February 12, 2019

Horiba, Ltd
Naoyuki Nomura
Medical Segment Strategy Office Assistant Section Leader
2 Miyanohigashi, Kisshoin, Minami-ku
Kyoto, 601-8510
Japan

Re: K183375
Trade/Device Name: Yumizen C1200 Glucose HK
Sodium Electrode
Potassium Electrode
Chloride Electrode
Yumizen C1200
Regulation Number: 21 CFR 862.1345
Regulation Name: Glucose test system
Regulatory Class: Class II
Product Code: CFR, JGS, CEM, CGZ, JJE
Dated: November 30, 2018
Received: December 6, 2018

Dear Naoyuki Nomura:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kellie B. Kelm -S

for Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
k183375

Device Name
Yumizen C1200, Yumizen C1200 Glucose HK, Sodium Electrode, Potassium Electrode, Chloride Electrode

Indications for Use *(Describe)*

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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) SUMMARY

"This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92."
"The assigned 510(k) number is: k183375.

Date of Summary:
02/08/2019

Product Name
Yumizen C1200

Sponsor
HORIBA, Ltd.
2 Miyanohigashi, Kisshoin, Minami-ku, Kyoto 601-8510, Japan

Correspondent
Naoyuki Nomura
2 Miyanohigashi, Kisshoin, Minami-ku, Kyoto 601-8510, Japan
+81-80-4358-0440
naoyuki.nomura@horiba.com

Device Trade or Proprietary Name

1. Clinical Chemistry Analyzer

Trade/Proprietary Name:	Yumizen C1200
Common or Usual Name:	Clinical Chemistry Analyzer
Device Class:	Class I
Regulation:	§862.2160
Classification Name:	Discrete photometric chemistry analyzer for clinical use
Product Code:	JJE: Analyzer, Chemistry (Photometric, Discrete), For Clinical Use
Review Panel	Clinical Chemistry

2. Glucose

Trade/Proprietary Name:	Yumizen C1200 Glucose HK
Common or Usual Name:	Glucose HK
Device Class:	Class II
Regulation:	§862.1345
Classification Name:	Glucose test system
Product Code:	CFR: Hexokinase, Glucose
Review Panel	Clinical Chemistry

3. ISE module

Trade/Proprietary Name:	Sodium Electrode
Common or Usual Name:	Sodium Electrode
Device Class:	Class II
Regulation:	§862.1665
Classification Name:	Sodium test system
Product Code:	JGS: Electrode, Ion Specific, Sodium
Review Panel	Clinical Chemistry

Trade/Proprietary Name: Potassium Electrode
Common or Usual Name: Potassium Electrode
Device Class: Class II
Regulation: §862.1600
Classification Name: Potassium test system
Product Code: CEM: Electrode, Ion Specific, Potassium
Review Panel Clinical Chemistry

Trade/Proprietary Name: Chloride Electrode
Common or Usual Name: Chloride Electrode
Device Class: Class II
Regulation: §862.1170
Classification Name: Chloride test system
Product Code: CGZ: Electrode, Ion-Specific, Chloride
Review Panel Clinical Chemistry

Substantial Equivalency

Investigational Device	Primary Predicate Device name	Primary predicate device manufacturer	k number
Yumizen C1200	DxC 700 AU Clinical Chemistry Analyzer	Beckman Coulter, Inc.	k161837
Yumizen C1200 Glucose HK	ABX PENTRA Glucose HK CP on Pentra C400 CLINICAL CHEMISTRY ANALYZER	HORIBA ABX SAS	k081276
Sodium Electrode	ISE reagents on DxC 700 AU Clinical Chemistry Analyzer	Beckman Coulter, Inc.	k161837
Potassium Electrode			
Chloride Electrode			

