Abbott

i-STAT CG4+ Cartridge

Intended for US only

NAME

i-STAT CG4+ Cartridge

INTENDED USE

The i-STAT CG4+ cartridge with the i-STAT 1 System is intended for use in the *in vitro* quantification of pH, partial pressure of oxygen (***P***O_2), and partial pressure of carbon dioxide (***P***CO_2) in arterial, venous, or capillary whole blood in point of care or clinical laboratory settings.

The i-STAT CG4+ cartridge with the i-STAT 1 System is intended for use in the *in vitro* quantification of lactate in arterial or venous whole blood in point of care or clinical laboratory settings.

Test	Intended Use
pH	pH, ***P***O_2, and ***P***CO_2 measurements are used in the diagnosis, monitoring, and treatment of respiratory, metabolic and acid-base disturbances.
Partial Pressure of Oxygen (***P***O_2)	
Partial Pressure of Carbon Dioxide (***P***CO_2)	
Lactate	Lactate measurements are used in (1) the diagnosis and treatment of lactic acidosis in conjunction with measurements of blood acid/base status, (2) monitoring tissue hypoxia and strenuous physical exertion, and (3) diagnosis of hyperlactatemia.

SUMMARY AND EXPLANATION / CLINICAL SIGNIFICANCE

Measured:

pH

pH is an index of the acidity or alkalinity of the blood with an arterial pH of <7.35 indicating an acidemia and >7.45 alkalemia[1].

Partial Pressure of Oxygen (*P*O_2)

PO_2 is a measurement of the tension or pressure of oxygen dissolved in blood. Low levels of *P*O_2 in whole blood, or hypoxemia, is generally characterized in three (3) ranges, mild hypoxemia (*P*O_2 in the range of 60 to 79 mmHg), moderate hypoxemia (*P*O_2 in the range of 40 to 59 mmHg), and severe hypoxemia (*P*O_2 < 40 mmHg)[2]. *P*O_2 levels can fluctuate depending on factors such as activity levels, sleep, breathing patterns, and underlying medical conditions that affect the lungs or heart. There are various mechanisms of hypoxemia such as ventilation/perfusion (V/Q) mismatch, right-to-left shunt, diffusion impairment, hypoventilation, and low inspired *P*O_2.

In mild hypoxemia, the blood oxygen levels (*P*O_2 of 60-79 mmHg/saturated O_2 (sO_2) 90 to 94%) are slightly lower than normal. Symptoms of mild hypoxia may include shortness of breath, rapid breathing, increased heart rate, fatigue and mild confusion. Mild hypoxemia can occur during activities such as strenuous exercise at high altitudes or due to mild respiratory conditions in patients with impaired lung function.

Moderate hypoxemia is characterized by a more significant decrease in blood oxygen levels (PO_2 of 40-59 mmHg/sO_2 85-89%), which can lead to more pronounced symptoms which may include severe shortness of breath, rapid breathing, increased heart rate, confusion and impaired coordination and headache. Moderate hypoxemia can occur due to various factors, including lung conditions (i.e. asthma or pneumonia), heart problems (i.e. heart failure), high altitudes, anemia or certain medications that affect breathing (i.e. sleep apnea).

Severe hypoxemia is a critical condition where in oxygen levels in the blood are dangerously low (PO_2 <40 mmHg/sO2 < 85%), leading to potentially life-threatening consequences. Symptoms of severe hypoxia may include: extreme shortness of breath, rapid and shallow breathing, weak pulse, confusion, and loss of consciousness. Severe hypoxia can result from conditions such as acute respiratory distress syndrome, severe lung infections, heart failure or carbon monoxide poisoning.

For risk stratification in critically ill patients, repeated PO_2 or oxygen saturation measurements over time in arterial whole blood are recommended.

Partial Pressure of Carbon Dioxide (PCO_2)

PCO_2 along with pH is used to assess acid-base balance. PCO_2, the respiratory component of acid-base balance, is a measure of the tension or pressure of carbon dioxide dissolved in the blood. PCO_2 represents the balance between cellular production of CO_2 and ventilatory removal of CO_2 and a change in PCO_2 indicates an alteration in this balance. Causes of primary respiratory acidosis (increase in PCO_2) are airway obstruction, sedatives and anesthetics, respiratory distress syndrome, and chronic obstructive pulmonary disease. Causes of primary respiratory alkalosis (decreased PCO_2) are hypoxia (resulting in hyperventilation) due to chronic heart failure, edema and neurologic disorders, and mechanical hyperventilation.

Lactate (Lac)

Lactate levels are generally characterized in three (3) ranges, normal (< 2.0 mmol/L), hyperlactatemia (moderate; 2.0 to 4.0 mmol/L) and lactic acidosis (high; > 4.0 mmol/L)[3]. Lactate levels can fluctuate depending on factors such as exercise, oxygen supply, and underlying medical conditions. Elevated levels of lactate are mainly found in conditions of hypoxia such as shock, hypovolemia, and left ventricular failure; also in conditions associated with diseases such as diabetes mellitus, neoplasia, and liver disease; and in conditions associated with drugs or toxins such as ethanol, methanol, or salicylates[4].

Hyperlactatemia (moderate lactate levels) is defined as a persistent, mild-to-moderate elevation (2.0-4.0 mmol/L) of blood lactate concentration. Hyperlactatemia is an indicator commonly used to detect tissue hypoperfusion, particularly in the case of sepsis[5-7], but also in trauma[8-10] and surgical[11-13] settings.

Lactic acidosis (high lactate levels > 4.0 mmol/L) is a condition in which there is an excessive accumulation of lactic acid in the blood, leading to a drop in pH levels (below 7.35)[8,10-12]. Lactic acidosis can be caused by several factors, including: hypoxia that can occur in conditions such as heart failure, shock, and respiratory failure, increased lactate production that can occur in conditions,
such as seizures, strenuous exercise, and liver disease, decreased lactate removal that can occur when the kidneys and liver are impaired and certain medication such as metformin and propofol.

For risk stratification in critically ill patients, repeated lactate measurements over time in arterial whole blood are recommended[14].

