510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:
k090109

B. Purpose for Submission:
Add new test to existing cleared system

C. Measurand:
Glucose

D. Type of Test:
Electrode technology

E. Applicant:
Epocal, Inc.

F. Proprietary and Established Names:
Blood Gas, Electrolyte And Metabolite Test Card

G. Regulatory Information:

1. Regulation section:
   21CFR Sec.- 862.1345-Glucose test system.
2. Classification:
   Class II
3. Product code:
   CGA - Glucose Oxidase, Glucose
4. Panel:
   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) 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 or venous whole blood in the laboratory or at the point of care in hospitals, nursing homes or other clinical care institutions.

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

3. Special conditions for use statement(s):
   For prescription use

4. Special instrument requirements:
   epoc Card Reader, epoc Host

I. Device Description:

The epoc glucose test is being added as an additional sensor to the existing single use test card that is used with the epoc Blood Analysis System. This test card is inserted into the epoc Reader and all analytical steps are performed automatically. Patient and user information may be entered into the mobile computing device (epoc Host) during the automated analysis cycle.
The epoc Blood Analysis System is an in vitro analytical system comprising a network of one or more epoc Readers designed to be used at the point of care (POC). The readers accept an epoc single use test card containing a group of sensors that perform diagnostic testing on whole blood. The blood test results are transmitted wirelessly to an epoc Host, which displays and stores the test results.
The epoc System is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of whole blood.
The test card panel configuration currently includes sensors for Sodium, Potassium, Ionized Calcium, pH, pCO2, pO2 and Hematocrit. This submission adds Glucose to this list of cleared tests.
To perform a blood test, a new test card is inserted into a card reader's card slot with white label face down. When fully inserted, the test card is automatically engaged in the reader.
Changes to the epoc Blood Analysis System required to introduce the Glucose test include:

- Developing a new Glucose sensor and adding it to the existing epoc test card, which was already designed to accommodate additional sensors;
- Modifications to the existing EpocHost software application to accommodate the new test;
- Labeling changes including indications for use for the Glucose test.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   i-STAT Model 300

2. Predicate 510(k) number(s):
   k001387

3. Comparison with predicate:

	epoc Blood Analysis System (Device)	**i-STAT Model 300 – Predicate k001387**	
Intended use	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 whole blood using the BGEM (Blood Gas Electrolyte Metabolite) test card panels.	The i-STAT Model 300 Portable Clinical Analyzer is intended to be used by trained medical professionals for use with i-STAT test cartridges and MediSense blood glucose test strips. i-STAT cartridges comprise a variety of clinical chemistry tests and test panels.	same
Where used	hospital	hospital	same
Measured parameters	Glucose, Sodium, Potassium, Ionized Calcium, pH, pCO2, pO2 and Hematocrit	Glucose and other various analytes such as Sodium, Potassium, Ionized Calcium, pH, pCO2, pO2 and Hematocrit	same
Sample type	Venous, arterial whole blood	Venous, arterial and capillary whole blood	same
Reportable range	Gluc 20 – 700 mg/dL	Gluc 20 – 700 mg/dL	same
Sample volume	95-125 µL	100 µL	same
Test card	Unit-use card with - on-board calibrator in sealed reservoir - an electrochemical multi-sensor array - port for sample introduction - fluid waste chamber	Unit-use cartridge with - on-board calibrator in sealed reservoir - an electrochemical multi-sensor array - port for sample introduction - fluid waste chamber	same
Test card storage	Room temperature until expiry date	Fridge storage until expiry date including max 2 weeks at room temperature	different
Sensor array	A laminated foil sensor module	A micro-fabricated chip-set	different
Tests/sensor components	Glu - glucose oxidase based amperometric peroxide detection	Glu - glucose oxidase based amperometric peroxide detection	same
Measurement temperature	37°C	37°C	same
Measurement sequence	Calibrate test card-introduce sample-measure	Introduce sample-calibrate test cartridge-measure	different
Measurement time	30sec from sample introduction	200 sec from sample introduction	different

