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

A. 510(k) Number:

k171971

B. Purpose for Submission:

New Device

C. Measurand:

Alkaline phosphate (ALP), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Blood urea nitrogen (BUN) and Creatinine (CREA)

D. Type of Test:

Quantitative, photometric/colorimetric

E. Applicant:

Lite-On Technology Corp.

F. Proprietary and Established Names:

Comprehensive Metabolic Panel
skyla Clinical Chemistry Analyzer
Minicare C300 Clinical Chemistry Analyzer

G. Regulatory Information:

Regulation description	Product Code	Device Class	Regulation Number	Panel
Alkaline Phosphatase test system	CJE	Class II	862.1050	Clinical Chemistry (75)
Blood Urea Nitrogen test system	CDN	Class II	862.1770	
Creatinine test system	CGX	Class II	862.1225	
Aspartate aminotransferase (AST/SGOT) test system	CIT	Class II	862.1100	
Alanine amino transferase (ALT/SGPT) test system	CKA	Class I	862.1030	
Analyzer, chemistry, centrifugal, for clinical use	JJG	Class I	862.2160	

H. Intended Use:

1. Intended use(s):

   See Indications for use below

2. Indication(s) for use:

   The Comprehensive Metabolic Panel is intended to be used for the quantitative determination of Alkaline Phosphate (ALP), Alanine Aminotransferase (ALP/GPT), Aspartate Aminotransferase (AST/GOT), Blood Urea Nitrogen (BUN) and Creatinine (CREA) in concentrations in lithium-heparinized venous whole blood, heparinized plasma, or serum in a clinical laboratory setting or point-of-care location.

   Alkaline phosphatase or its isoenzymes measurements are used in the diagnosis and treatment of liver, bone, parathyroid, and intestinal diseases.

   Alanine aminotransferase measurements are used in the diagnosis and treatment of certain liver diseases (e.g., viral hepatitis and cirrhosis) and heart diseases.

   Aspartate aminotransferase measurements are used in the diagnosis and treatment of certain types of liver and heart disease.

   Blood urea nitrogen measurements are used in the diagnosis and treatment of certain types of renal and metabolic diseases.

   Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

   The skyla Clinical Chemistry Analyzer is an in-vitro diagnostic device for the quantitative determination of clinical chemistry analytes in lithium-heparinized venous whole blood, heparinized plasma, or serum. It is for clinical laboratory and point-of-care use.

   The Minicare C300 Clinical Chemistry Analyzer is an in-vitro diagnostic device for the quantitative determination of clinical chemistry analytes in lithium-heparinized venous whole blood, heparinized plasma, or serum. It is for clinical laboratory and point-of-care use.

3. Special conditions for use statement(s):

   For prescription use only at point-of-care (POC) and clinical laboratory settings.

4. Special instrument requirements:

   skyla Clinical Chemistry Analyzer or Minicare C300 Clinical Chemistry Analyzer

I. Device Description:

The Comprehensive Metabolic Panel contains a set of dried reagents that are used in the quantitative testing of various substances in the blood sample. The Comprehensive Metabolic Panel reagent discs are designed to separate a heparinized venous whole blood sample into plasma and blood cells, quantity the amount of plasma and diluent through the metering function of disc, mix both of plasma and diluent, and deliver the mixture to each reaction wells where the dried reagent are present to initiate the chemical reactions that are then measured by analyzer. Alternately, the disc may also be used with heparinized plasma only and serum sample.

The skyla Clinical Chemistry System consists of a portable analyzer and single-use disposable reagent panel discs. The analyzers utilize precision photometric measurement technology, combined with the use of specific reagent panel disc, to measure the amount of substance in blood. The analyzer measures absorbance change of each reaction well in reagent panel disc and covert it to a concentration value for each analyte included on the panel.

