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

A. 510(k) Number:

k183375

B. Purpose for Submission:

New device

C. Measurands:

Glucose, sodium, potassium, and chloride

D. Type of Test:

Glucose – quantitative, enzymatic (glucose hexokinase)
Sodium, potassium, and chloride – quantitative, ion selective electrode

E. Applicant:

Horiba, Ltd.

F. Proprietary and Established Names:

Yumizen C1200 Glucose HK
Sodium Electrode
Potassium Electrode
Chloride Electrode
Yumizen C1200

G. Regulatory Information:

Regulation Section	Classification	Product Code	Panel
862.1345 Glucose test system	Class 2	CFR	Chemistry (75)
862.1665 Sodium test system		JGS	
862.1600 Potassium test system		CEM	
862.1170 Chloride test system		CGZ	
862.2160 analyzer Discrete photometric chemistry analyzer for clinical use.	Class 1	JJE	

H. Intended Use:

1. Intended use(s):

   Refer to Indications for Use

2. Indication(s) for use:

   The Yumizen C1200 Glucose HK reagent is intended for the quantitative in vitro diagnostic determination of glucose in human serum, plasma, and urine using a glucose hexokinase method by colorimetry. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.

   The sodium electrode is an ion selective electrode that is intended for use on the ion selective electrode (ISE) unit of the Yumizen C1200 analyzer. The sodium electrode is used to quantify the concentrations of sodium ions in serum, plasma, and urine. Measurements obtained by this device are used in the diagnosis and treatment of aldosteronism (excessive secretion of the hormone aldosterone), diabetes insipidus (chronic excretion of large amounts of dilute urine, accompanied by extreme thirst), adrenal hypertension, Addison's disease (caused by destruction of the adrenal glands), dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance.

   The potassium electrode is an ion selective electrode that is intended for use on the ion selective electrode (ISE) unit of the Yumizen C1200 analyzer. The potassium electrode is used to quantify the concentrations of potassium ions in serum, plasma, and urine. Measurements obtained by this device are used to monitor electrolyte balance in the diagnosis and treatment of diseases and conditions characterized by low or high blood potassium levels.

   The chloride electrode is an ion selective electrode that is intended for use on the ion selective electrode (ISE) unit of the Yumizen C1200 analyzer. The chloride electrode is used to quantify the concentrations of chloride ions in serum, plasma, and urine. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

   The Yumizen C1200 is an automatic chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. Applications include colorimetric and ion selective electrode. This analyzer is intended for professional use in a laboratory environment only. Tests performed using this analyzer are intended for in vitro diagnostic use.

3. Special conditions for use statement(s):

   For in vitro diagnostic use only.

4. Special instrument requirements:

   Yumizen C1200

I. Device Description:

The Yumizen C1200 is an automatic chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. Applications include colorimetric and ion selective electrode. This analyzer is intended for professional use in a laboratory environment only. Tests performed using this analyzer are intended for in vitro diagnostic use.

The Yumizen C1200 Glucose HK reagent consists of:

Reagent 1: TRIS Buffer, pH 7.8 100 mmol/L, Mg2+ 4 mmol/L, NAD+ 2.1 mmol/L and ATP 2.1 mmol/L.

Reagent 2: Hexokinase (HK) ≥ 7500 U/L, G-6-PDH ≥ 7500 U/L, and Mg^{2+} 4 mmol/L.

The ISE reagent consists of:

ISE Serum High Standard
ISE Serum Low Standard
ISE Urine High Standard
ISE Urine Low Standard
ISE Buffer (contains Formaldehyde < 1.0w/v%, Phosphoric acid < 1.0w/v%, Triethanolamine < 2.0w/v%)
Internal Standard

J. Substantial Equivalence Information:

1. Predicate device name(s):

   ABX PENTRA Glucose HK CP (Pentra C400 Analyzer)
   ISE reagents (DxC 700 AU Clinical Chemistry Analyzer)
   DxC 700 AU Clinical Chemistry Analyzer