1. Device Comparison between Yumizen C1200 and DxC 700 AU Clinical Chemistry Analyzer table

Item	Primary Predicate Device name DxC 700 AU Clinical Chemistry Analyzer k161837	Investigational Device Yumizen C1200
Manufactured by	Beckman Coulter, Inc.	JEOL Ltd.
Instrument type	Stand type	Same
Work station	Separate	Same
Throughput	Without ISE: 800 tests/h With ISE :1200 tests/h	Same
Sample treatment		
Sample type	Serum, Plasma, Urine, Cerebrospinal fluid (CSF)	Serum, Plasma, Urine
Sample input	Sample rack, STAT Table, Direct-line Sample Aspiration (For Automation Connections)	Sample tray, STAT Table
Sample volume	1.0 to 25.0 µL	Same
Parameters on board	60 photometric tests + 3 ISEs	45 photometric tests + 3 ISEs
Sample capacity	150 (15 racks × 10 samples)	84 (2 Sample tray × 42 samples)
Bar-code reader	Integrated	Same
Dilution of patient sample	Yes	Same
Reagent		
Type of reagent	Liquid	Same

Item	Primary Predicate Device name DxC 700 AU Clinical Chemistry Analyzer k161837	Investigational Device Yumizen C1200
Refrigerated	Reagent 1: 60 bottles capacity Reagent 2: 48 bottles capacity	Reagent 1: 45 bottles capacity Reagent 2: 45 bottles capacity
Sample Analysis		
Total reaction volume	Min: 120 µL, Max: 350 µL	Min: 80 µL, Max: 430 µL
Cuvette material	Glass	Plastic
	Washable cuvettes	Same
Number of cuvette	165	231
Wave length	Halogen lamp	Same
	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)
Type of measurement	Endpoint assay Reaction rate assay Fixed point assay Electrode method (ISE)	Endpoint assay (EPA) Reaction rate assay (RRA) 2-point assay (2PA) Constant rate assay (CRA) Immunoassay (IMA) Electrode method (ISE)
Physical characteristics		
Dimensions (W x D x H)	1250 × 890 mm × 1300 mm	1220 × 850 × 1108 mm
Weight	465 kg	450 kg

2. Comparison between Yumizen C1200 Glucose HK and the ABX PENTRA Glucose HK CP table

Item	Primary Predicate Device Name ABX Pentra Glucose HK CP k081276	Investigational Device Yumizen C1200 Glucose HK
Manufactured by	HORIBA ABX SAS	Same
Instrument	Pentra C400 CLINICAL CHEMISTRY ANALYZER	Yumizen C1200
Method	Enzymatic method using hexokinase coupled with glucose-6-phosphate dehydrogenase	Same
Sample type	Serum, Plasma, Urine	Same
Reagent format	Liquid	Same
Measuring Range	Serum: 0.11 - 50.00 mmol/L 1.98 – 900.00 mg/dL	Serum: 0.10 – 35.00 mmol/L 1.8 – 630.0 mg/dL
	Urine: 0.22 - 50.00 mmol/L 3.96 – 900.0 mg/dL	Urine: 0.47 - 35.0 mmol/L 8.5 – 630 .0 mg/dL
	Automatic post-dilution: Up to 150.00 mmol/L 2700 mg/dL	Automatic post-dilution: Up to 140.00 mmol/L 2520 mg/dL
Packaging	Reagent 1: 56 mL Reagent 2: 14 mL	Reagent 1: 6 × 39 mL Reagent 2: 6 × 13 mL
		Reagent 1: 4 × 57 mL Reagent 2: 3 × 26 mL
Calibrators	ABX PENTRA Multical	Yumizen C1200 Multical
Controls	ABX PENTRA N Control	Yumizen C1200 N Multi Control
	ABX PENTRA P Control	Yumizen C1200 P Multi Control
	ABX PENTRA Urine Control L/H	Yumizen C1200 Urine Level 1 Control
		Yumizen C1200 Urine Level 2 Control
Reagent stability	Open: Stable for 55 days on board	Open: Stable for 6 weeks on board
	Closed: Stable up to the expiry date on the label if stored at 2-8°C.	Same

Item	Primary Predicate Device name ISE reagents on DxC 700 AU Clinical Chemistry Analyzer k161837	Investigational Device Yumizen C1200
ISE parameters	NA, K, CL	Same
Potentiometry	Indirect	Same
Sample volume	20 µL for 3 parameters	22 µL for 3 parameters
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
Reagent	ISE Buffer Solution	ISE Buffer (IS)
	ISE Mid Standard Solution	Internal Standard
	ISE Reference Solution	
	ISE Internal Reference Solution	
	Na+/K+ Selectivity Check Solution	
Calibrator	Low Serum Standard	ISE Serum Standard Set (NA)
	High Serum Standard	
	Low/High Urine Standard	ISE Urine Standard Set
Measurement	Quantitative	Same
Sample Type	Serum, Plasma, Urine	Same
Measuring range	Serum	
	NA 50 – 200 mmol/L	NA 100 – 200 mmol/L
	K 1.0 – 10.0 mmol/L	K 1.5 – 10 mmol/L
	CL 50 – 200 mmol/L	CL 52 – 200 mmol/L
	Urine	
	NA 10 – 400 mmol/L	NA 10 – 400 mmol/L
	K 2.0 – 200.0 mmol/L	K 3 – 300 mmol/L
	CL 15 – 400 mmol/L	CL 15 – 400 mmol/L