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.[15]

Measured:

pH

pH is measured by direct potentiometry. In the calculation of results for pH, concentration is related to potential through the Nernst equation.

PO_2

PO_2 is measured amperometrically. The oxygen sensor is similar to a conventional Clark electrode. Oxygen permeates through a gas permeable membrane from the blood sample into an internal electrolyte solution where it is reduced at the cathode. The oxygen reduction current is proportional to the dissolved oxygen concentration.

PCO_2

PCO_2 is measured by direct potentiometry. In the calculation of results for *P*CO_2, concentration is related to potential through the Nernst equation.

Lactate (Lac)

Lactate is measured amperometrically. The enzyme lactate oxidase, immobilized in the lactate biosensor, selectively converts lactate to pyruvate and hydrogen peroxide (H_2O_2). The liberated hydrogen peroxide is oxidized at a platinum electrode to produce a current which is proportional to the sample lactate concentration.

$$\text{L-Lactate} + O_2 \xrightarrow{\text{Lactate Oxidase}} \text{Pyruvate} + H_2O_2$$

$$H_2O_2 \xrightarrow{\text{Platinum electrode}} 2H^+ + O_2 + 2e^-$$

Temperature "Correction" Algorithm

pH, *P*O_2, and *P*CO_2 are temperature-dependent quantities and are measured at 37°C. The pH, *P*O_2, and *P*CO_2 readings at a body temperature other than 37°C can be 'corrected' by entering the patient's temperature on the chart page of the analyzer. In this case, blood gas results will be displayed at both 37°C and the patient's temperature.

pH, *P*O_2, and *P*CO_2 at the patient's temperature (T_p) are calculated as follows[16]:

$$pH(T_p) = pH - 0.0147(T_p - 37) + 0.0065(7.4 - pH)(T_p - 37)$$

$$PO_2(T_p) = PO_2 \times 10^{\frac{5.49\times10^{-11}\,PO_2^{3.88} + 0.071}{9.72\times10^{-9}\,PO_2^{3.88} + 2.30}(T_p - 37)}$$

$$PCO_2(T_p) = PCO_2 \times 10^{0.019(T_p - 37)}$$

Calculated:

HCO_3, TCO_2, and BE

- Bicarbonate (HCO_3), the most abundant buffer in the blood plasma, is an indicator of the buffering capacity of blood. Regulated primarily by the kidneys, HCO_3 is the metabolic component of acid-base balance.
- Total Carbon Dioxide (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.

  - The calculated TCO_2 provided by the i-STAT 1 System is determined from the measured and reported values of pH and $\boldsymbol{P}CO_2$ according to a simplified and standardized form of the Henderson-Hasselbalch equation[16].

- Base excess (BE) of the extracellular fluid (ECF) or standard base excess is defined as the concentration of titratable base minus the concentration of titratable acid when titrating the average ECF (plasma plus interstitial fluid) to an arterial plasma pH of 7.40 at $\boldsymbol{P}CO_2$ of 40 mmHg at 37 °C. Excess concentration of base in the average ECF remains virtually constant during acute changes in the $\boldsymbol{P}CO_2$ and reflects only the non-respiratory component of pH-disturbances.

  When a cartridge includes sensors for both pH and $\boldsymbol{P}CO_2$, HCO_3, TCO_2 and BE are calculated[16].

  $\log HCO_3 = pH + \log \boldsymbol{P}CO_2 - 7.608$
  $TCO_2 = HCO_3 + 0.03\boldsymbol{P}CO_2$
  $BE_{ecf} = HCO_3 - 24.8 + 16.2(pH-7.4)$
  $BE_b = (1 - 0.014*Hb) * [\ HCO_3 - 24.8 + (1.43 * Hb + 7.7) * (pH - 7.4)\ ]$

sO_2

- Oxygen saturation (sO_2) is the amount of oxyhemoglobin expressed as a fraction of the total amount of hemoglobin able to bind oxygen (oxyhemoglobin plus deoxyhemoglobin).
- sO_2 is calculated from measured $\boldsymbol{P}O_2$ and pH and from HCO_3 calculated from measured $\boldsymbol{P}CO_2$ and pH[17]. However, this calculation assumes normal affinity of oxygen for hemoglobin. It does not take into account erythrocyte diphosphoglycerate (2,3-DPG) concentrations which affect the oxygen dissociation curve. The calculation also does not take into account the effects of fetal hemoglobin or dysfunctional hemoglobins (carboxy-, met-, and sulfhemoglobin). Clinically significant errors can result from incorporation of such an estimated sO_2 value for oxygen saturation in further calculations, such as shunt fraction, or by assuming the value obtained is equivalent to fractional oxyhemoglobin.

$$sO_2 = 100 \frac{(X^3 + 150X)}{X^3 + 150X + 23400}$$

where $X = \boldsymbol{P}O_2 \bullet 10^{(0.48(pH-7.4)-0.0013(HCO_3-25))}$

REAGENTS

Contents

Each i-STAT CG4+ cartridge contains a reference electrode, a ground electrode, potentiometric sensors and amperometric sensors for the measurement of specific analytes. It also contains a buffered aqueous calibrant solution with known concentrations of analytes and preservatives. A list of reactive ingredients relevant for the i-STAT CG4+ cartridge is indicated below:

Sensor	Reactive Ingredient	Biological Source	Minimum Quantity
pH	Hydrogen Ion (H^+)	N/A	6.66 pH
$\boldsymbol{P}CO_2$	Carbon Dioxide (CO_2)	N/A	25.2 mmHg
Lactate	Lactate	N/A	1.8 mmol/L
	Lactate Oxidase	*Aerococcus viridans*	0.001 IU

Warnings and Precautions

- For *in vitro* diagnostic use.
- DO NOT REUSE - cartridges are intended for single-use only.
- Although the sample is contained within the cartridge, cartridges should be disposed as biohazardous waste according to local, state, and national regulatory guidelines.
- The i-STAT 1 System automatically runs a comprehensive set of quality checks of instrument and cartridge performance each time a sample is tested. This internal quality system will suppress results by generating a Quality Check Code (QCC) if the instrument or cartridge does not meet certain specifications. To minimize the probability of delivering a result with medically significant error, the internal specifications are very stringent. It is typical for the system to suppress a very small percentage of results in normal operation given the stringency of these specifications. If, however, the instrument or cartridges have been compromised, results may be persistently suppressed, and one or the other must be replaced to restore normal operating conditions. Where unavailability of results while awaiting replacement of instruments or cartridges is unacceptable, Abbott Point of Care Inc. recommends maintaining both a backup analyzer and cartridges from an alternate lot number.
- Use a puncture device that provides free-flowing blood. Inadequate blood flow may produce erroneous results.
- Improperly filling and/or closing the cartridges may result in Quality Check Codes and/or inability to obtain results.

