July 26, 2019

Horiba ABX SAS
Caroline Ferrer
Regulatory Affairs Manager
Parc Euromedecine, Rue du Caducee – BP7290
Montpellier Cedex 4, 341184
France

Re: K191396
Trade/Device Name: Yumizen C1200 Calcium AS, Yumizen C1200 Creatinine Jaffe
Regulation Number: 21 CFR 862.1145
Regulation Name: Calcium Test System
Regulatory Class: Class II
Product Code: CJY, CGX
Dated: May 22, 2019
Received: May 24, 2019

Dear Caroline Ferrer:

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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-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, Ph.D.
Acting Director
Division of Chemistry and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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)*
k191396

Device Name
Yumizen C1200 Calcium AS
Yumizen C1200 Creatinine Jaffé

Indications for Use *(Describe)*

Yumizen C1200 Calcium AS reagent is a diagnostic reagent for quantitative in vitro determination of calcium in human serum, plasma and urine based on colorimetric method, using the clinical chemistry analyzer. Measurement of calcium is used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).

Yumizen C1200 Creatinine Jaffé reagent is a diagnostic reagent for quantitative in vitro determination of Creatinine in human serum, plasma and urine based on a kinetic method using alkaline picrate (Jaffé method). 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.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

SECTION 007 : 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.

510 (k) number : k191316

1- Date of Summary

Date submitted : 22nd May, 2019
Revised Date submitted : 23rd July,2019

2- Company

HORIBA ABX SAS
HORIBA MEDICAL
Parc Euromédecine
Rue du Caducée – BP 7290
34184 Montpellier cedex 4
France

3- Contact person

Contact Person: Caroline Ferrer (caroline.ferrer@horiba.com)
Telephone: + (33) 4 67 14 1843
Fax: + (33) 4 67 14 1517

4- Product Name

Yumizen C1200 C1200 Calcium AS (1300047910)
Yumizen C1200 Creatinine Jaffé (1300023842)

5- Device Name and Classification

- **Intended use**

The devices involved by the 510(k) submission file are the following :

- **Classification and Description**

Device's names	Intended Use
Yumizen C1200 Calcium AS	Yumizen C1200 Calcium AS reagent is a diagnostic reagent for quantitative in vitro determination of calcium in human serum, plasma and urine based on colorimetric method, using the clinical chemistry analyzer. Measurement of calcium is used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).
Yumizen C1200 Creatinine Jaffé	Yumizen C1200 Creatinine Jaffé reagent is a diagnostic reagent for quantitative in vitro determination of Creatinine in human serum, plasma and urine based on a kinetic method using alkaline picrate (Jaffé method). 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.

Trade/Proprietary Name:	Yumizen C1200 Calcium AS
Device Class:	Class II / 510(k) required
Classification Name:	§862.1145: Calcium test system
Product Code:	CJY
Panel:	Clinical Chemistry (75)

Trade/Proprietary Name:	Yumizen C1200 Creatinine Jaffé
Device Class:	Class II / 510(k) required
Classification Name:	§862.1225: Creatinine test system
Product Code:	CGX
Panel:	Clinical Chemistry (75)

6- Substantial Equivalence Information

The following tables show the similarities and differences and demonstrates substantial equivalence between the candidate device and its predicate device identified below.

a. Predicate Device Name and 510(k) number

Candidate device	Predicate device	Predicate Manufacturer	Predicate 510(k) number
Yumizen C1200 Calcium AS	ABX Pentra Calcium AS CP On ABX Pentra 400 / Pentra C400	HORIBA ABX SAS	K123171
Yumizen C1200 Creatinine Jaffé	ABX Pentra Creatinine 120 CP On ABX Pentra 400/ Pentra C400	HORIBA ABX SAS	K110530

The following tables show the similarities and differences and demonstrates substantial equivalence between the candidate device and its predicate device identified below.