Intended Use

1. Yumizen C1200 Glucose HK

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.

2. ISE module

This ISE unit is designed for making quantitative measurements of Na (sodium), K (potassium), and Cl (chloride) in serum, plasma, and urine samples. This unit is intended for professional use in a laboratory environment only.

2.1 Sodium Electrode

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.

2.2 Potassium Electrode

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.

2.3 Chloride Electrode

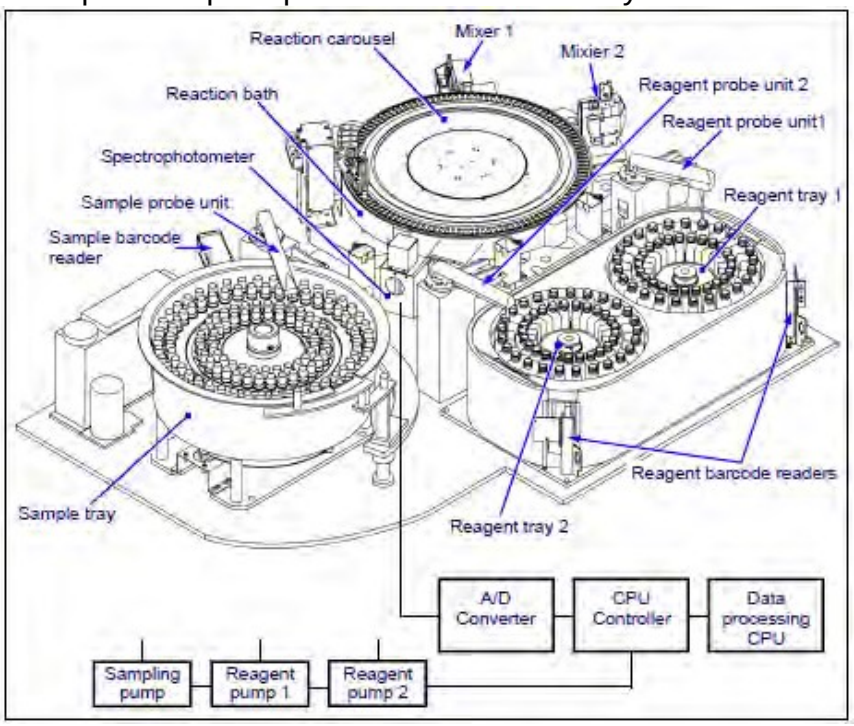
The chloride electrode is an ion selective electrode that is intended for use on the ion selective electrode (ISE) unit of the Yumizen C1200 analyzer. The chloride electrode is used to quantify the concentrations of chloride ions in serum, plasma, and urine. Chloride measurements are used in the diagnosis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

3. Yumizen C1200

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.

