal disease, overhydration and thiazide therapy.

Ionized Calcium (iCa)

Although most of the calcium in blood is bound to protein or complexed to smaller anionic species, the biologically active fraction of calcium is free ionized calcium. Through its role in a number of enzymatic reactions and in membrane transport mechanisms, ionized calcium is vitally important in blood coagulation, nerve conduction, neuromuscular transmission and in muscle contraction. Increased ionized calcium (hypercalcemia) may result in coma. Other symptoms reflect neuromuscular disturbances, such as hyperreflexia and/or neurologic abnormalities such as neurasthenia, depression or psychosis. Decreased ionized calcium (hypocalcemia) often results in cramps (tetany), reduced cardiac stroke work and depressed left ventricular function. Prolonged hypocalcemia may result in bone demineralization (osteoporosis) which can lead to spontaneous fractures. Measurements of ionized calcium have proven of value under the following clinical conditions: transfusion of citrated blood, liver transplantation, open heart surgery, neonatal hypocalcemia, renal disease, hyperparathyroidism, malignancy, hypertension and pancreatitis.

Glucose (Glu)

Glucose is a primary energy source for the body and the only source of nutrients for brain tissue. Measurements for determination of blood glucose levels are important in the diagnosis and treatment of patients suffering from diabetes and hypoglycemia. Some causes for increased values of glucose include diabetes mellitus, pancreatitis, endocrine disorders (e.g., Cushing's syndrome), drugs (e.g., steroids, thyrotoxicosis), chronic renal failure, stress, or I.V. glucose infusion. Some causes of decreased values of glucose include insulinoma, adrenocortical insufficiency, hypopituitarism, massive liver disease, ethanol ingestion, reactive hypoglycemia, and glycogen storage disease.

Blood Urea Nitrogen (BUN/Urea)

An abnormally high level of urea nitrogen in the blood is an indication of kidney function impairment or failure. Some other causes of increased values for urea nitrogen include prerenal azotemia (e.g., shock), postrenal azotemia, GI bleeding and a high protein diet. Some causes of decreased values for urea nitrogen include pregnancy, severe liver insufficiency, overhydration and malnutrition.

Creatinine (Crea)

Elevated levels of creatinine are mainly associated with abnormal renal function and occur whenever there is a significant reduction in glomerular filtration rate or when urine elimination is obstructed. The concentration of creatinine is a better indicator of renal function than urea or uric acid because it is not affected by diet, exercise, or hormones.

The creatinine level has been used in combination with BUN to differentiate between prerenal and renal causes of an elevated urea/BUN.

Hematocrit (Hct)

Hematocrit is a measurement of the fractional volume of red blood cells. This is a key indicator of the body's state of hydration, anemia or severe blood loss, as well as the blood's ability to transport oxygen. A decreased hematocrit can be due to either overhydration, which increases the plasma volume, or a decrease in the number of red blood cells caused by anemias or blood loss. An increased hematocrit can be due to loss of fluids, such as in dehydration, diuretic therapy, and burns, or an increase in red blood cells, such as in cardiovascular and renal disorders, polycythemia vera, and impaired ventilation.

Total Carbon Dioxide (TCO_2)

TCO_2 is a measure of carbon dioxide which exists in several states: CO_2 in physical solution or loosely bound to proteins, bicarbonate (HCO_3) or carbonate (CO_3) anions, and carbonic acid (H_2CO_3). Measurement of TCO_2 as part of an electrolyte profile is useful chiefly to evaluate HCO_3 concentration. TCO_2 and HCO_3 are useful in the assessment of acid-base imbalance (along with pH and $\boldsymbol{P}CO_2$) and electrolyte imbalance.

TEST PRINCIPLE

The i-STAT System uses direct (undiluted) electrochemical methods. Values obtained by direct methods may differ from those obtained by indirect (diluted) methods. [1]

Measured:

Sodium (Na), Potassium (K), Chloride (Cl) and ionized Calcium (iCa)

The respective analyte is measured by ion-selective electrode potentiometry. In the calculation of results, concentration is related to potential through the Nernst equation.

Glucose (Glu)

Glucose is measured amperometrically. Oxidation of glucose, catalyzed by the enzyme glucose oxidase, produces hydrogen peroxide (H_2O_2). The liberated H_2O_2 is oxidized at the electrode to produce a current proportional to the sample glucose concentration.

$$\beta\text{-D-glucose} + H_2O + O_2 \xrightarrow{\textit{glucose oxidase}} \text{D-gluconic acid} + H_2O_2$$

$$H_2O_2 \longrightarrow 2H^+ + O_2 + 2e^-$$

BUN/Urea

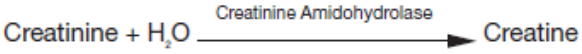
Urea is hydrolyzed to ammonium ions in a reaction catalyzed by the enzyme urease.

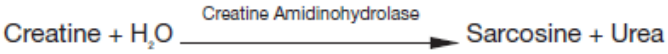
$$\text{Urea} + H_2O + 2H^+ \xrightarrow{\text{urease}} 2NH^+_4 + CO_2$$

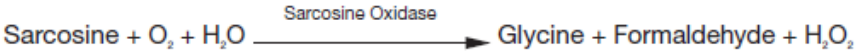
The ammonium ions are measured potentiometrically by an ion-selective electrode. In the calculation of results, concentration is related to potential through the Nernst Equation.

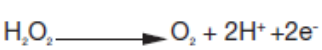
Creatinine (Crea)

Creatinine is measured amperometrically. It is hydrolyzed to creatine in a reaction catalyzed by the enzyme creatinine amidohydrolase. Creatine is then hydrolyzed to sarcosine by creatine amidinohydrolase. The oxidation of sarcosine, catalyzed by sarcosine oxidase, produces hydrogen peroxide (H_2O_2). The liberated hydrogen peroxide is oxidized at the platinum electrode to produce a current which is proportional to the sample creatinine concentration.