For additional warnings and precautions about the i-STAT System refer to the i-STAT 1 System Manual located at www.globalpointofcare.abbott.

Storage Conditions

- Refrigerated at 2-8°C (35-46°F) until expiration date.
- Room temperature at 18-30°C (64-86°F): Cartridges may be stored at room temperature for the time frame indicated on the cartridge box.

INSTRUMENTS

The i-STAT CG4+ cartridge is intended for use with the i-STAT 1 analyzer.

For a detailed description of the instrument and system procedures, refer to the i-STAT 1 System Manual located at www.globalpointofcare.abbott.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Arterial, venous or capillary whole blood.
Sample Volume: 95 µL

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

Test	Syringes*	Test Timing	Evacuated Tubes	Test Timing	Capillary	Test Timing
Lactate	Without anticoagulant	Immediately	Without anticoagulant	Immediately	Not applicable	Not applicable

Test	Syringes*	Test Timing	Evacuated Tubes	Test Timing	Capillary	Test Timing
	With balanced heparin anticoagulant or lithium heparin anticoagulant (syringe must be filled to labeled capacity)† • Mix thoroughly before filling cartridge.		With lithium heparin anticoagulant (tubes must be filled to labeled capacity)† • Mix thoroughly before filling cartridge.			
pH ***P***O_2 ***P***CO_2	Without anticoagulant	3 minutes	Without anticoagulant	3 minutes	With balanced heparin anticoagulant or lithium heparin anticoagulant (tubes must be filled to labeled capacity)† Note: Care should be taken to avoid exposure of the sample to air during the collection of the capillary whole blood specimen. When the specimen is exposed to air, the concentration of the analytes is changed, and the results may not reflect the true physiological level.	3 minutes
	With balanced heparin anticoagulant or lithium heparin anticoagulant (syringe must be filled to labeled capacity) • Maintain anaerobic conditions. • Mix thoroughly before filling cartridge.	10 minutes	With lithium heparin anticoagulant (tubes must be filled to labeled capacity) • Maintain anaerobic conditions. • Mix thoroughly before filling cartridge	10 minutes		

* Do Not Use Heparin lock flush solution syringes.

† Fill blood collection devices to capacity. Underfilling will cause higher heparin to blood ratios which may affect results.
Note: Do not use blood collection or transfer devices that would introduce air into the sample when pH, *P*O_2, or *P*CO_2 are being measured.

PROCEDURE FOR CARTRIDGE TESTING

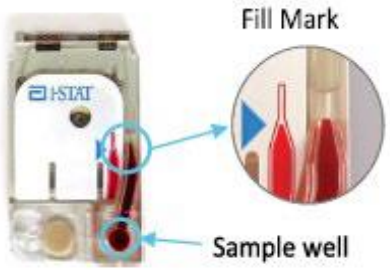
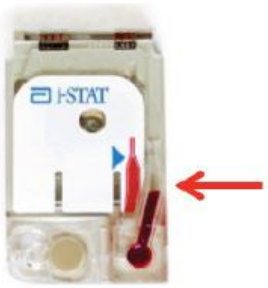
Each cartridge is sealed in a foil pouch for protection during storage--do not use if pouch has been punctured.

- A cartridge should not be removed from its protective pouch until it is at room temperature (18-30°C or 64-86°F). For best results, the cartridge and analyzer should be at room temperature.
- Since condensation on a cold cartridge may prevent proper contact with the analyzer, allow refrigerated cartridges to equilibrate at room temperature for 5 minutes for a single cartridge and 1 hour for an entire box before use.
- Use a cartridge immediately after removing it from its protective pouch. Prolonged exposure may cause a cartridge to fail a Quality Check.
- Do not return unopened, previously refrigerated cartridges to the refrigerator.
- Cartridges may be stored at room temperature for the time frame indicated on the cartridge box.

Filling and Sealing the Cartridge (after cartridge has been equilibrated and blood sample has been collected)

1. Place the cartridge on a flat surface.
2. Invert a lithium heparin blood collection tube at least 10 times. If sample was collected into a syringe, invert syringe for 5 seconds then roll the syringe between the palms (hands parallel to the ground) for 5 seconds, flip and roll for an additional 5 seconds. The blood in the hub of the syringe will not mix, therefore expelling 2 drops before filling a cartridge is desired. Note that it may be difficult to properly mix a sample in a 1.0 mL syringe.
3. Fill the cartridge immediately. Direct the hub of syringe or tip of the transfer device (capillary tube, pipette or dispensing tip) into the sample well of the cartridge.
4. Slowly dispense sample into the sample well until the sample reaches the fill mark indicated on the cartridge. Cartridge is properly filled when the sample reaches the ‘fill to’ mark and a small amount of sample is in the sample well (as displayed in the illustrations below). The sample should be continuous, no bubbles or breaks (see System Manual for details).
5. Fold the snap closure of the cartridge over the sample well.

Note: Every effort should be made to fill cartridges properly before inserting into the analyzer. The illustrations below are provided to support proper cartridge filling using representative cartridges.

Properly filled cartridge	The sample fills the sample chamber to the fill mark indicator  Full sample well, and no bubble appears in the sample pathway. 
Underfilled cartridge	The sample well is sufficiently filled, but the sample does not reach the fill mark indicator  The sample well is insufficiently filled, and the sample does not reach the fill mark indicator. 