K. Standard/Guidance Document Referenced (if applicable):

FDA Recognition No.	Standard	Title
5-4	IEC 60601-1	Medical Electrical Equipment - Part 1: General Requirements for Safety, 1988; Amendment 1, 1991-11, Amendment 2, 1995. (General)
5-28	IEC 60601-1-2:2001	Medical Electrical Equipment - Part 1-2: General Requirements for Safety - Collateral Standard: Electromagnetic Compatibility - Requirements and Tests
5-40	ISO 14971 (2007)*	Medical devices - Application of risk management to medical devices
7-100	ISO 15197 (2003)	In vitro diagnostic test systems - Requirements for in vitro whole blood glucose monitoring systems intended for use by patients for self testing in management of diabetes mellitus, First Edition 2003-05-01,
7-110	CLSI EP05-A2 (2004)	Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline
7-193	CLSI EP06-A	Evaluation of the Linearity of Quantitative Measurement
7-127	CLSI EP07-A2 (2005)	Interference Testing in Clinical Chemistry; Approved Guideline
7-92	CLSI EP09-A2 (2002)	Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition
7-104	CLSI H07-A3 (2000)	Procedure for Determining Packed Cell Volume by the Microhematocrit Method – Second Edition; Approved Standard – Third Edition
N/A	SW68 (2001)*	Medical device software – Software life cycle processes

* Used as a guideline for the design and development of the device

FDA Guidance Documents
Points to Consider for Portable Blood Glucose Monitoring Devices Intended for Bedside Use in the Neonate Nursery
Review Criteria for Assessment of Portable Blood Glucose In Vitro Diagnostic Devices Using Glucose Oxidase
Total Product Life Cycle for Portable Invasive Blood Glucose Monitoring Systems

L. Test Principle:

The glucose sensor comprises an immobilized enzyme first layer coated onto a gold electrode of the electrode module, with a diffusion barrier second layer.

The Epocal glucose electrode uses the enzyme glucose oxidase to convert glucose to hydrogen peroxide, and then uses an amperometric sensor to detect the enzymatically produced hydrogen peroxide. Peroxide detection is by redox mediated, horseradish peroxidase catalyzed, reduction on a gold electrode.

The enzyme layer immobilized on the electrode is further over-coated by a diffusion barrier layer whose composition and dimensions are selected to facilitate rapid transport of oxygen to the oxidase enzyme and assure that the enzymatic reaction rate

is regulated by the diffusion limited transport of glucose. The reduction current is proportional to the concentration of glucose in the test fluid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Point-of-Care (POC) Precision was demonstrated at a total of 4 POC clinical sites utilizing typical POC operators and different locations. In two of the sites, listed below, each operator performed a precision study. This comprised the testing of twelve (12) epoc cards on six (6) readers using venous blood samples collected from volunteers in green top (dry Na Heparin) vacutainers.

Site	**User**	N	Mean	**SD**	C.V. %
Level 1			**[mg/dL]**	**[mg/dL]**	
Baystate Heme Onco	Phlebotomist	10	42.8	1.9	4.4
Baystate Heme Onco	Lab Operator	12	43.2	1.8	4.2
Baystate Main Lab	Lab Operator	12	41.6	1.6	3.8
Baystate Main Lab	Med Tech	12	50	1.1	2.2
Level 2					
Huntsville Main Lab	Lab Operator	11	242.8	6.6	2.7
Huntsville Main Lab	Med Tech	11	229	5.3	2.3
Huntsville Main Lab	Lab Operator	11	233.4	6.8	2.9
Huntsville Main Lab	Phlebotomist	12	228.5	7	3.1

Aqueous precision testing was conducted at an additional two POC sites in Huntsville Hospital, Huntsville, Alabama, at the Surgical/Trauma ICU (STICU) and Cardiac-Vascular Intensive Care Unit (CVICU). This study was conducted to demonstrate precision by operators who typically run patient samples at a point-of-care sites. The three QC levels were tested in each location by three different operators, with one operator per level of fluid per site, for a total of six different users: 4 Respiratory Therapists (RT), 1 nurse and 1 Certified Registered Nurse Practitioner (CRNP).

	Low		Mid		High	
	STICU	CVICU	STICU	CVICU	STICU	CVICU
N	11	12	12	11	11	11
Mean mg/dL	48	46.6	109.7	106.8	258.9	256.9
SD	1.54	0.97	3.58	1.83	8.99	2.31
%CV	3.2	2.1	3.3	1.7	3.5	0.9

Studies were performed in-house to demonstrate the precision of the epoc glucose test. The table below shows the results of a twenty day precision study performed on 4 cartridge lots using aqueous controls at two levels L1 (213-277 mg/dL) and L3 (31-59 mg/dL). Each lot was tested for each level in

duplicate twice a day for 20 days.

