

## 12.1 General BGEM Test Card Specifications

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### 12.1.1 Indications for Use – epoc System

The **epoc Blood Analysis System** is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

The **Blood Gas Electrolyte and Metabolite (BGEM) Test Card** panel configuration includes sensors for Sodium, Potassium, ionized Calcium, pH, pCO<sub>2</sub>, pO<sub>2</sub>, Hematocrit, Lactate and Glucose.

**Sodium** and **Potassium** measurements from the epoc Blood Analysis System are used in diagnosis and treatment diseases involving electrolyte imbalance.

**Ionized Calcium** measurements from the epoc Blood Analysis System are used in diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany.

**pH, pCO<sub>2</sub>, pO<sub>2</sub> (blood gases)** measurements from the epoc Blood Analysis System are used in the diagnosis and treatment of life-threatening acid-base disturbances.

**Hematocrit** measurements from the epoc Blood Analysis System are used to distinguish normal from abnormal states of blood volume, such as anemia and erythrocytosis.

**Lactate** measurements from the epoc Blood Analysis System are used to evaluate the acid-base status and are used in the diagnosis and treatment of lactic acidosis (abnormally high acidity of the blood).

**Glucose** measurements from the epoc Blood Analysis System are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, and idiopathic hypoglycemia, and of pancreatic islet cell tumors.

## 12.2 Test Card Configuration

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The epoc Blood Gas and Electrolyte (BGE) Test Card and Blood Gas Electrolyte and Metabolytes (BGEM) Test Card include the following measured and calculated Test Results. (BGEM Test Card includes all tests on BGE Test Card):

### **epoc BGE**

Sodium Na+  
Potassium K+  
Ionized Calcium Ca++  
pH  
 $pCO_2$   
 $pO_2$   
Hematocrit Hct  
\*Total carbon dioxide cTCO<sub>2</sub>  
\*Bicarbonate cHCO<sub>3</sub><sup>-</sup>  
\*Base excess BE  
\*Oxygen saturation cSO<sub>2</sub>  
\*Hemoglobin cHgb

\* *calculated values*

### **epoc BGEM**

Sodium Na+  
Potassium K+  
Ionized Calcium Ca++  
pH  
 $pCO_2$   
 $pO_2$   
Lactate  
Glucose  
Hematocrit Hct  
\*Total carbon dioxide cTCO<sub>2</sub>  
\*Bicarbonate cHCO<sub>3</sub><sup>-</sup>  
\*Base excess BE  
\*Oxygen saturation cSO<sub>2</sub>  
\*Hemoglobin cHgb

\* *calculated values*

### 12.2.1 Storage Stability



Test Cards must be stored in their Card Pouch at Room Temperature, 15 to 30°C (59 to 86°F), at all times. Never fridge store or allow Test Cards to freeze.

### 12.2.2 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

### 12.2.3 Test Timing

The initiation of a test starts with establishing a communications link between the Host and Reader. Test Card is removed from Card Pouch. Card should be inserted immediately into Reader. During 165 second (approximate) calibration period User acquires blood sample for test. After calibration is complete Reader Indicator and epoc Host inform User that Card is ready to receive blood sample. Card is now ready for sample introduction, and sample can be introduced at any time thereafter for up to five (5) minutes after which the sample introduction period times-out, and can no longer accept sample. Approximately 30 seconds after sample introduction, Host displays analytical Test Results and card can be removed from Reader and discarded in biohazard waste.

## 12.2.4 Sample Type

Fresh whole blood from arterial, venous or capillary sources, introduced to the card using a Syringe or epoc Care-Fill™ Blood Collection Tube.

## 12.2.5 Sample Volume

>92µL, non-volumetric quantity

## 12.2.6 Sample Collection

epoc System is designed for point-of-care blood analysis. In general, it is recommended to test samples immediately after drawing a sample to obtain results that represent Patient status with greatest accuracy.

Samples without anticoagulant can always be used in this circumstance.



\*Always use ISO594-1 compliant Syringe for sample introduction. Verify that syringe to be used for sample collection is evaluated by Epocal prior to use.



The epoc System is intended to be used with fresh whole blood samples only.



Always wear protective gloves when handling blood samples.



The specimen used to fill a Test Card must be collected and handled properly to ensure that the results represent Patient's current status.



Blood samples must be collected according to the facility's policies and procedures. Always follow the specific instructions provided by other medical manufacturers when considering information in this section.



When anticoagulants are needed, use exclusively heparin for the anticoagulant.

See table below for additional options for specific tests and sample collection methods.

Test	Sample Collection Method <i>(see also references at end of Section)</i>		
	Syringes*	Evacuated Tubes	Capillary Tubes
pO <sub>2</sub>	<ul style="list-style-type: none"> <li>1 or 3ml plastic, non-iced<sup>1,2</sup></li> <li>Test in less than 30 min<sup>1,2</sup></li> </ul>	<ul style="list-style-type: none"> <li>Not recommended<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>epoc Care-Fill Capillary Tubes</li> </ul>
pH/pCO <sub>2</sub>	<ul style="list-style-type: none"> <li>1 or 3ml plastic</li> <li>Test in less than 30 min<sup>1,2</sup></li> </ul>	<ul style="list-style-type: none"> <li>Without anticoagulant</li> <li>With Li or Na heparin</li> </ul>	<ul style="list-style-type: none"> <li>epoc Care-Fill Capillary Tubes</li> </ul>
Ionized Calcium (Ca <sup>++</sup> )	<ul style="list-style-type: none"> <li>1 or 3ml plastic</li> <li>Without anticoagulant</li> <li>With Li or Na heparin only if &lt;10 IU/ml<sup>3</sup></li> <li>With balanced heparin only if &lt;70 IU/ml<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>Without anticoagulant</li> <li>With Li or Na heparin only if &lt;10 IU/ml<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>epoc Care-Fill Capillary Tubes</li> <li>Care-Fill capillary tubes contain 70 IU/ml of calcium balanced lithium heparin</li> </ul>

Hematocrit (Hct)	<ul style="list-style-type: none"> <li>• 1 or 3ml plastic</li> <li>• Immediate testing is recommended in order to avoid RBC settling. (Note: Re-suspension of RBC requires an air bubble of significant volume<sup>4</sup>)</li> </ul>	<ul style="list-style-type: none"> <li>• Without anticoagulant</li> <li>• With Li or Na heparin only (do not use EDTA)</li> </ul>	<ul style="list-style-type: none"> <li>• epoc Care-Fill Capillary Tubes</li> <li>• Immediate testing is recommended in order to avoid RBC settling</li> </ul>
All other tests	<ul style="list-style-type: none"> <li>• 1 or 3ml plastic</li> </ul>	<ul style="list-style-type: none"> <li>• Without anticoagulant</li> <li>• With Li or Na heparin</li> </ul>	<ul style="list-style-type: none"> <li>• epoc Care-Fill Capillary Tubes</li> </ul>

### 12.2.7 Analysis Time

Approximately 35 seconds after sample introduction for Blood Sample Tests.  
 Approximately 44 seconds after sample introduction for Aqueous Control Tests.

### 12.2.8 Interpretation of Results

If Patient Test Results are inconsistent with clinical assessment, a fresh Patient sample should be collected and tested on another card.

Look further in this Section for information on factors affecting results of various sensors. Certain substances, such as drugs, may affect the Test Results<sup>5-7</sup>.

### 12.2.9 Measurement Range (some values may be rounded)

Measured Parameters				
Test Name	Acronym	Units of Measure	Measurement Range	Normal Range <sup>7-9</sup>
pH	pH	pH units	6.5-8.0	7.35-7.45 arterial
				7.32-7.43 venous
Carbon Dioxide, Partial Pressure	$pCO_2$	mm Hg	5-250	35-48 arterial
				42-51 venous
		kPa	0.7-33.3	4.7-6.4 arterial
				5.4-6.8 venous
Oxygen, Partial Pressure	$pO_2$	mm Hg	5-750	83-108 arterial
		kPa	0.7-100	11.1-14.4 arterial
Sodium	Na+	mmol/L	85-180	138-146
		mEq/L		
Potassium	K+	mmol/L	1.5-12.0	3.5-4.5
		mEq/L		
Ionized Calcium	Ca <sup>++</sup>	mmol/L	0.25-4.0	1.15-1.33
		mg/dL	1.0-16.0	4.6-5.3
		mEq/L	0.5-8.0	2.3-2.7
Lactate	Lac	mmol/L	0.30 - 20.00	0.56 - 1.39
		mg/dL	2.7 - 180.2	5.0 - 12.5
		g/L	0.03 - 0.18	0.05 - 0.12
Glucose	Glu	mmol/L	1.1-38.5	4.1-5.5
		mg/dL	20-700	74-100
		g/L	0.20-7.00	0.74-1.00
Hematocrit	Hct	% PCV	10-75	38-51
		L/L	0.10-0.75	0.38-0.51

Calculated Parameters				
Hemoglobin	cHgb	g/dL	3.3-25	12-17
		mmol/L	2.0-15.5	7.4-10.6
		g/L	33-250	120-170
Actual Bicarbonate	cHCO <sub>3</sub> <sup>-</sup>	mmol/L	1-85	21-28 arterial
				22-29 venous
		mEq/L	1-85	21-28 arterial
				22-29 venous
Total Carbon Dioxide	cTCO <sub>2</sub>	mmol/L	1-85	22-29 arterial
				23-30 venous
		mEq/L	1-85	22-29 arterial
				23-30 venous
Base Excess of Extra Cellular Fluid	BE(ecf)	mmol/L	-30+30	-2+3
		mEq/L		
Base Excess of Blood	BE(b)	mmol/L	-30+30	-2+3
		mEq/L		
Oxygen Saturation	cSO <sub>2</sub>	%	0-100	94-98

### 12.2.10 References

1. CLSI C46-A2, Vol. 29, No. 8, Blood gas and pH analysis and related measurements- Approved Guideline—second edition, Wayne, Pennsylvania, USA, 2009.
2. CLSI H11-A4, Vol. 24, No. 28, Procedures for the collection of arterial blood specimens- Approved Standard, Wayne, Pennsylvania, USA, 2004.
3. CLSI C31-A2, Vol. 21, No. 10, Ionized Calcium Determinations: recollection variables, specimen, choice, collection and handling, approved guideline-second edition, Wayne, Pennsylvania, USA, 2001.
4. CLSI H7-A3, Vol. 20, No. 18, Procedures for determining packed cell volume by micro-hematocrit method- Approved Standard, Wayne, Pennsylvania, USA, 2000.
5. T.P. Moyer, L.M. Shaw, Chapters 33 of Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
6. D.S. Young, Effects of Drugs on Clinical Laboratory Tests, 3rd Edition, AACC Press, Washington DC, 1990.
7. N.W. Tietz, Clinical Guide to Laboratory Tests, 3rd Edition, W.B. Saunders Company, 1995.
8. Reference Ranges Table 56-1 in Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
9. B.E. Statland, Clinical Decision Levels for Lab Tests, Medical Economic Books, Oradell, NJ, 1987.

## 12.3 Sodium (Na<sup>+</sup>)

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### 12.3.1 General

Sodium is measured by potentiometry using an ion selective membrane electrode. The concentration of sodium ions is obtained from the measured potential using the Nernst equation. The epoc sodium measurement is an undiluted (direct) method. Values may differ from those obtained by dilutional (indirect) methods.<sup>1</sup>

### 12.3.2 Indications for Use

The sodium test, as part of the epoc Blood Analysis System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Measurement of sodium is used in diagnosis and treatment of diseases involving electrolyte imbalance.

### 12.3.3 Contents

Each Test Card incorporating a sodium test contains a sodium sensing electrode with a sodium selective membrane, a reference electrode and a calibrator fluid containing a known concentration of sodium salts.

### 12.3.4 Traceability

Values of sodium ion concentration assigned to controls and calibrator fluids are traceable to NIST standards.

### 12.3.5 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.3.6 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

### 12.3.7 Measurement Range

	Measurement Range	Normal Range <sup>2,3</sup>
Na <sup>+</sup>	85–180 mmol/L	138–146 mmol/L
	85–180 mEq/L	138–146 mEq/L

### 12.3.8 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the epoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A2<sup>4</sup> for method comparison studies, CLSI EP7-A2<sup>5</sup> for interference studies and CLSI EP5-A2<sup>12</sup> for precision studies.

## A. Precision Data

In the precision data tables below,  $SD_{WR}$  denotes within run standard deviation and  $SD_T$  denotes total standard deviation.

**In-house Precision 1:** Commercial aqueous blood gas and electrolyte controls run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 16 replicate measurements per lot per each control fluid level.

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mmol/L	113	0.9	0.8	1.2	1.1
Level 3	mmol/L	153	1.0	0.7	1.6	1.0

**In-house Precision 2:** Commercial aqueous blood gas and electrolyte controls run in a 20 day precision study<sup>12</sup> with 2 measurements each day per each control level. 4 manufactured lots, 6 different epoc Readers

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mmol/L	115	0.6	0.5	0.8	0.7
Level 3	mmol/L	153	0.7	0.5	1.0	0.6

**In-house Precision 3:** Whole blood samples run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 12 replicates per each blood sample per lot.

	Units	Mean	mean $SD_{WR}$	%CV
Blood level 1	mmol/L	147	0.9	0.6
Blood level 2	mmol/L	168	1.4	0.8

**Clinical Site Precision 1:** 10 replicates of commercial aqueous blood gas controls run by operators of the epoc system at 3 different point-of-care sites. Each precision study employed from 2 to 4 different epoc Readers.

High sodium level commercial aqueous blood gas control

	Units	Mean	$SD_{WR}$	%CV
Operator 1	mmol/L	158	1.3	0.8
Operator 2	mmol/L	155	0.8	0.5
Operator 3	mmol/L	157	1.3	0.8

Low sodium level commercial aqueous blood gas control

	Units	Mean	$SD_{WR}$	%CV
Operator 4	mmol/L	109	0.6	0.5
Operator 5	mmol/L	109	1.0	0.9
Operator 6	mmol/L	108	0.8	0.8
Operator 7	mmol/L	109	0.5	0.5

**Clinical Site Precision 2:** 10 replicates of different whole blood Patient samples run by different operators of the epoc system at different point-of-care sites. Each precision study employed 5 different epoc Readers.

	Units	Mean	$SD_{WR}$	%CV
Site 1	Operator 1 mmol/L	142	0.5	0.3
	Operator 2 mmol/L	143	1.5	1.0
Site 2	Operator 3 mmol/L	142	1.2	0.8
	Operator 4 mmol/L	143	0.8	0.6
	Operator 5 mmol/L	143	0.7	0.5
Site 3	Operator 6 mmol/L	141	0.7	0.5
	Operator 7 mmol/L	140	1.0	0.7

## B. Linearity Data

This study was performed in-house on multiple whole blood samples with sodium concentration spanning the reportable range. Linearity is reported versus an in-house standard ion selective electrode method with traceability to NIST standards.

	Test Range	Units	Slope	Intercept	R <sup>2</sup>
Na+	80-190	mmol/L	0.973	3.8	0.999

## C. Clinical Sites Method Comparison Data

Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>4</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set, Sxx and Syy are the pooled pair-wise imprecision of the comparative and epoc test methods respectively, Syx is the standard error and R is the correlation coefficient.

**Clinical Site Method Comparison 1:** In one (1) hospital study the epoc System was compared with the i-Stat 300<sup>6</sup> in the lab (2 test occasions) then in three (3) point-of-care sites:

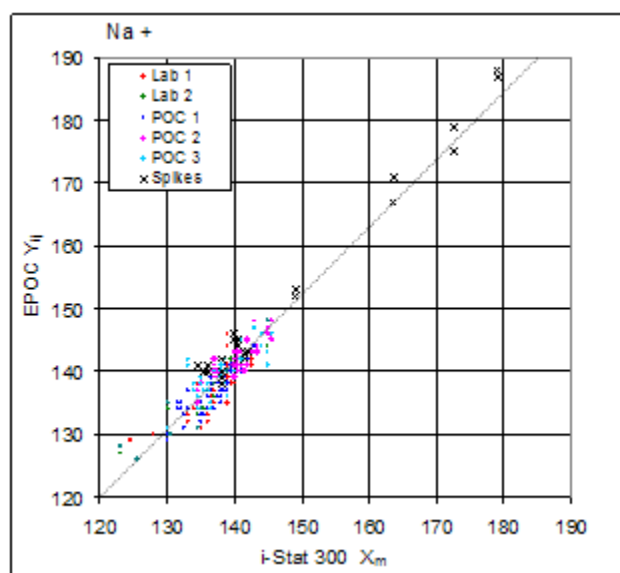
Method Comparison Summary Statistics: whole blood

X: i-Stat 300 test

Y: epoc test

Na+	Lab 1	Lab 2	POC 1	POC 2	POC 3	All	All*
N	34	24	35	27	22	142	156
Sxx	0.79	0.61	0.48	0.62	0.45	0.61	0.62
Syy	0.77	0.82	0.84	0.89	0.66	0.80	0.88
Intercept	22.2	8.4	5.3	27.9	28.9	8.8	-9.579
Slope	0.839	0.944	0.963	0.812	0.803	0.941	1.077
Syx	2.18	2.07	1.67	1.38	2.46	2.05	2.22
X min	125	123	130	135	130	123	123
X max	143	145	143	146	146	146	179
R	0.822	0.914	0.888	0.847	0.813	0.880	0.953

\*data set includes Patient samples spiked with NaCl for extended data range



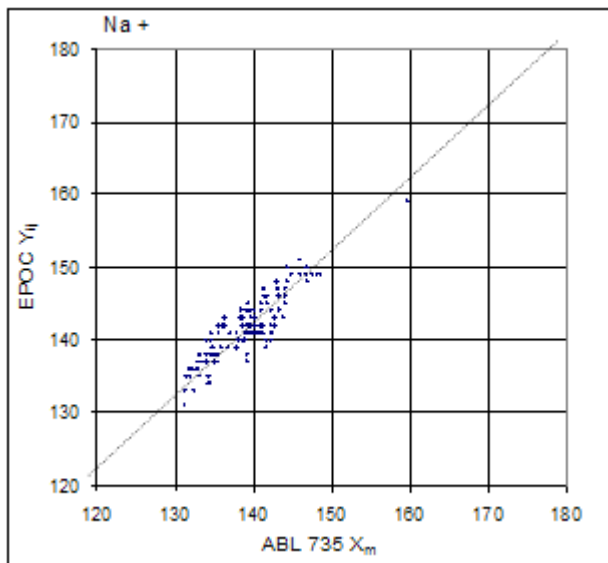
**Clinical Site Method Comparison 2:** In another hospital study the epoc System was compared with the Radiometer ABL 735<sup>7</sup> in the lab.