Overfilled cartridge	The sample well is overfilled, the sample exceeds the fill mark indicator  The sample well is overfilled, there is a bubble in the sample well. 

Performing Patient Analysis

1. Press the power button to turn on the analyzer.
2. Press 2 for *i-STAT Cartridge*.
3. Follow the analyzer prompts.
4. Scan the lot number on the cartridge pouch.
5. Continue normal procedures for preparing the sample, and filling and sealing the cartridge.
6. Push the sealed cartridge into the analyzer port until it clicks into place. Wait for the test to complete.
7. Review the results.

For additional information for cartridge testing, refer to the i-STAT 1 System Manual located at www.globalpointofcare.abbott.

Analysis Time

Approximately 130–200 seconds

Quality Control

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

1. A series of automated, on-line quality measurements that monitor the sensors, fluidics and instrumentation each time a test is performed.
2. A series of automated, on-line procedural checks monitors the user each time a test is performed.
3. Liquid materials are available to be used to verify the performance of a batch of cartridges when they are first received or when storage conditions are in question.
4. Traditional quality control measurements verify the instrumentation using an independent device, which simulates the characteristics of the electrochemical sensors in a way which stresses the performance characteristics of the instrumentation.

Each laboratory should follow local, state and national regulations regarding quality control materials.

For additional information on Quality Control, refer to the i-STAT 1 System Manual located at www.globalpointofcare.abbott.

Calibration Verification

Calibration Verification is a procedure intended to verify the accuracy of results over the entire measurement range of a test. While the Calibration Verification Set contains five levels, verification of the measurement range could be accomplished using the lowest, highest and mid-levels.

For additional information on Calibration Verification, refer to the i-STAT 1 System Manual located at www.globalpointofcare.abbott.

EXPECTED VALUES

TEST	UNITS *	REPORTABLE RANGE	REFERENCE RANGE *(arterial)*	REFERENCE RANGE *(venous)*
MEASURED				
pH	pH units	6.50 – 7.80	7.35 – 7.45 [18]	7.31 – 7.41**
PO_2	mmHg	5 – 700	80 – 105 [19]***	–
	kPa	0.7 – 93.3	10.7 – 14.0 [19]***	–
PCO_2	mmHg	5 – 130	35 – 45 [18]	41 – 51[18]
	kPa	0.67 – 17.33	4.67 – 6.00	5.47 – 6.80
Lactate	mmol/L	0.30 – 20.00	0.36 – 1.25 [4]****	0.90 – 1.70 [4]****
	mg/dL	2.7 – 180.2	3.2 – 11.3 [4]****	8.1 – 15.3 [4]****
CALCULATED				
HCO_3	mmol/L (mEq/L)	1.0 – 85.0	22 – 26**	23 – 28**
TCO_2	mmol/L (mEq/L)	5 – 50	23 – 27**	24 – 29**
BE	mmol/L (mEq/L)	(-30) – (+30)	(-2) – (+3) [18]	(-2) – (+3) [18]
sO_2	%	0 – 100	95 – 98 [19]	–

***** The i-STAT 1 System can be configured with the preferred units. Not applicable for pH test.

****** Calculated from Siggard-Andersen nomogram[1].

******* The reference ranges shown are for a healthy population. Interpretation of blood gas measurements depend on the underlying condition (e.g., patient temperature, ventilation, posture and circulatory status).

******** The i-STAT limits for whole blood listed above are similar to reference ranges derived from serum or plasma measurements with standard laboratory methods.

Unit Conversion

- ***P*O_2 and *P*CO_2:** To convert ***P***O_2 and ***P***CO_2 results from mmHg to kPa, multiply the mmHg value by 0.133.
- **Lactate:** To convert a Lactate result from mmol/L to mg/dL, multiply the mmol/L value by 9.01.

The reference ranges programmed into the analyzer and 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 CG4+ cartridge are traceable to the following reference materials or methods. The i-STAT 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.

pH

pH 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 materials SRMs 186-I, 186-II, 185, and 187.

PO_2

PO_2 values assigned to the i-STAT System controls and calibration verification materials are traceable to U.S. National Institute of Standards and Technology (NIST) standard reference materials via commercially available certified specialty medical gas standards.

PCO_2

PCO_2 values assigned to the i-STAT System controls and calibration verification materials are traceable to U.S. National Institute of Standards and Technology (NIST) standard reference materials via commercially available certified specialty medical gas standards.

Lactate

Presently, no international conventional reference measurement procedure or international conventional calibrator for lactate is available. Lactate values assigned to the i-STAT System controls and calibration verification materials are traceable to i-STAT System working calibrator prepared from sodium L-lactate (Sigma-Aldrich Fluka, >99 % purity).

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

To obtain additional information and technical support, refer to the company website at www.globalpointofcare.abbott.

PERFORMANCE CHARACTERISTICS

The typical performance of the i-STAT CG4+ cartridge tests with the i-STAT 1 System are shown below.

Precision

Precision data was collected based on CLSI guideline EP05-A3[20]. Precision studies were conducted using five (5) levels of aqueous materials for pH, PO_2, PCO_2, and lactate. Duplicates of each level were tested twice a day for a minimum of 20 days.

The mean, standard deviation (SD) and coefficient of variation (CV) observed for each test and level are summarized below. This is representative data; results in individual laboratories may vary.

Test	Units	Fluid Level	N	Mean	SD	CV (%)
pH	pH units	CV L1	84	6.5701	0.00457	0.07
		CV L2	84	7.0259	0.00218	0.03
		CV L3	83	7.4532	0.00242	0.03
		CV L4	84	7.6338	0.01049	0.14
		CV L5	84	7.9653*	0.00299	0.04
PO_2	mmHg	CV L1	84	71.0	2.10	2.96
		CV L2	84	82.6	1.89	2.29
		CV L3	83	108.9	2.22	2.03
		CV L4	84	138.8	2.90	2.09
		CV L5	84	372.9	7.35	1.97
PCO_2	mmHg	CV L1	84	89.41	1.443	1.61
		CV L2	84	56.28	0.726	1.29
		CV L3	83	29.37	0.412	1.40
		CV L4	84	22.69	0.758	3.34
		CV L5	84	12.19	0.418	3.43
Lactate	mmol/L	CV L1	84	19.791	0.2035	1.03
		CV L2	84	7.874	0.0676	0.86
		CV L3	83	2.110	0.0146	0.69
		CV L4	84	0.820	0.0148	1.80
		CV L5	84	0.410	0.0142	3.47

* Results outside of the reportable range may be displayed when testing with Calibration Verification material.