Hematocrit (Hct)

Hematocrit is determined conductometrically. The measured conductivity, after correction for electrolyte concentration, is inversely related to the hematocrit.

Total Carbon Dioxide (TCO_2)

The measured TCO_2 test method is calibrated to the International Federation of Clinical Chemistry (IFCC) TCO_2 reference method [2] with an algorithm based on the Henderson-Hasselbalch equation, which uses pH, ***P***CO_2, and ionic strength (Na) measurements.

Calculated:

Anion Gap (AnGap)

Anion Gap is calculated in the CHEM8+ cartridge as follows:

$$\text{Anion Gap (CHEM8+)} = (Na + K) - (Cl + (TCO_2 - 1))$$

For reporting the difference between the commonly measured cations sodium and potassium and the commonly measured anions chloride and bicarbonate the size of the anion gap reflects the unmeasured cations and anions and is therefore an analytical gap. Physiologically, a deficit of anions cannot exist, but, while relatively nonspecific, anion gap as calculated is useful for the detection of organic acidosis due to an increase in anions that are difficult to measure and in classifying metabolic acidosis into high and normal anion gap types.

Hemoglobin (Hb)

The i-STAT System provides a calculated hemoglobin result which is determined as follows:

hemoglobin (g/dL) = hematocrit (% PCV) x 0.34

hemoglobin (g/dL) = hematocrit (decimal fraction) x 34

To convert a hemoglobin result from g/dL to mmol/L, multiply the displayed result by 0.621. The calculation of hemoglobin from hematocrit assumes a normal MCHC.

eGFR (estimated Glomerular Filtration Rate)

Estimated Glomerular filtration rate is an index of kidney function, used to screen for and detect early kidney damage, to help diagnose chronic kidney disease (CKD), and to monitor kidney status.

The i-STAT Alinity can report a calculated eGFR result when a creatinine test result is obtained. The two calculation options are:

- The Modification of Diet in Renal Disease (MDRD) Study equation [3:]
  - **eGFR = 175 x $[S_{cr}]^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female) x (1.212 if African American)**, *where S_{cr} is serum creatinine (mg/dL), and age is expressed in years*.
- The Chronic Kidney Disease Epidemiology Collaboration formula (CKD-EPI):
  - **eGFR = 141x $\min(S_{cr}/k, 1)^{\alpha}$ x $\max(S_{cr}/k, 1)^{-1.209}$ x 0.993^{Age} x 1.018 [if female] x 1.159 [if Black]**, *where S_{cr} is serum creatinine (mg/dL), k is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of S_{cr}/k or 1, and max indicates the maximum of S_{cr}/k or 1*.

Limitations of the Procedure:

The formula is valid for adults between the ages of 18 and 120 years.

Warnings and Precautions:

eGFR >60 mL/min/1.73m^$_2$ does not exclude the possibility of mild renal disease. Further laboratory testing may be necessary to distinguish normal renal function from mild renal disease.

Creatinine-based estimating equations are not recommended for use with individuals with unstable creatinine concentrations, nor with persons with extremes in muscle mass and diet.

The MDRD eGFR equation has not been validated for those who are 70 years of age or older because muscle mass normally decreases with age. As a result, eGFR for patients older than 70 requires clinical correlation but is still regarded as a useful tool when caring for patients older than 70. [3]

See below for information on factors affecting results. Certain substances, such as drugs, may affect analyte levels in vivo. [4] If results appear inconsistent with the clinical assessment, the patient sample should be retested using another cartridge.

REAGENTS

Contents

Each i-STAT cartridge contains one reference electrode sensor, sensors for the measurement of specific analytes, and a buffered aqueous calibrant solution that contains known concentrations of analytes and preservatives. A list of reactive ingredients for the CHEM8+ cartridge is shown below:

Sensor	Reactive Ingredient	Biological Source	Minimum Quantity
Na	Sodium (Na^+)	N/A	121 mmol/L
K	Potassium (K^+)	N/A	3.6 mmol/L
Cl	Chloride (Cl^-)	N/A	91 mmol/L
iCa	Calcium (Ca^{2+})	N/A	0.9 mmol/L
Glu	Glucose	N/A	7 mmol/L
	Glucose Oxidase	*Aspergillus niger*	0.002 IU
BUN/Urea	Urea	N/A	4 mmol/L
	Urease	*Canavalia ensiformis*	0.12 IU
Crea	Creatinine	N/A	158.4 µmol/L
	Creatine Amidinohydrolase	Microbial	0.01 IU
	Creatinine Amidohydrolase	Microbial	0.02 IU
	Sarcosine Oxidase	Microbial	0.001 IU
TCO_2	Carbon Dioxide (CO_2)	N/A	25.2 mmHg

Warnings and Precautions

- For *in vitro* diagnostic use.
- Cartridges are intended for single-use only. Do not reuse.
- Refer to the i-STAT Alinity System Operations Manual for all warnings and precautions.

Storage Conditions

- Refrigeration at 2–8 ºC (35–46 ºF) until expiration date.
- Room Temperature at 18–30 ºC (64–86 ºF). Refer to the cartridge box for room temperature storage requirements.

INSTRUMENTS

The i-STAT CHEM8+ cartridge is intended for use with the i-STAT Alinity Instrument (Model No. AN-500).

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Arterial or venous whole blood

Sample volume: 95 µL

Blood Collection Options and Test Timing (time from collection to cartridge fill)

As higher heparin-to-blood ratios may affect results, fill blood collection tubes and syringes to capacity, following manufacturers' instructions.