The analyzer contains the following features and components:

- Compatibility with lithium-heparinized venous whole blood samples without the need for sample dilution.
- Operation by a colored touchscreen panel
- Fully automated system for simple operation
- Rapid analysis, reporting test results in approximately 15 minutes
- Power-on self-test capability, ensuring instrument stability
- Internal quality control functionality, ensuring reliable test results
- Built-in thermal printer for immediate printing of the test results

The Minicare C300 Clinical Chemistry Analyzer has the identical design and specifications of skyla Clinical Chemistry Analyzer, except the appearance and 2 additional USB ports.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Abaxis Piccolo

   Abaxis Piccolo Primary Health Panel Reagent Rotor

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

   k942782
   k950164

3. Comparison with predicate:

Assay

Similarities / Differences		
Item	Candidate Device Comprehensive Metabolic Panel k171971	Predicate Device Abaxis Piccolo Primary Health Panel Reagent Rotor k950164
Intended Use	Quantitative determination of alkaline phosphate, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen and creatinine concentrations in lithium-heparinized venous whole blood, heparinized plasma, or serum in a clinical laboratory setting or point-of-care location.	Same
Intended users	Clinical laboratories or point-of-care (POC) settings	Same
Specimen Type	Serum and lithium-heparinized venous whole blood or plasma	Same
Reportable range	ALT: 20 – 500 U/L ALP: 41 – 1500 U/L AST: 20 – 1000 U/L BUN: 2 – 120 mg/dL CREA: 0.6 – 20 mg/dL	ALT: 5 - 2000 U/L ALP: 5 - 2400 U/L AST: 5 – 2000 U/L BUN: 2 – 180 mg/dL CREA: 0.2 - 20 mg/dL
Detection Wavelength	ALT: 340 nm ALP: 405 nm AST: 340 nm BUN: 340 nm CREA: 546 nm	ALT: 340 - 405 nm ALP: 405 - 500 nm AST: 340 – 405 nm BUN: 340 - 405 nm CREA: 550 - 600 nm
Calibration	Bar-encode on each reagent disc with factory calibrated lot specific data	Same
Quality control	Internal quality control function for each reagent disc	Same
Reagent storage	2-8 °C (36-45 °F)	Same

Analyzers

Similarities / Differences		
Item	Candidate Device Skyla Clinical Chemistry Analyzer, Minicare C300 Clinical Chemistry Analyzer k171971	Predicate Device Abaxis Piccolo k942782
Intended Use	An in-vitro diagnostic device for the quantitative determination of clinical chemistry analytes in lithium-heparinized venous whole blood, heparinized plasma, or serum. It is for clinical laboratory and point-of-care use.	Same
Detector	Photodiode	Same
Method of measurement	Colorimetry (Absorbance)	Same
Blood separation function	Centrifugation technology integrated into the instrument	Same
Assay temperature	37 °C (98.6 °F)	Same
Test time	15 minutes	12 minutes
Light Source	LEDs	Xenon arc stroboscopic lamp
Power requirements	100-240 volts AC; 50-60 Hz; or 12 volts DC, 5.0A	100-240 volts AC; 50-60 Hz; or 15 volts DC, 5.0 A
Operating temperature	10-32 °C (50-90 °F)	15-32 °C (59-90 °F)
Sample volume	200 µL	100 µL

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

CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures

CLSI EP06-A Evaluation of Linearity of Quantitative Measurement Procedures

CLSI EP07-A2 Interference Testing in Clinical Chemistry

CLSI EP09-A3 Measurement Procedure Comparison and Bias Estimation Using Patient Samples

CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures

CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents

IEC 60601-1-2 Medical Electrical Equipment-Part 1-2: General Requirements for Basic Safety and Essential Performance

L. Test Principle:

ALP activity is enzymatically determined. *p*-Nitrophenyl phosphate that is hydrolyzed by ALP into a yellow colored product *p*-Nitrophenol which has an absorbance at a wavelength of 405 nm. The rate of the reaction is directly proportional to the enzyme activity.

$$p\text{-Nitrophenyl Phosphate} \xrightarrow{\text{ALP}} p\text{-Nitrophenol} + \text{Phosphate}$$

ALT activity is enzymatically determined. ALT catalyzes the reaction of alanine with α-ketoglutarate, converting them into glutamate and pyruvate. In the presence of NADH, lactate dehydrogenase converts pyruvate into lactate. In the course of the reaction NADH is oxidized to NAD+. The decrease of NADH absorbance is measured at a wavelength of 340 nm and is proportional to ALT activity.

$$\text{L-Alanine} + \alpha\text{-ketoglutarate} \xrightarrow{\text{ALT}} \text{Pyruvate} + \text{L-Glutamate}$$

$$\text{Pyruvate} + \text{NADH} + \text{H+} \xrightarrow{\text{LDH}} \text{L-Lactate} + \text{NAD+} + \text{H2O}$$