Whole blood precision was evaluated using arterial, venous, and capillary[1] specimens collected with anticoagulant. The repeatability analysis was conducted using the data collected across multiple point of care sites. For each sample type, samples were grouped into subintervals of the test reportable range for analysis and the results are summarized below.

Test	Units	Sample Type	Sample Range	N	Mean	SD	CV (%)
pH	pH units	Venous Whole Blood	6.500-7.300	9	7.0265	0.00235	0.03
			>7.300-7.450	154	7.3745	0.00668	0.09
			>7.450-7.800	12	7.5355	0.00732	0.10
		Arterial Whole Blood	6.500-7.300	9	7.2229	0.00262	0.04
			>7.300-7.450	124	7.3816	0.00486	0.07
			>7.450-7.800	43	7.4763	0.00690	0.09
		Capillary Whole Blood	6.500-7.300	3	7.2477	0.01355	0.19
			>7.300-7.450	121	7.4099	0.02084	0.28
			>7.450-7.800	32	7.4781	0.02609	0.35
PO_2	mmHg	Venous Whole Blood	10-40	125	26.2	0.91	3.49
			>40-50	21	43.1	0.98	2.26
			>50-100	24	59.3	1.32	2.23
			>100-250	3	227.7	2.65	1.16
			>250-700	8	508.4	6.96	1.37
		Arterial Whole Blood	>50-100	108	73.2	1.29	1.76
			>100-250	66	135.9	2.90	2.13
			>250-700	3	381.3	8.94	2.35
		Capillary Whole Blood	10-40	15	33.8	4.30	12.74
			>40-50	34	46.0	3.84	8.35
			>50-100	112	63.4	6.04	9.52
			>100-250	5	166.4	12.98	7.80
			>250-700	8	489.6	8.53	1.74

[1] The capillary whole blood clinical precision study design involved collection of capillary blood (from either two fingersticks or a single heelstick) into two (2) anticoagulated capillary tubes, and using each tube to fill an i-STAT CG4+ cartridge.

Test	Units	Sample Type	Sample Range	N	Mean	SD	CV (%)
PCO_2	mmHg	Venous Whole Blood	5.0-35.0	23	30.17	0.379	1.26
			>35.0-50.0	119	46.48	0.639	1.38
			>50.0-62.5	31	57.05	0.687	1.20
			>62.5-130.0	10	117.05	1.650	1.41
		Arterial Whole Blood	5.0-35.0	48	33.24	0.393	1.18
			>35.0-50.0	105	44.55	0.641	1.44
			>50.0-62.5	16	61.33	1.100	1.79
			>62.5-130.0	6	77.18	1.080	1.40
		Capillary Whole Blood	5.0-35.0	47	32.31	1.736	5.37
			>35.0-50.0	105	40.00	2.258	5.64
			>50.0-62.5	3	58.35	1.967	3.37
			>62.5-130.0	1	68.20	2.263	3.32
Lactate	mmol/L	Venous Whole Blood	0.30-1.00	100	0.639	0.0127	1.99
			>1.00-5.00	81	1.549	0.0206	1.33
			>5.00-20.00	20	12.476	0.0756	0.61
		Arterial Whole Blood	0.30-1.00	55	0.653	0.0138	2.11
			>1.00-5.00	76	1.771	0.0184	1.04
			>5.00-20.00	3	8.120	0.0252	0.31

Method Comparison

Method comparison was demonstrated in a study based on CLSI guideline EP09c-ED3[21]. Heparinized arterial and venous whole blood specimens collected across multiple point of care sites were evaluated using i-STAT CG4+ cartridges on the i-STAT 1 analyzer against the comparative method. For pH and ***P***O_2, the first replicate result from the i-STAT 1 analyzer was compared to the singlicate result of the comparative method. For ***P***CO_2 and lactate, the first replicate result from the i-STAT CG4+ cartridge was compared to the mean result of the comparative method.

Two (2) capillary specimens collected from skin puncture with balanced heparin capillary tubes from each study subject across multiple point of care sites. One (1) tube was used to test in singlicate on the i-STAT CG4+ cartridge and the other tube was used to test in singlicate on the comparative method.

The arterial, venous, and capillary data were pooled and a Passing-Bablok linear regression analysis for pH, ***P***O_2, and ***P***CO_2 was performed using the singlicate result from the i-STAT CG4+ cartridges on the i-STAT 1 analyzer versus the result from the comparative method and summarized in the table below. In the method comparison table, N is the number of specimens in the data set, and r is the correlation coefficient.

Test (units)	Comparative Method		N	Slope	Intercept	r	Xmin	Xmax	Medical Decision Level	Bias at Medical Decision Level
	Arterial/ Venous	Capillary								
pH (pH units)	RAPIDPoint 500/500e	RAPIDPoint 500/500e	551	1.00	-0.01	0.98	6.559	7.745	7.30	-0.0080
									7.35	-0.0080
									7.40	-0.0080
PO_2 (mmHg)	RAPIDPoint 500/500e	RAPIDPoint 500/500e	557	1.01	-1.29	0.99	10.9	691.7	30	-0.9
									45	-0.7
									60	-0.6
PCO_2 (mmHg)	i-STAT G3+	i-STAT G3+	475	1.03	-0.30	0.99	7.4	125.8	35.0	0.67
									45.0	0.95
									50.0	1.08
									70.0	1.64

The arterial and venous data were pooled, and a Passing-Bablok linear regression analysis for Lactate was performed using the singlicate result from the i-STAT CG4+ cartridges on the i-STAT 1 analyzer versus the result from the comparative method and summarized in the table below.