	CHEM8+ Sample Collection
Syringe	**Without anticoagulant** • Maintain anaerobic conditions prior to filling this cartridge. • Mix sample immediately before filling cartridge. • Fill cartridge within 3 minutes of sample collection. **With balanced heparin anticoagulant** • Maintain anaerobic conditions prior to filling this cartridge.

	• Mix sample immediately before filling cartridge. • Fill cartridge within 10 minutes of sample collection.
Evacuated Tube	**Without anticoagulant** • Maintain anaerobic conditions prior to filling this cartridge. • Mix sample immediately before filling cartridge. • Fill cartridge within 3 minutes of sample collection. **With lithium heparin anticoagulant** • Maintain anaerobic conditions prior to filling this cartridge. • Mix sample immediately before filling cartridge. • Fill cartridge within 10 minutes of sample collection
Fill cartridge directly from skin puncture	**Not Recommended**

PROCEDURE FOR CARTRIDGE TESTING

Preparation for Use:

1. Individual cartridges may be used after standing five minutes at room temperature. An entire box of cartridges should stand at room temperature for one hour.
2. All cartridges should be used immediately after opening pouch.
3. If the pouch has been punctured, the cartridge should not be used.
4. Do not return cartridges to the refrigerator after bringing them to room temperature.

How to Perform Patient Testing

1. From the Home screen, touch "**Perform Patient Test**". This initiates the patient testing pathway.
2. To begin, follow instructions on the screen to "**Scan or Enter OPERATOR ID**"
3. Follow instructions on the screen to "**Scan or Enter PATIENT ID**"
4. Continue to follow prompts on the screen to proceed with patient testing. "**Scan (CARTRIDGE POUCH) Barcode**", Scanning is required. Information cannot be entered manually.
5. The Screen for selecting sample type will display if more than one sample type is applicable; select sample type if applicable.
6. Follow instructions on the screen to "**Close and Insert Filled Cartridge**". The action buttons at the bottom of the screen allow forward, backward and pause functionality.
7. Once the cartridge is inserted, "**Contacting Cartridge**" will display followed by the countdown bar. The following alerts are also displayed: **"Cartridge locked in instrument. Do not attempt to remove the Cartridge**" and "**Testing - Instrument Must Remain Level**".
8. When the test is complete, the test results are displayed.

Analysis Time

Approximately 130–200 seconds.

Quality Control

The i-STAT Alinity System quality control regimen comprises various aspects, with a system design that reduces the opportunity for error, including:

1. The i-STAT Alinity System automatically runs a comprehensive set of quality checks of analyzer and cartridge performance each time a sample is tested. This internal quality system will suppress results if the analyzer or cartridge does not meet certain internal specifications.
2. Aqueous-based control solutions are available for verifying the integrity of newly received cartridges.

3. In addition, the instrument performs internal electronic checks and calibration during each test cycle, and the Electronic Simulator test provides an independent check on the ability of the instrument to take accurate and sensitive measurements of voltage, current and resistance from the cartridge. The instrument will pass or fail this electronic test depending on whether or not it measures these signals within limits specified in the instrument software.

For additional information on Quality Control, refer to the i-STAT Alinity System Operations Manual located at www.pointofcare.abbott.

Calibration Verification

Standardization is the process by which a manufacturer establishes "true" values for representative samples. A multi-point calibration is derived for each sensor by this standardization process. These calibration curves are stable over many lots.

A one-point calibration is performed each time a cartridge requiring calibration is used. During the first part of the testing cycle, the calibrant solution is automatically released from its foil pack and is positioned over the sensors. The signals produced by the sensors' responses to the calibrant solution are measured. This one-point calibration adjusts the offset of the stored calibration curve. Next, the instrument automatically moves the sample over the sensors and the signals produced by the sensors' responses to the sample are measured. While coefficients are used rather than graphic calibration curves, the calculation of the result is equivalent to reading the sample's concentration from an adjusted calibration curve.

EXPECTED VALUES

TEST	UNITS *	REPORTABLE RANGE	REFERENCE RANGE *arterial*	*venous*
MEASURED				
Na	mmol/L (mEq/L)	100–180	138–146 [5]	
K	mmol/L (mEq/L)	2.0–9.0	3.5–4.9 [5] **	
Cl	mmol/L (mEq/L)	65–140	98–109 [5]	
iCa	mmol/L	0.25–2.50	1.12–1.32 [6]	
	mg/dL	1.0–10.0	4.5–5.3 [6]	
Glu	mmol/L	1.1–38.9	3.9–5.8 [6]	
	mg/dL	20–700	70–105 [6]	
	g/L	0.20–7.00	0.70–1.05 [6]	
BUN/Urea Nitrogen	mg/dL	3–140	8–26 [5]	
Urea	mmol/L	1–50	2.9–9.4 [5]	
	mg/dL	6–300	17–56 [5]	
	g/L	0.06–3.00	0.17–0.56 [5]	
Crea	mg/dL	0.2–20.0	0.6–1.3 [7]	
	µmol/L	18–1768	53–115	
Hematocrit/Hct	% PCV***	15–75	38–51 **** [5]	
	Fraction	0.15–0.75	0.38–0.51 [5]	
TCO_2	mmol/L	5–50	23–27 *****	24–29 *****
CALCULATED				
AnGap	mmol/L	(-10)–(+99)	10–20 [6]	
Hemoglobin/Hb	g/dL	5.1–25.5	12–17 [5]	

TEST	UNITS *	REPORTABLE RANGE	REFERENCE RANGE *arterial*	*venous*
	g/L	51–255	120–170 [5]	
	mmol/L	3.2–15.8	7–11 [5]	
estimated Glomerular Filtration Rate (eGFR)	mL/min/1.73m^2	0 – 60	>90	
estimated Glomerular Filtration Rate – Black/African American (eGFR-a)	mL/min/1.73m^2	0 – 60	>90	

* The i-STAT System can be configured with the preferred units. (See "Unit Conversion" below.)