Glucose [mg/dL]	**L1**	**L3**
N	**320**	**320**
Mean	241.9	50.2
S_{WR}	4.72	1.1
Within run CV%	1.95%	2.19%
S_{DD}	2.86	0.43
Day to day CV%	1.18%	0.09%
S_T	5.52	1.18
Total CV%	2.30%	2.30%

Studies were performed in-house to demonstrate the precision of the epoc glucose sensor. The table below shows the results of a study conducted on whole blood samples prepared to five concentrations of glucose, using cards from four different lots and testing over 100 cards/blood sample on 50 different readers. The test was performed within 12 min for each sample.

Fluid	Lot	n	avg	SD	%CV
20	09072-8	4	25.4	1.2	4.8%
	09096-7	24	22.1	1.2	5.2%
	09097-7	29	22.7	1.0	4.6%
	09098-7	45	22.4	1.0	4.4%
20 Combined		102	22.5	1.2	5.4%
120	09072-8	10	121.5	2.6	2.1%
	09096-7	15	124.0	1.5	1.2%
	09097-7	28	123.6	2.9	2.3%
	09098-7	45	124.1	3.4	2.8%
120 Combined		98	123.7	3.0	2.4%
200	09072-8	8	210.0	2.6	1.2%
	09096-7	19	216.5	7.0	3.2%
	09097-7	31	214.3	6.9	3.2%
	09098-7	43	217.9	10.2	4.7%
200 Combined		101	215.9	8.5	3.9%
300	09072-8	2	302.1	2.1	0.7%
	09096-7	26	314.4	8.5	2.7%
	09097-7	32	309.2	17.9	5.8%
	09098-7	45	312.5	11.3	3.6%
300 Combined		105	311.8	13.1	4.2%
500	09072-8	4	529.7	23.8	4.5%
	09096-7	25	554.2	14.6	2.6%
	09097-7	30	544.8	17.1	3.1%
	09098-7	44	548.9	17.8	3.2%
500 Combined		103	548.3	17.6	3.2%

b. Linearity/assay reportable range:

The reportable range of the assay, 20 to 700 mg/dL is supported by the linearity study. This study was performed in-house using blood samples as per CLSI EP6-A recommendations for evaluation of linearity. A total of nine blood samples, with theoretical concentrations of 29, 83, 137, 212, 298, 406, 492, 578, 675 mg/dL were prepared from two pools of blood, which were evaluated by comparison with in-house reference instruments with traceability to NIST standards. Regression analysis was performed as per CLSI EP6-A. The summary is given in the table below.

	Slope	Intercept	R^2	Range
Glu [mg/dL]	0.9996	0.64	0.9989	20-700

Another study was performed in-house on multiple whole blood samples with Glucose values spanning the reportable range. Three types of samples were considered, namely, normal hematocrit-normal venous blood pO2, normal hematocrit– hypoxic venous blood and elevated hematocrit-normal venous blood pO2. Linearity is reported versus two in-house standard whole blood glucose methods with traceability to NIST standards.

Type of blood sample	Slope	Intercept	R2	Test range	Units
43% Hct, 30mmHg pO2	1.022	-3.32	0.9997	20-700	mg/dL
62% Hct, 30mmHg pO2	1.018	-4.04	0.9996	20-700	mg/dL
43% Hct, <20mmHg pO2	0.955	0.33	0.9995	20-700	mg/dL

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The epoc System's test card comprises an on-board calibration material. This calibration fluid in the test card is prepared gravimetrically. Its concentration is measured for each batch with in house secondary reference instruments. Each reference instrument is calibrated with fluids having NIST traceable glucose concentrations and periodically verified using NIST SRM 965B serum based glucose solutions.

Stability is based on real time studies.

