i-STAT G Cartridge

Intended for use with the i-STAT 1 Analyzer (REF 04P75-01 & 03P75-06)

NAME

i-STAT G Cartridge – REF 03P83-25

INTENDED USE

The test for glucose, as part of the i-STAT System, is intended for use in the *in vitro* quantification of glucose in arterial, venous, or capillary whole blood.

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.

SUMMARY AND EXPLANATION/CLINICAL SIGNIFICANCE

Measured:

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.

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:

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.

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

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

See below for information on factors affecting results. Certain substances, such as drugs, may affect analyte levels *in vivo*. [2] 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 (when potentiometric sensors are included in the cartridge configuration), 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 i-STAT G cartridge is shown below:

Sensor	Reactive Ingredient	Biological Source	Minimum Quantity
Glu	Glucose	N/A	7 mmol/L
	Glucose Oxidase	*Aspergillus niger*	0.002 IU

Warnings and Precautions

- For *in vitro* diagnostic use.
- Cartridges are intended for single-use only. Do not reuse.
- Refer to the i-STAT 1 System Manual for all warnings and precautions.

Storage Conditions

- Refrigerated at 2-8°C (35-46°F) until expiration date.
- Room Temperature at 18-30°C (64-86°F). Refer to the cartridge box for shelf life.

INSTRUMENTS

The i-STAT G cartridge is intended for use with the i-STAT 1 analyzer REF 04P75-01 (Model 300-G) and REF 03P75-06 (Model 300W).

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types
Arterial, venous or capillary whole blood.
Sample Volume: 65 µL

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

Analyte	Syringes	Test Timing	Evacuated Tubes	Test Timing	Capillary Tubes	Test Timing
Glucose	Without anticoagulant	3 minutes	Without anticoagulant	3 minutes	With balanced heparin anticoagulant or lithium heparin if labeled for the measurement of electrolytes	3 minutes
	With balanced heparin anticoagulant or lithium heparin anticoagulant (syringe must be filled per manufacturer's recommendation) • Remix thoroughly before filling cartridge.	30 minutes	With lithium heparin anticoagulant (tubes must be filled per manufacturer's recommendation) • Remix thoroughly before filling cartridge,	30 minutes		

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. Mix the sample thoroughly. 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 after mixing. 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. The sample should be continuous, no bubbles or breaks (see System Manual for details).
5. Fold the snap closure over the sample well.

Performing Patient Analysis

1. Press the power button to turn on the handheld.
2. Press 2 for *i-STAT Cartridge*.
3. Follow the handheld 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 handheld 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.pointofcare.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 monitors the sensors, fluidics, and instrumentation each time a test is performed.
2. A series of automated, on-line procedural checks that 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. The performance of this procedure is not a manufacturer's system instruction.

4. Traditional quality control measurements that verify the instrumentation using an independent device, which simulates the characteristics of the electrochemical sensors in a way that stresses the performance characteristics of the instrumentation.

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

Calibration Verification
Calibration Verification is a procedure intended to verify the accuracy of results over the entire measurement range of a test. The performance of this procedure is not a manufacturer's system instruction. However, it may be required by regulatory or accreditation bodies. While the Calibration Verification Set contains five levels, verification of the measurement range could be accomplished using the lowest, highest and mid-levels.

EXPECTED VALUES

TEST	UNITS *	REPORTABLE RANGE	REFERENCE RANGE [3] *(arterial)*	*(venous)*
MEASURED				
	mmol/L	1.1–38.9	3.9–5.8	
Glu	mg/dL	20–700	70–105	
	g/L	0.20–7.00	0.70–1.05	

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

Unit Conversion:

- **Glucose (Glu):** To convert mg/dL to mmol/L, multiply the mg/dL value by 0.055.

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

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 analyte in the i-STAT G cartridge is 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.

Glucose (Glu)
The i-STAT System test for glucose measures glucose amount-of-substance concentration in the plasma fraction of arterial, venous, or capillary whole blood (dimension mmol L^{-1}) for *in vitro* diagnostic use. Glucose values assigned to 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.

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

PERFORMANCE CHARACTERISTICS

The typical performance data summarized below was collected in health care facilities by health care professionals trained in the use of the i-STAT System and comparative methods.

Precision

Precision data was collected in multiple sites as follows: Duplicates of each control fluid were tested in the morning and in the afternoon on five days for a total of 20 replicates. The averaged statistics are presented below.