AST activity is enzymatically determined. When the test sample reacts with the substrate-enzyme reagent, AST converts L-Aspartic acid and α-ketoglutarate into monosodium glutamate and amide acetate. amide acetate is subsequently converted into malate by malate dehydrogenase while NADH undergoes oxidation to NAD+. The decrease of NADH absorbance is measured at a wavelength of 340 nm and is proportional to AST activity.

$$\text{L-asparate} + \alpha\text{-ketoglutarate} \xrightarrow{\text{AST}} \text{oxaloactate} + \text{L-glutamate}$$

$$\text{oxaloactate} + \text{NADH} \xrightarrow{\text{MDH}} \text{malate} + \text{NAD+}$$

BUN is enzymatically determined. Urea undergoes a urease catalyzed hydrolysis, thus producing ammonia and carbon dioxide. In a glutamate dehydrogenase (GLDH) catalyzed reaction ammonia reacts with 2-oxoglutarate yielding L-glutamate. In the process of this reaction, NADH is oxidized to NAD+ which in turn undergoes a color reaction. The rate of change of absorbance at wavelength of 340 nm is measured and proportional to the BUN concentration.

$$\text{Urea} + \text{H2O} \xrightarrow{\text{Urease}} \text{2NH3} + \text{CO2}$$

$$\text{NH3} + \text{2-Oxoglutarate} + \text{NADH} \xrightarrow{\text{GLDH}} \text{L-Glutamate} + \text{H2O} + \text{NAD+}$$

CREA is determined through the endpoint enzymatic reaction approach. Creatinine amidohydrolase hydrolyzes CREA to creatine. Then creatine is converted into sarcosine through catalysis of creatine amidinohydrolase. Furthermore, sarcosine oxidase oxidizes sarcosine, yielding glycine, formalehyde and peroxide (H2O2) in the process. The enzyme peroxidase processes hydrogen peroxide, 2,4,6-3 hydroxy-benzoic acid (TBHBA) and 4-amine triazolam alternate pyrazol (4-AAP), forming a quinoneimine dye as a product. The dye formation is measured at wavelength of 546 nm and is proportional to the amount of creatinine in the sample.

$$\text{Creatinine} + H_2O \xrightarrow{\text{Creatinine amidohyrolase}} \text{Creatine}$$

$$\text{Creatine} + H_2O \xrightarrow{\text{Creatine amidohyrolase}} \text{Sarcosine} + \text{Urea}$$

Estimated Glomerular Filtration Rate (eGFR)
eGFR is the kidney filtrate per minute, which is calculated from creatinine results. It is used to assess renal function. Calculation of the eGFR is performed by the skyla Clinical Chemistry Analyzer using the patient's age, gender and race. The equation is shown below. For African American, multiply the eGFR value by 1.212.

eGFR = 175 x (Scr)-1.154 x (Age)-0.203 x (0.742 if female)

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   Analytical performance was established using the skyla Clinical Chemistry Analyzer; performance is also representative of the Minicare C300 Clinical Chemistry Analyzer.

   a. Internal Precision/Reproducibility:
   Internal precision was conducted using CLSI EP5-A3 guideline. The study was performed using three levels (low, middle, high) of patient serum samples. Each level was tested on 3 skyla Clinical Chemistry Analyzers and 1 lot of Comprehensive Metabolic Panel disc in duplicates with 2 runs per day over 20 days. The results of the within-run and total precision for one representative analyzer are summarized below:

Test System	N	Level	Mean	Within-run		Total	
				SD	CV (%)	SD	CV (%)
ALP (U/L)	80	1	71.9	1.8	2.5	1.8	2.5
		2	788.8	33.9	4.3	33.9	4.3
		3	1403.1	23.4	1.7	24.2	1.7
ALT (U/L)	80	1	39.9	2.7	6.7	2.7	6.8
		2	194.6	6.1	3.1	6.3	3.2
		3	478.0	14.5	3.0	14.8	3.1