Method Comparison Summary Statistics: whole blood

X: Radiometer ABL 735

Y: epoc test

Na+	Lab
N	77
Sxx	0.78
Syy	0.79
Intercept	19.1
Slope	0.881
Syx	1.81
X min	131
X max	160
R	0.924



## D. Limitations and Interferences

Similar to other dry reagent methods, a decrease (increase) of total protein will increase (decrease) Na<sup>+</sup> by 1.3mM/(g/dL) versus a direct method. The epoc Na<sup>+</sup> result tracks the reading of an indirect (dilutional) method<sup>1,8,9</sup>.

Concordant with direct methods, hyperlipidemia does not affect the Na<sup>+</sup> measurement<sup>7,8</sup>. The effect of Intralipid was tested up to 5% (lipid vol)/(plasma vol) and was found to be clinically insignificant.

Whole blood specimens should not be over-diluted with liquid anti-coagulants or other solutions used in therapies as this may alter results. Refer to 12.2.6 Sample Collection

Interference testing<sup>4</sup> was performed in-house on the epoc sodium sensor. In each of these tests a whole blood specimen was aliquoted into two (2) samples. The test sample was spiked by addition of an interferent, while the control sample was spiked by the addition of the solvent of the interferent. The sodium bias between the mean of six (6) replicates on both the control sample and the test sample with added interferent was calculated.

Clinically significant interfering substances are itemized below:

- Sodium heparin will give erroneously high Na<sup>+</sup> results
- 20 mmol/L β-hydroxybutyrate will decrease Na<sup>+</sup> by 3 mmol/L
- 20 mmol/L lactate will decrease Na<sup>+</sup> by 4 mmol/L
- 16 mmol/L bromide will increase sodium by 5 mmol/L
- Samples contaminated with benzalkonium salts used as coatings for in-dwelling lines may cause significant elevation of sodium results<sup>10</sup>. For proper line-flushing procedures refer to CLSI H-11<sup>11</sup>.

The following levels of exogenous interferences were tested and found to be clinically insignificant: 447 mg/dL ethanol, 1 mmol/L sodium pentothal, 4.3 mmol/L acetyl salicylate, 0.4 mmol/L ascorbate, 4.3 mmol/L salicylate, 0.7 mmol/L iodide, 2.2 mmol/L ibuprofen, 1.66 mmol/L acetaminophen, 2 mmol/L ammonium, 4 mmol/L lithium, 10 mmol/L bromide, 3 μmol/l dobutamide, 2.5 mmol/L tolbutamide.

The following levels of endogenous interferences were tested and found to be clinically insignificant: 8 mmol/L KCl, 3mmol/L CaCl<sub>2</sub>, 10 to 120 mmHg pCO<sub>2</sub>, pH 6.9 to 7.7, +20 mmol/L bicarbonate, 10 mmol/L lactate, +20% PCV Hct, 9.1 mmol/L cholesterol, 1 mmol/L cysteine, 0.26 mmol/L bilirubin, +2 mmol/L phosphate.

## E. References

1. M.G. Scott, V.A. LeGrys and J.S. Klutts, Chapter 27 of Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
2. Reference Ranges Table 56-1 in Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
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4. CLSI. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition, CLSI document EP9-A2 (ISBN 1-56238-472-4), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
5. CLSI. Interference Testing in Clinical Chemistry; Approved Guideline, CLSI document EP7-A2 (ISBN 1-56238-480-5), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
6. i-STAT 300, Abbott Point of Care Inc., 104 Windsor Center Drive, East Windsor, NJ 08520, "i-STAT" is a registered trademark of Abbott Laboratories.
7. Radiometer ABL 735, Radiometer Medical Aps, Åkandevvej 21, DK-2700 Brønshøj, Denmark, "Radiometer" and "ABL" are registered trademarks of Radiometer Medical Aps.
8. G. Dimeski, R. J. Barnett, "Effects of Total Plasma Protein Concentration on Plasma Sodium, Potassium and Chloride Measurements by an Indirect Ion Selective Electrode Measurement System", Critical Care and Resuscitation, 7, 12-15, 2005.
9. G.B. Levy, "Determination of Sodium with Ion-Selective Electrodes", Clinical Chemistry, 27, 1435-1437, 1981.
10. CLSI. Blood Gas and pH Analysis and Related Measurements; Approved Guideline, CLSI document C46-A (ISBN 1-56238-444-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2001.
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12. CLSI. Evaluation of Precision in Clinical Chemistry Devices; Approved Guideline-Second Edition, CLSI document EP5-A2 (ISBN 1-56238-542-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.

## 12.4 Potassium (K<sup>+</sup>)

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Potassium is measured by potentiometry using an ion selective membrane electrode. The concentration of potassium ions is obtained from the measured potential using the Nernst equation. The epoc potassium measurement is an undiluted (direct) method. Values may differ from those obtained by dilutional (indirect) methods.<sup>1</sup>

### 12.4.1 Indications for Use

The potassium test, as part of the epoc Blood Analysis System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Measurement of potassium is used in diagnosis and treatment of diseases involving electrolyte imbalance.

### 12.4.2 Contents

Each Test Card incorporating a potassium test contains a potassium sensing electrode with a potassium selective membrane, a reference electrode and a calibrator fluid containing a known concentration of potassium salts.

### 12.4.3 Traceability

Values of potassium ion concentration assigned to controls and calibrator fluids are traceable to NIST standards

### 12.4.4 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.4.5 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

### 12.4.6 Measurement Range

	Measurement Range	Normal Range <sup>2</sup>
K <sup>+</sup>	1.5 – 12 mmol/L	3.5 – 4.5 mmol/L
	1.5 – 12 mEq/L	3.5 – 4.5 mEq/L

### 12.4.7 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the epoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A2<sup>3</sup> for method comparison studies, CLSI EP7-A2<sup>4</sup> for interference studies and CLSI EP5-A2<sup>9</sup> for precision studies.

## A. Precision Data

In the precision data tables below,  $SD_{WR}$  denotes within run standard deviation and  $SD_T$  denotes total standard deviation.

**In-house Precision 1:** Commercial aqueous blood gas and electrolyte controls run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 16 replicate measurements per lot per each control fluid level.

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mmol/L	2.2	0.02	0.9	0.03	1.5
Level 3	mmol/L	6.7	0.06	0.9	0.07	1.1

**In-house Precision 2:** Commercial aqueous blood gas and electrolyte controls run in a 20 day precision study<sup>9</sup> with two (2) measurements each day per each control level. four (4) manufactured lots, six (6) different epoc Readers

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mmol/L	2.2	0.02	1.0	0.03	1.2
Level 3	mmol/L	6.6	0.05	0.8	0.06	1.0

**In-house Precision 3:** Whole blood samples run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 12 replicates per each blood sample per lot.

	Units	Mean	mean $SD_{WR}$	%CV
Blood level 1	mmol/L	4.3	0.04	1.0
Blood level 2	mmol/L	6.2	0.05	0.8

**Clinical Site Precision 1:** 10 replicates of commercial aqueous blood gas controls run by operators of the epoc system at 3 different point-of-care sites. Each precision study employed from two (2) to four (4) different epoc Readers.

High potassium level commercial aqueous blood gas control.

	Units	Mean	$SD_{WR}$	%CV
Operator 1	mmol/L	6.8	0.05	0.7
Operator 2	mmol/L	6.7	0.06	0.9
Operator 3	mmol/L	6.7	0.09	1.3

Low potassium level commercial aqueous blood gas control.

	Units	Mean	$SD_{WR}$	%CV
Operator 4	mmol/L	2.0	0.01	0.6
Operator 5	mmol/L	2.0	0.03	1.6
Operator 6	mmol/L	2.0	0.05	2.5
Operator 7	mmol/L	2.0	0.02	1.0

**Clinical Site Precision 2:** 10 replicates of different whole blood Patient samples run by different operators of the epoc system at different point-of-care sites. Each precision study employed 5 different epoc Readers.

	Units	Mean	$SD_{WR}$	%CV
Site 1	Operator 1 mmol/L	4.0	0.05	1.3
	Operator 2 mmol/L	4.0	0.00	0.0
Site 2	Operator 3 mmol/L	3.7	0.00	0.0
	Operator 4 mmol/L	3.8	0.03	0.8
	Operator 5 mmol/L	3.7	0.03	0.9
Site 3	Operator 6 mmol/L	3.6	0.03	0.9
	Operator 7 mmol/L	4.1	0.05	1.2

## B. Linearity Data

This study was performed in-house on multiple whole blood samples with potassium concentration spanning the reportable range. Linearity is reported versus an in-house standard ion selective electrode method with traceability to NIST standards.

Test Range	Units	Slope	Intercept	R <sup>2</sup>
K+ 1.5-12	mmol/L	1.006	0.03	0.999

## C. Clinical Sites Method Comparison Data

Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>3</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set, Sxx and Syy are the pooled pair-wise imprecision of the comparative and epoc test methods respectively, Syx is the standard error and R is the correlation coefficient.

**Clinical Site Method Comparison 1:** In one hospital study the epoc System was compared with the i-Stat 300<sup>5</sup> in the lab (two test occasions) then in three (3) point-of-care sites.

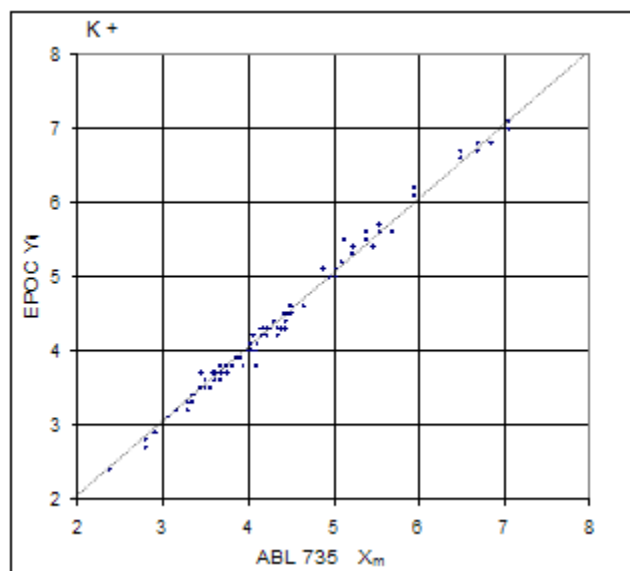
Method Comparison Summary Statistics: whole blood

X: i-Stat 300 test

Y: epoc test

K+	Lab 1	Lab 2	POC 1	POC 2	POC 3	All	All*
N	34	24	35	27	22	142	146
Sxx	0.040	0.061	0.040	0.061	0.030	0.047	0.048
Syy	0.043	0.052	0.045	0.045	0.045	0.046	0.049
Intercept	-0.164	-0.144	-0.171	-0.134	0.134	-0.044	-0.018
Slope	1.056	1.042	1.051	1.057	0.971	1.021	1.013
Syx	0.088	0.114	0.057	0.077	0.114	0.094	0.094
X min	2.5	3.0	2.6	2.9	3.3	2.5	2.5
X max	6.1	4.8	5.1	4.9	6.7	6.7	7.8
R	0.991	0.979	0.993	0.993	0.988	0.989	0.993

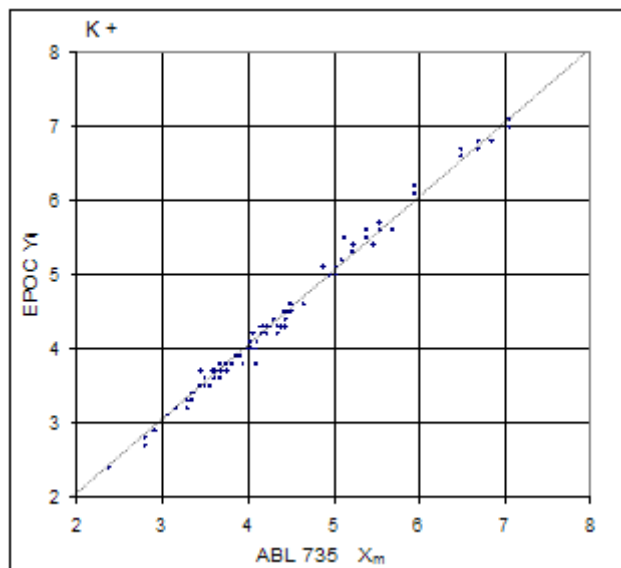
\*data set includes Patient samples spiked with KCl for extended data range



**Clinical Site Method Comparison 2:** In another hospital study the epoc was compared with the Radiometer ABL 735<sup>6</sup> in the lab.

1. Method Comparison Summary Statistics: whole blood
2. X: Radiometer ABL 735
3. Y: epoc test

K+	Lab
N	77
Sxx	0.057
Syy	0.044
Intercept	-0.073
Slope	1.026
Syx	0.090
X min	2.4
X max	7.1
R	0.996



#### D. Limitations and Interferences

Sample hemolysis will cause elevated potassium values. Improper sample collection technique may cause variation in potassium values due to hemolysis<sup>1</sup>.

Whole blood specimens should not be over-diluted with liquid anti-coagulants or other solutions used in therapies as this may alter results. Refer to 12.2.6 Sample Collection

Interference testing<sup>4</sup> was performed in-house on the epoc potassium sensor. In each of these tests a whole blood specimen was aliquoted into two samples. The test sample was spiked by addition of an interferent, while the control sample was spiked by the addition of the solvent of the interferent. The potassium bias between the mean of six (6) replicates on both the control sample and the test sample with added interferent was calculated.

Clinically significant interfering substances are itemized below:

Samples contaminated with benzalkonium salts used as coatings for in-dwelling lines may cause significant elevation of potassium results<sup>7</sup>. For proper line-flushing procedures refer to CLSI H11-A4<sup>8</sup>.

The following levels of exogenous interferences were tested and found to be clinically insignificant: 447 mg/dL ethanol, 1 mmol/L sodium pentothal, 4.3 mmol/L acetyl Salicylate, 0.4 mmol/L ascorbate, 4.3 mmol/L salicylate, 0.7 mmol/L iodide, 2.2 mmol/L ibuprofen, 1.66 mmol/L acetaminophen, 2 mmol/L ammonium, 4 mmol/L lithium, 38 mmol/L bromide, 3 µmol/l dobutamide, 2.5mmol/L tolbutamide.

The following levels of endogenous interferences were tested and found to be clinically insignificant: 20 mmol/L NaCl, 3mmol/L CaCl<sub>2</sub>, 10 to 120 mmHg pCO<sub>2</sub>, pH 6.9 to 7.7, +20 mmol/L bicarbonate, 10 mmol/L lactate, +20% PCV Hct, 3% to 11% total protein, 0.8% lipids, 9.1 mmol/L cholesterol, 20 mmol/L β-hydroxybutyrate, 1 mmol/L cysteine, 0.26 mmol/L bilirubin, +2 mmol/L phosphate.

## E. References

1. M.G. Scott, V.A. LeGrys and J.S. Klutts, Chapter 27 of Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
2. Reference Ranges Table 56-1 in Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
3. CLSI. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition, CLSI document EP9-A2 (ISBN 1-56238-472-4), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
4. CLSI. Interference Testing in Clinical Chemistry; Approved Guideline, CLSI document EP7-A2 (ISBN 1-56238-480-5), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
5. i-STAT 300, Abbott Point of Care Inc., 104 Windsor Center Drive, East Windsor, NJ 08520, "i-STAT" is a registered trademark of Abbott Laboratories.
6. Radiometer ABL 735, Radiometer Medical Aps, Åkandevvej 21, DK-2700 Brønshøj, Denmark, "Radiometer" and "ABL" are registered trademarks of Radiometer Medical Aps.
7. CLSI. Blood Gas and pH Analysis and Related Measurements; Approved Guideline, CLSI document C46-A (ISBN 1-56238-444-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2001.
8. CLSI. Procedures for the Collection of Arterial Blood Specimens; Approved Standard, CLSI document H11-A4 (ISBN 1-56238-545-3), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.
9. CLSI. Evaluation of Precision in Clinical Chemistry Devices; Approved Guideline-Second Edition, CLSI document EP5-A2 (ISBN 1-56238-542-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.