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

   k081276
   k161837
   k161837

3. Comparison with predicate:

Similarities and Differences – Glucose reagent

Item	Predicate Device ABX Pentra **Glucose** HK CP (k081276)	Candidate Device Yumizen C1200 **Glucose** HK (k183375)
Intended use	For quantitative in vitro diagnostic determination of glucose in human serum, plasma and urine using glucose hexokinase method by colorimetry.	Same
Method	Enzymatic method using hexokinase coupled with glucose-6-phosphate dehydrogenase	Same
Sample type	Serum, Plasma, Urine	Same
Reagent format	Liquid	Same
Reagent stability	Open: Stable for 55 days on board	Same
	Closed: Stable up to the expiry date on the label if stored at 2-8°C.	Same
Measuring Range – serum/plasma	1.98 – 900.00 mg/dL	1.8 – 630.0 mg/dL
Measuring Range – urine	3.96 – 900.0 mg/dL	8.5 – 630 .0 mg/dL
Automatic post-dilution	up to 2700 mg/dL	up to 2520 mg/dL

Similarities and Differences – Sodium, Potassium and Chloride

Item	Predicate Device ISE reagents on DxC 700 AU Clinical Chemistry Analyzer (k161837)	Candidate Device Sodium Electrode, Potassium Electrode, Chloride Electrode (k183375)
Intended use	For the quantitative determination of sodium, potassium and chloride concentrations in human serum, plasma, and urine.	Same
Sodium Electrode	Crown ether membrane	Same
Potassium Electrode	Crown ether membrane	Same
Chloride Electrode	Super-layer solid molecule orientation membrane	Same
Reference Electrode	Sealed silver/silver chloride electrode	Same
Sample Types	Serum, Plasma, Urine	Same
Measuring range	Serum and plasma: Cl 50 - 200 mmol/L	Same
	Urine Na 10 – 400 mmol/L	Same
	Urine Cl 15 – 400 mmol/L	Same
Measuring range	Serum/plasma Na 50 - 200 mmol/L	Na 100 - 200 mmol/L
	Serum/plasma K 1.0 – 10.0 mmol/L	K 1.5 – 10 mmol/L
	Urine K 2.0 – 200.0 mmol/L	K 2 – 300 mmol/L

Similarities and Differences - Analyzer

Item	Predicate Device DxC 700 AU Clinical Chemistry Analyzer (k161837)	Candidate Device Yumizen C1200 (k183375)
Intended Use	Automated chemistry analyzer that measures analytes in samples, in combination with appropriate reagents, calibrators, quality control (QC) material and other accessories. The system is for in vitro diagnostic use only.	Same
Throughput	Without ISE: 800 tests/h With ISE :1200 tests/h	Same
Sample volume	1.0 to 25.0 µL	Same
Bar-code reader	Integrated	Same
Auto dilution feature	Yes	Same
Type of reagent	Liquid	Same
Sample type	Serum, Plasma, Urine, Cerebrospinal fluid (CSF)	Serum, Plasma, Urine
Sample capacity	150 (15 racks × 10 samples)	84 (2 Sample tray × 42 samples)
Total reaction volume	Min: 120 µL, Max: 350 µL	Min: 80 µL, Max: 430 µL
Wavelengths	340 to 800 nm	340 to 884 nm
	13 wavelengths: 340, 380, 410, 450, 480, 520,540, 570, 600, 660, 700, 750 and 800 nm (maximum of 2 wavelengths)	14 wavelengths: 340, 410, 451, 478, 505, 545, 571, 596, 658, 694, 751, 805, 845 and 884 nm (maximum of 2 wavelengths)
Cuvette Material	Glass	Plastic
Dimensions (W x D x H)	1250 × 890 mm × 1300 mm	1220 × 850 × 1108 mm
Weight	465 kg	450 kg
Number of cuvettes	165	231

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

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition.

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.

CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition.

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline.

CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.

CLSI C28-A3: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline; Third Edition.

L. Test Principle:

Glucose – Glucose in the sample is phosphorylated by hexokinase (HK) in the presence of adenosine triphosphate (ATP) and magnesium ions to produce glucose-6-phosphate (G-6-P) and adenosine diphosphate (ADP). Glucose-6-phosphate dehydrogenase (G- 6-PDH) specifically oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD+) to nicotinamide adenine dinucleotide (NADH), reduced. The change in absorbance at 340/410 nm is proportional to the amount of glucose present in the sample.

Sodium/Potassium/Chloride – The ISE module employs membrane electrodes for sodium, potassium and chloride that are specific for each ion of interest in the sample. An electrical potential is developed according to the Nernst Equation for a specific ion. When compared to the Internal Solution, this electrical potential is translated into voltage and then into the ion concentration of the sample.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   Precision studies were performed in accordance with CLSI EP05-A3.