** The reference range for potassium has been reduced by 0.2 mmol/L from the range cited in Reference 5 to account for the difference in results between serum and plasma.

*** PCV, packed cell volume.

**** The reference ranges for hematocrit and hemoglobin span both female and male populations.

***** Calculated from Siggard-Andersen nomogram. [8]

Unit Conversion

- **Ionized Calcium (iCa):** To convert mmol/L to mg/dL, multiply the mmol/L value by 4. To convert mmol/L to mEq/L, multiply the mmol/L value by 2.
- **Glucose (Glu):** To convert mg/dL to mmol/L, multiply the mg/dL value by 0.055.
- **BUN/Urea**: To convert a BUN result in mg/dL to a urea result in mmol/L, multiply the BUN result by 0.357. To convert a urea result in mmol/L to a urea result in mg/dL, multiply the mmol/L result by 6. To convert a urea result in mg/dL to a urea result in g/L, divide the mg/dL result by 100.
- **Creatinine (Crea):** To convert mg/dL to µmol/L, multiply the mg/dL value by 88.4.
- **Hematocrit (Hct):** To convert a result from % PCV (packed cell volume) to fraction packed cell volume, divide the % PCV result by 100. For the measurement of hematocrit, the i-STAT System can be customized to agree with methods calibrated by the microhematocrit reference method using either K_3EDTA or K_2EDTA anticoagulant. Mean cell volumes of K_3EDTA anticoagulated blood are approximately 2–4% less than K_2EDTA anticoagulated blood. While the choice of anticoagulant affects the microhematocrit method to which all hematocrit methods are calibrated, results from routine samples on hematology analyzers are independent of the anticoagulant used. Since most clinical hematology analyzers are calibrated by the microhematocrit method using K_3EDTA anticoagulant, the i-STAT System default customization is K_3EDTA.

i-STAT Alinity does not have default reference ranges programmed into the instrument. The reference ranges shown above are intended to be used as guides for the interpretation of results. Since reference ranges may vary with demographic factors such as age, gender and heritage, it is recommended that reference ranges be determined for the population being tested.

METROLOGICAL TRACEABILITY

The measured analytes in the i-STAT CHEM8+ cartridge are traceable to the following reference materials or methods. The i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods.

Sodium (Na), Potassium (K), Chloride (Cl) and Ionized Calcium (iCa)
The respective analyte values assigned to the i-STAT System controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard

reference material SRM956.

Glucose (Glu)
The i‑STAT System test for glucose measures glucose amount-of-substance concentration in the plasma fraction of arterial, venous whole blood (dimension mmol L‑1) for *in vitro* diagnostic use. Glucose values assigned to the i‑STAT System controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material SRM965.

Blood Urea Nitrogen (BUN/Urea)
The i‑STAT System test for blood urea nitrogen/urea measures blood urea nitrogen/urea amount-of substance concentration in the plasma fraction of arterial, venous whole blood (dimension mmol L^{-1}) for *in vitro* diagnostic use. BUN/urea values assigned to the i‑STAT System controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material SRM909.

Creatinine (Crea)
The i‑STAT System test for creatinine measures creatinine amount-of-substance concentration in the plasma fraction of arterialor venous whole blood (dimension µmol L^{-1}) for *in vitro* diagnostic use. Creatinine values assigned to the i‑STAT System controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material SRM967.

Hematocrit (Hct)
The i‑STAT System test for hematocrit measures packed red blood cell volume fraction in arterialor venous whole blood (expressed as the % packed cell volume) for *in vitro* diagnostic use. Hematocrit values assigned to i‑STAT System working calibrators are traceable to the Clinical and Laboratory Standards Institute (CLSI) H7-A3 procedure for determining packed cell volume by the microhematocrit method. [9]

Total carbon dioxide (TCO_2)
The i-STAT System test for total carbon dioxide (TCO2) measures the amount-of-substance total concentration of all forms of carbon dioxide in the plasma fraction of arterial, venous, or capillary whole blood (dimension mmol L^{-1}) for *in vitro* diagnostic use. TCO_2 values assigned to the i-STAT System controls and calibration verification materials are traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Reference Measurement Procedure for Substance Concentration Determination for Total Carbon Dioxide in Blood, Plasma or Serum. [2]

Additional information regarding metrological traceability is available from Abbott Point of Care Inc.

PERFORMANCE CHARACTERISTICS

The performance data summarized for Sodium, Glucose and Hematocrit was collected by professionals trained in the use of the i‑STAT Alinity System and comparative methods. The performance data summarized for all other tests listed below was collected at Abbott Point of Care. Representative cartridges were used to collect the data.

Precision*
A multiday precision study was performed with aqueous calibration verification materials in representative cartridges. Duplicates of each aqueous fluid were tested twice a day for 20 days.