## 12.5 Ionized Calcium (Ca<sup>++</sup>)

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**NOTE** – **Ca<sup>++</sup>** and **iCa** are equivalent analyte acronyms that stand for Ionized Calcium

Ionized calcium is measured by potentiometry using an ion selective membrane electrode. The concentration of calcium ions is obtained from the measured potential using the Nernst equation.

### 12.5.1 Indications for Use

The ionized calcium test, as part of the epoc Blood Analysis System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Measurement of Ionized Calcium is used in diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany.

### 12.5.2 Contents

Each Test Card incorporating an ionized calcium test contains a calcium ion sensing electrode with a calcium selective membrane, a reference electrode and a calibrator fluid containing a known concentration of calcium salts.

### 12.5.3 Traceability

Values of calcium ion concentration assigned to controls and calibrator fluids are traceable to NIST standards

### 12.5.4 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.5.5 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

### 12.5.6 Measurement Range

	Measurement Range	Normal Range <sup>1</sup>
Ca <sup>++</sup>	0.25 – 4.00 mmol/L	1.15 – 1.33 mmol/L
	1.0 - 16.0 mg/dL	4.6 - 5.3 mg/dL
	0.5 – 8.0 mEq/L	2.3 – 2.7 mEq/L

### 12.5.7 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the epoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A2<sup>2</sup> for method comparison studies, CLSI EP7-A2<sup>3</sup> for interference studies and CLSI EP5-A2<sup>11</sup> for precision studies.

## A. Precision Data

In the precision data tables below,  $SD_{WR}$  denotes within run standard deviation and  $SD_T$  denotes total standard deviation.

**In-house Precision 1:** Commercial aqueous blood gas and electrolyte controls run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 16 replicate measurements per lot per each control fluid level.

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mmol/L	2.18	0.03	1.4	0.04	1.7
Level 3	mmol/L	0.66	0.01	1.5	0.01	1.9

**In-house Precision 2:** commercial aqueous blood gas and electrolyte controls run in a 20 day precision study<sup>11</sup> with 2 measurements each day per each control level. 4 manufactured lots, 6 different epoc Readers

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mmol/L	2.20	0.02	1.0	0.03	1.3
Level 3	mmol/L	0.67	0.01	1.3	0.01	1.8

**In-house Precision 3:** whole blood samples run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 12 replicates per each blood sample per lot.

	Units	Mean	mean $SD_{WR}$	%CV
Blood level 1	mmol/L	1.35	0.02	1.4
Blood level 2	mmol/L	2.20	0.03	1.2

**Clinical Site Precision 1:** 10 replicates of commercial aqueous blood gas controls run by operators of the epoc system at 3 different point-of-care sites. Each precision study employed from 2 to 4 different epoc Readers.

High ionized calcium level commercial aqueous blood gas control

	Units	Mean	$SD_{WR}$	%CV
Operator 1	mmol/L	0.57	0.01	1.9
Operator 2	mmol/L	0.56	0.01	0.9
Operator 3	mmol/L	0.57	0.01	1.7

Low ionized calcium level commercial aqueous blood gas control

	Units	Mean	$SD_{WR}$	%CV
Operator 4	mmol/L	1.53	0.02	1.3
Operator 5	mmol/L	1.53	0.02	1.5
Operator 6	mmol/L	1.55	0.03	1.7
Operator 7	mmol/L	1.56	0.02	1.2

**Clinical Site Precision 2:** 10 replicates of different whole blood Patient samples run by different operators of the epoc system at different point-of-care sites. Each precision study employed 5 different epoc Readers.

	Units	Mean	$SD_{WR}$	%CV
Site 1	Operator 1 mmol/L	1.20	0.02	1.5
	Operator 2 mmol/L	1.21	0.02	1.9
Site 2	Operator 3 mmol/L	1.19	0.02	1.7
	Operator 4 mmol/L	1.21	0.03	2.1
	Operator 5 mmol/L	1.20	0.02	1.6
Site 3	Operator 6 mmol/L	1.23	0.02	1.8
	Operator 7 mmol/L	1.24	0.02	1.9

## B. Linearity Data

This study was performed in-house on multiple whole blood samples with ionized calcium concentration spanning the reportable range. Linearity is reported versus an in-house standard ion selective electrode method with traceability to NIST standards.

	Test Range	Units	Slope	Intercept	R <sup>2</sup>
Ca <sup>++</sup>	0.6-3.7	mmol/L	1.017	-0.01	0.998

## C. Clinical Sites Method Comparison Data

Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>2</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set, Sxx and Syy are the pooled pair-wise imprecision of the comparative and epoc test methods respectively, Syx is the standard error and R is the correlation coefficient.

**Clinical Site Method Comparison 1:** In one hospital study the epoc was compared with the i-Stat 300<sup>4</sup> in the lab (two test occasions) then in three point-of-care sites.

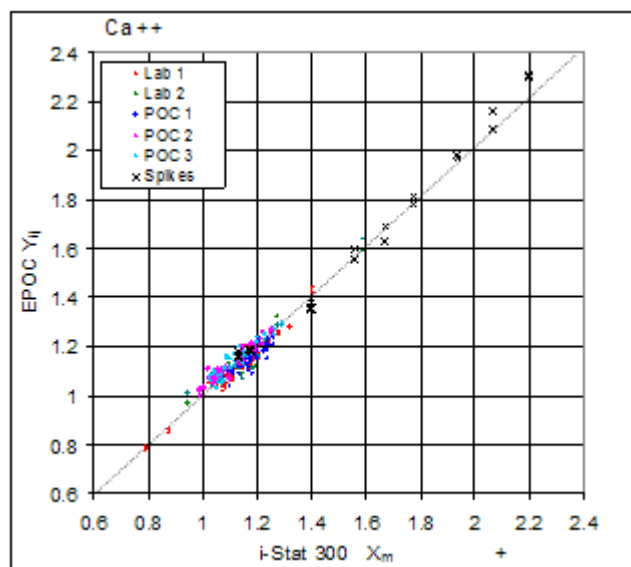
Method Comparison Summary Statistics: whole blood

X: i-Stat 300 test

Y: epoc test

Ca <sup>++</sup>	Lab 1	Lab 2	POC 1	POC 2	POC 3	All	All*
N	34	24	35	28	22	143	156
Sxx	0.016	0.019	0.014	0.017	0.015	0.016	0.016
Syy	0.011	0.014	0.017	0.014	0.015	0.014	0.015
Intercept	0.003	0.050	0.157	0.106	0.103	0.102	-0.026
Slope	0.980	0.953	0.851	0.925	0.923	0.908	1.021
Syx	0.025	0.033	0.020	0.016	0.024	0.029	0.031
X min	0.8	0.9	1.1	1.0	1.0	0.8	0.80
X max	1.4	1.6	1.3	1.3	1.3	1.6	2.20
R	0.974	0.961	0.891	0.978	0.939	0.943	0.985

\*data set includes Patient samples spiked with CaCl<sub>2</sub> for extended data range



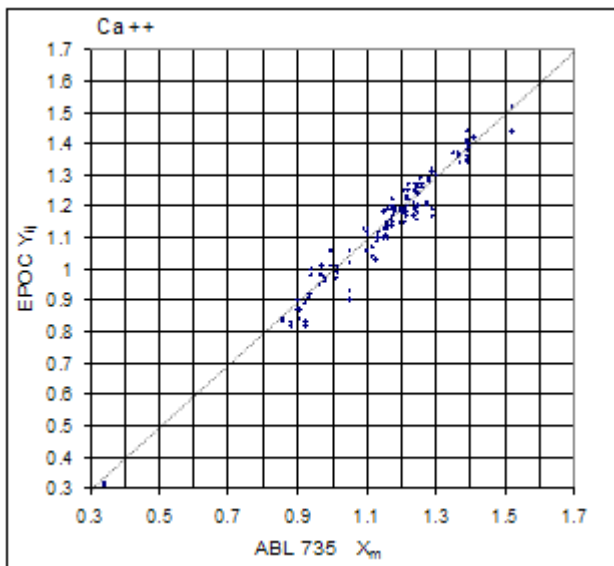
**Clinical Site Method Comparison 2:** In another hospital study the epoc was compared with the Radiometer ABL 735<sup>5</sup> in the lab.

Method Comparison Summary Statistics: whole blood

X: Radiometer ABL 735

Y: epoc test

Ca++	Lab
N	77
Sxx	0.023
Syy	0.016
Intercept	-0.045
Slope	1.025
Syx	0.040
X min	0.34
X max	1.52
R	0.981



#### D. Limitations and Interferences

Specimen choice, collection technique, anti-coagulant type and level as well as sample handling will affect the concentration of ionized calcium<sup>6</sup>.

Exposure of the sample to air will affect pH,  $p\text{CO}_2$ ,  $p\text{O}_2$  and ionized calcium results due to the sample equilibration with the gas levels in the air, with pH affected by the  $p\text{CO}_2$  change<sup>7</sup> and ionized calcium affected by the pH change<sup>8</sup>. Air contains less than 1 mmHg  $p\text{CO}_2$  and about 150-180 mmHg  $p\text{O}_2$ . Do not introduce air bubbles into a collection device. If present, air bubbles should be removed immediately after collection.

Whole blood specimens should not be over-diluted with liquid anti-coagulants or other solutions used in therapies as this may alter results. Refer to 12.2.6 Sample Collection

Interference testing<sup>3</sup> was performed in-house on the ionized calcium sensor. In each of these tests a whole blood specimen was aliquoted into two samples. The test sample was spiked by addition of interferent, while the control sample was spiked by the addition of the solvent of the interferent. The ionized calcium bias between the mean of six replicates on both the control sample and the test sample with added interferent was calculated.

Clinically significant interfering substances are itemized below:

20 mmol/L  $\beta$ -hydroxybutyrate will decrease  $\text{Ca}^{++}$  by 0.038 mmol/L

10 mmol/L lactate will decrease  $\text{Ca}^{++}$  by 0.04 mmol/L

4.3 mmol/L salicylate or acetyl salicylate will decrease  $\text{Ca}^{++}$  by 0.06 mmol/L

10 mmol/L bromide will increase  $\text{Ca}^{++}$  by 0.05 mmol/L

Samples contaminated with benzalkonium salts used as coatings for in-dwelling lines may cause significant elevation of ionized calcium results<sup>9</sup>. For proper line-flushing procedures refer to CLSI H-11<sup>10</sup>.

Highly heparinized samples will decrease the  $i\text{Ca}^{6}$ ; balanced heparin or low heparin collection tubes/syringes are recommended.

The following levels of exogenous interferences were tested and found to be clinically insignificant: 447 mg/dL ethanol, 1 mmol/L sodium pentothal, 0.4 mmol/L ascorbate, 1 mmol/L iodide, 2.2 mmol/L ibuprofen, 1.66 mmol/L acetaminophen, 2 mmol/L ammonium, 4 mmol/L lithium, 3 µmol/L dobutamide, 2.5mmol/L tolbutamide.

The following levels of endogenous interferences were tested and found to be clinically insignificant: 20 mmol/L NaCl, 8 mmol/L KCl, 10 to 120 mmHg  $p\text{CO}_2$ , pH 6.9 to 7.7, +20 mmol/L bicarbonate, 7 mmol/L lactate, +20% PCV Hct, 0.8% lipids, 9.1 mmol/L cholesterol, 1 mmol/L cysteine, 0.26 mmol/L bilirubin, +2 mmol/L phosphate.

## E. References

1. Reference Ranges Table 56-1 in Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
2. CLSI. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition, CLSI document EP9-A2 (ISBN 1-56238-472-4), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
3. CLSI. Interference Testing in Clinical Chemistry; Approved Guideline, CLSI document EP7-A2 (ISBN 1-56238-480-5), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
4. i-STAT 300, Abbott Point of Care Inc., 104 Windsor Center Drive, East Windsor, NJ 08520, "i-STAT" is a registered trademark of Abbott Laboratories.
5. Radiometer ABL 735, Radiometer Medical Aps, Åkandevvej 21, DK-2700 Brønshøj, Denmark, "Radiometer" and "ABL" are registered trademarks of Radiometer Medical Aps.
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11. CLSI. Evaluation of Precision in Clinical Chemistry Devices; Approved Guideline-Second Edition, CLSI document EP5-A2 (ISBN 1-56238-542-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.

## 12.6 Hematocrit (Hct) and Calculated Hemoglobin (cHgb)

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### 12.6.1 Measured values

Hematocrit is measured by ac conductometry using two (2) gold electrodes. The conductance of the blood sample in the fluidic path between the two (2) electrodes, after correction for variable plasma conductivity through the measurement of sodium concentration, is inversely proportional to the hematocrit value.

### 12.6.2 Calculated Values

Hemoglobin concentration is calculated from the measured hematocrit according to the relation<sup>1,2</sup>

$$\text{cHgb (g/dL)} = \text{Hct (decimal fraction)} \times 34$$

The relation above assumes a normal Mean Corpuscular Hemoglobin Concentration, MCHC of 34%<sup>1,2</sup>.

### 12.6.3 Indications for Use

The Hct test, as part of the epoc Blood Analysis System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Measurement of Hct distinguishes normal from abnormal states of blood volume, such as anemia and erythrocytosis.

### 12.6.4 Contents

Each Test Card incorporating a Hct test contains two (2) gold sensing electrodes and a calibrator fluid containing a known concentration of dissolved electrolytes with a known conductivity.

### 12.6.5 Traceability

Hematocrit values assigned to controls and calibrator fluids are traceable to the standard method for measuring packed cell volume by the microhematocrit method – applicable standard CLSI H7-A3<sup>3</sup>

### 12.6.6 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.6.7 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

## 12.6.8 Measurement Range

	Measurement Range	Normal Range <sup>4</sup>
Hct	10 – 75 %	38 – 51 %
	0.10 – 0.75	0.38 – 0.51 L/L
cHgb	3.3 – 25 g/dL	12 – 17 g/dL
	2.0 – 15.5 mmol/L	7.4 – 10.6 mmol/L
	33 – 250 g/L	120 – 170 g/L

## 12.6.9 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the epoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A2<sup>5</sup> for method comparison studies, CLSI EP7-A2<sup>6</sup> for interference studies and CLSI EP5-A2<sup>9</sup> for precision studies.

### A. Precision Data

In the precision data tables below,  $SD_{WR}$  denotes within run standard deviation and  $SD_T$  denotes total standard deviation.

**In-house Precision 1:** commercial hematocrit controls run in a 20 day precision study<sup>9</sup> with 2 measurements each day per each control level. 4 manufactured lots, 6 different epoc Readers

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	%PCV	25.3	0.4	1.5	0.4	1.6
Level 3	%PCV	46.1	0.7	1.5	0.7	1.5

**In-house Precision 2:** whole blood samples run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 12 replicates per each blood sample per lot.

	Units	Mean	mean $SD_{WR}$	%CV
Blood level 1	%PCV	44.0	0.7	1.6
Blood level 2	%PCV	22.0	0.7	3.0

**Clinical Site Precision:** 10 replicates of whole blood Patient samples run by different operators of the epoc system at different point-of-care sites. Each precision study employed 5 different epoc Readers.

		Units	Mean	$SD_{WR}$	%CV
Site 1	Operator 1	%PCV	40	0.6	1.4
	Operator 2	%PCV	40	0.5	1.3
Site 2	Operator 3	%PCV	39	0.6	1.6
	Operator 4	%PCV	41	0.5	1.2
Site 3	Operator 5	%PCV	40	0.6	1.4
	Operator 6	%PCV	40	0.8	2.0
	Operator 7	%PCV	38	0.7	1.9

## B. Linearity Data

This study was performed in-house on multiple whole blood samples with hematocrit level spanning the reportable range. Linearity is reported versus an in-house standard spun hematocrit method.

	Test Range	Units	Slope	Intercept	R <sup>2</sup>
Hct	0-75	% PCV	1.005	-0.58	0.999

## C. Clinical Sites Method Comparison Data

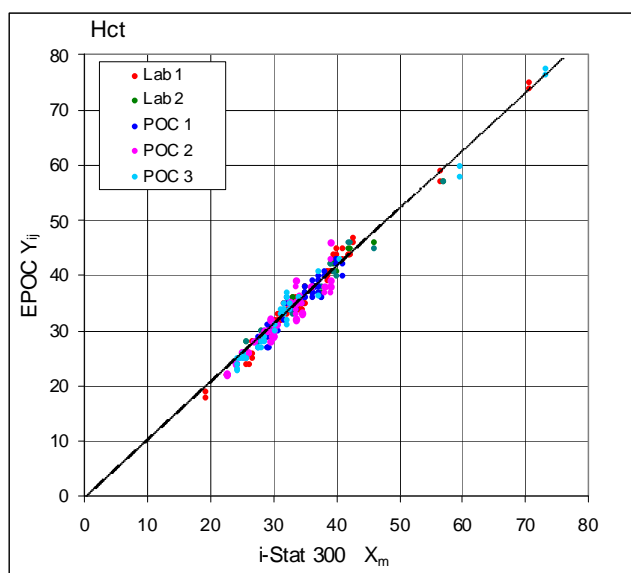
Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>5</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set, Sxx and Syy are the pooled pair-wise imprecision of the comparative and epoc test methods respectively, Syx is the standard error and R is the correlation coefficient.

**Clinical Site Method Comparison 1:** In one hospital study the epoc System was compared with the i-Stat 300<sup>7</sup> in the lab (two test occasions) then in three (3) point-of-care sites.