b. Yumizen C1200 Calcium AS (1300047910)

i. Comparison with predicate Device : Similarities

Item	Predicate K123171	Candidate
Device Name	ABX Pentra Calcium AS CP On ABX Pentra 400 / Pentra C400	Yumizen C1200 Calcium AS (1300047910)
Manufactured by	HORIBA ABX SAS	HORIBA ABX SAS
Intended Use	Diagnostic reagent for quantitative in vitro determination of calcium in human serum, plasma and urine based on a colorimetric method, using the ABX Pentra 400 Clinical Chemistry analyzer. Measurement of calcium is used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).	Diagnostic reagent for quantitative in vitro determination of calcium in human serum, plasma and urine based on colorimetric method, using the clinical chemistry analyzer. Measurement of calcium is used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).
Sample type	Serum, plasma, urine	Same
Reagent format	Liquid	Same
Measurement	Quantitative	Same
Method	Colorimetry	Same
Shelf-life	Reagents, in unopened cassettes, are stable up to the expiry date on the label if stored between 2-8°C, protected from light	Stable up to the expiry date on the label if stored at 2-8°C.
Analytical Range	**Measuring Range** Serum/Plasma: 4.0 – 18.05 mg/dL Urine: 0.64 – 18.05 mg/dL	**Measuring Range** Serum, Plasma: 1.00 -4.50 mmol/L **or** 4.0- 18.05 mg/dL Urine: 0.16 - 4.5 mmol/L **or** 0.64 -18.05 mg/dL

Item	Predicate K123171	Candidate
	Automatic post-dilution: Serum/plasma: up to 13.50 mmol/L **or** 54.15 mg/dL with Automatic post-dilution. Urine: up to 13.50 mmol/L **or** 54.15 mg/dL with the automatic post-dilution.	**Automatic post-dilution:** Serum/ Plasma: up to 13.5 mmol/L **or** 54.15 mg/dL with the automatic post-dilution. Urine: up to 13.5 mmol/L **or** 54.15 mg/dL with the automatic post-dilution.
Reference range	Serum/Plasma: 8.6 -10.3 mg/dL Urine : Male: <300 mg/24h Female : <250 mg/24h	Serum/Plasma : 8.6-10.2 mg/dL Urine : Men: < 300 mg/24h Women: < 250 mg/24h

ii. Comparison with predicate Device: Differences

Item	Predicate K123171	Candidate
Device Name	ABX Pentra Calcium AS CP On ABX Pentra 400 / Pentra C400	Yumizen C1200 Calcium AS (1300047910)
Instrument	ABX Pentra 400 / Pentra C400	Yumizen C1200 Clinical chemistry analyzer
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
Packaging & Number of tests	Serum, plasma: 285 tests Urine : 285 tests	Serum, plasma: 6 x 290 tests Urine: 6 x 290 tests
On board Stability	Once opened, the reagent cassette placed in the refrigerated ABX Pentra 400 compartment is stable for 70 days.	Once opened, the reagent cassette placed in the refrigerated compartment is stable for 6 weeks.

Item	Predicate K123171	Candidate
Discussion on the analysis differences : 1. Instrument: Yumizen C1200 Calcium AS is used on Yumizen C1200 (See 2.) 2. Controls: 2 separate levels of controls for Yumizen C1200 Urine Level 1 and Level 2(same for ABX Pentra) 3. Packaging : Candidate offers more number of tests than the predicate. 4. Reagent stability: the on board stability of Yumizen C1200 Calcium AS is shorter. Stability depends on the reagent composition and cassette capacity.		