Test	Units	Aqueous Cal Ver	n	Mean	SD (Standard Deviation)	CV (%) [Coefficient of Variation (%)]
Na	mmol/L	Very Low Abnormal	80	99.5	0.32	0.3

Test	Units	Aqueous Cal Ver	n	Mean	SD (Standard Deviation)	CV (%) [Coefficient of Variation (%)]
	or mEq/L	Low Abnormal	80	121.2	0.32	0.3
		Normal	80	133.7	0.34	0.3
		High Abnormal	80	160.8	0.38	0.2
		Very High Abnormal	80	180.2	0.56	0.3
K	mmol/L	Very Low Abnormal	80	2.31	0.010	0.4
		Low Abnormal	80	2.90	0.015	0.5
		Normal	80	3.81	0.023	0.6
		High Abnormal	80	6.16	0.026	0.4
		Very High Abnormal	80	7.81	0.039	0.5
Cl	mmol/L	Very Low Abnormal	80	63.3	0.59	0.9
		Low Abnormal	80	72.9	0.71	1.0
		Normal	80	91.7	0.75	0.8
		High Abnormal	80	112.4	0.90	0.8
		Very High Abnormal	80	124.1	1.08	0.9
iCa	mmol/L	Very Low Abnormal	80	0.32	0.006	2.0
		Low Abnormal	80	0.82	0.008	1.0
		Normal	80	1.29	0.012	1.0
		High Abnormal	80	1.56	0.015	1.0
		Very High Abnormal	80	2.38	0.027	1.1
Glu	mg/dL	Very Low Abnormal	80	26.9	0.42	1.6
		Low Abnormal	80	41.0	0.34	0.8
		High Abnormal	80	125.0	0.32	0.3
		Very High Abnormal	80	286.7	0.77	0.3
		Highest Abnormal	80	600.6	3.47	0.6
BUN	mg/dL	Very Low Abnormal	80	4.6	0.19	4.1
		Low Abnormal	80	6.6	0.15	2.3
		Normal	80	11.5	0.19	1.6
		High Abnormal	80	54.3	0.66	1.2
		Very High Abnormal	80	108.4	1.07	1.0
Crea	mg/dL	Low Abnormal	80	0.27	0.028	10.3
		Normal	80	1.05	0.025	2.4
		High Abnormal	80	3.83	0.083	2.2
		Very High Abnormal	80	14.63	0.403	2.8
Hct	%PCV	Very Low Abnormal	80	16.9	0.46	2.7
		Low Abnormal	80	33.9	0.51	1.5
		High Abnormal	80	55.2	0.49	0.9
		Very High Abnormal	80	65.0	0.39	0.6
TCO_2	Mmol/L	Very Low Abnormal	80	9.2	0.24	2.6
		Low Abnormal	80	14.9	0.40	2.7
		Normal	80	19.6	0.58	3.0
		High Abnormal	80	29.7	0.86	2.9
		Very High Abnormal	80	42.0	1.37	3.3

*Note: Representative data, individual laboratories may vary from these data.

Method Comparison

Method comparison was demonstrated in a study comparing the i-STAT Alinity to the i-STAT 1 Wireless (i-STAT 1W) using representative cartridges. The studies were based on CLSI guideline EP9-A3. [10] Whole blood samples anticoagulated with lithium heparin were evaluated. Samples were analyzed in duplicate on both systems. A weighted Deming regression analysis was performed using the first replicate result from the i-STAT Alinity versus the mean of the duplicates from the i-STAT 1W.

In the method comparison table, n is the number of specimens, and r is the correlation coefficient.

Test	Units		Comparative Method i-STAT 1W
Na	mmol/L	n	174
		Slope	1.0
		r	0.999
		intercept	-1
		X_{min}	115
		X_{max}	173
K	mmol/L	n	195
		Slope	1.00
		r	1.00
		intercept	-0.01
		X_{min}	2.0
		X_{max}	9.0
Cl	mmol/L	n	189
		Slope	1.01
		r	0.999
		intercept	-0.76
		X_{min}	66
		X_{max}	140
iCa	mmol/L	n	194
		Slope	1.005
		r	1.000
		intercept	-0.001
		X_{min}	0.40
		X_{max}	2.44
Glu	mg/dL	n	188
		Slope	1.00
		r	1.000
		intercept	1.17
		X_{min}	24
		X_{max}	671
BUN/Urea	mg/dL	n	194
		Slope	1.01
		r	0.999
		intercept	-0.02
		X_{min}	3
		X_{max}	137

Test	Units		Comparative Method i-STAT 1W
Crea	mg/dL	n	194
		Slope	0.988
		r	0.999
		intercept	0.003
		X_{min}	0.2
		X_{max}	19.2
Hct	%PCV	n	229
		Slope	1.02
		r	0.993
		intercept	-0.36
		X_{min}	18
		X_{max}	70
TCO_2	mmol/L	n	195
		Slope	0.980
		r	0.994
		intercept	0.3
		X_{min}	10
		X_{max}	49

FACTORS AFFECTING RESULTS

The following substances were evaluated in plasma for relevant analytes at the test concentrations recommended in CLSI guideline EP7-A2 [11] unless otherwise noted. For those identified as an interferant the interference is described.

Substance	Test Concentration (mmol/L)	Analyte	Interference (Yes/No)	Comment
Acetaldehyde	0.045 [12]	Glu	No	
		Crea	No	
Acetaminophen	1.32	Na	No	
		K	No	
		Cl	No	
		iCa	Yes	Decreased results
		Glu	No	
		BUN	No	
		Crea	Yes	Increased results
Acetaminophen (therapeutic)	0.132 [12]	iCa	No	
		Glu	No	
		Crea	No	
Acetoacetate	2.0	Glu	No	
Acetylcysteine	10.2	Na	No	
		K	No	
		Cl	Yes	Increased results
		iCa	Yes	Decreased results