   Repeatability Precision – Glucose serum and urine

   The sponsor evaluated the repeatability of the glucose method by analyzing two concentrations of control materials and five concentrations of patient samples for both serum and urine matrices. The data was collected using one instrument system and one reagent lot, and twenty replicates were collected per sample by one trained technician.

Results are summarized below:

Sample	Serum		Urine	
	Mean	CV %	Mean	CV %
Control N	91.91	1.1	23.85	0.5
Control P	275.02	0.7	294.27	0.6
Sample 1	9.92	1.1	11.13	0.9
Sample 2	30.80	0.9	17.07	1.0
Sample 3	96.52	0.8	178.71	0.5
Sample 4	272.07	0.8	353.08	0.8
Sample 5	556.09	0.5	570.28	0.6

Total Precision - Glucose serum and urine

The sponsor evaluated the total precision of the glucose method by analyzing two concentrations of control materials and five concentrations of patient samples for both serum and urine matrices. The data was collected using three instrument systems and one reagent lot, and four replicates were collected per sample per day over 20 days by one trained technician.

Results are summarized below:

Samples	Serum		Urine	
	Mean (mg/dL)	CV %	Mean (mg/dL)	CV %
Control N	92.70	1.5	25.04	4.0
Control P	255.24	1.4	279.65	3.0
Sample 1	12.65	2.3	11.87	3.6
Sample 2	30.63	1.8	16.64	3.4
Sample 3	103.56	1.7	174.80	3.2
Sample 4	259.29	1.6	324.70	3.3
Sample 5	571.87	1.6	537.47	4.3

Repeatability Precision – ISE Serum and Urine

The sponsor evaluated the repeatability of the sodium, potassium and chloride assays in serum by analyzing four levels of control materials and four levels of patient samples. Repeatability of the ISE methods in urine was evaluated by analyzing two levels of control materials and four levels of patient samples.

The data was collected using one instrument system and three reagent lots, and twenty replicates were collected per sample by three trained technicians.

Results from one representative lot are summarized below:

Serum

Sample	Sodium		Potassium		Chloride	
	Mean (mmol/L)	%CV	Mean (mmol/L)	%CV	Mean (mmol/L)	%CV
Control N	134.68	0.2	4.336	0.2	115.47	0.3
Control P	135.37	0.2	6.689	0.3	114.5	0.2
Control N2	123.1	0.2	3.865	0.3	91.7	0.3
Control P2	155.18	0.2	6.567	0.3	112.17	0.3
Sample 1	126.81	0.3	2.779	0.3	90.89	0.3
Sample 2	139.61	0.3	4.067	0.3	102.29	0.4
Sample 3	149.51	0.3	5.896	0.2	113.09	0.4
Sample 4	165.83	0.3	6.742	0.3	130.35	0.3

Urine

Sample	Sodium		Potassium		Chloride	
	Mean (mmol/L)	%CV	Mean (mmol/L)	%CV	Mean (mmol/L)	%CV
Control N	86.65	0.3	31.104	0.4	66.09	0.4
Control P	178.09	0.4	83.115	0.4	171.54	0.3
Sample 1	28.36	1.2	29.176	0.3	30.78	2.2
Sample 2	103.53	0.3	68.365	0.5	106.76	0.8
Sample 3	186.54	0.3	118.05	0.4	190.33	0.6
Sample 4	331.45	0.3	218.953	0.5	292	0.3

Total Precision - ISE serum and urine

The sponsor evaluated the total precision of the ISE methods by analyzing four concentrations of control materials and four concentrations of patient samples for both serum and urine matrices. The data was collected using three instrument systems and one reagent lot, and four replicates were collected per sample per day over 20 days by one trained technician. Results are summarized below:

Serum Samples	Sodium		Potassium		Chloride	
	Mean (mmol/L)	CV (%)	Mean (mmol/L)	CV (%)	Mean (mmol/L)	CV (%)
Control N	134.09	0.4	4.296	0.5	113.49	0.4
Control P	134.22	0.3	6.599	0.6	111.34	0.4
Control N2	122.41	0.4	3.814	0.7	90.77	0.4
Control P2	154.02	0.3	6.514	0.5	111.51	0.4
Low sample	126.47	0.3	2.800	1.6	90.25	0.3
Middle sample	139.09	0.3	4.058	0.6	101.59	0.3
High sample	148.82	0.3	5.861	0.6	112.36	0.3
Spiked sample	164.53	0.4	6.706	0.8	129.46	0.4