Test System	N	Level	Mean	Within-run		Total	
				SD	CV (%)	SD	CV (%)
AST (U/L)	80	1	36.9	3.0	8.1	3.6	9.7
		2	282.4	6.2	2.2	6.3	2.2
		3	839.7	18.4	2.2	18.9	2.3
BUN (mg/dL)	80	1	14.46	0.52	3.6	0.55	4.5
		2	23.29	0.73	3.1	0.79	3.4
		3	106.86	2.77	2.6	3.26	3.0
Crea (mg/dL)	80	1	1.17	0.09	8.1	0.10	8.5
		2	7.52	0.32	4.3	0.32	4.3
		3	15.65	0.37	2.4	0.40	2.6

b. External Precision studies (serum)

Precision at external POC sites was evaluated as described in CLSI EP5-A3 guideline. The study was performed at 3 point of care settings in 3 outpatient clinics. Each site used 2 analyzers and a total of 9 POC operators. Three levels of human serum were prepared (low, middle, high). The samples were tested by POC operators on the skyla Clinical Chemistry Analyzers in 2 replicates per run, 2 runs per day for 20 days (N=80). The within run, total SD, and percent CVs were calculated. The results for the three POC sites are summarized in the tables below:

Test System	Site	Level	Mean (U/L)	Within-run		Total	
				SD	CV (%)	SD	CV (%)
Serum ALP	POC 1	Serum 1	71.9	2.3	3.2	2.4	3.4
		Serum 2	785.6	31.7	4.0	32.4	4.1
		Serum 3	1407.3	38.9	2.8	42.3	3.0
	POC 2	Serum 1	72.2	2.1	2.9	2.1	2.9
		Serum 2	787	28.1	3.6	30.1	3.8
		Serum 3	1405.1	20.5	1.5	25.9	1.8
	POC 3	Serum 1	71.9	1.7	2.3	1.7	2.3
		Serum 2	784.1	27.1	3.5	32.8	4.2
		Serum 3	1405.9	36.8	2.6	37.5	2.7
	Combined	Serum 1	72.0			1.8	2.56
		Serum 2	785.5			29.3	3.73
		Serum 3	1406.0			33.3	2.36

Test System	Site	Level	Mean	Within-run		Total	
				SD	CV (%)	SD	CV (%)
Serum ALT	POC 1	Serum 1	40.5	2.3	5.7	2.4	5.8
		Serum 2	193.9	5.6	2.9	5.6	2.9
		Serum 3	474.5	11.9	2.5	12.6	2.7
	POC 2	Serum 1	40.7	2.3	5.6	2.3	5.6
		Serum 2	192.3	5.0	2.6	5.4	2.8
		Serum 3	477.2	9.8	2.0	10.8	2.3
	POC 3	Serum 1	40.6	2.0	5.0	2.2	5.3
		Serum 2	194.8	5.9	3.0	6.7	3.4
		Serum 3	478.2	14.8	3.1	14.8	3.1
	Combined	Serum 1	40.6			2.0	5.0
		Serum 2	193.6			5.8	3.0
		Serum 3	476.7			12.3	206

Test System	Site	Level	Mean	Within-run		Total	
				SD	CV (%)	SD	CV (%)
Serum AST	POC 1	Serum 1	40.3	2.9	7.3	3.1	7.65
		Serum 2	283.5	4.7	1.6	5.0	1.8
		Serum 3	842.5	13.8	1.6	13.9	1.6
	POC 2	Serum 1	40.1	3.3	8.2	3.4	8.6
		Serum 2	279.7	5.6	2.0	5.8	2.1
		Serum 3	839.6	10.0	1.2	11.7	1.4
	POC 3	Serum 1	40.0	2.93	7.3	3.4	8.4
		Serum 2	286.0	5.5	1.9	7.2	2.5
		Serum 3	843.3	16.3	1.9	16.5	2.0
	Combined	Serum 1	40			2.9	7.3
		Serum 2	283			6.2	2.2
		Serum 3	841			14.3	1.7

Test System	Site	Level	Mean	Within-run		Total	
				SD	CV (%)	SD	CV (%)
Serum BUN	POC 1	Serum 1	14.43	0.48	3.3	0.50	3.5
		Serum 2	2.43	0.78	3.3	0.78	3.3
		Serum 3	106.67	3.14	2.9	3.57	3.4
	POC 2	Serum 1	14.59	0.43	3.0	0.49	3.4
		Serum 2	23.36	0.88	3.8	0.94	4.0
		Serum 3	106.35	2.53	2.4	3.37	3.2
	POC 3	Serum 1	14.52	0.46	3.1	0.49	3.4
		Serum 2	23.40	0.86	3.7	0.94	4.0
		Serum 3	105.82	3.12	2.9	3.40	3.25
	Combined	Serum 1	14.51			0.48	3.3
		Serum 2	23.40			0.81	3.5
		Serum 3	106.28			3.29	3.1