Substance	Test Concentration (mmol/L)	Analyte	Interference (Yes/No)	Comment
		Glu	Yes	Decreased results
		BUN	No	
		Crea	Yes	Increased results
Acetylcysteine (therapeutic)	0.3 [13 14]	Cl	No	
		iCa	No	
		Glu	No	
		Crea	No	
Ascorbate	0.34	Na	No	
		K	No	
		Cl	No	
		iCa	No	
		Glu	No	
		BUN	No	
		Crea	Yes	Increased by up to 0.3 mg/dL
Bicarbonate	35.0	Crea	No	
Bilirubin	0.342	Crea	No	
Bromide	37.5	Na	Yes	Increased results. Use another method.
		K	Yes	Increased results and rate of star (***) outs. Use another method.
		Cl	Yes	Increased results. Use another method.
		iCa	Yes	Increased results. Use another method.
		Glu	Yes	Decreased results. Use another method.
		BUN	Yes	Decreased result and increased rate of star (***) outs. Use another method.
		Hct	Yes	Increased rate of star (***) outs.
Bromide (therapeutic)	2.5 [15 16 17]	Na	No	
		K	No	
		Cl	Yes	Increased results. Use another method.
		iCa	No	
		Glu	Yes	Decreased results
		BUN	No	
		Crea	Yes	Increased results
		Hct	No	
Calcium Chloride	5.0	Crea	No	
Creatine	0.382	Crea	Yes	Increased by up to 0.3 mg/dL. See Other Factors Affecting Results below for Creatine.

Substance	Test Concentration (mmol/L)	Analyte	Interference (Yes/No)	Comment
Dopamine	0.006	Glu	No	
		Crea	No	
Formaldehyde	0.133 [12]	Glu	No	
		Crea	No	
β-Hydroxybutyrate	6.0 [18]	Na	No	
		K	No	
		Cl	No	
		iCa	No	
		Glu	No	
		BUN	No	
		Crea	No	
Glycolic Acid	10.0	Crea	Yes	Decreased results. Use another method.
Hydroxyurea	0.92	Glu	Yes	Increased results. Use another method.
		BUN	Yes	Increased results.
		Crea	Yes	Increased results. Use another method.
Iodide	2.99	Cl	Yes	Increased results.
	0.4	Cl	No	
Lactate	6.6	Na	No	
		K	No	
		Cl	No	
		iCa	Yes	Decreased results by up to 0.07 mmol/L.
		Glu	No	
		BUN	No	
		Crea	No	
Leflunomide	0.03	iCa	Yes	Decreased results
Magnesium Chloride	1.0	Na	No	
		K	No	
		iCa	Yes	Increased results by up to 0.04 mmol/L.
Maltose	13.3	Glu	No	
Methyldopa	0.071	Crea	No	
Nithiodote (Sodium thiosulfate)	16.7 [19]	Na	Yes	Increased results
		K	Yes	Decreased results
		Cl	Yes	Increased results
		iCa	Yes	Decreased results
		Glu	Yes	Decreased results
		BUN	Yes	Decreased results
		Crea	Yes	Increased results
Pyruvate	0.31	Glu	No	

Substance	Test Concentration (mmol/L)	Analyte	Interference (Yes/No)	Comment
		Crea	No	
Salicylate	4.34	Na	No	
		K	No	
		Cl	Yes	Increased results. Use another method.
		iCa	Yes	Decreased results
		Glu	No	
		BUN	No	
		Crea	No	
Salicylate (therapeutic)	0.5 [20]	Cl	No	
		iCa	Yes	Decreased results by up to 0.03 mmol/L
Thiocyanate	6.9	Cl	Yes	Increased results. Use another method
		iCa	Yes	Decreased results. Use another method.
		Glu	Yes	Decreased results
		BUN	No	
Thiocyanate (therapeutic)	0.5 [12]	Glu	No	
Uric Acid	1.4	Glu	No	
		Crea	No	

The degree of interference at concentrations other than those reported above might not be predictable. It is possible that interfering substances other than those tested may be encountered.

Relevant comments regarding interference of Acetaminophen, Acetylcysteine, Bromide, Hydroxyurea, Iodide, Leflunomide, Nithiodote and Salicylate and are noted below:

- Acetaminophen has been shown to interfere with i-STAT ionized calcium and creatinine results at a 1.32 mmol/L, a toxic concentration that is proscribed by the CLSI guideline. Acetaminophen at 0.132 mmol/L, which represents the upper end of the therapeutic concentration range, has been shown not to significantly interfere with i-STAT ionized calcium and creatinine results.
- Acetylcysteine has been tested at two levels: the CLSI recommended level of 10.2 mmol/L and a concentration of 0.30 mmol/L. The latter is 3 times the peak therapeutic plasma concentration associated with treatment to reverse acetaminophen poisoning. APOC has not identified a therapeutic condition that would lead to levels consistent with the CLSI recommended level.
- Bromide was tested at two levels: the CLSI recommended level and a therapeutic plasma concentration level of 2.5 mmol/L. The latter is the peak plasma concentration associated with halothane anesthesia, in which bromide is released. APOC has not identified a therapeutic condition that would lead to levels consistent with the CLSI recommended level.
- Hydroxyurea has been shown to interfere with glucose, BUN and creatinine results at 0.92 mmol/L. Hydroxyurea is a DNA synthesis inhibitor used in the treatment sickle cell anemia, HIV infection, and various types of cancer. The malignancies that it is used to treat include melanoma, metastatic ovarian cancer, and chronic myelogenous leukemia. It is also used in the treatment of polycythemia vera, thrombocythemia, and psoriasis. At typical doses ranging from 500 mg to 2 g/day, concentrations of hydroxyurea in a patient's blood may be sustained at approximately 100 to 500 µmol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.