Urine Samples	Sodium		Potassium		Chloride	
	Mean (mmol/L)	CV (%)	Mean (mmol/L)	CV (%)	Mean (mmol/L)	CV (%)
Control N	85.31	0.7	31.131	0.7	60.40	1.8
Control P	179.90	0.4	84.269	0.6	162.60	1.2
Low sample	27.93	1.5	29.388	1.6	24.29	3.1
Middle sample	103.29	0.5	68.638	0.7	100.79	0.7
High sample	187.18	0.4	117.706	1.1	199.13	0.4
Spiked sample	335.21	0.7	222.108	1.3	323.05	0.6

b. Linearity/assay reportable range:

Linearity studies were performed in accordance with CLSI EP06-A guideline. Test samples spanning the claimed measuring ranges were prepared and analyzed for each analyte. The results of the linearity studies supported the claimed measuring ranges, as summarized below:

Analyte / Matrix	Measuring Range
Glucose Serum / Plasma	1.8 to 630 mg/dL
Glucose Urine	8.5 to 630 mg/dL
Sodium Serum / Plasma	100 to 200 mmol/L
Sodium Urine	10 to 400 mmol/L
Potassium Serum / Plasma	1.5 to 10 mmol/L
Potassium Urine	3 to 300 mmol/L
Chloride Serum / Plasma	52 to 200 mmol/L
Chloride Urine	15 to 400 mmol/L

The sponsor also performed a study to evaluate the auto-dilute feature available for serum and urine glucose measurements. The study protocol and acceptance criteria were reviewed and found to be acceptable. The results of the study supported the sponsor's claim that samples with glucose concentrations above 630 mg/dL can be diluted onboard the analyzer to obtain results up to 2520 mg/dL for serum, plasma and urine.

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

The calibrators are traceable to commercially available reference materials for glucose, sodium, potassium, and chloride.

d. Detection limit:

The sponsor performed limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) studies for the Glucose assay according to the CLSI EP17-A2 guideline. Results are summarized in the table below.

Parameter	LoB	LoD	LoQ
Serum/Plasma (mg/dL)	0.39	0.75	1.8
Urine (mg/dL)	0.20	1.00	3.5

The sponsor chose to use 1.8 mg/dL as the lowest reportable value for serum and 8.5 mg/dL as the lowest reportable value for urine.

The sponsor performed LoQ studies for the ISE assays according to the CLSI EP17-A2 guideline. Samples at 11 different concentrations were analyzed in replicates of four over four days using two lots of reagent. The LoQ was defined as the highest concentration meeting the following total error goals: 7.0% for serum sodium, 8.0% for serum potassium, 7.4% for serum chloride and 17.6% for urine sodium, potassium and chloride.

Results are summarized in the table below.

Parameter	LoQ
Serum/Plasma Sodium (mmol/L)	32.05
Urine Sodium (mmol/L)	9.71
Serum/Plasma Potassium (mmol/L)	0.909
Urine Potassium (mmol/L)	0.258
Serum/Plasma Chloride (mmol/L)	22.59
Urine Chloride (mmol/L)	7.00

The upper and lower limits of the measuring range for the sodium, potassium and chloride assays are supported by the LoQ studies and the linearity studies (described under section M.2.b above).

e. *Analytical specificity:*

Interference studies were performed according to the CLSI EP07-A2 guideline. Potential interferents were spiked into serum and urine sample pools and tested on the candidate device. The sponsor defined interference as a bias of ≥ 10%. None of the compounds in the table below caused interference up to and including the concentrations listed.