Test System	Site	Level	Mean	Within-run		Total	
				SD	CV (%)	SD	CV (%)
Serum CREA	POC 1	Serum 1	0.97	0.06	5.8	0.07	7.0
		Serum 2	7.36	0.25	3.3	0.25	3.4
		Serum 3	15.75	0.35	2.2	0.36	2.3
	POC 2	Serum 1	1.28	0.08	6.4	0.09	6.8
		Serum 2	7.62	0.22	2.9	0.25	3.2
		Serum 3	15.62	0.45	2.9	0.48	3.1
	POC 3	Serum 1	1.07	0.07	6.7	0.07	6.8
		Serum 2	7.36	0.27	3.7	0.30	4.0
		Serum 3	15.45	0.41	2.7	0.46	3.0
	Combined	Serum 1	1.11			0.08	7.0
		Serum 2	7.45			0.27	3.7
		Serum 3	15.6			0.43	2.8

c. External precision studies (whole blood)

Whole blood precision was performed at 3 point of care settings in 3 outpatient clinics. Three levels of whole blood samples were tested in ten replicates by 3 POC (total 9 operators) using twelve analyzers in one day. The results are summarized in the following table:

			ALP (U/L)			ALT (U/L)			AST(g/dL)			BUN (mg/dL)			CREA (mg/dL)		
Site	OP	Level	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%
1	1	Low	56.9	2.51	4.4	28	2.7	9.7	32	2.7	8.6	11.0	0.24	2.2	0.9	0.05	5.5
	2	Low	61.5	3.57	5.8	30	2.2	7.5	29	1.9	6.4	10.9	0.21	2.0	0.9	0.07	7.4
	3	Low	61.9	2.69	4.3	31	2.5	8.1	31	2.9	9.3	10.5	0.36	3.5	0.9	0.07	7.3
	1	Med	744.9	12.06	1.6	294	4.1	1.4	459	6.4	1.4	30.9	0.72	2.3	7.7	0.17	2.2
	2	Med	749.9	15.79	2.1	294	3.4	1.2	459	5.4	1.2	31.1	0.88	2.8	7.6	0.27	3.5
	3	Med	757.7	13.57	1.8	298	6.5	2.2	31.6	2.7	8.6	30.6	1.18	3.9	7.6	0.45	5.9
	1	High	1341.0	10.84	0.8	402	6.6	1.6	29.3	1.9	6.4	93.7	3.06	3.3	16.5	0.6	3.6
	2	High	1322.5	11.33	0.9	397	12.9	3.2	30.9	2.9	9.3	92.3	2.96	3.2	16.6	0.62	3.8
	3	High	1315.1	17.22	1.3	401	9.8	2.4	458.6	6.4	1.4	93.8	2.77	3.0	16.6	1.05	6.3
2	1	Low	75.9	2.64	3.5	37	1.0	2.8	458.6	5.4	1.2	10.7	0.33	3.1	0.8	0.05	6.8
	2	Low	68.5	2.84	4.1	37	1.3	3.6	455.6	13.1	2.9	10.5	0.32	3.0	0.7	0.04	5.9
	3	Low	66.0	3.97	6.0	37	1.1	2.9	814.1	3.2	0.4	10.3	0.20	1.9	0.8	0.05	6.3
	1	Med	781.6	12.69	1.6	228	3.2	1.4	800.6	1.6	0.2	16.1	0.45	2.8	3.6	0.17	4.8
	2	Med	766.5	10.83	1.4	230	4.5	2.0	798.0	3.6	0.5	16.2	0.42	2.6	3.7	0.16	4.4