- Iodide has been tested at the CLSI recommended level of 2.99 mmol/L, which is close to the peak concentration after a lethal dose. A lethal dose is reported to be in the range of 2–4 grams , which equates to 3.1–6.3 mmol/L assuming the dose is fully distributed in a typical blood [21] volume of 5 L. Iodide can be used to treat thyroid disease (i.e., hyperthyroidism). A study showed serum iodide reaches mean peak concentration between 1.8 mg/L (0.014 mmol/L) and 2.2 mg/L (0.017 mmol/L) after a month of supplementation at 50 mg/day. [22] Iodide has been shown to interfere with i-STAT chloride results at 2.99 mmol/L. The lowest concentration tested at APOC of 0.4 mmol/L has been shown to not significantly interfere with i-STAT chloride results. APOC has not identified a therapeutic condition that would lead to levels consistent with the CLSI recommended level.
- Leflunomide has been shown to interfere with ionized calcium results at 0.03 mmol/L. Leflunomide is an isoxazole immunomodulatory agent that inhibits dihydroorotate dehydrogenase, an enzyme involved in *de novo* pyrimidine synthesis, and that has antiproliferative activity. It is used in the treatment of some immune diseases. Following oral administration, leflunomide is metabolized to an active metabolite, teriflunomide, which is responsible for essentially all its *in vivo* activity. The active metabolite teriflunomide reaches a plasma concentration of 8.5 µg/mL (0.031 mmol/L) after a 100 mg loading dose and the steady state concentration is maintained at 63 µg/mL (0.23 mmol/L) after 24 weeks of maintenance dose at 25 mg/day [23] when treating inflammatory polyarthropathy.
- Nithiodote (sodium thiosulfate) has been shown to interfere with sodium, potassium, chloride, ionized calcium, glucose, BUN and creatinine results at 16.7 mmol/L. Nithiodote (sodium thiosulfate) is indicated for the treatment of acute cyanide poisoning. The journal article titled "Falsely increased chloride and missed anion gap elevation during treatment with sodium thiosulfate" indicated that sodium thiosulfate could be used in the treatment of calciphylaxis indicating that "the highest concentration likely to be seen in plasma [is] after infusion of a 12.5 g dose of sodium thiosulfate pentahydrate. Assuming that the 12.5 g dose of sodium thiosulfate pentahydrate is distributed in a typical blood volume of 5 L with a hematocrit of 40%, the peak sodium thiosulfate plasma concentration expected is 16.7 mmol/L." [19]
- Salicylate has been shown to interfere with i-STAT chloride and ionized calcium results at 4.34 mmol/L, a toxic concentration that is proscribed by the CLSI guideline. Salicylate at 0.5 mmol/L, which represents the upper end of the therapeutic concentration range, has been shown not to significantly interfere with i-STAT chloride results and has been shown to decrease ionized calcium results by approximately 0.03 mmol/L.

OTHER FACTORS AFFECTING RESULTS

Factor	Analyte	Effect
Sodium heparin	Na	Sodium heparin may increase sodium results up to 1 mmol/L. [24]
Venous stasis	iCa	Venous stasis (prolonged tourniquet application) and forearm exercise may increase ionized calcium due to a decrease in pH caused by localized production of lactic acid. [25]
Line draw	Hct	Low hematocrit results can be caused by contamination of flush solutions in arterial or venous lines. Back flush a line with a sufficient amount of blood to remove intravenous solutions, heparin, or medications that may contaminate the sample. Five to six times the volume of the catheter, connectors, and needle is recommended.
Heparin	iCa	Heparin binds calcium. Each unit of heparin added per mL of blood will decrease ionized calcium by 0.01 mmol/L. [25] Therefore, the correct ratio of heparin anticoagulant to blood must be achieved during sample collection. Intravenous injection of 10,000 units of heparin has been shown in adults to cause a significant decrease of ionized calcium of about 0.03 mmol/L. [25] Use only non-heparinized sample transfer devices when using i-STAT System's aqueous control and calibration verification materials.

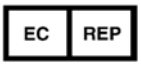
Factor	Analyte	Effect
Exposing the sample to air	iCa	Exposing the sample to air will cause an increase in pH due to loss of CO_2, which will decrease ionized calcium.
	TCO_2	Exposing the sample to air allows CO_2 to escape, which causes TCO_2 to be underestimated.
Hemodilution	Na	Hemodilution of the plasma by more than 20% associated with priming cardiopulmonary bypass pumps, plasma volume expansion or other fluid administration therapies using certain solutions may cause clinically significant error on sodium, chloride and ionized calcium results. These errors are associated with solutions that do not match the ionic characteristics of plasma. To minimize these errors when hemodiluting by more than 20%, use physiologically balanced multi-electrolyte solutions containing low-mobility anions (e.g., gluconate).
	Cl	
	iCa	
Cold temperature	K	Potassium values will increase in iced specimens.
Allowing blood to stand (without exposure to air)	K	If heparinized whole blood is allowed to stand before testing, potassium values will first decrease slightly, then increase over time.
	Glu	Glucose values will decrease in whole blood samples over time. Venous blood glucose is as much as 7 mg/dL less than capillary blood glucose as a result of tissue utilization. [26]
	TCO_2	Allowing blood samples to stand (without exposure to air) before testing causes TCO_2 to be overestimated due to metabolic processes.
Sample type	K	Serum Potassium results may be 0.1 to 0.7 mmol/L higher than Potassium results from anticoagulated samples due to the release of Potassium from platelets [1] and red blood cells during the clotting process.
Sample mixing	Hct	Samples from 1 mL syringes should not be used to determine hematocrit if testing is delayed.
Under fill or partial draw	TCO_2	The use of partial draw tubes (evacuated tubes that are adjusted to draw less than the tube volume, e.g., a 5 mL tube with enough vacuum to draw only 3 mL) is not recommended due to the potential for decreased TCO_2 values. Underfilling blood collection tubes may also cause decreased TCO_2 results. Care must be taken to eliminate "bubbling" of the sample with a pipette when filling a cartridge to avoid the loss of CO_2 in the blood.
pH dependence	Glu	The dependence of the i-STAT glucose test with respect to pH is as follows: values below pH 7.4 at 37 °C decrease results by approximately 0.9 mg/dL (0.05 mmol/L) per 0.1 pH unit. Values above pH 7.4 at 37 °C increase results by approximately 0.8 mg/dL (0.04 mmol/L) per 0.1 pH unit.
PO_2 dependence	Glu	The dependence of the i-STAT glucose test with respect to ***P***O_2 is as follows: oxygen levels of less than 20 mmHg (2.66 kPa) at 37 °C may decrease results.
Creatine	Creatinine	The normal range of creatine concentration in plasma is 0.17–0.70 mg/dL (13–53 µmol/L) in males and 0.35–0.93 mg/dL (27–71 µmol/L) in females. [12] Creatine may be elevated in patients using creatine supplements, experiencing muscle trauma or other primary or secondary myopathies, taking statins for hyperlipidemia control, or in patients with hyperthyroidism or a rare genetic defect of the creatine transporter protein.