No controls available with assay. The manufacturer recommends using commercially available controls to comply with federal, state and local regulatory requirements that oversee the institution.

d. Detection limit:

The detection limit of 20 mg/dL for the epoc was verified by demonstrating acceptable precision near 20 mg/dL as described above. A study was conducted on whole blood samples at 20 ng/mL glucose using cards from four different lots and testing over 100 cards/blood sample on 50 different readers. The test was performed within 12 min for each sample. The observed %CV was ≤5.2%.

e. Analytical specificity:

Interference testing 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. Anticoagulants:

- Citrate had no significant effect up to 15mM (441mg/dL), after which it decreases the glucose reading by -0.28%/mMCitrate, i.e. -0.01%/(mg/dLCitrate); therefore it is not recommended to use collection devices containing citrate as additive.
- Na fluoride had no significant effect up to 10mM (42mg/dL), after which it decreases the glucose reading by -0.1%/mMNaF, i.e. -0.024%/(mg/dLNaF); therefore it is not recommended to use collection devices containing Na fluoride as additive.
- Oxalate had no significant effect up to 20mM (128mg/dL), after which it decreases the glucose reading by -0.29%/mMOxalate, i.e. -0.045%/(mg/dLOxalate); therefore it is not recommended to use devices tubes containing oxalate as additive.
- Iodide had no significant effect up to 28µM (0.47mg/dLKI), after which it decreases the glucose reading by as much as (-0.16mg/dL)/µMI-, i.e. (-9.5mg/dL)/(mg/dLKI). Iodide concentrations higher than 0.4mMI– (6.7mMKI) will trigger iQC.
- Bromide had no significant effect up to 28mM (224mg/dLNaBr), after which it decreases the glucose reading by (-0.23 mg/dL)/mMBr, i.e. (-0.029mg/dL)/(mg/dLNaBr).
- N-acetyl cysteine had no significant effect up to 500µM (8mg/dL), after which it will trigger iQC.
- L-cysteine had no significant effect up to 750µM (9mg/dL), after which it will trigger iQC.
- Gallamine triethiodide (Flaxedil) had no significant effect up to 11µM (1mg/dL), after which it decreases the glucose reading by (–0.27mg/dL)/µMgallamine triethiodide, i.e. (–3mg/ dL)/(mg/dLgallamine triethiodide).
- Thiocyanate had no significant effect up to 1mM (5.9mg/dLKSCN), after which it decreases the glucose reading with -1.7%/mMSCN, i.e. (–0.29mg/dL)/(mg/dLKSCN).

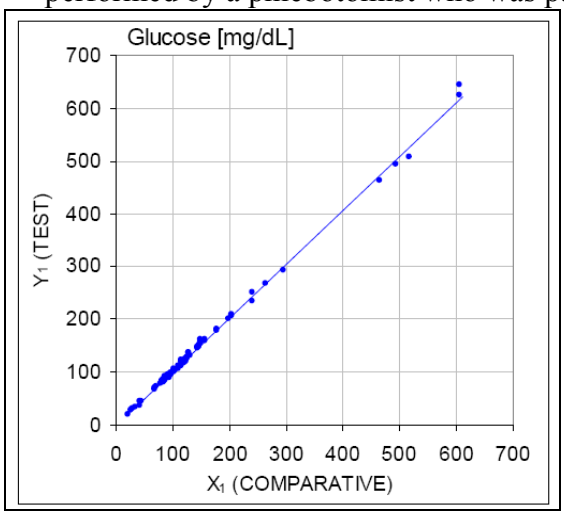
- Uric acid had no significant effect up to 700µM (11.8mg/dL), after which it decreases the glucose reading by (-3.5mg/dL)/mMUric Acid, i.e. (–0.21mg/dL)/(mg/dLUric Acid).
- Mannose had no significant effect up to 3.5mM (63mg/dL), after which it will increase the glucose reading by +3.8%/mMMannose, i.e. (+0.21%)/(mg/dLMannose).
- Xylose had no significant effect up to 3mM (45mg/dL), after which it will increase the glucose reading by +7.5%/mMXylose, i.e. (+0.5%)/(mg/dLXylose).

f. Assay cut-off:
Not Applicable

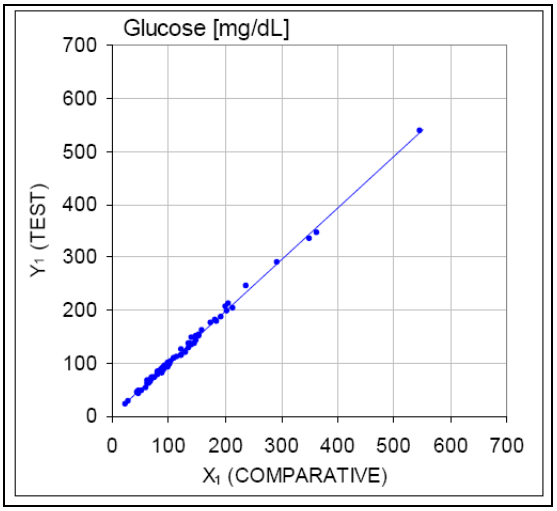
2. Comparison studies:

a. Method comparison with predicate device:

The applicant evaluated the performance of the new epoc tests on patient specimens (capillary, arterial and venous) in clinical settings including at the point of care. The reference instrument was the predicate device, i.e. iSTAT Abbott Point of Care analyzers using CG8 cartridges and a Roche Hitachi analyzer. Comparison testing to the predicate device was performed in two locations: central lab and Hematology-Oncology-POC site. The testing was performed by a phlebotomist who was part of the POC-coordination staff.



i-STAT



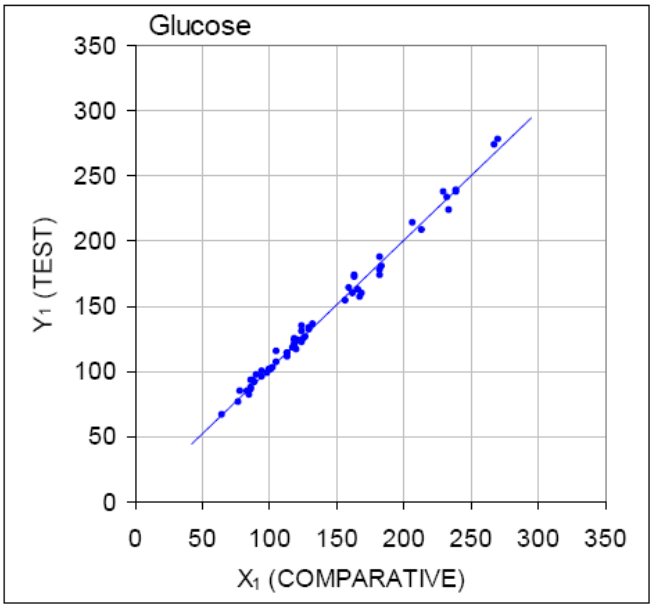
Hitachi

Device compared against i-STAT						Device compared against Hitachi					
N	**slope**	**intercept**	**R**	**Range**		**N**	**slope**	**intercept**	**R**	**Range**	
80	1.031	-2.2	0.999	20	605.5	73	0.971	-0.2	0.998	20	605.5

Combined					
N	**Slope**	**Intercept**	**R**	**Range**	
160	1.022	-2.338	0.999	20	605.5

Additionally, the applicant evaluated the performance of the new epoc glucose sensor on patient specimens in clinical settings including at the point of care at Huntsville Hospital. Comparison testing to the predicate device was first performed in the laboratory and then thereafter in three non-lab locations: CVICU, Neurological Intensive Care Unit (NICU)-stroke and STICU. The method comparison study was conducted on 58 blood specimens against predicate device at point-of-care, in three different sites.

N	slope	intercept	R_2	Range	
58	1.006	0.7	0.993	65	268.5



b. *Matrix comparison:*

i. Effect of anticoagulant

The effect of anticoagulant was evaluated on patient samples that were collected using heparinized and non-heparinized collection devices. This study was performed at various POC sites of a hospital. The data was analyzed using EP9-2A methodology. The table below shows the method comparison summary versus the predicate device.

Heparinized					
N	**slope**	**intercept**	**R^2**	**Range**	
29	0.994	2	0.992	78	266.5
Unheparinized					
29	1.019	-0.7	0.994	65	268.5
Combined					
58	1.006	0.7	0.993	65	268.5

ii. Venous versus arterial blood

Clinical data from method comparison studies performed in field trials at several hospitals and POC locations, on patient samples of whole blood, were analyzed separately as arterial and venous. The data was analyzed according to CLSI guideline EP09-2A. The table below shows the method comparison summary versus the predicate device.

N	slope	intercept	R^2	Range	
Arterial					
100	0.991	1.89	0.995	26	355
Venous					
114	1.028	-3.03	0.998	20	605.5
Combined					
214	1.02	-1.874	0.997	20	605.5

iii. Effect of altitude

A method comparison study was performed at an altitude of over 2000m (~6600 ft) against ABL800 Flex Radiometer whole blood instrument. The data was analyzed using EP9-2A methodology. The table in figure 5.12 shows the method comparison summary.