			ALP (U/L)			ALT (U/L)			AST(g/dL)			BUN (mg/dL)			CREA (mg/dL)		
Site	OP	Level	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%
	3	Med	767.7	13.32	1.7	230	7.9	3.4	32.4	2.2	6.7	16.1	0.65	4.0	3.9	0.27	6.9
	1	High	1312.6	13.13	1.0	397	9.8	2.5	28.3	2.2	7.8	111.0	2.98	2.7	16.4	0.63	3.8
	2	High	1311.5	18.92	1.4	401	9.6	2.4	32.5	2.6	8.1	110.5	4.78	4.3	15.8	0.56	3.5
	3	High	1330.0	16.05	1.2	408	10.8	2.6	105.5	6.5	6.2	110.1	4.11	3.7	16.1	0.68	4.2
3	1	Low	99.4	2.91	2.9	41	3.3	8.1	102.6	6.4	6.2	7.4	0.33	4.5	0.8	0.05	7.0
	2	Low	101.0	2.54	2.5	39	1.2	3.0	104.4	7.9	7.6	7.4	0.29	3.9	0.7	0.05	7.0
	3	Low	106.5	3.50	3.3	41	3.9	9.4	817.9	15.8	1.9	7.4	0.23	3.1	0.7	0.04	5.9
	1	Med	677.9	8.88	1.3	219	9.5	4.3	833.3	15.8	1.9	29.0	1.03	3.6	4.7	0.14	3.0
	2	Med	665.0	10.02	1.5	224	5.3	2.3	841.1	11.2	1.3	29.1	0.68	2.3	4.6	0.22	4.7
	3	Med	682.0	4.67	0.7	225	5.6	2.5	40.7	2.1	5.1	28.2	1.05	3.7	4.8	0.33	6.8
	1	High	1405.8	18.27	1.3	476	8.9	1.9	37.8	2.9	7.8	91.4	3.98	4.4	14	0.75	5.3
	2	High	1419.3	9.87	0.7	480	14.9	3.1	40.4	1.4	3.5	93.8	3.30	3.5	14.1	0.62	4.4
	3	High	1398.4	19.68	1.4	481	9.1	1.9	264.7	8.3	3.1	94.7	4.02	4.2	14.4	0.93	6.5

d. Linearity/assay reportable range:

The linearity studies of alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, blood urea nitrogen and creatinine were conducted in accordance to CLSI EP6-A guideline. A high and a low human serum pool sample were proportionally mixed to create 9 intermediate dilutions that span the claimed measuring range of each analyte test. The observed values were plotted against the expected values and linear regression analysis was performed. The summary results are provided in the table below.

Analyte	**Concentration Tested**	**R^2**	**Slope**	**Intercept**	**Claimed Measuring Range**
ALP (U/L)	30 – 2083	0.9967	1.0417	10.329	41 – 1500
ALT (U/L)	17 – 535	0.9999	0.9985	0.4839	20 – 500
AST (U/L)	16 – 1021.3	0.9984	1.0006	0.0405	20 – 1000
BUN (mg/dL)	1.8 – 126.9	0.9979	0.9588	0.7389	2 – 120
CREA (mg/dL)	0.48 – 21.48	0.9993	0.9988	-0.0015	0.6 – 20

The results of the linearity study support the sponsor's claimed measuring ranges (as described in the table above).

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

Traceability
The calibrators are traceable to Siemens ADVIA Chemistry analyzer method calibration to below reference material or method. The calibration parameters of each test system were established internally, and are unique with each reagent lot. The calibration information is bar-encoded on each reagent disc.

Assay	Reference material / method
ALT	The ADVIA ALT method is traceable to the IFCC reference method via patient sample correlation.
ALP	The ADVIA ALP method is traceable to the IFCC reference method via patient sample correlation.
AST	The ADVIA AST method is traceable to the IFCC reference method via patient sample correlation.
BUN	The ADVIA BUN method is traceable to the CDC reference method, which uses reference materials from the National Institute of Standards and Technology (NIST). via patient sample correlation.
CREA	The ADVIA CREA_2 method is traceable to the IDMS Reference Method via correlation of patient samples and reference material SRM967 from the National Institute of Standards and Technology (NIST).

f. Detection limit:

The limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) were determined according to CLSI EP17-A2 guideline. Human serum samples were diluted with BSA to obtain the blank for the LoB studies and low concentration samples for LoD and LoQ studies. LoB was determined by running three blank samples in triplicate on two skyla Clinical Chemistry Analyzers with two reagent disc lots per day for ten days (N=60). LoD and LoQ were performed using serum samples containing very low concentrations of the analyte tested in triplicate using 2 lots of reagents disc for ten days (N=60).