c. Yumizen C1200 Creatinine Jaffé

i. Comparison with predicate Device : Similarities

Item	Predicate K110530	Candidate
Device Name	ABX Pentra Creatinine 120 CP On ABX Pentra 400/ Pentra C400	Yumizen C1200 Creatinine Jaffé (1300023842).
Intended Use	Diagnostic reagent for quantitative in vitro determination of Creatinine in human serum, plasma and urine based on a kinetic method using alkaline picrate (Jaffé method). 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.	Diagnostic reagent for quantitative in vitro determination of Creatinine in human serum, plasma and urine based on a kinetic method using alkaline picrate (Jaffé method). 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.
Manufactured by	HORIBA ABX SAS	HORIBA ABX SAS
Sample type	Serum, plasma, urine	Same
Reagent format	Liquid	Same
Measurement	Quantitative	Same
Method	Colorimetry	Same
Analytical Range	**Measuring Range** Serum/Plasma: 0.22 to 18.08 mg/dL Urine: 2.90 to 282.50 mg/dL	**Measuring Range** Serum, plasma: 20 µmol/L to 1600 µmol/L **or** 0.23 to 18.08 mg/dL Urine: 261 µmol/L to 25000 µmol/L **or** 3 to 282.5 mg/dL

Item	Predicate K110530	Candidate
	Automatic post-dilution: Serum, plasma: up to 4800 µmol/L **or** 54.24 mg/dL with the automatic post-dilution. Urine: up to 75000 µmol/L **or** 847.5 mg/dL with the automatic post-dilution	**Automatic post-dilution:** Serum, plasma: up to 4800 µmol/L**or** 54.24 mg/dL with the automatic post-dilution. Urine: up to 75000 µmol/L **or** 847.5 mg/dL with the automatic post-dilution.
Reference range	Serum, plasma: Men 7.0 - 12.0 mg/L 0.70- 1.20 µmol/L 62 - 106 µmol/L Women 5.0 - 9.0 mg/L 0.50-0.90 µmol/L 44 - 80 µmol/L Urine (24 hours): Men 14 - 26 mg/kg/day 124 - 230 µmol/kg/day Women 11 - 20 mg/kg/day 97 - 177 µmol/kg	Serum, plasma: Men 7.0 - 12.0 mg/L 0.70- 1.20 µmol/L 62 - 106 µmol/L Women 5.0 - 9.0 mg/L 0.50-0.90 µmol/L 44 - 80 µmol/L Urine (24 hours) Men 14 - 26 mg/kg/day 124 - 230 µmol/kg/day Women: 11 - 20 mg/kg/day 97 - 177 µmol/kg/day

ii. Comparison with predicate Device: Differences

Item	Predicate K110530	Candidate
Device Name	ABX Pentra Creatinine 120 CP On ABX Pentra 400/ Pentra C400	Yumizen C1200 Creatinine Jaffé (1300023842).
Instrument	ABX Pentra 400 Clinical Chemistry Analyzer	Yumizen C1200 Clinical chemistry analyzer
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
Calibrators	ABX Pentra Multical	Yumizen C1200 Multical
Number of tests	120 tests	6 x 315 tests
Packaging	Cassette of : R1= 27.5 mL R2= 8 mL	Cassette of : R1: 6 x 32 mL R2: 6 x 11 mL
Sample Volume	10 µL/test	5.0 µL/test
Shelf-life	In unopened cassettes, stable up to 36 months if stored at 2-8°C	Stable up to the expiry date on the label if stored at 2-8°C. Store protected from light.
On board Stability	Once opened, the reagent cassette placed in the refrigerated (2-8ºC) ABX Pentra 400 compartment is stable: **19 days**	Once opened, the reagent cassette placed in the refrigerator compartment (2-8ºC) is stable for : **7 days**
Calibration Stability	The reagent is calibrated on Day 0. The calibration stability is checked by testing 2 control specimens. The calibration stability is at least 3 days.	The reagent is calibrated on Day 0. The calibration stability is checked by testing 2 control specimens. The calibration stability is 24 hours.