Test (units)	Comparative Method	N	Slope	Intercept	r	Xmin	Xmax	Medical Decision Level	Bias at Medical Decision Level
Lactate (mmol/L)	i-STAT CG4+	345	0.97	-0.01	1.00	0.31	20.00	5.00	-0.140

The method comparison results for capillary whole blood for pH, ***P***O_2, and ***P***CO_2 are shown in the table below.

Test (units)	Comparative Method	N	Slope	Intercept	r	Xmin	Xmax
pH (pH units)	RAPIDPoint 500/500e	193	1.01	-0.08	0.97	6.607	7.709
PO_2 (mmHg)	RAPIDPoint 500/500e	192	1.08	-5.47	0.99	14.0	554.0
PCO_2 (mmHg)	i-STAT G3+	184	1.05	-0.54	0.98	8.9	125.8

The bias at the medical decision levels for native capillary whole blood specimens for pH, ***P***O_2, and ***P***CO_2 are shown in the table below.

Test (units)	N	Min	Max	Medical Decision Level	Bias	
					Estimate	95% CI
pH (pH units)	178	7.259	7.531	7.30	-0.0166	(-0.0341, 0.0007)
				7.35	-0.0104	(-0.0207, 0.0000)
				7.40	-0.0041	(-0.0095, 0.0013)
PO_2 (mmHg)	178	31	139	30	-3.3	(-6.1, -0.4)
				45	-2.1	(-3.7, -0.4)
				60	-0.9	(-2.1, 0.0)
PCO_2 (mmHg)	175	23.1	78.6	35.0	1.18	(0.48, 1.75)
				45.0	1.84	(1.04, 2.46)
				50.0	2.17	(1.15, 3.03)
				70.0	3.49	(1.40, 5.49)

Method comparisons will vary from site to site due to differences in sample handling, comparative method calibration and other site-specific variables.

Linearity

Linearity studies were performed based on guidance from CLSI EP06-Ed2[22]. The results using lithium heparin whole blood samples demonstrated linearity across the reportable range of the analytes described in the **EXPECTED VALUES** section above.

LIMITATIONS OF THE PROCEDURE

The analyte results should be assessed in conjunction with the patient's medical history, clinical examination, and other findings. If results appear inconsistent with the clinical assessment, the patient sample should be retested using another cartridge.

Interference Testing

Interference studies were based on CLSI guideline EP07 3rd edition[23]. The substances listed were evaluated in lithium heparin whole blood for relevant analytes. For those identified as an interferent the interference is described.

Substance*	Substance Concentration mmol/L	mg/dL	Test	Interference (Yes/No)	Comment
Acetaldehyde[a]	0.045 [2]	0.2	Lactate	No	
Acetaminophen	1.03 [2]	15.6	pH	No	
			$\boldsymbol{P}O_2$	No	
			$\boldsymbol{P}CO_2$	No	
			Lactate	No	
Acetyl Cysteine (N-Acetyl-Cysteine)	0.92 [24,25]	15.0	Lactate	No	
Ascorbic Acid (L-Ascorbic Acid)	0.298	5.25	Lactate	No	
Atracurium (Atracurium Besylate)[a]	0.0287	3.57	pH	No	
			$\boldsymbol{P}O_2$	No	
			$\boldsymbol{P}CO_2$	No	
β-Hydroxybutyric Acid[a]	6.0 [26]	62.46	Lactate	No	
Bilirubin	0.684	40	pH	No	
			$\boldsymbol{P}O_2$	No	
			$\boldsymbol{P}CO_2$	No	
			Lactate	No	
Bromide [a] (Lithium Bromide) [27-29]	2.5	21.7	Lactate	No	Refer to comment below.
	37.5	325.7	Lactate	Yes	Use Another Method. Decreased results >10.0 mmol/L bromide. Refer to comment below.
Calcium (Calcium Chloride)	5.0	20	pH	No	
			$\boldsymbol{P}O_2$	No	
			$\boldsymbol{P}CO_2$	No	
Dopamine (Dopamine Hydrochloride)	4.06 µmol/L	0.0621	Lactate	No	
Ethanol	130	600	pH	No	
			$\boldsymbol{P}O_2$	No	
			$\boldsymbol{P}CO_2$	No	
Formaldehyde [a]	0.133 [2]	0.399	Lactate	No	
Glycolic Acid [a]	10.0 [2]	76.05	Lactate	Yes	Increased results >0.8 mmol/L glycolic acid. Refer to comment below.
Hemoglobin	10 g/L	1000	pH	No	
			$\boldsymbol{P}O_2$	No	
			$\boldsymbol{P}CO_2$	No	
			Lactate	No	
Hydroxyurea	0.405	3.08	Lactate	No	
Ibuprofen	1.06	21.9	pH	No	
			$\boldsymbol{P}O_2$	No	
			$\boldsymbol{P}CO_2$	No	
Intralipid 20%	N/A	2684	pH	No	

Substance*	Substance Concentration		Test	Interference (Yes/No)	Comment
	mmol/L	mg/dL			
			PO_2	No	
			PCO_2	No	
		3579	Lactate	No	
Morphine (Morphine Sodium Salt)	0.0273	0.78	pH	No	
			PO_2	No	
			PCO_2	No	
Potassium (Potassium Chloride)	8	59.6	pH	No	
			PO_2	No	
			PCO_2	No	
Pyruvate (Lithium Pyruvate)	0.570	5	Lactate	No	
Salicylate (Lithium Salicylate)	0.207	2.86	Lactate	No	
Sodium (Sodium Chloride)	170	993.48	pH	No	
			PO_2	No	
			PCO_2	No	
Thiocyanate (Lithium Thiocyanate)	0.898 [2,30]	5.22	Lactate	No	
Thiopental	1.66	40.2	pH	No	
			PO_2	No	
			PCO_2	No	
Triglyceride	16.94	1500	pH	No	
			PO_2	No	
			PCO_2	No	
			Lactate	No	
Uric Acid	1.4	23.5	Lactate	No	

[a] The test concentration for this substance is not included in CLSI guideline EP37 1st edition[31].
*The compound tested to evaluate the interfering substance is presented in parenthesis.