N	slope	intercept	R^2	Range	
26-100 mg/dL					
39	0.986	-1.9	0.975	26	97
100-300 mg/dL					
26	1.009	-4.1	0.985	100	290
300-631 mg/dL					
16	1.032	-5.9	0.978	301	631.5
26-631 mg/dL					
81	1.031	-6.12	0.998	26	631.5

3. Clinical studies:
   a. *Clinical Sensitivity:*
      Not Applicable

   b. *Clinical specificity:*
      Not Applicable

   c. Other clinical supportive data (when a. and b. are not applicable):
      Not Applicable

4. Clinical cut-off:
   Not Applicable

5. Expected values/Reference range:

Non-diabetic patient glucose reference range is 74 – 100 mg/dL*

* *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.*

N. Instrument Name:

epoc Blood Analysis System with BGEM Test Card (BGE Test Card plus Glucose)

O. System Descriptions:

1. Modes of Operation:
   Single sample mode of operation for sample reader, Host Personal Digital Assistant (PDA) can link to up to seven readers and actively control up to 4 readers in the analysis mode.
2. Software:
   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:
   Yes ___X____ or No _____
   The applicant has provided software documentation that supports good software life-cycle processes.
3. Specimen Identification:
   Hand entry or Bar-Code
4. Specimen Sampling and Handling:
   Single sample using syringe
5. Calibration:
   Unitized calibrator fluid
6. Quality Control:
   Internal Quality control and recommendation of commercially available external quality control material

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Effect of Hematocrit

Hematocrit effect was evaluated in six glucose level blood linearity studies performed at four different hematocrit levels.

The hematocrit was evaluated by centrifugation using the micro-hematocrit method. The reference mean glucose concentration was computed from the average of at least two in house reference instruments with traceability to NIST standards. The percent bias for each sample tested was within 10% of the reference mean for each level and each level of glucose demonstrated acceptable precision and there was no correlation between the glucose result and the hematocrit.

The summary is presented in the Table below. Each sample was tested on 6 cards, i.e. duplicates from 3 different lots and each individual sample fell within 10% of the reference mean:

Hct [PCV]	Glu level	Ref. mean [mg/dL]	epoc mean [mg/dL]	Mean 95%conf [mg/dL]	epoc %CV	epoc bias [mg/dL]	epoc bias percent
30	35	33.7	34.9	2.1	8.40%	1.2	3.56%
30	60	54.5	55.6	1	2.50%	1.1	2.02%
30	130	128.7	127.9	1.2	1.30%	-0.7	-0.62%
30	200	209.3	212.6	3.2	2.10%	3.2	1.58%
30	400	407.2	425.4	7.9	2.60%	18.2	4.47%
30	600	608.3	601.4	14.8	3.30%	-7	-1.13%
43	35	36.6	36	1.1	1.20%	-0.6	-1.64%
43	50	49.2	46.4	0.8	3.80%	-2.7	-5.69%
43	100	96.8	95.4	1.8	5.70%	-1.4	-1.45%
43	130	129.9	128.4	2.7	2.20%	-1.5	-1.15%
43	200	204.7	205.3	2	2.60%	0.6	0.29%
43	350	330.7	346.4	10.8	2.40%	15.7	4.75%
43	650	670.5	690.5	32.4	4.00%	20	2.98%
52	35	34	35.9	2.1	5.80%	1.9	5.59%
52	60	55.7	55.8	1	2.70%	0.1	0.18%
52	130	130.7	129.7	1.2	1.50%	-0.9	-0.77%
52	200	216	210.2	3.2	1.30%	-5.8	-2.69%
52	400	416.7	417.3	7.9	2.00%	0.7	0.14%
52	600	615.2	596.2	14.8	5.10%	-18.9	-3.09%
62	35	29.7	31.6	0.6	2.10%	1.9	6.40%
62	50	46.8	45.9	0.4	1.20%	-1	-1.92%
62	100	95.4	93.9	1.9	1.80%	-1.5	-1.57%
62	130	127.5	121.7	1.3	1.00%	-5.8	-4.55%
62	200	205.1	201.6	3.5	1.30%	-3.4	-1.71%
62	350	326	336	3.2	2.50%	10	3.07%
62	650	666	685.3	9.8	2.20%	19.2	2.90%

Table – Summary of Glucose Blood Linearity Results at Various Hct Levels

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.