Test	Units	Aqueous Control	Mean	SD (Standard Deviation)	CV (%) [Coefficient of Variation (%)]
Glu	mg/dL	Level 1	41.8	0.68	1.6
		Level 3	289	2.4	0.8

Method Comparison

Method comparison data was collected using CLSI guideline EP9-A. [4]

Deming regression analysis [5] was performed on the first replicate of each sample. In the method comparison table, n is the number of specimens in the data set, Sxx and Syy refer to estimates of imprecision based on the duplicates of the comparative and the i-STAT methods respectively, Sy.x is the standard error of the estimate, and r is the correlation coefficient.*

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

* The usual warning relating to the use of regression analysis is summarized here as a reminder. For any analyte, "if the data is collected over a narrow range, the estimate of the regression parameters are relatively imprecise and may be biased. Therefore, predictions made from these estimates may be invalid" [5]. The correlation coefficient, r, can be used as a guide to assess the adequacy of the comparative method range in overcoming this problem. As a guide, the range of data can be considered adequate if r>0.975.

Glucose/Glu (mg/dL)		Beckman Coulter LX20®	Bayer 860	Dade Dimension RxL-Xpand
Venous blood samples were collected in lithium heparin Vacutainer® tubes and analyzed in duplicate on the i-STAT System. A portion of the specimen was centrifuged and the plasma portion analyzed in duplicate on comparative methods within 20 minutes of collection.	n	35	40	32
	Sxx	2.21	4.71	0.98
	Syy	0.69	0.96	0.59
	Slope	1.03	0.99	1.01
	Int't	-3.39	-1.67	-0.85
	Sy.x	0.91	0.70	1.57
	Xmin	45	58	48
	Xmax	297	167	257
	r	0.999	0.993	0.998

FACTORS AFFECTING RESULTS

The following substances were evaluated in plasma for the Glucose analyte at the test concentrations recommended in CLSI guideline EP7-A2 [6] 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 [7]	Glu	No	
Acetaminophen	1.32	Glu	Yes	Increased results
Acetaminophen (therapeutic)	0.132 [7]	Glu	No	
Acetoacetate	2.0	Glu	No	
Acetylcysteine	10.2	Glu	Yes	Decreased results.

Substance	Test Concentration (mmol/L)	Analyte	Interference (Yes/No)	Comment
Acetylcysteine (therapeutic)	0.3 [8 9]	Glu	No	
Ascorbate	0.34	Glu	No	
Bromide	37.5	Glu	Yes	Decreased results. Use another method.
Bromide (therapeutic)	2.5 [10 11 12]	Glu	Yes	Decreased results
β-Hydroxybutyrate	6.0 [13]	Glu	No	
Dopamine	0.006	Glu	No	
Formaldehyde	0.133 [7]	Glu	No	
Hydroxyurea	0.92	Glu	Yes	Increased results. Use another method.
Lactate	6.6	Glu	No	
Maltose	13.3	Glu	No	
Nithiodote (Sodium thiosulfate)	16.7 [14]	Glu	Yes	Decreased results
Pyruvate	0.31	Glu	No	
Salicylate	4.34	Glu	No	
Thiocyanate	6.9	Glu	Yes	Decreased results
Thiocyanate (therapeutic)	0.5 [7]	Glu	No	
Uric Acid	1.4	Glu	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, and Nithiodote are noted below:

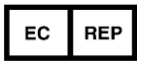
- Acetaminophen has been shown to interfere with glucose results in the i-STAT G cartridge, at a concentration prescribed by the CLSI guideline, 1.32 mmol/L, which represents a toxic concentration of acetaminophen. Acetaminophen at 0.132 mmol/L, which represents the upper end of the therapeutic concentration, has been shown not to significantly interfere with i-STAT glucose results for i-STAT G cartridge.
- Acetylcysteine has been tested at two levels: the CLSI recommended level and a concentration of 0.30 mmol/L. The latter is 3 times the peak plasma therapeutic 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. Acetylcysteine at a concentration of 10.2 mmol/L decreased i-STAT glucose results, while acetylcysteine at a concentration of 0.3 mmol/L did not significantly interfere with i-STAT glucose results.
- Bromide has been 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. Bromide tested at concentrations of 2.5 and 37.5 mmol/L decreased i-STAT glucose results.
- Hydroxyurea is a DNA synthesis inhibitor used in the treatment of various forms of cancer, sickle cell anemia, and HIV infection. This drug is used to treat malignancies including 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 patients' blood may be sustained at approximately 100 to 500 µmol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.
- 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." [14]

OTHER FACTORS AFFECTING RESULTS

Factor	Analyte	Effect
Allowing blood to stand	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. [15]
pH dependence	Glu	The dependence of the i-STAT glucose with respect to pH is as follows: Values below 7.4 at 37°C decrease results by approximately 0.9 mg/dL (0.05 mmol/L) per 0.1 pH units. Values above 7.4 at 37°C increase results by approximately 0.8 mg/dL (0.04 mmol/L) per 0.1 pH units.
PO_2 dependence	Glu	The dependence of the i-STAT glucose 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.

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 company website at www.pointofcare.abbott.

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

EC REP
EMERGO EUROPE
Prinsessegracht 20
2514 AP The Hague
The Netherlands

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