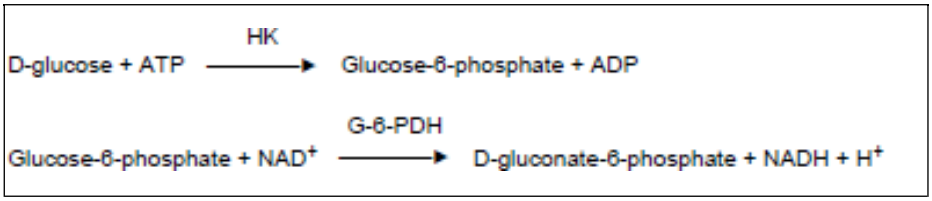
Methodology

1. The chemistry principles of Operations
   The operation principle of Yumizen C1200 system is as follows



   The reagent probe (RPP) dispenses reagent 1 (R1) from reagent tray 1 (RTT1) to a clean reaction cuvette on the reaction carousel (RRV).
   The sample probe (SPP) dispenses the sample in the quantity required for the test from the sample tray (STT) into the RRV now containing R1.
   Sample dilution is possible if necessary. The diluent is placed in the RTT and dispensed into the reaction cuvette. Next, the sample is dispensed into the same cuvette by the SPP and mixed with the mixing rod. Now the diluted sample is in the reaction cuvette. The SPP dispenses the diluted sample in the reaction cuvette in which R1 required for the test has already been dispensed. The dispensed sample and R1 are mixed in the reaction cuvette. Next, reagent 2/2 early (e) is dispensed from the RTT as required. The contents are then mixed for the length of time required by the test. Photometric measurement data is collected by the spectrophotometer every 13.5 seconds to calculate concentration at each measurement point, which are posted to the workstation. The reaction cuvettes are washed with detergent and tepid water and blank measurement is performed for each wavelength.

2. The measuring assay of glucose
   Glucose is phosphorylated by hexokinase (HK) in the presence of adenosine triphosphate (ATP) and magnesium ions to produce glucose-6-phospage (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.



3. The measuring assay of Electrodes
   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.
   Each of the selected electrodes is composed of the following membrane
   - ✓ NA: Crown ether membrane
   - ✓ K: Crown ether membrane
   - ✓ CL: Super-layer solid molecule orientation membrane

Performance Data

1. Yumizen C1200 Glucose HK

1.1 Measuring Range

The limit of detection and quantitation was determined according to the CLSI guideline EP17-A2.

The reagent linearity was determined according to CLSI guideline EP06-A.

The limit of quantitation and the linearity studies showed that claimed measuring ranges are appropriate.

	Limit of quantitation	Measuring range
Serum / plasma	1.8 mg/dL 0.10 mmol/L	1.8 to 630.0 mg/dL 0.10 to 35.00 mmol/L
Urine	3.5 mg/dL 0.19 mmol/L	8.5 to 630.0 mg/dL 0.47 to 35.00 mmol/L
Post-dilution	NA	In serum / plasma /urine Up to 2520.0 mg/dL Up to 140.00 mmol/L

1.2 Accuracy and Precision

1.2.1 Repeatability (within-run precision)

2 level controls and 5 samples of low, middle, and high concentrations were tested 20 times.

	Serum				Urine			
	Mean value		CV %		Mean value		CV %	
	mg/dL	mmol/L	mg/dL	mmol/L	mg/dL	mmol/L	mg/dL	mmol/L
Control N	91.91	5.106	1.1	1.1	23.85	1.325	0.5	0.6
Control P	275.02	15.278	0.7	0.7	294.27	16.348	0.6	0.6
Sample 1	9.92	0.551	1.1	1.0	11.13	0.617	0.9	0.8
Sample 2	30.80	1.711	0.9	0.9	17.07	0.949	1.0	0.9
Sample 3	96.52	5.362	0.8	0.8	178.71	9.928	0.5	0.5
Sample 4	272.07	15.115	0.8	0.8	353.08	19.616	0.8	0.8
Sample 5	556.09	30.894	0.5	0.5	570.28	31.682	0.6	0.6

1.2.2 Reproducibility (total precision)

2 level controls and 5 patient samples of low, middle and high level concentrations were tested in duplicate for 20 days (2 series per day) according to the CLSI guideline EP05-A3.

	Serum				Urine			
	Mean value		CV %		Mean value		CV %	
	mg/dL	mmol/L	mg/dL	mmol/L	mg/dL	mmol/L	mg/dL	mmol/L
Control N	92.70	5.150	1.5	1.5	25.04	1.391	4.0	4.0
Control P	255.24	14.180	1.4	1.4	279.65	15.536	3.0	3.1
Sample 1	12.65	0.703	2.3	2.2	11.87	0.660	3.6	3.6
Sample 2	30.63	1.702	1.8	1.8	16.64	0.924	3.4	3.4
Sample 3	103.56	5.753	1.7	1.7	174.80	9.711	3.2	3.2
Sample 4	259.29	14.405	1.6	1.6	324.70	18.039	3.3	3.3
Sample 5	571.87	31.770	1.6	1.6	537.47	29.859	4.3	4.3

1.3 Interferences

The Interferences were determined according to the CLSI guideline EP07-A2.