Discussion on the analysis differences :

1. Instrument: Yumizen C1200 Creatinine Jaffé is used on Yumizen C1200
2. Packaging: Yumizen C1200 Creatinine Jaffé offers more reagent per cassette including more number of tests that depends on packaging and cassette capacity.
3. Reagent stability: the on board stability of Yumizen C1200 Creatinine Jaffé is shorter but has longer shelf-life when un-opened. Stability depend on reagent composition and cassette capacity.
4. Calibration stability: Yumizen C1200 Creatinine Jaffé is shorter

7- Special Control/Guidance Document Referenced

a. Standards Followed

The following standards & FDA guidance documents have been used to support this submission:

CLSI Guidelines:

- **CLSI EP05-A3:**Evaluation of Precision of Quantitative Measurement Procedures– Third Edition - October 2014
- **CLSI EP17-A2:** Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures – Second Edition - June 2012
- **CLSI EP09-A3:** Measurement Procedure Comparison and Biais Estimation Using Patient Samples– Third Edition - August 2013
- **CLSI EP06-A:** Evaluation of the Linearity of Quantitative measurement Procedures A Statistical Approach – First Edition – April 2003
- **CLSI C28-A3:** Defining, Establishing, and Verifying Reference Intervals in the Clinical laboratory- Third Edition – November 2008
- **CLSI EP25-A** : Evaluation of Stability of In Vitro Diagnostic reagents- First Edition- September 2009

b. FDA Guidances Followed

- Guidance for Industry and FDA Staff : Format for Traditional and Abbreviated 510(k)s – 2005
- Refuse To Accept (RTA) Policy for 510(k) – Guidance for Industry and Food and Drug Administration Staff Document issued on: February 21, 2019.
- Guidance for Industry and FDA Staff : eCopy Program for Medical Device Submissions – 2015

c. Others Guidances followed

- Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745)

8- Analytical Performance Characteristics

8.1 Measuring Range

- **Yumizen C1200 Calcium AS**

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 range is appropriate.

- Results :

	Limit of detection	Limit of quantitation	Linearity	Measuring range
Serum / plasma	0.12 mmol **or** 0.48 mg/dL	0.14 mmol/L **or** 0.57 mg/dL	0.00 to 4.84 mmol/L **or** 0.00 to 19.40 mg/dL	1.00 - 4.50 mmol/L **or** 4.0 -18.05 mg/dL
Serum/ plasma Post-dilution	NA	NA	Up to 13.5 mmol/L **or** 54.15 mg/dL	Up to 13.5 mmol/L **or** 54.15 mg/dL
Urine	0.06 mmol/L **or** 0.24 mg/dL	0.16 mmol/L **or** 0.64 mg/dL	0.00 to 4.84 mmol/L **or** 0.00 -18.60 mg/dL	0.16 to 4.5 mmol/L **or** 0.64 -18.05 mg/dL
Urine Post-dilution	NA	NA	Up to 13.5 mmol/L **or** 54.15 mg/dL	Up to 13.5 mmol/L **or** 54.15 mg/dL

- **Yumizen C1200 Creatinine Jaffé**

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 range is appropriate.

➢ Results :

	Limit of detection	Limit of quantitation	Linearity	Measuring range
Serum / plasma	3.83 µmol **or** 0.04mg/dL	20 µmol/L **or** 0.23 mg/dL	0 - 2226.59 µmol/L **or** 0.00- 25.16 mg/dL	20 -1600 µmol/L **or** 0.23 - 18.08 mg/dL
Serum/ plasma Post-dilution	NA	NA	Until 4800 µmol/L or **or** Until 54.24 mg/dL	Until 4800 µmol/L **or** Until 54.24 mg/dL
Urine	81.91 µmol/L **or** 0.93 mg/dL	235.61 µmol/L **or** 2.66 mg/dL	0 to 26896.10 µmol/L **or** 0 to 303.93 mg/dL	261 to 25000 µmol/L **or** 3 to 282.5 mg/dL
Urine Post-dilution	NA	NA	Until 75000 µmol/L **or** 875.5 mg/dL	Until 75000 µmol/L **or** 875.5 mg/dL

8.2 Accuracy and Precision

Repeatability (within-run precision) and Reproducibility (total precision)

- **Yumizen C1200 Calcium AS**

Serum/Plasma :

Within run : CV limits, for the low (1.8 mmol/L), middle (2.4 mmol/L) and high level (3.4 mmol/L) are 1.2 %
Total precision: CV limits, for the low (1.8 mmol/L), middle (2.4 mmol/L) and high level (3.4 mmol/L) are 1.6 %.