Serum Glucose		Urine Glucose	
Hemoglobin	501 mg/dL	Hemoglobin	501 mg/dL
Triglycerides	569 mg/dL	Total Bilirubin	27.20 mg/dL
Total Bilirubin	35.53 mg/dL	Ascorbic Acid	5.98 mg/dL
Direct Bilirubin	21.09 mg/dL	pH	1.7 – 11.2
Acetylsalicylic Acid	65.16 mg/dL	Specific gravity	1.000 - 1.030
Ascorbic Acid	5.98 mg/dL		
Ibuprofen	50.1 mg/dL		
Acetaminophen	20 mg/dL		

Serum Sodium, Potassium, Chloride	
Hemoglobin	0.5 g/dL
Triglycerides	52.1 mmol/L
Total Bilirubin	396 µmol/L
Total Protein	121.13 g/L
Urea	71.9 mmol/L
Salicylic Acid	0.53 mmol/L
Imipramine	2.50 µmol/L
Procainamide	102 µmol/L
Chlorpromazine	6.30 µmol/L
Erythromycin	81.6 µmol/L
Ampicillin	150 µmol/L

Urine Sodium, Potassium, Chloride	
Hemoglobin	1.25 g/dL
Total Bilirubin	256 µmol/L
Total Protein	3.31 g/L
Urea	988.3 mmol/L
Ascorbic Acid	3.40 mmol/L

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Glucose

Serum and urine samples were tested using the Glucose HK reagent on the Yumizen C1200 and compared with the Pentra C400 Clinical Chemistry Analyzer. A single replicate was analyzed on both the candidate and comparator method. The equation for the regression line using the Passing Bablok method was obtained and is summarized below:

Analyte	N	Intercept	Slope	Correlation (R^2)
Glucose in serum (mg/dL)	141	-2.453	1.005	0.996
Glucose in urine (mg/dL)	100	0.975	1.007	0.999

Sodium, Potassium, Chloride

Serum and urine samples were tested using the ISE module of the Yumizen C1200 and compared with the AU400 Analyzer. The equation for the linear regression analysis was obtained and is summarized below:

Analyte	N	Intercept	Slope	Correlation (R^2)
Sodium in serum (mmol/L)	165	1.371	0.987	0.995
Sodium in urine (mmol/L)	194	-1.256	1.001	1.000
Potassium in serum (mmol/L)	170	0.023	0.994	0.999

Analyte	N	Intercept	Slope	Correlation (R^2)
Potassium in urine (mmol/L)	198	-0.128	0.983	0.999
Chloride in serum (mmol/L)	172	0.818	0.992	0.998
Chloride in urine (mmol/L)	194	0.525	0.991	1.000

The sponsor also performed a second method comparison study to evaluate the performance of the candidate device when using lithium heparin plasma samples. For glucose, lithium heparin plasma samples were evaluated on the candidate device and the Pentra C400 analyzer with ABX Pentra Glucose HK reagent. For sodium, potassium, and chloride, lithium heparin plasma samples were evaluated on the candidate device and the Olympus AU400 Clinical Chemistry Analyzer. Results are summarized below:

Analyte	N	Intercept	Slope	Correlation (R^2)
Glucose	56	-0.070	0.991	0.999
Sodium	171	0.200	1.000	0.997
Potassium	173	0.010	1.000	0.999
Chloride	173	-1.568	1.019	0.998

b. Matrix comparison:

The performance of the device with serum and lithium heparin plasma samples was evaluated in the method comparison section above.

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:

Glucose
Serum: 70 - 115 mg/dL
Urine: < 15 mg/dL

Sodium
Serum: 136 - 145 mmol/L
Urine: 40 - 220 mmol/day

Potassium
Serum: 3.5 - 5.1 mmol/L
Urine: 25 - 235 mmol/day

Chloride
Serum: 98 - 107 mmol/L
Urine: 110 - 250 mmol/day

References

Tietz NW, Clinical Guide for Laboratory Tests 3rd edition.

Walker HK, et al. Clinical Methods: The History, Physical, and Laboratory Examinations 3rd edition.

Thomas L. Clinical Laboratory Diagnostics. 1st edition.

N. Instrument Name:

Yumizen C1200

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:

   Specimens are identified using the built-in barcode reader.

4. Specimen Sampling and Handling:

   Instructions on specimen sampling and handling are provided in the reagent labeling.

5. Calibration:

   Instructions on calibration are provided in the reagent labeling. For glucose, calibration stability is defined as 6 weeks, and users are instructed to recalibrate with every new reagent lot and when quality control values fall outside of the established ranges. For sodium, potassium, and chloride, users are instructed to calibrate daily, after maintenance, and after replacing the ISE Buffer, Internal Standard, electrode, or consumable items.

6. Quality Control:

   The sponsor recommends that controls be assayed daily and/or after a calibration. The frequency of controls should correspond to laboratory guidelines and follow federal, state and local guidelines.

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.