Method Comparison Summary Statistics: whole blood

1. X: i-Stat 300 test
2. Y: epoc test

Hct	Lab 1	Lab 2	POC 1	POC 2	POC 3	All
N	34	23	35	28	22	142
Sxx	0.49	0.66	0.46	0.67	0.69	0.58
Syy	0.69	0.42	0.65	0.57	0.80	0.64
Intercept	-1.5	1.3	0.0	-0.4	-0.4	-1.1
Slope	1.086	1.006	1.034	1.027	1.051	1.066
Syx	1.28	1.17	1.05	1.48	1.82	1.36
X min	19	24	28	23	24	19
X max	73	57	41	39	60	73
R	0.995	0.990	0.964	0.955	0.976	0.987

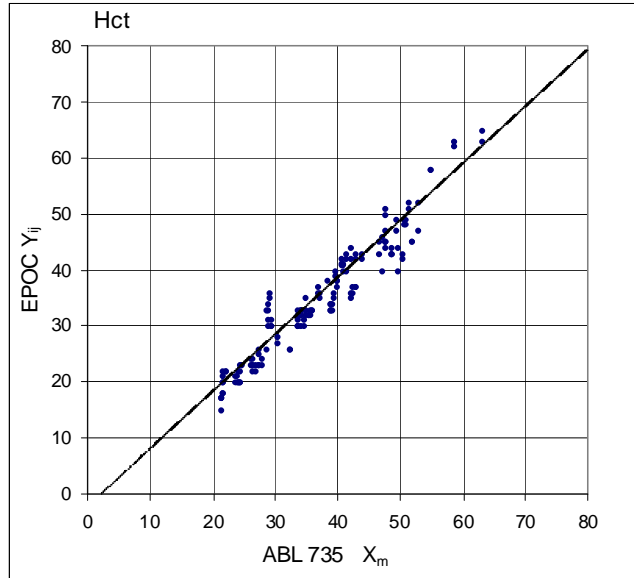


**Clinical Site Method Comparison 2:** In another hospital study the epoc was compared with the Radiometer ABL 735<sup>8</sup> in the lab. (The ABL 735 hematocrit value is calculated from the measured hemoglobin.)

Method Comparison Summary Statistics: whole blood

1. X: Radiometer ABL 735
2. Y: epoc test

Hct	Lab
N	77
Sxx	1.42
Syy	1.16
Intercept	-2.3
Slope	1.006
Syx	2.84
X min	21
X max	63
R	0.964



## D. Limitations and Interferences

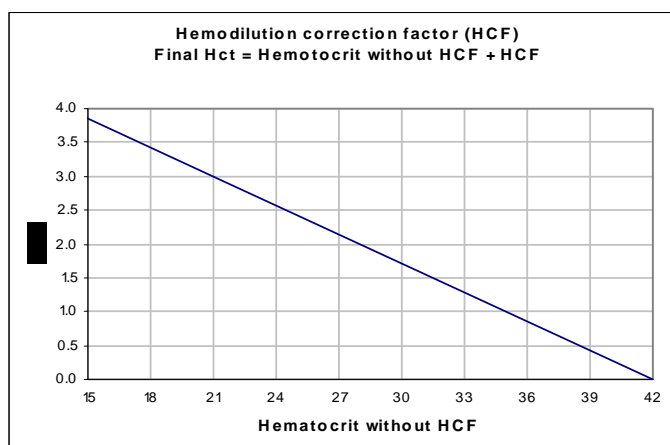
Blood samples must be well mixed in order to obtain accurate hematocrit results. The best way to ensure this is to test the sample immediately after collection. For samples where testing delays of greater than one minute occur, cells should be thoroughly re-mixed by rolling the sample between the hands for several rotations in both directions. *Note* – Thin diameter collection devices (for example, 1cc syringes or epoc Care-Fill™ Capillary Tubes) may be difficult to re-mix. Therefore, it is recommended that testing from these devices not be delayed. Refer to 12.2.6 Sample Collection

Interference testing<sup>6</sup> was performed in-house on the epoc hematocrit sensor. In each of these tests a whole blood specimen was aliquoted into two samples. The test sample was spiked by addition of interferent, while the control sample was spiked by the addition of the solvent of the interferent. The hematocrit bias between the mean of six replicates on both the control sample and the test sample with added interferent was calculated.

Clinically significant interfering substances are itemized below:

- Total protein content will affect the hematocrit results as follows: an increase (decrease) of 1 g/dL of total protein will increase (decrease) the hematocrit value by approximately 1% PCV. Total protein levels vary with the clinical populations<sup>4</sup>. Low total protein values may be found in neonates, burned Patients, Patients receiving large volumes of IV fluids and Patients undergoing cardiopulmonary bypass (CPB) and extra-corporeal membrane oxygenation (ECMO).

For the case of hemodilution, the user should activate the **hemodilution correction factor** or “HCF” in the epoc Host (see sections 6 and 7 for details). The HCF corrects hematocrit for low protein in blood samples known to be diluted with fluids that do not contain protein. There is no HCF applied for Hct over 42%. The differences between no HCF and HCF algorithm are illustrated in the figure to the right.



It is recommended that each practice verify the use of the HCF algorithm as well as the time interval that the HCF should be selected during the recovery period.

- A significant increase in white blood cell count may increase the hematocrit result.
- Abnormally high lipids may increase hematocrit results.

The following levels of exogenous interferences were tested and found to be clinically insignificant: 447 mg/dL ethanol, 1 mmol/L sodium pentothal, 4.3 mmol/L acetyl salicylate, 0.4 mmol/L ascorbate, 4.3 mmol/L salicylate, 1 mmol/L iodide, 2.2 mmol/L ibuprofen, 4 mmol/L lithium, 19 mmol/L bromide.

The following levels of endogenous interferences were tested and found to be clinically insignificant: 0.8% lipids, 9.1 mmol/L cholesterol, 20 mmol/L β-hydroxybutyrate, 1 mmol/L cysteine, 0.26 mmol/L bilirubin, +2 mmol/L phosphate.

## E. References

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5. CLSI. *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition*, CLSI document EP9-A2 (ISBN 1-56238-472-4), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
6. CLSI. *Interference Testing in Clinical Chemistry; Approved Guideline*, CLSI document EP7-A2 (ISBN 1-56238-480-5), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
7. i-STAT 300, Abbott Point of Care Inc., 104 Windsor Center Drive, East Windsor, NJ 08520, "i-STAT" is a registered trademark of Abbott Laboratories.
8. Radiometer ABL 735, Radiometer Medical Aps, Åkandevvej 21, DK-2700 Brønshøj, Denmark, "Radiometer" and "ABL" are registered trademarks of Radiometer Medical Aps.
9. CLSI. *Evaluation of Precision in Clinical Chemistry Devices; Approved Guideline-Second Edition*, CLSI document EP5-A2 (ISBN 1-56238-542-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.

## 12.7 pH

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pH is measured by potentiometry using an pH selective membrane electrode. The concentration of hydrogen ions is obtained from the measured potential using the Nernst equation.

### 12.7.1 Indications for Use

The pH test, as part of the epoc Blood Analysis System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Measurement of pH,  $pCO_2$ ,  $pO_2$  (blood gases) is used in the diagnosis and treatment of life-threatening acid-base disturbances.

### 12.7.2 Contents

Each Test Card incorporating a pH test contains a hydrogen ion sensing electrode with a hydrogen ion selective membrane, a reference electrode and a calibrator fluid containing a known concentration of pH buffer salts.

### 12.7.3 Traceability

Values of pH assigned to controls and calibrator fluids are traceable to NIST standards

### 12.7.4 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.7.5 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

### 12.7.6 Measurement Range

	Measurement Range	Normal Range <sup>1</sup>
pH	6.5 – 8.0	7.35 – 7.45 arterial 7.32 – 7.43 venous

### 12.7.7 Temperature Correction

pH is a temperature dependent quantity, measured at 37°C on the epoc System. The pH value can be corrected to the Patient's temperature. Patient temperature is entered on the Test Information Page of the Reader Tab on the epoc Host (see epoc System Operation section of System Manual).

The pH at the Patient's temperature (T) is calculated as follows<sup>2</sup>

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

## 12.7.8 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the ePoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A2<sup>3</sup> for method comparison studies, CLSI EP7-A2<sup>4</sup> for interference studies and CLSI EP5-A2<sup>10</sup> for precision studies.

### A. Precision Data

In the precision data tables below,  $SD_{WR}$  denotes within run standard deviation and  $SD_T$  denotes total standard deviation.

**In-house Precision 1:** commercial aqueous blood gas and electrolyte controls run on 20 sequential manufactured lots using at least 8 different ePoc Readers, with 16 replicate measurements per lot per each control fluid level.

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	pH units	6.992	0.007	0.10	0.010	0.15
Level 3	pH units	7.673	0.007	0.09	0.011	0.14

**In-house Precision 2:** commercial aqueous blood gas and electrolyte controls run in a 20 day precision study<sup>10</sup> with 2 measurements each day per each control level. 4 manufactured lots, 6 different ePoc Readers

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	pH units	6.986	0.006	0.09	0.008	0.11
Level 3	pH units	7.676	0.005	0.07	0.006	0.08

**In-house Precision 3:** whole blood samples run on 20 sequential manufactured lots using at least 8 different ePoc Readers, with 12 replicates per each blood sample per lot.

	Units	Mean	mean $SD_{WR}$	%CV
Blood level 1	pH units	7.200	0.007	0.09
Blood level 2	pH units	7.700	0.009	0.12

**Clinical Site Precision 1:** 10 replicates of commercial aqueous blood gas controls run by operators of the ePoc system at 3 different point-of-care sites. Each precision study employed from 2 to 4 different ePoc Readers.

High pH level commercial aqueous blood gas control

	Units	Mean	$SD_{WR}$	%CV
Operator 1	pH units	7.679	0.004	0.05
Operator 2	pH units	7.672	0.005	0.07
Operator 3	pH units	7.685	0.009	0.12

Low pH level commercial aqueous blood gas control

	Units	Mean	$SD_{WR}$	%CV
Operator 4	pH units	7.101	0.005	0.07
Operator 5	pH units	7.094	0.006	0.08
Operator 6	pH units	7.088	0.013	0.18
Operator 7	pH units	7.079	0.006	0.08

**Clinical Site Precision 2:** 10 replicates of different whole blood Patient samples run by different operators of the epoc system at different point-of-care sites. Each precision study employed 5 different epoc Readers.

	Units	Mean	SD <sub>WR</sub>	%CV
Site 1	Operator 1 pH units	7.365	0.006	0.08
	Operator 2 pH units	7.368	0.005	0.07
Site 2	Operator 3 pH units	7.322	0.005	0.07
	Operator 4 pH units	7.335	0.006	0.08
	Operator 5 pH units	7.303	0.009	0.12
Site 3	Operator 6 pH units	7.266	0.006	0.08
	Operator 7 pH units	7.381	0.004	0.05

## B. Linearity Data

This study was performed in-house on multiple whole blood samples with pH values spanning the reportable range. Linearity is reported versus an in-house standard pH electrode method with traceability to NIST standards.

Test Range	Units	Slope	Intercept	R <sup>2</sup>
pH 6.4-7.9	pH units	1.021	-0.15	0.998

## C. Clinical Sites Method Comparison Data

Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>3</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set, Sxx and Syy are the pooled pair-wise imprecision of the comparative and epoc test methods respectively, Syx is the standard error and R is the correlation coefficient.

**Clinical Site Method Comparison 1:** In one hospital study the epoc was compared with the i-Stat 300<sup>6</sup> in the lab (two test occasions) then in three point-of-care sites.

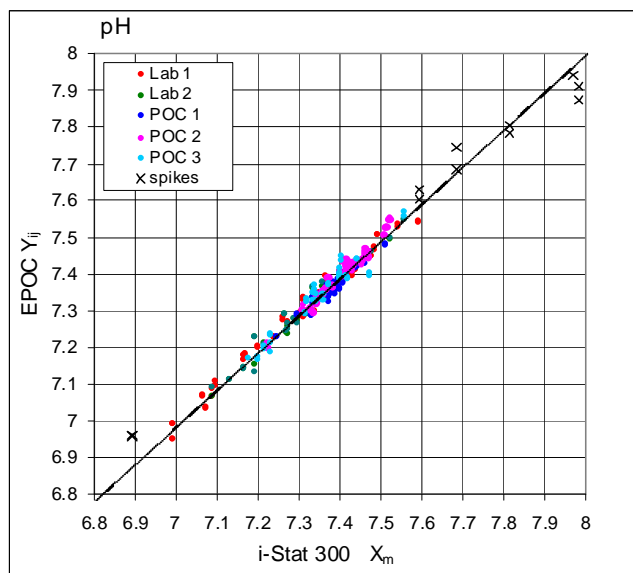
Method Comparison Summary Statistics: whole blood

X: i-Stat 300 test

Y: epoc test

pH	Lab 1	Lab 2	POC 1	POC 2	POC 3	All	All*
N	34	24	35	27	22	142	149
Sxx	0.016	0.012	0.010	0.010	0.015	0.013	0.014
Syy	0.005	0.006	0.006	0.006	0.008	0.006	0.007
Intercept	0.152	0.006	0.448	-0.772	-0.367	0.029	0.251
Slope	0.978	0.999	0.938	1.104	1.050	0.995	0.966
Syx	0.019	0.021	0.013	0.015	0.024	0.018	0.020
X min	6.991	7.085	7.243	7.223	7.174	6.991	6.770
X max	7.592	7.557	7.507	7.522	7.557	7.592	7.982
R	0.993	0.985	0.961	0.981	0.985	0.987	0.991

\*data set includes Patient samples spiked with NaOH for extended data range



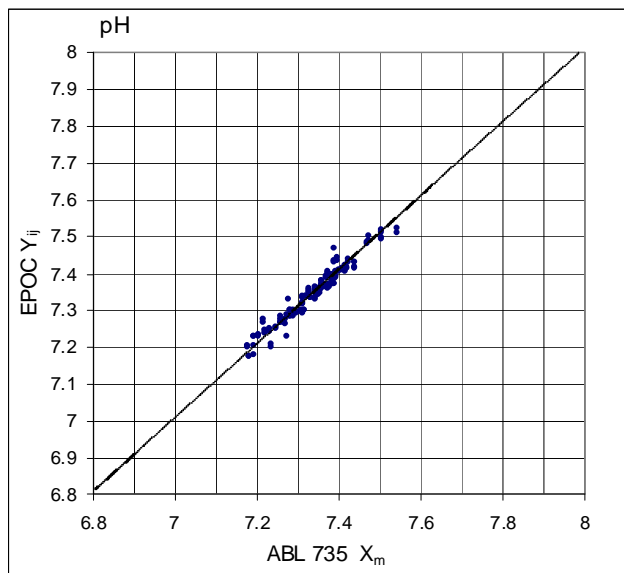
**Clinical Site Method Comparison 2:** In another hospital study the epoc was compared with the Radiometer ABL 735<sup>7</sup> in the lab.

Method Comparison Summary Statistics: whole blood

X: Radiometer ABL 735

Y: epoc test

pH	Lab
N	77
Sxx	0.011
Syy	0.010
Intercept	0.366
Slope	0.952
Syx	0.017
X min	7.175
X max	7.542
R	0.975



#### D. Limitations and Interferences

Exposure of the sample to air will affect pH,  $p\text{CO}_2$ ,  $p\text{O}_2$  and ionized calcium results due to the sample equilibration with the gas levels in the air, with pH affected by the  $p\text{CO}_2$  change<sup>9</sup> and ionized calcium affected by the pH change<sup>8</sup>. Air contains less than 1 mmHg  $p\text{CO}_2$  and about 150-180 mmHg  $p\text{O}_2$ . Do not introduce air bubbles into a collection device. If present, air bubbles should be removed immediately after collection.

Whole blood specimens should not be over-diluted with liquid anti-coagulants or other solutions used in therapies as this may alter results. Refer to 12.2.6 Sample Collection

Interference testing<sup>4</sup> was performed in-house on the epoc pH sensor. In each of these tests a whole blood specimen was aliquoted into two samples. The test sample was spiked by addition of interferent, while the control sample was spiked by the addition of the solvent of the interferent. The pH bias between the mean of six replicates on both the control sample and the test sample with added interferent was calculated.

Clinically significant interfering substances are itemized below:

Samples contaminated with benzalkonium salts used as coatings for in-dwelling lines may cause lower pH results<sup>2</sup>. For proper line-flushing procedures refer to CLSI H11-A4<sup>5</sup>.

The following levels of exogenous interferences were tested and found to be clinically insignificant: 447 mg/dL ethanol, 1 mmol/L sodium pentothal, 4.3 mmol/L acetyl salicylate, 0.4 mmol/L ascorbate, 4.3 mmol/L salicylate, 1 mmol/L iodide, 2.2 mmol/L ibuprofen, 1.66 mmol/L acetaminophen, 2 mmol/L ammonium, 4 mmol/L lithium, 35 mmol/L bromide.

The following levels of endogenous interferences were tested and found to be clinically insignificant: 20 mmol/L NaCl, 8 mmol/L KCl, 3 mmol/L CaCl<sub>2</sub>, 10 to 120 mmHg  $p\text{CO}_2$ , pH 6.9 to 7.7, +20 mmol/L bicarbonate, 10 mmol/L lactate, +20% PCV Hct, 3% to 11% total protein, 0.8% lipids, 9.1 mmol/L cholesterol, 20 mmol/L  $\beta$ -hydroxybutyrate, 1 mmol/L cysteine, 0.26 mmol/L bilirubin, +2 mmol/L phosphate.