The calculated bias was within the 10% acceptance criteria on serum and urine samples for up to the following concentrations.

Serum		Urine	
Hemoglobin	501 mg/dL (290 µmol/L)	Hemoglobin	501 mg/dL (290 µmol/L)
Triglycerides	569 mg/dL (6.50 mmol/L)	Total Bilirubin	27.20 mg/dL (465 µmol/L)
Total Bilirubin	35.53 mg/dL (607 µmol/L)	Ascorbic Acid	5.98 mg/dL (340 µmol/L)
Direct Bilirubin	21.09 mg/dL (360 µmol/L)	Modification of the pH of the samples	No impact on glucose assay measurement
Acetylsalicylic Acid	65.16 mg/dL (3.62 mmol/L)	Specific gravity	1.000 - 1.030
Ascorbic Acid	5.98 mg/dL (340 µmol/L)		
Ibuprofen	50.1 mg/dL (2.43 mmol/L)		
Acetaminophen	20 mg/dL (1324 µmol/L)		

1.4 Matrix comparison on predicate device

This protocol was according to the CLSI guideline EP09-A3. 56 plasma samples were evaluated on Yumizen C1200 using Yumizen C1200 Glucose HK reagent and with the Pentra C400 Clinical Chemistry Analyzer with ABX PENTRA Glucose HK reagent (Predicate device). The equation for the regression line using Passing Bablok was obtained.

Passing Bablok	N	Intercept	Slope	Correlation - r
Glucose in plasma (mg/dL)	56	-0.070	0.991	0.999
Glucose in plasma (mmol/L)		0.013	0.988	0.999

1.5 Method comparison with a predicate device

Yumizen C1200 was compared with Pentra C400 Clinical Chemistry Analyzer. 140 (in serum) and 100 (in urine) patient samples were correlated with a commercial reagent taken as reference according to the CLSI guideline EP09-A3. The equation for the regression line using Passing Bablok was obtained.

Passing Bablok	N	Intercept	Slope	Correlation - r
Glucose in serum (mg/dL)	141	-2.453	1.005	0.996
Glucose in urine (mg/dL)	100	0.975	1.007	0.999

1.6 Reagent Stability

1.6.1 Closed stability

The closed stability was determined according to the CLSI guideline EP25-A.

Stable up to the expiry date on the label if stored at 2 - 8 degree C.

1.6.2 Open stability

Stable up to the expiry date on the label if stored at the refrigerated compartment is stable for 6 weeks.

1.7 Reference Range

The Reference Range was determined according to the CLSI guideline EP28-A3c.

50 normal samples (25 women + 25 men) in serum were assayed with the method in evaluation. Each sample was assayed in duplicates. The mean of the duplicate results for each subject was compared against reference ranges cited in literature. The verification studied support in the following reference ranges which were established through literature.

Serum: 70 to 115 mg/dL (3.89 to 6.39 mmol/L)

Urine: < 15 mg/dL (< 0.84 mmol/L)

Reference

Thomas L. Clinical Laboratory Diagnostics. 1st ed. Frankfurt: TH-Books Verlagsgesellschaft; 1998. p. 131-7, 1368.

2 ISE module on Yumizen C1200

2.1 Measuring Range

The measuring range of the Sodium, Potassium and Chloride Electrodes on Yumizen C1200 was validated by the linearity studies.

Parameters	Measuring range
NA in serum (mmol/L)	100 to 200
K in serum (mmol/L)	1.5 to 10
CL in serum (mmol/L)	52 to 200
NA in urine (mmol/L)	10 to 400
K in urine (mmol/L)	3 to 300
CL in urine (mmol/L)	15 to 400

2.2 Accuracy and Precision

2.2.1 Repeatability (within-run precision)

The Repeatability was determined by analyzing 2 level controls, 3 samples of low, middle and high level concentration and the spiked samples were tested 20 times by 3 reagent Lots.