Sample	N	Mean (mmol/L)	Mean (mg/dL)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Yumizen C1200 N Multi Control	240	**2.22**	**8.91**	**0.6**	0.8	1.0	0.0	**1.5**
Yumizen C1200 P Multi Control	240	**3.04**	**12.21**	**0.5**	0.7	1.1	0.4	**1.4**
Sample 1	240	**1.60**	**6.41**	**0.8**	0.8	1.1	0.4	**1.7**
Sample 2	240	**2.42**	**9.70**	**0.6**	1.2	0.6	0.4	**1.6**
Sample 3	240	**3.66**	**14.68**	**0.5**	1.1	1.0	0.8	**1.8**

Although the %CV of Total Precision is superior to the Acceptance criteria for some samples, the p-value with 5% acceptable remains acceptable for all the samples tested.

Urine :

Within run : CV limits, for the low (1.0mM), middle (2.5mM) and high level (4.0mM) are 3.0 %.
Total precision: CV limits, for the low (1.0mM), middle (2.5mM) and high level (4.0mM) are 4.0%.

Sample	N	Mean (mmol/L)	Mean (mg/dL)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Yumizen C1200 Urine Level 1 Control	240	**1.90**	**7.62**	**0.7**	1.4	3.4	0.5	**3.8**
Yumizen C1200 Urine Level 2 Control	240	**2.80**	**11.23**	**0.5**	1.4	3.6	0.0	**3.9**
Sample 1	240	**0.73**	**2.92**	**1.6**	1.0	1.8	0.0	**2.6**
Sample 2	240	**1.53**	**6.12**	**0.8**	1.3	1.4	0.0	**2.1**
Sample 3	240	**2.07**	**8.28**	**0.7**	1.5	1.0	0.0	**2.0**
Sample 4	240	**3.59**	**14.40**	**0.6**	1.0	1.1	0.4	**1.7**
Sample 5	240	**4.26**	**17.07**	**0.6**	0.9	1.2	0.3	**1.6**

The results are within the specifications.

- **Yumizen C1200 Creatinine Jaffé**

Serum/Plasma :

Within run : CV limit, for the low, middle and high level are respectively 4.5 %, 3.4 % and 1.8 %.

Total precision : CV limit, for the low, middle and high level are respectively 6.0 %, 4.5 % and 2.4 %.

Sample	N	Mean (µmol/L)	Mean (mg/dL)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Yumizen C1200 N Multi Control	240	160.04	1.81	**0.6**	1.6	1.3	0.0	**2.1**
Yumizen C1200 P Multi Control	240	463.07	5.23	**0.5**	1.6	1.1	0.1	**2.1**
Sample 1	240	48.86	0.55	**1.9**	1.8	1.8	0.0	**3.1**
Sample 2	240	137.77	1.56	**1.5**	1.5	1.9	0.0	**2.9**
Sample 3	240	580.92	6.56	**0.5**	1.8	0.9	0.0	**2.0**
Sample 4	240	1006.9	11.38	**0.4**	1.5	1.0	0.0	**1.9**
Sample 5	240	1465.33	16.56	**0.4**	2.4	0.5	0.0	**2.5**

Although the %CV of Total Precision is superior to the Acceptance criteria for some samples, the p-value with 5% acceptable remains acceptable for sample 5.