The LoB is the 95th percentile value from 60 measurements of a near zero of sample over 10 days.
The LoD was calculated using the following formula: $LoD = LoB + c\beta * SD_S$.
In the equation, $c\beta = 1.645/(1-(1/(4*f))$, where f is the degrees of freedom, and SD_S is the standard deviation of the low concentration sample.

LoQ is defined as the concentration at which measured total error is less than the pre-defined total error of ±30%.

The results of LoB, LoD and LoQ are summarized below table.

Analyte	LoB	LoD	LoQ	Claimed Measuring Range
ALP (U/L)	2.350	4.405	4.405	41 – 1500
ALT (U/L)	2.701	5.228	5.228	20 – 500
AST (U/L)	6.695	12.089	11.690	20 – 1000
BUN (mg/dL)	0.795	1.526	1.526	2 – 120
CREA (mg/dL)	0.108	0.262	0.262	0.6 – 20

g. *Analytical specificity:*

To determine the effects of potential endogenous and exogenous interference, the sponsor conducted an analytical specificity study according to CLSI EP07-A2 guideline. Different known concentrations of the interferent were tested in triplicate on two concentration of each analyte: level 1 (within normal range) and level 2 (high level at abnormal range). Samples were tested using the skyla Clinical Chemistry Analyzer with the Comprehensive Metabolic Panel (ALP, ALT, AST, BUN and CREA). The sponsor defined significant interference as bias >10% between the test and control samples.

Analyte	Highest concentrations tested that did not show significant interference			
	Hemolysis (Hemoglobin)	Icterus Bilirubin (unconjugated)	Icterus Bilirubin (conjugated)	Lipemia (Intralipid)
ALP	600 mg/dL	66.4 mg/dL	32.7 mg/dL	1032 mg/dL
ALT	243 mg/dL	60.3 mg/dL	18.2 mg/dL	411 mg/dL
AST	202 mg/dL	15.9 mg/dL	32.7 mg/dL	189.9 mg/dL
BUN	600 mg/dL	66.4 mg/dL	29.3 mg/dL	1032 mg/dL
CREA	224 mg/dL	13.1 mg/dL	2.6 mg/dL	390.8 mg/dL

Substances	Effect of exogenous substances		
	Test Concentration	Affected Test Item	Effect
Acetaminophen	20 mg/dL	No significant interference	
Acetylsalicylic acid	65 mg/dL	No significant interference	
Ampicillin	5 mg/dL	No significant interference	
Ascorbic acid	6 mg/dL	No significant interference	
Caffeine	6 mg/dL	No significant interference	
Cephalothin	30 mg/dL	No significant interference	
Cimetidine	2 mg/dL	No significant interference	
Ibuprofen	50 mg/dL	CREA	11.8% increase
Salicylic acid	60 mg/dL	ALT	16.3% decrease
Theophylline	4 mg/dL	ALP	14.4% decrease

The interfering substance with significant interference (>10% bias) are as follows:

- ALP concentrations are decreased by 14.4% when 4 mg/dL Theophylline is present in the sample.
- Salicylic Acid at 60 mg/dL causes a 16.3% decrease in ALT levels.
- Creatinine levels are increased by 11.8% in the presence of 50 mg/dL Ibuprofen.

h. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

POC Method comparison, whole blood and serum
The method comparison study was performed at three POC sites using 8 analyzers and s total of 9 POC operators. A total of 120 lithium heparinized venous whole blood and serum samples were tested using the skyla Clinical Chemistry Analyzer and Comprehensive Metabolic Panel and compared to matched serum samples analyzed using ALP, ALT, AST, BUN and Creatinine assays on the Beckman Coulter AU2700. The results of the overall performance of the device at all the sites are summarized in the tables below.