## E. References

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2. CLSI. Blood Gas and pH Analysis and Related Measurements; Approved Guideline, CLSI document C46-A (ISBN 1-56238-444-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2001.
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4. CLSI. Interference Testing in Clinical Chemistry; Approved Guideline, CLSI document EP7-A2 (ISBN 1-56238-480-5), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
5. CLSI. Procedures for the Collection of Arterial Blood Specimens; Approved Standard, CLSI document H11-A4 (ISBN 1-56238-545-3), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.
6. i-STAT 300, Abbott Point of Care Inc., 104 Windsor Center Drive, East Windsor, NJ 08520, "i-STAT" is a registered trademark of Abbott Laboratories.
7. Radiometer ABL 735, Radiometer Medical Aps, Åkandevvej 21, DK-2700 Brønshøj, Denmark, "Radiometer" and "ABL" are registered trademarks of Radiometer Medical Aps.
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## 12.8 $p\text{CO}_2$ and Calculated Values: $\text{cHCO}_3^-$ , $\text{cTCO}_2$ and BE

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### 12.8.1 Measured values

$p\text{CO}_2$  is measured by potentiometry using a membrane covered pH sensing electrode<sup>9,10</sup>. The electrode voltage is proportional to the dissolved carbon dioxide concentration through the Nernst equation.

### 12.8.2 Calculated Values<sup>1</sup>

**NOTE** – alternate analyte acronyms for  $\text{cHCO}_3^-$  are  $\text{HCO}_3^-$ -act or  $\text{HCO}_3^-$

Calculated bicarbonate:  $\text{LOG cHCO}_3^- = \text{pH} + \text{LOG } p\text{CO}_2 - 7.608$

Calculated  $\text{TCO}_2$ :  $\text{cTCO}_2 = \text{cHCO}_3^- + 0.0307p\text{CO}_2$

Base Excess (extra cellular fluid):  $\text{BE(ecf)} = \text{cHCO}_3^- - 24.8 + 16.2(\text{pH} - 7.4)$

Base Excess (blood):  $\text{BE(b)} = (1 - 0.014\text{cHgb}) * (\text{cHCO}_3^- - 24.8 + (1.43 * \text{cHgb} + 7.7) * (\text{pH} - 7.4))$

Applicable standards: CLSI C46-A<sup>1</sup>.

### 12.8.3 Indications for Use

The  $p\text{CO}_2$  test, as part of the epoc Blood Analysis System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Measurement of pH,  $p\text{CO}_2$ ,  $p\text{O}_2$  (blood gases) is used in the diagnosis and treatment of life-threatening acid-base disturbances.

### 12.8.4 Contents

Each Test Card incorporating a  $p\text{CO}_2$  test contains a pH sensing electrode overlaid with a bicarbonate containing membrane, a carbon dioxide permeable membrane, a reference electrode and a calibrator fluid containing a known concentration of dissolved carbon dioxide.

### 12.8.5 Traceability

Dissolved carbon dioxide concentration values assigned to controls and calibrator fluids are traceable to NIST standards via commercially available certified medical gas standards.

### 12.8.6 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.8.7 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

## 12.8.8 Measurement Range

	Measurement Range	Normal Range <sup>2</sup>	
		Arterial	Venous
$p\text{CO}_2$	5 – 250 mm Hg	35 – 48 mm Hg	41 – 51 mm Hg
	0.7 – 33.3 kPa	4.7 – 6.4 kPa	5.4 – 6.8 kPa
$\text{cHCO}_3^-$	1 – 85 mmol/L	21 – 28 mmol/L	22 – 29 mmol/L
	1 – 85 mEq/L	21 – 28 mEq/L	22 – 29 mEq/L
$\text{cTCO}_2$	1 – 85 mmol/L	22 – 29 mmol/L	23 – 30 mmol/L
	1 – 85 mEq/L	22 – 29 mEq/L	23 – 30 mEq/L
BE	-30 – 30 mmol/L	-2 – +3 mmol/L	-2 – +3 mmol/L
	-30 – 30 mEq/L	-2 – +3 mEq/L	-2 – +3 mEq/L

## 12.8.9 Temperature Correction

$p\text{CO}_2$  is a temperature dependent quantity, measured at 37°C on the epoc System. The  $p\text{CO}_2$  value can be corrected to the Patient's temperature. Patient temperature is entered on the Test Information Page of the Reader Tab on the epoc Host (see epoc System Operation section of System Manual).

The  $p\text{CO}_2$  at the Patient's temperature (T) is calculated as follows<sup>1</sup>

$$p\text{CO}_2 (T) = p\text{CO}_2 \times 10^{0.019(T - 37)}$$

## 12.8.10 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the epoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A2<sup>4</sup> for method comparison studies, CLSI EP7-A2<sup>7</sup> for interference studies and CLSI EP5-A2<sup>11</sup> for precision studies.

### A. Precision Data

In the precision data tables below,  $SD_{WR}$  denotes within run standard deviation and  $SD_T$  denotes total standard deviation.

**In-house Precision 1:** commercial aqueous blood gas and electrolyte controls run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 16 replicate measurements per lot per each control fluid level.

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mm Hg	86.2	1.9	2.2	2.4	2.8
Level 3	mm Hg	24.1	0.5	2.1	0.7	3.0

**In-house Precision 2:** commercial aqueous blood gas and electrolyte controls run in a 20 day precision study<sup>11</sup> with 2 measurements each day per each control level. 4 manufactured lots, 6 different epoc Readers

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mm Hg	80.6	1.9	2.4	2.4	2.9
Level 3	mm Hg	22.5	0.4	1.6	0.6	2.5

**In-house Precision 3:** whole blood samples run on 20 sequential manufactured lots using at least eight (8) different epoc Readers, with 12 replicates per each blood sample per lot.

	Units	Mean	mean $SD_{WR}$	%CV
Blood level 1	mm Hg	65.0	1.5	2.3
Blood level 2	mm Hg	90.0	2.9	3.2

**Clinical Site Precision 1:** 10 replicates of commercial aqueous blood gas controls run by operators of the epoc system at three (3) different point-of-care sites. Each precision study employed from two (2) to four (4) different epoc Readers.

Low  $pCO_2$  level commercial aqueous blood gas control

	Units	Mean	$SD_{WR}$	%CV
Operator 1	mm Hg	21.2	0.4	1.9
Operator 2	mm Hg	21.2	0.5	2.3
Operator 3	mm Hg	20.5	1.1	5.2

High  $pCO_2$  level commercial aqueous blood gas control

	Units	Mean	$SD_{WR}$	%CV
Operator 4	mm Hg	69.0	1.2	1.7
Operator 5	mm Hg	70.2	1.2	1.7
Operator 6	mm Hg	68.2	1.3	1.8
Operator 7	mm Hg	67.2	1.3	1.9

**Clinical Site Precision 2:** 10 replicates of different whole blood Patient samples run by different operators of the epoc system at different point-of-care sites. Each precision study employed 5 different epoc Readers.

		Units	Mean	$SD_{WR}$	%CV
Site 1	Operator 1	mm Hg	52.3	2.0	3.8
	Operator 2	mm Hg	49.9	0.9	1.9
Site 2	Operator 3	mm Hg	56.9	0.9	1.5
	Operator 4	mm Hg	55.4	1.4	2.5
	Operator 5	mm Hg	58.9	1.1	1.9
Site 3	Operator 6	mm Hg	61.7	1.8	2.9
	Operator 7	mm Hg	41.5	0.9	2.1

## B. Linearity Data

This study was performed in-house on multiple whole blood samples with  $pCO_2$  values spanning the reportable range. Linearity is reported versus an in-house standard blood gas method with traceability to NIST standards.

	Test Range	Units	Slope	Intercept	$R^2$
$pCO_2$	10-230	mm Hg	1.058	-3.6	0.998

## C. Clinical Sites Method Comparison Data

Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>4</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set,  $S_{xx}$  and  $S_{yy}$  are the pooled pair-wise imprecision of the comparative and epoc test methods respectively,  $S_{yx}$  is the standard error and R is the correlation coefficient.

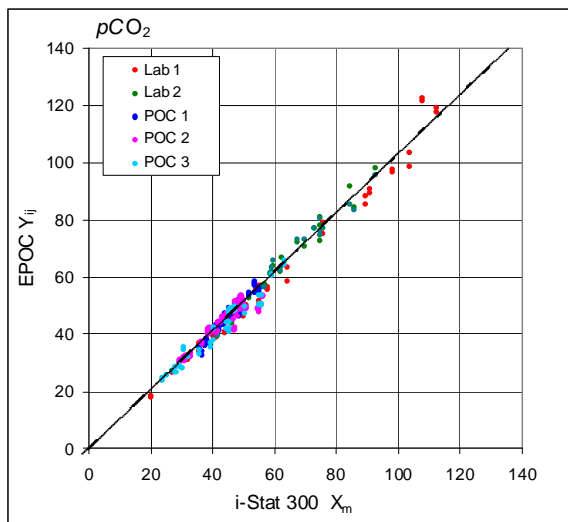
**Clinical Site Method Comparison 1:** In one hospital study the epoc was compared with the i-Stat 300<sup>5</sup> in the lab (two test occasions) then in three (3) point-of-care sites.

Method Comparison Summary Statistics: whole blood

X: i-Stat 300 test

Y: epoc test

pCO <sub>2</sub>	Lab 1	Lab 2	POC 1	POC 2	POC 3	All
N	34	24	35	28	22	143
Sxx	1.4	2.1	0.6	1.5	1.7	1.5
Syy	1.3	1.3	0.6	1.1	1.2	1.1
Intercept	-2.0	-1.2	-6.1	5.0	1.0	-0.9
Slope	1.048	1.055	1.167	0.911	0.983	1.041
Syx	3.1	2.3	1.6	2.3	2.4	2.4
X min	19.7	26.7	35.6	29.1	23.6	19.7
X max	112.2	92.5	54.4	55.6	63.0	112.2
R	0.993	0.991	0.967	0.949	0.978	0.990



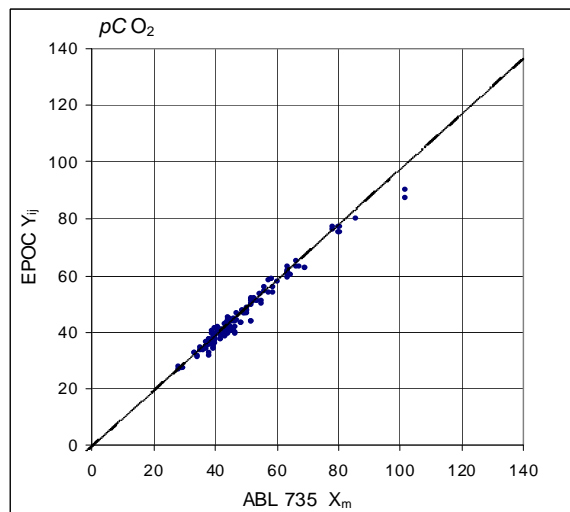
**Clinical Site Method Comparison 2:** In another hospital study the epoc was compared with the Radiometer ABL 735<sup>6</sup> in the lab.

Method Comparison Summary Statistics: whole blood

X: Radiometer ABL 735

Y: epoc test

pCO <sub>2</sub>	Lab
N	77
Sxx	1.5
Syy	0.8
Intercept	1.6
Slope	0.924
Syx	1.97
X min	27.6
X max	101.5
R	0.987



## D. Limitations and Interferences

Exposure of the sample to air will affect pH,  $p\text{CO}_2$ ,  $p\text{O}_2$  and ionized calcium results due to the sample equilibration with the gas levels in the air, with pH affected by the  $p\text{CO}_2$  change<sup>3</sup> and ionized calcium affected by the pH change<sup>8</sup>. Air contains less than 1 mmHg  $p\text{CO}_2$  and about 150-180 mmHg  $p\text{O}_2$ . Do not introduce air bubbles into a collection device. If present, air bubbles should be removed immediately after collection.

Whole blood specimens should not be over-diluted with liquid anti-coagulants or other solutions used in therapies as this may alter results. Refer to 12.2.6 Sample Collection

Interference testing<sup>7</sup> was performed in-house on the epoc  $p\text{CO}_2$  sensor. In each of these tests a whole blood specimen was aliquoted into two samples. The test sample was spiked by addition of interferent, while the control sample was spiked by the addition of the solvent of the interferent. The  $p\text{CO}_2$  bias between the mean of six replicates on both the control sample and the test sample with added interferent was calculated.

Clinically significant interfering substances are itemized below:

Bromide will increase the  $p\text{CO}_2$  by 0.19 mmHg/mM bromide

The following levels of exogenous interferences were tested and found to be clinically insignificant: 447 mg/dL ethanol, 1 mmol/L sodium pentothal, 4.3 mmol/L acetyl salicylate, 0.4 mmol/L ascorbate, 4.3 mmol/L salicylate, 2.2 mmol/L ibuprofen, 1.66 mmol/L acetaminophen, 2 mmol/L ammonium, 4 mmol/L lithium, 0.4 mmol/L iodide, 25 mmol/L bromide.

The following levels of endogenous interferences were tested and found to be clinically insignificant: 20 mmol/L NaCl, 8 mmol/L KCl, 3 mmol/L  $\text{CaCl}_2$ , pH 6.9 to 7.7, +20 mmol/L bicarbonate, 10 mmol/L lactate, +20% PCV Hct, 3% to 11% total protein, 0.8% lipids, 9.1 mmol/L cholesterol, 20 mmol/L  $\beta$ -hydroxybutyrate, 1 mmol/L cysteine, 0.26 mmol/L bilirubin, +2 mmol/L phosphate.

## E. References

1. CLSI. Blood Gas and pH Analysis and Related Measurements; Approved Guideline, CLSI document C46-A (ISBN 1-56238-444-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2001.
2. Reference Ranges Table 56-1 in Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
3. M.G. Scott, V.A. LeGrys and J.S. Klutts, Chapter 27 of Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
4. CLSI. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition, CLSI document EP9-A2 (ISBN 1-56238-472-4), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
5. i-STAT 300, Abbott Point of Care Inc., 104 Windsor Center Drive, East Windsor, NJ 08520, "i-STAT" is a registered trademark of Abbott Laboratories.
6. Radiometer ABL 735, Radiometer Medical Aps, Åkandevvej 21, DK-2700 Brønshøj, Denmark, "Radiometer" and "ABL" are registered trademarks of Radiometer Medical Aps.
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## 12.9 $pO_2$ and Calculated Oxygen Saturation: $cSO_2$

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### 12.9.1 Measured values

$pO_2$  is measured by amperometry using a membrane covered oxygen sensing cathode electrode. The oxygen reduction current is proportional to the dissolved oxygen concentration<sup>10</sup>

### 12.9.2 Calculated Values<sup>1</sup>

**NOTE** – alternate analyte acronym for  $cSO_2$  is **O2SAT**

$$cSO_2 = 100(X^3 + 150X) / (X^3 + 150X + 23400)$$

$$X = pO_2 * 10^{(0.48(pH-7.4)-0.0013(cHCO_3-25))}$$

Because oxygen saturation also depends on the level of carbon monoxide and 2,3 diphosphoglycerate in the blood, as well as the effects of dysfunctional hemoglobins (carboxy-, met- and sulfhemoglobin), the above equation does not account for variations in these values, the oxygen saturation that is reported should only be used as an estimate of the actual value<sup>2, 3</sup>. Clinically significant errors can result from incorporation of such an estimated value for oxygen saturation in further calculations, such as shunt fraction, or by assuming the value obtained is equivalent with fractional oxyhemoglobin.

Oxygen saturation is a useful predictor of the amount of oxygen that is available for tissue perfusion. Some causes for decreased values of  $cSO_2$  include low  $pO_2$  or impaired ability of hemoglobin to carry oxygen.

### 12.9.3 Indications for Use

The  $pO_2$  test, as part of the epoc Blood Analysis System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Measurement of pH,  $pCO_2$ ,  $pO_2$  (blood gases) is used in the diagnosis and treatment of life-threatening acid-base disturbances.

### 12.9.4 Contents

Each Test Card incorporating a  $pO_2$  test contains a sensing electrode with a oxygen permeable membrane, a reference electrode, a counter electrode and a calibrator fluid containing a known concentration of dissolved oxygen.

### 12.9.5 Traceability

Dissolved oxygen concentration values assigned to controls and calibrator fluids are traceable to NIST standards via commercially available certified medical gas standards.

### 12.9.6 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.9.7 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

## 12.9.8 Measurement Range

	Measurement Range	Normal Range <sup>4</sup> Arterial
$pO_2$	5 - 750 mm Hg 0.7 - 100 kPa	83 - 108 mm Hg 11.1 - 14.4 kPa
$cSO_2$	0 - 100 %	94 - 98 %

## 12.9.9 Temperature Correction

$pO_2$  is a temperature dependent quantity, measured at 37°C on the epoc System. The  $pO_2$  value can be corrected to the Patient's temperature. Patient temperature is entered on the Test Information Page of the Reader Tab on the epoc Host (see epoc System Operation section of System Manual).