This is representative data and results may vary from study to study due to matrix effects. Viscosity, surface tension, turbidity, ionic strength and pH are common causes of matrix effects. It is possible that interfering substances other than those tested may be encountered. The degree of interference at concentrations other than those listed might not be predictable.

- Relevant comments regarding interference of Bromide and Glycolic acid are noted below:
  - Bromide at 2.5 mmol/L is the peak plasma concentration associated with halothane anesthesia, in which bromide is released. Bromide may result in an increased rate of star outs (***).
  - Glycolic acid is a product of ethylene glycol metabolism. Unexpected increased lactate concentrations caused by glycolic acid may be a clue to the possibility of ethylene glycol ingestion as the cause of an otherwise unknown high anion gap metabolic acidosis [32,33]. In a study of 35 patients who had ingested ethylene glycol, initial glycolic acid concentrations of 0 to 38 mmol/L corresponded to ethylene glycol levels of 0.97 – 130.6 mmol/L[33].

Factors Affecting Results

Note: The calculated values are affected when the factor affecting results impacts the analyte used in the calculations. See calculated value equations in **TEST PRINCIPLES** section.

Factor	Test	Effect
Exposing the sample to air or partially filling a blood collection	***P***O_2	Exposure of the sample to air will cause an increase in ***P***O_2 when values are below 150 mmHg and a decrease in ***P***O_2 when values are above 150 mmHg (approximate ***P***O_2 of room air).
	pH	Exposing the sample to air allows CO_2 to escape which causes ***P***CO_2

Factor	Test	Effect
device	***P***CO_2	to decrease and pH to increase and HCO_3 and TCO_2 to be under-estimated.
Venous stasis	pH	Venous stasis (prolonged tourniquet application) and forearm exercise may decrease pH due to localized production of lactic acid.
Hemodilution	pH	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, ionized calcium and pH 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).
Cold temperature	***P***O_2	Do not ice samples before testing - ***P***O_2 results may be falsely elevated in cold samples. Do not use a cold cartridge - ***P***O_2 results may be falsely decreased if the cartridge is cold.
Sample collection	***P***O_2	Use a puncture device that provides free-flowing blood. Inadequate blood flow may produce erroneous results.
	pH	
	PCO_2	
	Lactate	
	Lactate	Special collection procedures are necessary to prevent changes in lactate both during and after the blood is drawn. For steady state lactate concentrations, patients should be at rest for 2 hours and fasting. Venous samples should be obtained without the use of a tourniquet or immediately after the tourniquet is applied. Both venous and arterial samples may be collected into heparinized syringes.
Allowing blood to stand (without exposure to air)	pH	pH decreases on standing anaerobically at room temperature at a rate of 0.03 pH units per hour[1].
	PO_2	Standing anaerobically at room temperature will decrease ***P***O_2 at a rate of 2–6 mmHg per hour[1].
	PCO_2	Allowing blood to stand (without exposure to air) before testing will increase ***P***CO_2 by approximately 4 mmHg per hour[1]. Calculated HCO_3 and TCO_2 results are over-estimated, if blood is allowed to stand (without exposure to air), due to metabolic processes.
	Lactate	Samples for lactate should be analyzed immediately after drawing as lactate increases by as much as 70% within 30 minutes at 25 °C due to glycolysis[4].
Under fill or partial draw	***P***CO_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 ***P***CO_2, HCO_3 and TCO_2 values. Underfilling blood collection tubes may also cause decreased ***P***CO_2, HCO_3 and 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.
PO_2 dependence	Lactate	The dependence of the i-STAT Lactate test with respect to ***P***O_2 is as follows: oxygen levels of less than 25 mmHg (3.33 kPa) at 37 °C may decrease results.
Method of calculation	sO_2	Calculated sO_2 values from a measured ***P***O_2 and an assumed oxyhemoglobin dissociation curve may differ significantly from the direct measurement [16].
Clinical conditions	HCO_3	Causes of primary metabolic acidosis (decrease calculated HCO_3) are ketoacidosis, lactate acidosis (hypoxia), and diarrhea. Causes of primary metabolic alkalosis (increase calculated HCO_3) are vomiting and antacid treatment.

KEY TO SYMBOLS

Symbol	Definition/Use
	2 months room temperature storage at 18-30°C
	Use by or expiration date. An expiration date expressed as YYYY-MM-DD means the last day the product can be used.
	Manufacturer's lot number or batch code. The lot number or batch will appear adjacent to this symbol.
	Sufficient for <n> tests
	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
	For prescription use only.