Control in serum		Control N			Control P			Control N2			Control P2		
		Lot1	Lot2	Lot3	Lot1	Lot2	Lot3	Lot1	Lot2	Lot3	Lot1	Lot2	Lot3
NA	Mean value (mmol/L)	133.80	134.68	134.55	134.55	135.37	135.84	122.13	123.10	123.25	154.39	155.18	154.66
	CV (%)	0.2	0.2	0.3	0.2	0.2	0.3	0.2	0.2	0.2	0.2	0.2	0.2
K	Mean value (mmol/L)	4.296	4.336	4.333	6.643	6.689	6.700	3.825	3.865	3.866	6.536	6.567	6.553
	CV (%)	0.1	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.4	0.2	0.3	0.3
CL	Mean value (mmol/L)	114.04	115.47	114.24	112.75	114.50	113.45	91.21	91.70	91.64	112.01	112.17	111.72
	CV (%)	0.2	0.3	0.4	0.3	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.3
Patient sample in serum		Low sample			Middle sample			High sample			Spiked sample		
		Lot1	Lot2	Lot3	Lot1	Lot2	Lot3	Lot1	Lot2	Lot3	Lot1	Lot2	Lot3
NA	Mean value (mmol/L)	125.85	126.81	126.74	138.64	139.61	139.18	148.72	149.51	148.84	165.20	165.83	164.90
	CV (%)	0.2	0.3	0.2	0.2	0.3	0.3	0.3	0.3	0.3	0.2	0.3	0.3
K	Mean value (mmol/L)	2.773	2.779	2.784	4.041	4.067	4.065	5.847	5.896	5.899	6.688	6.742	6.733
	CV (%)	0.2	0.3	0.3	0.3	0.3	0.2	0.2	0.2	0.3	0.3	0.3	0.3
CL	Mean value (mmol/L)	90.61	90.89	90.46	101.81	102.29	101.71	112.79	113.09	112.46	130.18	130.35	129.65
	CV (%)	0.2	0.3	0.2	0.2	0.4	0.3	0.4	0.4	0.3	0.3	0.3	0.3

Control in urine		Control N			Control P		
		Lot1	Lot2	Lot3	Lot1	Lot2	Lot3
NA	Mean value (mmol/L)	85.75	86.68	86.65	178.97	179.04	178.09
	CV (%)	0.3	0.3	0.3	0.3	0.3	0.4
K	Mean value (mmol/L)	31.102	31.160	31.104	83.437	83.453	83.115
	CV (%)	0.5	0.5	0.4	0.4	0.4	0.4
CL	Mean value (mmol/L)	62.04	62.48	66.09	163.60	162.67	171.54
	CV (%)	0.4	0.3	0.4	0.2	0.2	0.3

Patient sample in urine		Low sample			Middle sample			High sample			Spiked sample		
		Lot1	Lot2	Lot3	Lot1	Lot2	Lot3	Lot1	Lot2	Lot3	Lot1	Lot2	Lot3
NA	Mean value (mmol/L)	27.69	28.44	28.36	103.54	104.24	103.53	188.09	187.72	186.54	336.99	334.35	331.45
	CV (%)	1.0	0.8	1.2	0.2	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.3
K	Mean value (mmol/L)	29.373	29.309	29.176	68.765	68.922	68.365	118.831	118.845	118.050	220.783	221.125	218.953
	CV (%)	0.5	0.3	0.3	0.4	0.3	0.5	0.4	0.3	0.4	0.5	0.5	0.5
CL	Mean value (mmol/L)	24.13	25.79	30.78	102.07	104.55	106.76	199.91	199.77	190.33	322.88	318.66	292.00
	CV (%)	1.1	0.8	2.2	0.2	0.4	0.8	0.3	0.3	0.6	0.4	0.3	0.3

2.2.2 Reproducibility (total precision)

The Reproducibility was determined according to according to the CLSI guideline EP05-A3.

2 level controls, 3 samples of low, middle and high concentrations and the spiked samples were tested in duplicate for 20 days (2 series per day).

serum	NA in serum		K in serum		CL in serum	
	Mean value (mmol/L)	CV (%)	Mean value (mmol/L)	CV (%)	Mean value (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	NA in urine		K in urine		CL in urine	
	Mean value (mmol/L)	CV (%)	Mean value (mmol/L)	CV (%)	Mean value (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

2.3 Interferences

This protocol was determined according to the CLSI EP07-A2.

The calculated bias was within the 10% acceptance criteria on Sodium, Potassium and Chloride serum and urine samples for up to the following concentrations.