The  $pO_2$  at the Patient's temperature (T) is calculated as follows<sup>2</sup>

$$pO_2(T) = pO_2 \times 10^{\frac{5.49 \times 10^{-11} pO_2^{3.88} + 0.071}{9.71 \times 10^{-9} pO_2^{3.88} + 2.30} (T-37)}$$

## 12.9.10 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the epoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A2<sup>5</sup> for method comparison studies, CLSI EP7-A2<sup>6</sup> for interference studies and CLSI EP5-A2<sup>11</sup> for precision studies.

### A. Precision Data

In the precision data tables below,  $SD_{WR}$  denotes within run standard deviation and  $SD_T$  denotes total standard deviation.

**In-house Precision 1:** commercial aqueous blood gas and electrolyte controls run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 16 replicate measurements per lot per each control fluid level.

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mm Hg	74.9	2.4	3.1	2.8	3.8
Level 3	mm Hg	140.1	2.4	1.7	2.8	2.0

**In-house Precision 2:** commercial aqueous blood gas and electrolyte controls run in a 20 day precision study<sup>11</sup> with 2 measurements each day per each control level. 4 manufactured lots, 6 different epoc Readers

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 1	mm Hg	78.4	1.9	2.5	2.6	3.3
Level 3	mm Hg	141.2	1.8	1.3	2.2	1.6

**In-house Precision 3:** whole blood samples run on 20 sequential manufactured lots using at least 8 different epoc Readers, with 12 replicates per each blood sample per lot.

	Units	Mean	mean $SD_{WR}$	%CV
Blood level 1	mm Hg	38.0	2.2	5.9
Blood level 2	mm Hg	70.0	2.4	3.5

**Clinical Site Precision 1:** 10 replicates of commercial aqueous blood gas controls run by operators of the epoc system at 3 different point-of-care sites. Each precision study employed from 2 to 4 different epoc Readers.

High  $pO_2$  level commercial aqueous blood gas control

	Units	Mean	SD <sub>WR</sub>	%CV
Operator 1	mm Hg	136.3	4.1	3.0
Operator 2	mm Hg	139.8	2.0	1.4
Operator 3	mm Hg	138.1	3.1	2.2

Low  $pO_2$  level commercial aqueous blood gas control

	Units	Mean	SD <sub>WR</sub>	%CV
Operator 4	mm Hg	67.5	2.3	3.5
Operator 5	mm Hg	67.4	3.3	4.9
Operator 6	mm Hg	70.1	3.2	4.6
Operator 7	mm Hg	70.8	4.0	5.6

**Clinical Site Precision 2:** 10 replicates of different whole blood Patient samples run by different operators of the epoc system at different point-of-care sites. Each precision study employed 5 different epoc Readers.

	Units	Mean	SD <sub>WR</sub>	%CV
Site 1 Operator 1	mm Hg	28.6	1.7	6.0
Operator 2	mm Hg	32.9	1.8	5.5
Site 2 Operator 3	mm Hg	33.9	1.2	3.5
Operator 4	mm Hg	30.0	1.5	5.0
Operator 5	mm Hg	40.1	1.2	3.1
Site 3 Operator 6	mm Hg	61.8	3.5	5.6
Operator 7	mm Hg	74.6	2.9	3.9

## B. Linearity Data

This study was performed in-house on multiple whole blood samples with  $pO_2$  values spanning the reportable range. Linearity is reported versus an in-house standard blood gas method with traceability to NIST standards.

	Test Range	Units	Slope	Intercept	R <sup>2</sup>
pO <sub>2</sub>	10-750	mm Hg	1.022	-3.9	0.999

## C. Clinical Sites Method Comparison Data

Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>5</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set, Sxx and Syy are the pooled pair-wise imprecision of the comparative and epoc test methods respectively, Syx is the standard error and R is the correlation coefficient.

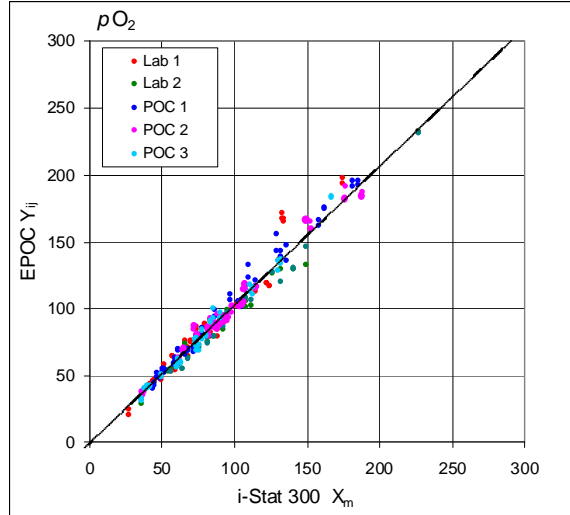
**Clinical Site Method Comparison 1:** In one hospital study the epoc was compared with the i-Stat 300<sup>6</sup> in the lab (two test occasions) then in three point-of-care sites.

Method Comparison Summary Statistics: whole blood

X: i-Stat 300 test

Y: epoc test

pO <sub>2</sub>	Lab 1	Lab 2	POC 1	POC 2	POC 3	All
N	34	23	35	28	22	142
Sxx	2.6	4.3	3.2	6.2	2.7	4.6
Syy	1.7	3.5	3.0	2.9	2.6	2.7
Intercept	-6.5	-3.1	-1.3	0.3	-3.9	-1.7
Slope	1.142	1.006	1.083	1.041	1.090	1.053
Syx	8.5	4.5	4.5	4.9	4.2	6.6
X min	26.0	35.0	43.5	36.0	35.5	26.0
X max	174.5	226.5	185.0	187.5	166.0	226.5
R	0.977	0.995	0.995	0.990	0.994	0.978



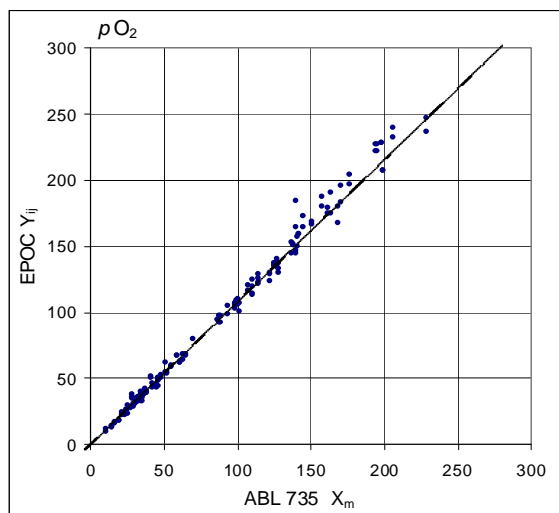
**Clinical Site Method Comparison 2:** In another hospital study the epoc was compared with the Radiometer ABL 735<sup>7</sup> in the lab.

Method Comparison Summary Statistics: whole blood

X: Radiometer ABL 735

Y: epoc test

pO <sub>2</sub>	Lab
N	77
Sxx	3.4
Syy	3.7
Intercept	-0.8
Slope	1.117
Syx	5.1
X min	10.2
X max	278.5
R	0.997



#### D. Limitations and Interferences

Exposure of the sample to air will affect pH,  $p\text{CO}_2$ ,  $p\text{O}_2$  and ionized calcium results due to the sample equilibration with the gas levels in the air, with pH affected by the  $p\text{CO}_2$  change<sup>2</sup> and ionized calcium affected by the pH change<sup>9</sup>. Air contains less than 1 mmHg  $p\text{CO}_2$  and about 150-180 mmHg  $p\text{O}_2$ . Do not introduce air bubbles into a collection device. If present, air bubbles should be removed immediately after collection.

Whole blood specimens should not be over-diluted with liquid anti-coagulants or other solutions used in therapies as this may alter results. Refer to 12.2.6 Sample Collection

Interference testing<sup>8</sup> was performed in-house on the epoc  $p\text{O}_2$  sensor. In each of these tests a whole blood specimen was aliquoted into two samples. The test sample was spiked by addition of interferent, while the control sample was spiked by the addition of the solvent of the interferent. The  $p\text{O}_2$  bias between the mean of six replicates on both the control sample and the test sample with added interferent was calculated.

Clinically significant interfering substances are itemized below: None identified.

The following levels of exogenous interferences were tested and found to be clinically insignificant: 447 mg/dL ethanol, 1 mmol/L sodium pentothal, 4.3 mmol/L acetyl salicylate, 0.4 mmol/L ascorbate, 4.3 mmol/L salicylate, 1 mmol/L iodide, 2.2 mmol/L ibuprofen, 1.66 mmol/L acetaminophen, 2 mmol/L ammonium, 4 mmol/L lithium, 37.5 mmol/L bromide, 2.7% halothane.

The following levels of endogenous interferences were tested and found to be clinically insignificant: 20 mmol/L NaCl, 8 mmol/L KCl, 3 mmol/L CaCl<sub>2</sub>, 10 to 120 mmHg  $p\text{CO}_2$ , pH 6.9 to 7.7, +20 mmol/L bicarbonate, 10 mmol/L lactate, +20% PCV Hct, 3% to 11% total protein, 0.8% lipids, 9.1 mmol/L cholesterol, 20 mmol/L  $\beta$ -hydroxybutyrate, 1 mmol/L cysteine, 0.26 mmol/L bilirubin, +2 mmol/L phosphate.

## E. References

1. J.W. Severinghaus, Simple and accurate equations for human blood O<sub>2</sub> dissociation computations, *J. Appl. Physiol.*, 46, 1979, p. 599-602.
2. CLSI. Blood Gas and pH Analysis and Related Measurements; Approved Guideline, CLSI document C46-A (ISBN 1-56238-444-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2001.
3. M.G. Scott, V.A. LeGrys and J.S. Klutts, Chapter 27 of Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
4. Reference Ranges Table 56-1 in Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St. Louis, 2006.
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6. i-STAT 300, Abbott Point of Care Inc., 104 Windsor Center Drive, East Windsor, NJ 08520, "i-STAT" is a registered trademark of Abbott Laboratories.
7. Radiometer ABL 735, Radiometer Medical Aps, Åkandevvej 21, DK-2700 Brønshøj, Denmark, "Radiometer" and "ABL" are registered trademarks of Radiometer Medical Aps.
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## 12.10 Lactate (Lac)

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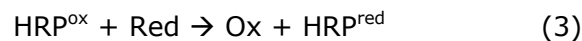
### 12.10.1 Measured values

*Lactate* is measured by amperometry<sup>1</sup>. The sensor comprises an immobilized enzyme first layer coated onto a gold electrode of the electrode module, with a diffusion barrier second layer. The lactate oxidase enzyme is employed to convert lactate to hydrogen peroxide,

Lactate Oxidase



and then uses an amperometric sensor to detect the enzymatically produced hydrogen peroxide. Peroxide detection is by redox mediated (ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt), horseradish peroxidase (HRP) catalyzed, reduction on a gold electrode.



The reduction current is proportional to the concentration of lactate in the test fluid.

### 12.10.2 Indications for Use

The *Lactate* test, as part of the epoc Blood Analysis System, is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Lactate measurements are used to evaluate the acid-base status and are used in the diagnosis and treatment of lactic acidosis (abnormally high acidity of the blood).

### 12.10.3 Contents

Each test card incorporating a *Lactate* test contains a sensing electrode with a redox mediated enzymatic membrane covered with an oxygen permeable diffusion layer, a reference electrode, a counter electrode and a calibrator fluid containing a known concentration of lactate.

### 12.10.4 Traceability

Certified standard reference material for lactate is not available at present. Lactate values assigned to controls and calibration verification materials are traceable to a working calibrator prepared from Sodium L-Lactate from Sigma-Aldrich Co., Item Number 71718, >99% purity.

### 12.10.5 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.10.6 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

## 12.10.7 Measurement Range

	Measurement Range	Normal Range <sup>2</sup>
Lactate	2.7 – 180.2 mg/dL	5.0 – 12 mg/dL
	0.30 - 20.00 mmol/L	0.56 - 1.39 mmol/L
	0.03 – 0.18 g/L	0.05 – 0.12 g/L

## 12.10.8 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the epoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A<sup>3</sup> for method comparison studies, CLSI EP7-A<sup>4</sup> for interference studies, CLSI EP6-A<sup>7</sup> for linearity studies and CLSI EP5-A<sup>5</sup> for precision studies.

### A. Precision Data

In the precision data tables below, SD<sub>WD</sub> denotes within-day standard deviation, SD<sub>DD</sub> denotes day-to-day standard deviation and SD<sub>T</sub> denotes total standard deviation.

**In-house Precision (CLSI EP5-A):** Four (4) card lots using at least 40 epoc Readers with replicate measurements were run in-house twice a day for twenty days for each fluid.

Lactate mM	All	
	L1	L3
<b>N</b>	320	320
<b>Mean</b>	7.99	0.94
<b>SWD</b>	0.39	0.03
<b>SDD</b>	0.32	0.03
<b>ST</b>	0.51	0.04
<b>Total CV%</b>	6.3%	4.7%

**Aqueous Clinical Site Precision:** 14-15 replicates of commercial aqueous blood gas, electrolytes and metabolites controls were run by potential end users of the epoc system at 2 different point-of-care sites. Each precision study employed at least 5 different epoc Readers. Three lots of cards were used.

Aqueous Control Precision			Lactate, mM			
Site	User	QC Level	N	Mean	SD	%CV
1	Operator 1	L3	15	0.95	0.031	3.3%
1	Operator 2	L3	15	0.94	0.027	2.9%
1	Operator 3	L2	14	2.88	0.05	1.8%
1	Operator 4	L2	15	2.91	0.08	2.8%
2	Operator 1	L1	15	7.34	0.57	7.8%
2	Operator 2	L1	15	7.45	0.42	5.6%

**Blood Clinical Site Precision:** 15 replicates of venous whole blood at two (2) different lactate concentrations were run by potential end users of the epoc system at two (2) different point-of-care sites. Each precision study employed at least five (5) different epoc Readers. Four (4) card lots were used in this study.

Whole Blood Precision			Lactate, mM			
Site	User	Level	N	Mean	SD	%CV
1	Operator 1	WB L1	15	10.24	0.62	6.0%
1	Operator 2	WB L1	15	10.27	0.34	3.3%
2	Operator 1	WB L2	15	2.77	0.07	2.7%
2	Operator 2	WB L2	15	2.67	0.12	4.7%

## B. Linearity Data

*Whole Blood Linearity Study (CLSI EP6-A):* This study was performed in-house on multiple whole blood samples with *Lactate* values spanning the reportable range. Linearity is reported versus theoretical lactate values based on gravimetric mixtures of high and low lactate samples (as measured using an in-house standard whole blood lactate method with traceability to NIST standards). Four (4) card lots were used in this study.

Test Range	Slope	Intercept	R <sup>2</sup>
0.3 - 20.1 mM	1.001	0.271	0.999

## C. Clinical Sites Method Comparison Data

Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>3</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set, Sxx and Syy are the pooled pair-wise imprecision of the comparative and epoc test methods respectively, Syx is the standard error and R is the correlation coefficient.

Method comparison studies were performed at two (2) hospitals. At one hospital 99 venous samples were tested. At another hospital both 43 arterial and 44 capillary samples were tested. Sample lactate concentrations on the comparison device varied from 0.57 to 14.57 mmol/L.

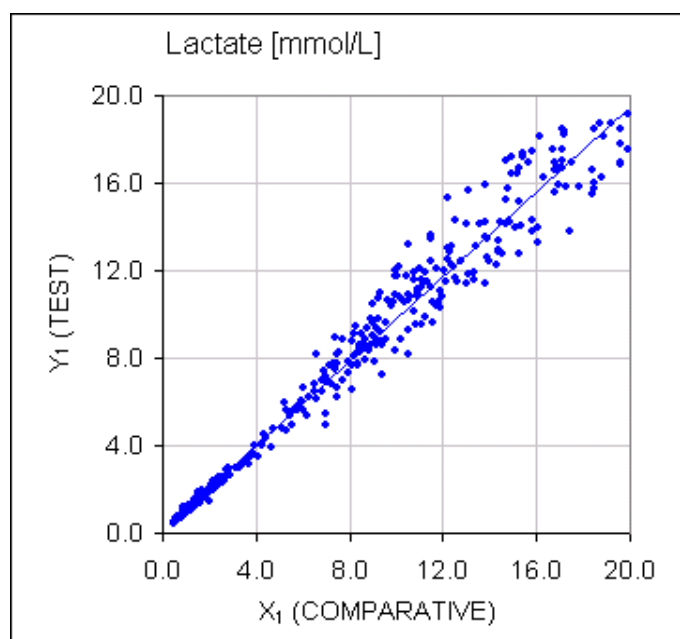
In these studies epoc was compared with the i-STAT 300 analyzer<sup>6</sup>.

Method Comparison Summary Statistics: whole blood—venous, arterial, capillary

X: i-STAT CG4+ cartridges

Y: epoc test

epoc Lactate vs. i-STAT	
N	373
Sxx	0.215
Syy	0.530
intercept	0.132
slope	0.967
Syx	0.948
X min	0.48
X max	19.95
R <sup>2</sup>	0.9711



Lactate Scatter Plot versus i-STAT 300 with CG4+ cartridges

## F. Limitations and Interferences

Interference testing<sup>4</sup> was performed in-house on the epoc lactate sensor. In each of these tests a pooled human serum specimen was aliquoted into two (2) samples. The test sample was spiked by addition of interferent, while the control sample was spiked by the addition of the solvent of the interferent. The lactate bias between the mean of six (6) replicates on both the control sample and the test sample with added interferent was calculated.