<table>
<tr><th>Factor</th><th>Analyte</th><th>Effect</th></tr>
<tr><td>CO_2 dependence</td><td>Creatinine</td><td>The dependence of the i-STAT creatinine test with respect to carbon dioxide (CO_2) is as follows:
For creatinine results ≤ 2.0 mg/dL, no correction for $\boldsymbol{P}CO_2$ is required.
For creatinine results > 2.0 mg/dL, the following correction applies:
$creatinine_{corrected}$ = creatinine * (1+ 0.0025 * ($\boldsymbol{P}CO_2$ - 40))</td></tr>
<tr><td>Erythrocyte sedimentation</td><td>Hct</td><td>• The measurement of certain blood samples with high erythrocyte sedimentation rates (ESR) may be affected by analyzer angle. While testing blood samples, beginning 90 seconds after the cartridge is inserted, the analyzer should remain level until a result is obtained. A level surface includes running the handheld in the downloader/ recharger.
• Hematocrit results can be affected by the settling of red blood cells in the collection device. The best way to avoid the effect of settling is to test the sample immediately. If there is a delay in testing of a minute or more, the sample must be remixed thoroughly.</td></tr>
<tr><td>White Blood Cell Count (WBC)</td><td>Hct</td><td>Grossly elevated white blood cell counts may increase results.</td></tr>
<tr><td>Lipids</td><td>Hct</td><td>Abnormally high lipids may increase results. Interference from lipids will be about two thirds the size of the interference from protein.</td></tr>
<tr><td>Total Protein</td><td>Hct</td><td>Hematocrit results are affected by the level of total protein as follows:
<table>
<tr><th>Displayed Result</th><th>Total Protein (TP) < 6.5 g/dL</th><th>Total Protein (TP) > 8.0 g/dL</th></tr>
<tr><td>HCT < 40 %PCV</td><td>Hct decreased by ~1% PCV for each decrease of 1 g/dL TP</td><td>Hct increased by ~1% PCV for each increase of 1 g/dL TP</td></tr>
<tr><td>HCT > 40 %PCV</td><td>Hct decreased by ~0.75 % PCV for each decrease of 1 g/dL TP</td><td>Hct increased by ~0.75 % PCV for each increase of 1 g/dL TP</td></tr>
</table>
• Total protein levels may be low in neonatal and burn patient populations, as well as in additional clinical populations listed in Statland. [5] Total protein levels may also be decreased in patients undergoing cardiopulmonary bypass (CPB) or extracorporeal membrane oxygenation (ECMO) and with patients receiving large volumes of saline-based intravenous (IV) fluids. Care should be taken when using hematocrit results from patients with total protein levels below the adult reference range (6.5 to 8 g/dL).
• The CPB sample type can be used to correct the hematocrit result for the dilutional effect of the pump prime in cardiovascular surgery. The CPB algorithm assumes that cells and plasma are diluted equally and that the pump priming solution has no added albumin or other colloid or packed red blood cells. Since perfusion practices vary, it is recommended that each practice verify the use of the CPB sample type and the length of time in which the CPB sample type should be used during the recovery period. Note that for hematocrit values above 30% PCV, the CPB correction is ≤ 1.5% PCV; the size of the correction at this level should not impact transfusion decisions.</td></tr>
<tr><td>Sodium</td><td>Hct</td><td>The sample electrolyte concentration is used to correct the measured conductivity prior to reporting hematocrit results. Factors that affect sodium will therefore also affect hematocrit.</td></tr>
</table>

Factor	Analyte	Effect
Clinical Condition	Anion Gap	The calculated anion gap may be only slightly increased in diarrhea and renal failure, but elevated (often >25) due to an increase in organic anions in lactic acidosis, ketoacidosis (alcoholic, diabetic, starvation) and uremia, an increase in inorganic anions in uremia, an increase in anions from drugs such a salicylate and carbenicillin or toxins such as methanol and ethanol.

For BUN/Urea, endogenous ammonium ions will not affect results.

KEY TO SYMBOLS

Symbol	Definition/Use
	14 days room temperature storage at 18–30 ^{0}C.
	Use by or expiration date. The expiration date, expressed as YYYY-MM-DD, indicates the last day the product may be used.
	Manufacturer's lot number or batch code. The lot number or batch code appears adjacent to this symbol.
	Sufficient for <n> tests.
	Authorized representative for Regulatory Affairs in the European Community.
	Temperature limitations. The upper and lower limits for storage are adjacent to upper and lower arms.
	Catalog number, list number, or reference.
	Do not reuse.
	Manufacturer.
	Consult instructions for use or see System Manual for instructions.
	*In vitro* diagnostic medical device.
	Compliance to the European directive on *in vitro* diagnostic devices (98/79/EC)
	For prescription use only.

Additional Information: to obtain additional product information and technical support, refer to the Abbott company website at www.pointofcare.abbott.

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