NA, K, CL in serum		NA, K, CL in urine	
Hemoglobin	0.5 g/dL	Hemoglobin	1.25 g/dL
Triglycerides	52.1 mmol/L	Total Bilirubin	256 µmol/L
Total Bilirubin	396 µmol/L	Protein	3.31 g/L
Total protein	121.13 g/L	Urea	988.3 mmol/L
Urea	71.9 mmol/L	Ascorbic acid	3.40 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		

2.4 Matrix comparison on predicate device

This protocol was according to the CLSI guideline EP09-A3.

Plasma samples were evaluated on Yumizen C1200 and Olympus AU400 Clinical Chemistry Analyzer. The equation for the regression line using Passing Bablok was obtained.

Passing Bablok	N	Min (mmol/L)	Max (mmol/L)	Intercept	Slope	Correlation - r
NA	171	102.9	188.9	0.200	1.000	0.997
K	173	1.76	9.53	0.010	1.000	0.999
CL	173	53.1	178.4	-1.568	1.019	0.998

2.5 Method comparison with a reference device

Yumizen C1200 was compared with Olympus AU400 Clinical Chemistry Analyzer.

The patient samples were correlated with a commercial ISE module taken as reference according to the CLSI guideline EP09-A3.

The equation for the regression line using Passing Bablok was obtained.

Passing Bablok	N	Intercept	Slope	Correlation - r
NA in serum	165	1.371	0.987	0.995
K in serum	170	0.023	0.994	0.999
CL in serum	172	0.818	0.992	0.998
NA in urine	194	-1.256	1.001	1.000
K in urine	198	-0.128	0.983	0.999
CL in urine	194	0.525	0.991	1.000

2.6 Electrodes Stability

The protocol of this study was followed by JEOL internal protocol.

The evaluation was performed using the same parameter checked in manufacturing of the electrodes.

2.6.1 Closed stability

Stable up to the expiry date on the label if stored at 0-40 degree C.

2.6.2 Open stability

Stable for 3 months from opened.

2.7 Reference Range

The Reference Range was determined according to the CLSI EP28-A3c.

80 normal samples (23 women + 57 men) in serum and plasma were assayed with the method in evaluation. Each sample was assayed in duplicates. The mean of the duplicate results for each subject was compared against reference ranges cited from literature. The verification studies supported in the following reference ranges which were established through literature.

NA in serum and plasma: 136 to 145 mmol/L[1]

K in serum and plasma: 3.5 to 5.1 mmol/L[1]

(The reference range of K in plasma is about 0.5 mmol/L lower than in serum)[2]

CL in serum and plasma: 98 to 107 mmol/L[1]

The expected values based on 24 hours urine out-put were cited from the literature.

NA in urine: 40 to 220 mmol/day[1]

K in urine: 25 to 125 mmol/day[1]

CL in urine: 110 to 250 mmol/day[1]

Reference:

1. Tietz NW, Clinical Guide for Laboratory Tests 3rd edition. WB Saunders Company, Philadelphia, PA, pp. 610-611 (1995)

2. Walker HK,et al. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition, Boston: Butterworths, pp 884-887(1990)

Non clinical tests

The non clinical studies tests conclude that the safety and effectiveness of the devices are not compromised.
Yumizen C1200 meets the following.

ISO 14971: 2007	Medical devices - Application of risk management to medical devices
IEC 61326-2-6:2012	Electrical equipment for measurement, control and laboratory use — EMC requirements — Part 2-6: Particular requirements — *In vitro* diagnostic (IVD) medical equipment
IEC 61326-1: 2012	Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 1: General requirements
IEC 61010-1: 2010	Safety requirements for electrical equipment for measurement, control, and laboratory use — Part 1 General requirements
IEC 61010-2-010: 2014	Safety requirements for electrical equipment for measurement, control and laboratory use - Part 2-010: Particular requirements for laboratory equipment for the heating of materials
IEC 61010-2-101: 2015	Safety requirements for electrical equipment for measurement, control, and laboratory use — Part 2-101: Particular requirements for *in vitro* diagnostic (IVD) medical equipment
IEC 62304: 2006	Medical device software — software life-cycle processes
IEC 60825-1 2014	Safety of laser products - Part 1: Equipment classification and requirements

Conclusion

The data presented demonstrate that the Yumizen C1200 glucose, sodium, potassium, and chloride assays are substantially equivalent to the predicate devices.