Summary Result of Method Comparison, Lithium heparin whole blood

Analyte	**Correlation Coefficient**	**Slope**	**Intercept**	**N**	**Sample range tested**
ALP	0.9987	0.9963	1.5568	221	41 – 1421 U/L
ALT	0.9978	1.0029	-0.1760	185	20 – 491 U/L

Analyte	Correlation Coefficient	Slope	Intercept	N	Sample range tested
AST	0.9989	1.0013	1.0197	174	20 – 998 U/L
BUN	0.9981	0.9935	-0.0710	210	2.4 – 118 mg/dL
CREA	0.9978	1.0121	-0.0737	191	0.6 – 19.7 mg/dL

Summary Result of Method Comparison, Serum

Analyte	Correlation Coefficient	Slope	Intercept	N	Sample range
ALP	0.9987	1.0020	2.9364	221	42 – 1422 U/L
ALT	0.9985	0.9916	2.5606	185	20 – 486 U/L
AST	0.9986	0.9996	1.2770	174	20 – 994 U/L
BUN	0.9981	1.0017	0.1119	210	2.7 – 120 mg/dL
CREA	0.9977	1.0064	-0.0455	191	0.6 - 19.8 mg/dL

b. Matrix comparison:

Studies were performed using matched serum, lithium heparin venous whole blood, and lithium heparinized plasma. A total of 40 human samples were analyzed using the skyla Clinical Chemistry Analyzer. The linear regression analyses are as follows:

Test	Matrix	Slope	Intercept	Correlation Coefficient	Sample range
ALP (U/L)	Serum vs. Plasma	0.994	1.5	0.9997	44-1407
	WB vs. Serum	0.996	1.4	0.9997	45-1392
ALT (U/L)	Serum vs. Plasma	1.002	-1.3	0.9998	21-485
	WB vs. Serum	0.993	1.2	0.9997	21-592
AST (U/L)	Serum vs. Plasma	0.988	3.6	0.9987	20-953
	WB vs. Serum	0.988	3.8	0.9989	20-998
BUN (mg/dL)	Serum vs. Plasma	1.011	-0.45	0.9989	7.7-90.2
	WB vs. Serum	0.982	0.71	0.9990	7.8-91.7
CREA (mg/dL)	Serum vs. Plasma	0.960	0.13	0.9965	0.7-19.3
	WB vs. Serum	1.004	-0.02	0.9971	0.6-19.8

The results of the matrix comparison study support the sponsor claim that serum, lithium heparin plasma and venous lithium heparin whole blood samples can be tested with these assays.

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:

   The following expected values are provided in the product insert based on the literature[1]:

Analyte		Reference range	Reference range (SI units)
ALP		37 – 108 U/L	37 – 108 U/L
ALT		10 - 40 U/L	10 - 40 U/L
AST		10 – 42 U/L	10 – 42 U/L
BUN		9 – 23 mg/dL	3.2 – 8.2 mmol urea/L
Creatinine	Male	0.7 – 1.3 mg/dL	62 – 115 µmol/L
	Female	0.6 – 1.1 mg/dL	53 – 97 µmol/L

[1]C. A. Burtis, E. R. Ashwood, and D. E. Bruns. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 4th ed., Elsevier Saunders, St. Louis, 2006

N. Instrument Name:

skyla Clinical Chemistry Analyzer
Minicare C300 Clinical Chemistry Analyzer

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ____X____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___X___

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ____X____ or No _____

3. Specimen Identification:

   The user can utilize an external barcode scanner or touch screen display to manually enter patient information.

4. Specimen Sampling and Handling:

   The following type of sampling devices are acceptable on the Skyla Chemistry Clinical Chemistry Analyzer and Minicare C300 Clinical Chemistry Analyzer:

   - lithium-heparinized venous whole blood
   - heparinized plasma
   - serum

5. Calibration:
   The Analyzer performs automatic system calibrations every time the instrument is powered on. The barcode on every manufactured reagent disc contains all information required for calibration of the test items. The analyzer will automatically read the barcode information during testing.

6. Quality Control:

   The sponsor recommends using BIO-RAD Lyphochek Assayed Chemistry Control / two levels (Level 1 and Level 2). The following recommendations are included in package insert:

   - Quality control should be performed on each day the instrument is used.
   - Users should follow local, state and federal regulations for quality control materials testing.
   - Quality control should be analyzed when a new lot of discs are used on the analyzer.
   - Quality control should be performed after analyzer has been turned off for any reason or reinitializing the analyzer.
   - Quality control should be performed after routine maintenance procedures.
   - Before a new batch of reagents is used for testing.

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

Not applicable.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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