Unacceptable interference bias was defined as producing a significant error more than 5% of the time.

Significant interfering substances are itemized below:

- Acetaminophen will have no significant effect up to 0.81 mM after which it will increase the lactate reading up to 306  $\mu\text{M}/\text{mM}$  Tylenol. Because the therapeutic upper limit for acetaminophen is 0.20 mM, interfering levels of acetaminophen should only be encountered in overdose situations
- Iodide will decrease the lactate reading up to -1.2mM/mM of Iodide up to an Iodide concentration of 0.67 mM. Above 0.67 mM Iodide the decrease will be -1.2mM.
- Bromide will have no significant effect up to 25.4 mM after which it will decrease the lactate reading up to 14.6  $\mu\text{M}/\text{mM}$  Bromide.
- Thiocyanate will have no significant effect up to 2.7 mM after which it will decrease the lactate reading by up to 96.6  $\mu\text{M}/\text{mM}$  thiocyanate.
- N-Acetylcysteine will have no significant effect up to 3.7 mM after which it will decrease the lactate reading by up to 96.3  $\mu\text{M}/\text{mM}$  N-Acetylcysteine.

Ethylene glycol ingestion and metabolism has been shown to produce falsely elevated lactate measurements\*. Ethylene glycol plus three metabolism products - Glycolic Acid, Glyoxylic Acid and Oxalic Acid - were tested for interference. Ethylene Glycol and Oxalic Acid do not interfere significantly.

- Glycolic Acid will have no significant effect up to 0.87 mM after which it will increase the lactate reading up to 142  $\mu\text{M}/\text{mM}$  glycolic acid.
- Glyoxylic Acid will have no significant effect up to 0.85 mM after which it will increase the lactate reading up to 373  $\mu\text{M}/\text{mM}$  glyoxylic acid.

\* CMAJ, April 10, 2007, 176(8), p.1097 "Falsely elevated point-of-care lactate measurement after ingestion of ethylene glycol"

The following levels of exogenous interferences were tested and found to be insignificant: 1.66mM (25mg/dL) acetaminophen, 630 $\mu\text{mol}/\text{L}$  (12.5mg/dL) Na ascorbate, 20mmol/L (588 mg/dL) citrate, 100  $\mu\text{mol}/\text{L}$  (~2mg/dL) L-dopa, 9mmol/L (263mg/dL) EDTA, 4.84mmol/L (30mg/dL) ethylene glycol, 105  $\mu\text{mmol}/\text{L}$  (0.441mg/dL) Na fluoride, 71  $\mu\text{mol}/\text{L}$  Methyldopa, 2.55mmol/L oxidized glutathione, 2.55mmol/L reduced glutathione, 132  $\mu\text{mol}/\text{L}$  (1.0mg/dL) hydroxyurea, 292 $\mu\text{mol}/\text{L}$  (4mg/dL) isoniazide (nydrazid), 81  $\mu\text{mol}/\text{L}$  (1.5 mg/dL) K Oxalate, 0.037 mmol/L (1.2 mg/dL) Quinidine.

The following levels of endogenous interferences were tested and found to be insignificant: +342 $\mu\text{mol}/\text{L}$  (+29.0mg/dL) bilirubin conjugated, +342  $\mu\text{mol}/\text{L}$  (+20.1mg/dL) bilirubin unconjugated, +13mmol/L (+503.1mg/dL) cholesterol, +1500 $\mu\text{mol}/\text{L}$  (+18mg/dL) L-cysteine, +0.8% lipids, pH (+0.4, -0.4), 3% to 10% total protein, 1.4 mM (+ 23.5 mg/dL) Uric Acid. Low hematocrit did not interfere down to a level of 21 % hematocrit and high hematocrit did not interfere up to a level of 61 % hematocrit. Triglycerides did not show significant interference up to a level of 37 mM (1430 mg/dL). pO<sub>2</sub> partial pressures below 20mmHg (2.67kPa) may decrease lactate values.

## G. References

1. P. D’Orazio, M.E. Meyerhoff, “Electrochemistry and Chemical Sensors”, Chapter 4 in Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-Fourth Edition, C.A. Burtis, E.R. Ashwood, and D.E. Burns eds., Elsevier Saunders, St.Louis, 2006.
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3. CLSI. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition, CLSI document EP9-A2 (ISBN 1-56238-472-4), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
4. CLSI. Interference Testing in Clinical Chemistry; Approved Guideline, CLSI document EP7-A2 (ISBN 1-56238-480-5), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2002.
5. CLSI. Evaluation of Precision in Clinical Chemistry Devices; Approved Guideline-Second Edition, CLSI document EP5-A2 (ISBN 1-56238-542-9), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.
6. i-STAT 300, Abbott Point of Care Inc., 104 Windsor Center Drive, East Windsor, NJ 08520, “i-STAT” is a registered trademark of Abbott Laboratories.
7. CLSI. Evaluation of the Linearity of Quantitative Measurement Procedures; Approved Guideline, CLSI document EP6-A (ISBN 1-56238-498-8), CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2003.

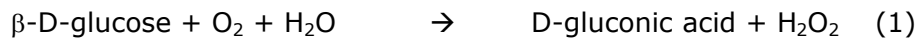
## 12.11 Glucose (Glu)

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### 12.11.1 Measured values

*Glucose* is measured by amperometry<sup>1</sup>. The sensor comprises an immobilized enzyme first layer coated onto a gold electrode of the electrode module, with a diffusion barrier second layer. The glucose oxidase enzyme is employed to convert glucose to hydrogen peroxide,

#### Glucose Oxidase



and then uses an amperometric sensor to detect the enzymatically produced hydrogen peroxide. Peroxide detection is by redox mediated (ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt), horseradish peroxidase (HRP) catalyzed, reduction on a gold electrode.



The reduction current is proportional to the concentration of glucose in the test fluid.

### 12.11.2 Indications for Use

The *Glucose* test, as part of the epoc Blood Analysis System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, idiopathic hypoglycemia and of pancreatic islet cell tumors.

### 12.11.3 Contents

Each Test Card incorporating a *Glucose* test contains a sensing electrode with a redox mediated enzymatic membrane covered with an oxygen permeable diffusion layer, a reference electrode, a counter electrode and a calibrator fluid containing a known concentration of glucose.

### 12.11.4 Traceability

Glucose concentration values assigned to controls and calibrator fluids are traceable to NIST standards.

### 12.11.5 Sample Collection

Refer to 12.2.6 Sample Collection

### 12.11.6 Additional Information

Refer to section "03 - epoc System Operation" of the epoc System Manual for detailed sample collection and system operating instructions for conducting a blood test.

Refer to section "09 - Quality Assurance" of the epoc System Manual for quality control requirements.

## 12.11.7 Measurement Range

	Measurement Range	Normal Range <sup>2</sup>
Glucose	20 - 700 mg/dL	74 - 100 mg/dL
	1.1 - 38.5 mmol/L	4.1 - 5.5 mmol/L
	0.20 - 7.00 g/L	0.74 - 1.00 g/L

## 12.11.8 Performance Data

Typical performance data summarized below were obtained in-house as well as in healthcare facilities by healthcare professionals trained in the use of the epoc System. Experimental designs conformed to applicable CLSI guidelines.

Applicable standards include: CLSI EP9-A2<sup>3</sup> for method comparison studies, CLSI EP7-A2<sup>4</sup> for interference studies and CLSI EP5-A<sup>5</sup> for precision studies.

### A. Precision Data

In the precision data tables below,  $SD_{WR}$  denotes within run standard deviation and  $SD_T$  denotes total standard deviation.

**In-house Precision 1:** commercial aqueous blood gas and electrolyte controls run on 5 sequential manufactured lots using at least 8 different epoc Readers, with 16 replicate measurements per lot per each control fluid level.

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 3	mg/dL	51.1	1.2	2.3	1.6	3.1
Level 1	mg/dL	242.6	5.5	2.3	6.0	2.5

**In-house Precision 2:** commercial aqueous blood gas and electrolyte controls run in a 20 day precision study<sup>5</sup> with 2 measurements each day per each control level for each of 4 manufactured lots using 6 different epoc Readers

	Units	Mean	$SD_{WR}$	%CV	$SD_T$	%CV
Level 3	mg/dL	50.2	1.1	2.2	1.2	2.3
Level 1	mg/dL	241.9	4.7	2.0	5.5	2.3

**In-house Precision 3:** whole blood samples run on 5 sequential manufactured lots using at least 8 different epoc Readers, with 12 replicates per each blood sample per lot.

	Units	Mean	mean $SD_{WR}$	%CV
Blood level 1	mg/dL	80.0	1.2	1.5
Blood level 2	mg/dL	210.0	5.8	2.7

**In-house Precision 4:** whole blood samples were spiked at five levels of glucose and were tested with 100 replicates per each blood sample; each sample was tested within 12 minutes in two runs; each run was performed simultaneously on 50 different epoc Readers; a mix of four manufactured lots were included in this test.

	Units	Mean	mean SD	%CV
Blood level 1	mg/dL	22.5	1.2	5.4
Blood level 2	mg/dL	123.7	3.0	2.4
Blood level 3	mg/dL	215.9	8.5	3.9
Blood level 4	mg/dL	311.8	13.1	4.2
Blood level 5	mg/dL	548.3	17.6	3.2

**Clinical Site Precision 1:** 12 replicates of venous blood where glycolysis was allowed for a certain period of time was run by four different operators of the epoc system in a clinical environment. Each precision study employed 6 different epoc Readers.

### Low glucose level blood

	Units	Mean	SD <sub>WR</sub>	%CV
Operator 1	mg/dL	42.8	1.9	4.4
Operator 2	mg/dL	43.2	1.8	4.3
Operator 3	mg/dL	41.6	1.6	3.8
Operator 4	mg/dL	50.0	1.1	2.2

**Clinical Site Precision 2:** 12 replicates of venous blood spiked with glucose was run by four different operators of the epoc system in a clinical environment. Each precision study employed 6 different epoc Readers.

### High glucose level blood

	Units	Mean	SD <sub>WR</sub>	%CV
Operator 5	mg/dL	242.8	6.6	2.7
Operator 6	mg/dL	229.0	5.3	2.3
Operator 7	mg/dL	233.4	6.8	2.9
Operator 8	mg/dL	228.5	7.0	3.1

**Clinical Site Precision 3:** 10-12 replicates of commercial aqueous blood gas, electrolytes and metabolites controls were run by operators of the epoc system at 2 different point-of-care sites. Each precision study employed 5-6 different epoc Readers.

### Low glucose level commercial aqueous blood gas electrolyte and metabolite control

	Units	Mean	SD <sub>WR</sub>	%CV
Operator 1	mg/dL	48.0	1.5	3.2
Operator 2	mg/dL	46.6	1.0	2.1

### Medium glucose level commercial aqueous blood gas electrolyte and metabolite control

	Units	Mean	SD <sub>WR</sub>	%CV
Operator 3	mg/dL	109.7	3.6	3.3
Operator 4	mg/dL	106.8	1.8	1.7

### High glucose level commercial aqueous blood gas electrolyte and metabolite control

	Units	Mean	SD <sub>WR</sub>	%CV
Operator 5	mg/dL	258.9	9.0	3.5
Operator 6	mg/dL	256.9	2.3	0.9

## B. Linearity Data

This study was performed in-house on multiple whole blood samples with *Glucose* values spanning the reportable range. Three types of samples were considered, i.e. normal hematocrit-normal venous blood  $pO_2$ , normal hematocrit- hypoxic blood sample and elevated hematocrit-normal venous blood  $pO_2$ . Linearity is reported versus two in-house standard whole blood glucose method with traceability to NIST standards.

Type of blood sample	Test Range	Units	Slope	Intercept	R <sup>2</sup>
43% Hct, 30mmHg pO <sub>2</sub>	20-700	mg/dL	1.022	-3.32	0.9997
62% Hct, 30mmHg pO <sub>2</sub>	20-700	mg/dL	1.018	-4.04	0.9996
43% Hct, <20mmHg pO <sub>2</sub>	20-700	mg/dL	0.955	+0.33	0.9995

## C. Clinical Sites Method Comparison Data

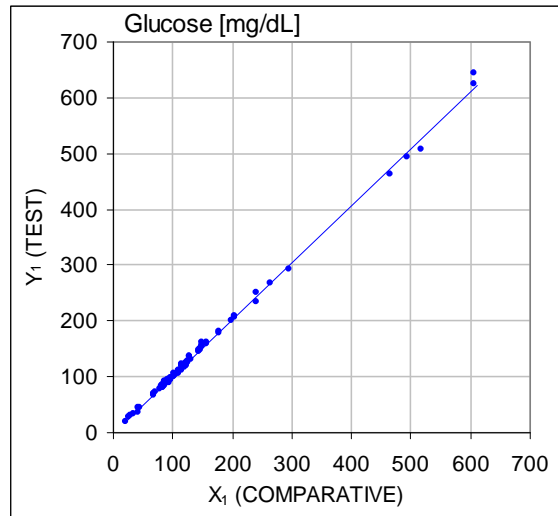
Linear regression analysis was performed on the method comparison data in accordance with CLSI EP9-A2<sup>3</sup>. In the method comparison statistics table, N is the number of Patient specimens in the data set, S<sub>xx</sub> and S<sub>yy</sub> are the pooled pair-wise imprecision of the comparative and epoc test methods respectively, S<sub>yx</sub> is the standard error and R is the correlation coefficient.

**Clinical Site Method Comparison 1:** In one hospital study the epoc was compared with the i-Stat 300<sup>6</sup> in the lab and in one point-of-care site.

Method Comparison Summary Statistics: whole blood

X: i-Stat 300 CG8 cartridges test  
Y: epoc test

Glu All  
N 80  
Sxx 0.93  
Syy 3.4  
Intercept -2.2  
Slope 1.031  
Syx 5.6  
X min 20.0  
X max 605.5  
R 0.999



The precision in whole blood was assessed from the pooling of within method pairs from the method comparison data. This is shown in the table below.

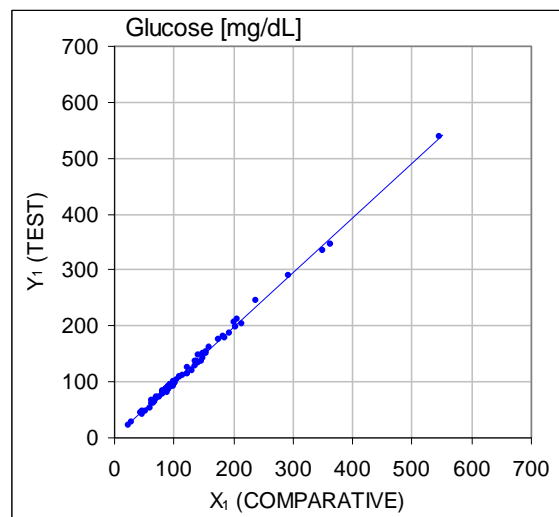
	Glucose [mg/dL]		
	20-70	70-200	200-700
Range	20-70	70-200	200-700
N	10	59	11
Average reading	44.8	116.4	383.8
Pair Precision (SD)	0.80	2.44	7.08
%CV	1.8%	2.1%	1.8%

**Clinical Site Method Comparison 2:** In another hospital study the epoc was compared simultaneously with the Roche-Hitachi<sup>7</sup> instrument in the lab and with iSTAT 300<sup>6</sup>. The summaries are presented in the tables below. The correlation plots are illustrated on the next page.

Method Comparison Summary Statistics: whole blood

X: Roche-Hitachi P800-D2400 test  
Y: epoc test

Glu All  
N 73  
Sxx  
Syy 3.6  
Intercept -0.2  
Slope 0.971  
Syx 3.0  
X min 23.0  
X max 546.0  
R 0.998

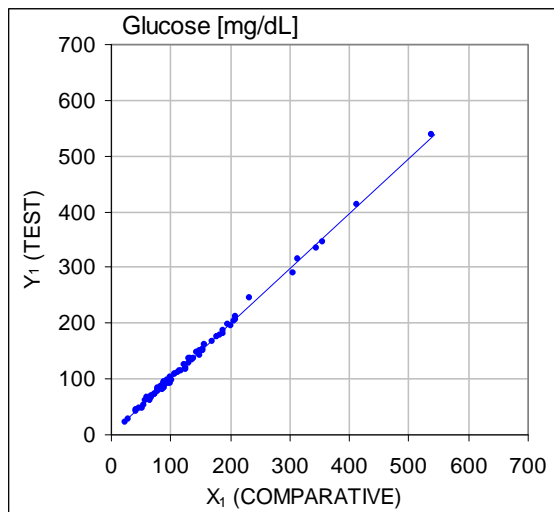


## Method Comparison Summary Statistics: whole blood

X: i-Stat 300 G cartridges test

Y: epoc test

Glu	All
N	80
Sxx	3.25
Syy	4.25
Intercept	-1.33
Slope	1.003
Syx	4.45
X min	22.5
X max	517.5
R	0.999



The precision in whole blood was assessed from the pooling of within method pairs from the method comparison data. This is shown in the table below.