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

REFERENCES

1. Pruden, E. L., Siggaard-Andersen, O., and Tietz, N. W. (1994) Blood Gases and pH In *Teitz Textbook of Clinical Chemistry*, 2nd Ed. Burtis CA, Ashwood ER, eds. W.B. Saunders, Philidelphia.
2. Wu, A. H. B. (2006) *Tietz Clinical Guide to Laboratory Tests*, 4th Ed., W.B. Saunders Elsevier, St. Louis, MO
3. Rivers, E., Nguyen, B., Havstad, S., Ressler, J., Muzzin, A., Knoblich, B. *et al.* (2001) Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med.* **345**, 1368-1377
4. Sacks, D. B. (1994) Carbohydrates In *Teitz Textbook of Clinical Chemistry*, 2nd Ed. Burtis CA, Ashwood ER, eds. W.B. Saunders, Philidelphia, PA.
5. Dellinger, R. P., Levy, M. M., Carlet, J. M., Bion, J., Parker, M. M., Jaeschke, R. *et al.* (2008) Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med.* **36**, 296-327
6. Jones, A. E., and Puskarich, M. A. (2009) Sepsis-induced tissue hypoperfusion. *Crit Care Clin.* **25**, 769-779, ix
7. Shapiro, N. I., Fisher, C., Donnino, M., Cataldo, L., Tang, A., Trzeciak, S. *et al.* (2010) The feasibility and accuracy of point-of-care lactate measurement in emergency department patients with suspected infection. *J Emerg Med.* **39**, 89-94
8. Blow, O., Magliore, L., Claridge, J. A., Butler, K., and Young, J. S. (1999) The golden hour and the silver day: detection and correction of occult hypoperfusion within 24 hours improves outcome from major trauma. *J Trauma.* **47**, 964-969
9. Crowl, A. C., Young, J. S., Kahler, D. M., Claridge, J. A., Chrzanowski, D. S., and Pomphrey, M. (2000) Occult hypoperfusion is associated with increased morbidity in patients undergoing early femur fracture fixation. *J Trauma.* **48**, 260-267
10. Paladino, L., Sinert, R., Wallace, D., Anderson, T., Yadav, K., and Zehtabchi, S. (2008) The utility of base deficit and arterial lactate in differentiating major from minor injury in trauma patients with normal vital signs. *Resuscitation.* **77**, 363-368
11. Bakker, J., and de Lima, A. P. (2004) Increased blood lacate levels: an important warning signal in surgical practice. *Crit Care.* **8**, 96-98
12. Husain, F. A., Martin, M. J., Mullenix, P. S., Steele, S. R., and Elliott, D. C. (2003) Serum lactate and base deficit as predictors of mortality and morbidity. *Am J Surg.* **185**, 485-491
13. Rossi, A. F., Khan, D. M., Hannan, R., Bolivar, J., Zaidenweber, M., and Burke, R. (2005) Goal-directed medical therapy and point-of-care testing improve outcomes after congenital heart surgery. *Intensive Care Med.* **31**, 98-104
14. Godinjak, A., Jusufovic, S., Rama, A., Iglica, A., Zvizdic, F., Kukuljac, A. *et al.* (2017) Hyperlactatemia and the Importance of Repeated Lactate Measurements in Critically Ill Patients. *Med Arch.* **71**, 404-407
15. Tietz, N. W., Pruden, E. L., and Siggaard-Andersen, O. (1994) Electrolytes In *Teitz Textbook of Clinical Chemistry*, 2nd Ed. Burtis CA, Ashwood ER, eds. W.B. Saunders, Philidelphia.
16. CLSI. *Blood Gas and pH Analysis and Related Measurements*. CLSI document C46-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2001
17. Severinghaus, J. W. (1979) Simple, accurate equations for human blood O2 dissociation computations. *J Appl Physiol Respir Environ Exerc Physiol.* **46**, 599-602
18. Painter, P. C., Cope, J. Y., and Smith, J. L. (1994) "Reference Ranges, Table 41-20" In *Teitz Textbook of Clinical Chemistry*, 2nd Ed. Burtis CA, Ashwood ER, eds. W.B. Saunders, Philidelphia.
19. Statland, B. E. (1987) *Clinical Decision Levels for Lab Tests*, 2nd Ed., Medical Economics Books, Oradell, N.J.
20. CLSI. *Evaluation of Precision of Quantitative Measurement Procedures.* 3rd ed. CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014
21. CLSI. *Measurement Procedure Comparison and Bias Estimation using Patient Samples.* 3rd ed. CLSI guideline EP09c. Wayne, PA: Clinical and Laboratory Standards Institute; 2018
22. CLSI. *Evaluation of the Linearity of Quantitative Measurement Procedures*. 2nd ed. CLSI guideline EP06, Wayne, PA: Clinical and Laboratory Standards Institute; 2020.
23. CLSI. *Interference Testing in Clinical Chemistry*. 3rd ed. CLSI document EP07. Wayne, PA: Clinical and Laboratory Standards Institute; 2018
24. Ventura, P., Panini, R., Pasini, M. C., Scarpetta, G., and Salvioli, G. (1999) N -Acetyl-cysteine reduces homocysteine plasma levels after single intravenous administration by increasing thiols urinary excretion. *Pharmacol Res.* **40**, 345-350

25. Whillier, S., Raftos, J. E., Chapman, B., and Kuchel, P. W. (2009) Role of N-acetylcysteine and cystine in glutathione synthesis in human erythrocytes. *Redox Rep.* **14**, 115-124
26. Charles, R. A., Bee, Y. M., Eng, P. H., and Goh, S. Y. (2007) Point-of-care blood ketone testing: screening for diabetic ketoacidosis at the emergency department. *Singapore Med J.* **48**, 986-989
27. Hankins, D. C., and Kharasch, E. D. (1997) Determination of the halothane metabolites trifluoroacetic acid and bromide in plasma and urine by ion chromatography. *J Chromatogr B Biomed Sci Appl.* **692**, 413-418
28. Karch, S. (2008) Dissociative Anesthetics. In: *Karch's Pathology of Drug Abuse*, 4th ed. Boca Raton, FL: CRC Press
29. Morrison, J. E., Jr., and Friesen, R. H. (1990) Elevated serum bromide concentrations following repeated halothane anaesthesia in a child. *Can J Anaesth.* **37**, 801-803
30. Schulz, V. (1984) Clinical pharmacokinetics of nitroprusside, cyanide, thiosulphate and thiocyanate. *Clin Pharmacokinet.* **9**, 239-251
31. CLSI. *Supplemental Tables for Interference Testing in Clinical Chemistry*. 1st ed. CLSI supplement EP37. Wayne, PA: Clinical and Laboratory Standards Institute; 2018
32. Morgan, T. J., Clark, C., and Clague, A. (1999) Artifactual elevation of measured plasma L-lactate concentration in the presence of glycolate. *Crit Care Med.* **27**, 2177-2179
33. Porter, W. H., Crellin, M., Rutter, P. W., and Oeltgen, P. (2000) Interference by glycolic acid in the Beckman synchron method for lactate: a useful clue for unsuspected ethylene glycol intoxication. *Clin Chem.* **46**, 874-875

Abbott Point of Care Inc.
100 and 200 Abbott Park Road
Abbott Park, IL 60064 · USA

IVD

Rx ONLY