	Glucose [mg/dL]		
Range	20-70	70-200	200-700
N	16	53	11
Average reading	53.5	113.4	299.0
Pair Precision (SD)	1.32	3.18	8.73
%CV	2.47%	2.81%	2.92%

### D. Consolidated Method Comparison Study Focusing on Low End Glucose Range

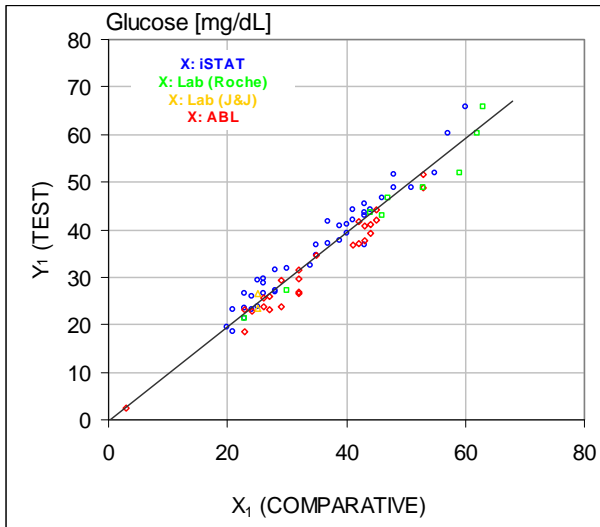
We evaluated the performance of the epoc glucose sensor in the low end range of glucose concentrations on Patient samples in clinical settings including at the point of care at several different hospitals. The results shown below include method comparison data against i-STAT<sup>6</sup> (whole blood method), ABL 800 Flex<sup>8</sup> (whole blood method), Roche-Hitachi<sup>7</sup> (plasma method) and J&J (plasma method). We supplemented the above mentioned clinical results with an in-house full duplicate method comparison<sup>3</sup> against iSTAT<sup>6</sup> and ABL705<sup>8</sup>. In this study high hematocrit blood samples were prepared by removing half of the plasma volume from a venous sample that was allowed to glycolyse. The hematocrit of these specimens was tested by micro-centrifugation method<sup>10</sup> and found to be ~62%, i.e. characteristic to the upper range of the neonatal blood<sup>9</sup>. After the glucose reached ~20mg/dL, it was spiked to cover uniformly the low range glucose, i.e. 20-80 mg/dL specific to neonatal population<sup>9</sup>. One sample was treated with Hexokinase, NADH-β and ATP in order to obtain a zero glucose concentration.

The data was processed as per CLSI EP9-A2 recommendations<sup>3</sup>. The correlation plot and bias plot are presented in the figures below. The test results versus the various reference instruments (X) are color coded.

epoc Low End Study	All points	Lab (plasma)	iSTAT	ABL	Roche	J&J
N	78	11	40	27	9	2
Sxx	1.0		0.6	1.6		
Syy	1.1	1.4	1.1	1.0	1.5	0.7
Intercept	-0.2	1.1	1.0	-2.2	0.8	
Slope	0.984	0.936	0.992	0.990	0.942	
Syx	2.9	2.1	2.55	2.16	2.21	
X min	1.5	23.0	20	1.5	23	25
X max	63.0	63.0	60	53	63	25
R <sup>2</sup>	0.947	0.960	0.948	0.971	0.946	
Decision Level	40	40	40	40	40	
Bias	-0.8	-1.4	0.7	-2.6	-1.52	
Bias 95% Conf. Hi	-0.3	-0.5	1.3	-1.9	-0.18	
Bias 95% Conf. Lo	-1.3	-2.3	0.1	-3.3	-2.86	

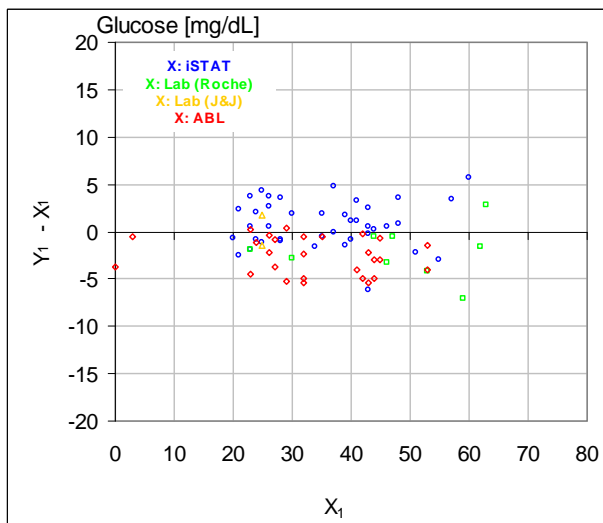
Method Comparison Summary Statistics: whole blood

- X (blue circles): i-Stat 300 G cartridges (whole blood) test
- X (green squares): Roche Hitachi Lab (plasma) test
- X (red diamonds): ABL 705 (whole blood) test
- X (yellow triangles): J&J Lab (plasma) test
- Y: epoc test



Low end glucose range, correlation plot versus various comparative instruments

Low end glucose range, bias plot versus various comparative instruments



## E. Method Comparison Study Focusing on Capillary Blood Specimens

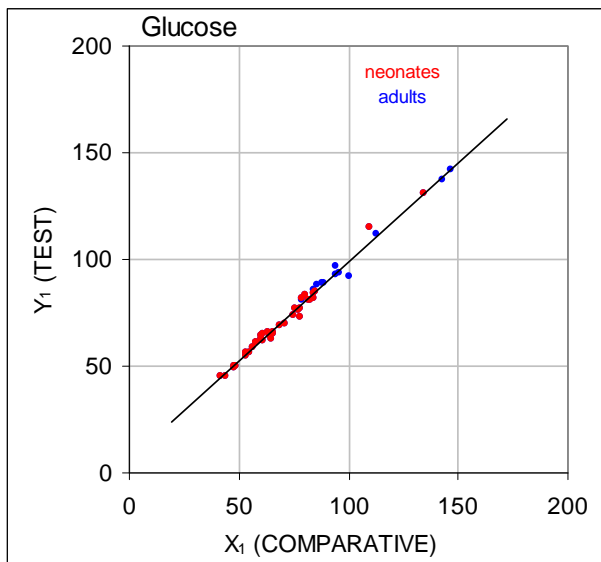
We evaluated the performance of the epoc tests on authentic capillary blood specimens in clinical settings at the point of care. The comparative method was i-STAT Abbott Point of Care<sup>6</sup> analyzers using CG8 cartridges and Radiometer CLINITUBE capillaries. Comparison testing was performed at four (4) locations: NICU, Well-baby Nursery and two (2) different outpatient drawing areas. There were a total of 48 samples collected, of which 24 in full duplicate. Of the 48 samples, 12 were adult blood specimens and 36 were neonatal blood specimens, represented with blue and red respectively in the figures below.

The data was processed as per CLSI EP9-A2 recommendations<sup>3</sup>. The correlation plot and bias plot are presented in the figures below. The test results versus the patient age are color coded.

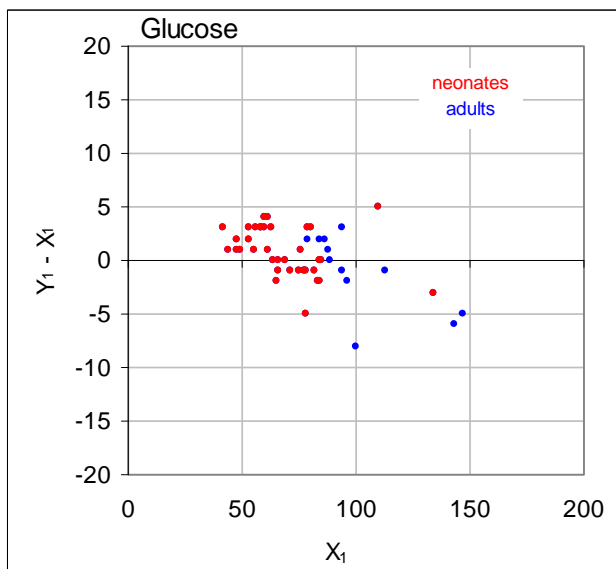
Method Comparison Summary Statistics: capillary blood

X: i-Stat 300 test

Y: epoc test



N	48
Sxx	1.13
Syy	1.80
intercept	5.1
slope	0.935
Syx	2.42
X min	42.5
X max	147
R	0.9942



## F. Limitations and Interferences

Interference testing<sup>4</sup> was performed in-house on the epoc *glucose* sensor. In each of these tests a whole blood specimen was aliquoted into two samples. The test sample was spiked by addition of interferent, while the control sample was spiked by the addition of the solvent of the interferent. The *glucose* bias between the mean of six replicates on both the control sample and the test sample with added interferent was calculated.

Clinically significant interfering substances are itemized below:

- Anticoagulants:
  - Citrate will have no significant effect up to 15mM (441mg/dL), after which it will decrease the glucose reading by  $-0.28\%/mM_{\text{Citrate}}$ , i.e.  $-0.01\%/(\text{mg/dL}_{\text{Citrate}})$ ; therefore we do not recommend using collection devices containing citrate as additive.
  - Na fluoride will have no significant effect up to 10mM (42mg/dL), after which it will decrease the glucose reading by  $-0.1\%/mM_{\text{NaF}}$ , i.e.  $-0.024\%/(\text{mg/dL}_{\text{NaF}})$ ; therefore we do not recommend using collection devices containing Na fluoride as additive.
  - Oxalate will have no significant effect up to 20mM (128mg/dL), after which it will decrease the glucose reading by  $-0.29\%/mM_{\text{Oxalate}}$ , i.e.  $-0.045\%/(\text{mg/dL}_{\text{Oxalate}})$ ; therefore we do not recommend using devices tubes containing oxalate as additive.
- Iodide will have no significant effect up to  $28\mu\text{M}$  ( $0.47\text{mg/dL}_{\text{KI}}$ ), after which it will decrease glucose reading by as much as  $(-0.16\text{mg/dL})/\mu\text{M}_{\text{I}^-}$ , i.e.  $(-9.5\text{mg/dL})/(\text{mg/dL}_{\text{KI}})$ . Iodide concentrations higher than  $0.4\text{mM}_{\text{I}^-}$  ( $6.7\text{mM}_{\text{KI}}$ ) will trigger iQC.
- Bromide will have no significant effect up to  $28\text{mM}$  ( $224\text{mg/dL}_{\text{NaBr}}$ ), after which it will decrease glucose reading by  $(-0.23\text{mg/dL})/mM_{\text{Br}^-}$ , i.e.  $(-0.029\text{mg/dL})/(\text{mg/dL}_{\text{NaBr}})$ .
- N-acetyl cysteine will have no significant effect up to  $500\mu\text{M}$  ( $8\text{mg/dL}$ ), after which it will trigger iQC.
- L-cysteine will have no significant effect up to  $750\mu\text{M}$  ( $9\text{mg/dL}$ ), after which it will trigger iQC.
- Gallamine triethiodide (Flaxedil) will have no significant effect up to  $11\mu\text{M}$  ( $1\text{mg/dL}$ ), after which it will decrease the glucose reading by  $(-0.27\text{mg/dL})/\mu\text{M}_{\text{gallamine triethiodide}}$ , i.e.  $(-3\text{mg/dL})/(\text{mg/dL}_{\text{gallamine triethiodide}})$ .
- Thiocyanate will have no significant effect up to  $1\text{mM}$  ( $5.9\text{mg/dL}_{\text{KSCN}}$ ), after which it will decrease the glucose reading with  $-1.7\%/mM_{\text{SCN}^-}$ , i.e.  $(-0.29\text{mg/dL})/(\text{mg/dL}_{\text{KSCN}})$ .
- Uric acid will have no significant effect up to  $700\mu\text{M}$  ( $11.8\text{mg/dL}$ ), after which it will decrease the glucose reading by  $(-3.5\text{mg/dL})/mM_{\text{Uric Acid}}$ , i.e.  $(-0.21\text{mg/dL})/(\text{mg/dL}_{\text{Uric Acid}})$ .
- Mannose will have no significant effect up to  $3.5\text{mM}$  ( $63\text{mg/dL}$ ), after which it will increase the glucose reading by  $+3.8\%/mM_{\text{Mannose}}$ , i.e.  $(+0.21\%)/(\text{mg/dL}_{\text{Mannose}})$ .
- Xylose will have no significant effect up to  $3\text{mM}$  ( $45\text{mg/dL}$ ), after which it will increase the glucose reading by  $+7.5\%/mM_{\text{Xylose}}$ , i.e.  $(+0.5\%)/(\text{mg/dL}_{\text{Xylose}})$ .

The following levels of exogenous interferences were tested and found to be clinically insignificant:  $1.66\text{mM}$  ( $25\text{mg/dL}$ ) acetaminophen,  $0.09\text{mmol/L}$  ( $10\text{mg/dL}$ ) anidulafungin,  $500\mu\text{mol/L}$  ( $8.2\text{mg/dL}$ ) N-acetyl cysteine,  $3.3\text{mmol/L}$  ( $60\text{mg/dL}$ ) acetyl salicylate,  $630\mu\text{mol/L}$  ( $12.5\text{mg/dL}$ ) Na ascorbate,  $28\text{mmol/L}$  ( $224\text{mg/dL}$ ) bromide,  $15\text{mmol/L}$  ( $441\text{mg/dL}$ ) citrate,  $89.2\mu\text{mol/L}$  ( $4.5\text{mg/dL}$ ) clindamycin hydrochloride,  $0.1\text{mmol/L}$  ( $0.65\text{mg/dL}$ ) K cyanide,  $6.15\text{nmol/L}$  ( $507\text{ng/dL}$ ) digoxin,  $66\mu\text{mol/L}$  ( $2.2\text{mg/dL}$ ) dobutamine,  $100\mu\text{mol/L}$  ( $1.9\text{mg/dL}$ ) dopamine HCl,  $50\mu\text{mol/L}$  ( $\sim 1\text{mg/dL}$ ) L-dopa,  $9\text{mmol/L}$  ( $263\text{mg/dL}$ ) EDTA,  $12\mu\text{mol/L}$  ( $0.2\text{mg/dL}$ ) ephedrine,  $87\text{mM}$  ( $400\text{mg/dL}$ ) ethanol,  $4.84\text{mmol/L}$  ( $30\text{mg/dL}$ ) ethylene glycol,  $1.78\mu\text{mol/L}$  ( $60\mu\text{g/dL}$ ) famotidine,  $10\text{mmol/L}$  ( $42\text{mg/dL}$ ) Na fluoride,  $1\text{mmol/L}$  ( $18\text{mg/dL}$ ) fructose,  $181\mu\text{mol/L}$  ( $6\text{mg/dL}$ ) furosemide,

3.3mmol/L (59mg/dL) galactose, 11 $\mu$ mol/L (1mg/dL) gallamine triethiodide (flaxedil), 238 $\mu$ mol/L (10mg/dL) gentamicin, 4.5 $\mu$ mol/L (200 $\mu$ g/dL) glipizide, 1.1mmol/L (28.5mg/dL) glucosamine, 2.55mmol/L<sub>RBC</sub> oxidized glutathione, 2.55mmol/L<sub>RBC</sub> reduced glutathione, 400 $\mu$ mol/L (5mg/dL) guaiacol, 80U/ml heparin, 0.4mmol/L (14.5mg/dL) hydrocortisone, 2.5mmol/L (19mg/dL) hydroxyurea, 292 $\mu$ mol/L (4mg/dL) isoniazide (nydrazid), 48.6 $\mu$ mol/L (1.76mg/dL) levofloxacin, 1mmol/L (34mg/dL) linezolid, 13.3mmol/L (479mg/dL) maltose, 3.5mmol/L (90mg/dL) mannose, 71 $\mu$ mol/L (1.7mg/dL) methyl dopa, 77.4 $\mu$ mol/L (2.9mg/dL) 6 $\alpha$ -methyl prednisolone, 0.7mM (12mg/dL) metronidazole, 17.4 $\mu$ M (0.6mg/dL) omeprazole, 102 $\mu$ mol/L (2.4mg/dL) procainamide, 4.22 $\mu$ mol/L (0.12mg/dL) promethazine hydrochloride, 37 $\mu$ mol/L (1.2mg/dL) quinidine, 1.67 $\mu$ mol/L (40 $\mu$ g/dL) salbutamol (albuterol), 4.34mmol/L (60mg/dL) salicylic acid, 1.96 $\mu$ mol/L (60 $\mu$ g/dL) sertaline, 1mmol/L (5.8mg/dL) thiocyanate, 413 $\mu$ mol/L (10mg/dL) sodium penthotal, 1mmol/L (31mg/dL) tolazamide (tolinase), 2.37mmol/L (64mg/dL) tolbutamide, 69 $\mu$ mol/L (10mg/dL) vancomycin, 21.3 $\mu$ mol/L (1mg/dL) vitamin K1, 3mmol/L (45mg/dL) xylose.

The following levels of endogenous interferences were tested and found to be clinically insignificant: +20mmol/L (168mg/dL) Na bicarbonate, +86 $\mu$ mol/L (+7.3mg/dL) bilirubin conjugated, +510  $\mu$ mol/L (+30mg/dL) bilirubin unconjugated, +13mmol/L (+298mg/dL) cholesterol, 15 to 140 mmHg *p*CO<sub>2</sub>, +500 $\mu$ mol/L (+6mg/dL) L-cysteine, +20mmol/L (+256mg/dL) Na  $\beta$ -hydroxybutyrate, +20mmol/L (+180mg/dL) Na L-lactate, +0.8% lipids, +59.2 $\mu$ mol/L (+1.9mg/dL) norepinephrine, pH 6.7 to 7.7, +20% PCV Hct, 3.4% to 10.4% total protein, +11.2mmol/L (+1g/dL) triglycerides, +500 $\mu$ mol/L (+8.4mg/dL) uric acid.

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