Urine :

Within run : CV limit accepted, for the low, middle and high level are respectively 4.5 %, 3.8 % and 3.8 % for urine.

Total precision : CV limit accepted, for the low, middle and high level are respectively 6.0 %, 5.0 % and 5.0 % for urine.

Sample	N	Mean (µmol/L)	Mean (mg/dL)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Yumizen C1200 Urine Level 1 Control	240	**5344**	**60.38**	**0.8**	1.7	1.0	0.0	**2.1**
Yumizen C1200 Urine Level 2 Control	240	**13295**	**150.24**	**0.5**	1.6	1.3	0.0	**2.1**
Sample 1	240	**492**	**5.56**	**3.4**	3.5	3.6	1.3	**6.2**
Sample 2	240	**1020**	**11.52**	**2.1**	2.1	1.9	0.0	**3.5**
Sample 3	240	**8222**	**92.91**	**0.8**	1.8	0.0	0.3	**2.0**
Sample 4	240	**12692**	**143.42**	**0.8**	2.9	0.0	0.0	**3.0**
Sample 5	240	**19188**	**216.83**	**0.7**	1.8	0.0	0.3	**2.0**

Although the %CV of Total Precision is superior to the Acceptance criteria, the p-value with 5% acceptable remains acceptable for the sample 1.

8.3 Interferences

The Interferences were determined according to the CLSI guideline EP07-A2.
The acceptable bias is defined at +/-10% of the value without interfering substances.
These data in the following table represent the highest values for which no interferences higher than 10% have been observed.

- **Yumizen C1200 Calcium AS**

Serum/plasma		
Hemoglobin	290µmol/L	500 mg/dL
Triglycerides	5.66 mmol/l	495 mg/dL
Total Bilirubin	562 µmol/L	32.9 mg/dL
Direct Bilirubin	410 µmol/L	24 mg/dL
Acetylsalicylic Acid	3.62 mmol/L	65.16 mg/dL
Ascorbic Acid	340 µmol/L	5.98 mg/dL
Ibuprofen	2.43 mmol/L	50.10 mg/dL
Acetaminophen	1324 µmol/L	20 mg/dL

Urine		
Hemoglobin	290 µmol/L	500 mg/dL
Triglycerides	5.19 mmol/l	454 mg/dL
Direct Bilirubin	328 µmol/L	19.2 mg/dL
Ascorbic Acid	340 µmol/L	5.98 mg/dL
Ibuprofen	2.43 mmol/L	50.10 mg/dL
Glucose	81 mmol/L	1463.4 mg/dL

- **Yumizen C1200 Creatinine Jaffé**

Serum/plasma		
Hemoglobin	290 µmol/L	500 mg/dL
Triglycerides	5.80 mmol/l	507.50 mg/dL
Total Bilirubin	397 µmol/L	23.24 mg/dL
Direct Bilirubin	635 µmol/L	37.15 mg/dL
Acetylsalicylic Acid	2.72 mmol/L	48.87 mg/dL
Ascorbic Acid	255 µmol/L	4.49 mg/dL
Ibuprofen	2.43 mmol/L	50.10 mg/dL
Acetaminophen	1324 µmol/L	20 mg/dL
Glucose	38 mmol/L	682 mg/dL
Total Proteins	36 to 101 g/L	

Urine		
Hemoglobin	290 µmol/L	500 mg/dL
Triglycerides	4.50 mmol/l	393.75 mg/dL
Direct Bilirubin	537 µmol/L	31.39 mg/dL
Ascorbic Acid	340 µmol/L	5.98 mg/dL

8.4 Matrix comparison on predicate device

- **Yumizen C1200 Calcium AS**

Study materials :

Anticoagulant : heparin-lithium
Samples: individual donors

Description :

108 plasma samples were evaluated on Yumizen C1200 analyzer using Yumizen C1200 Calcium AS reagent and with the Horiba Pentra C400 analyzer with Horiba Pentra reagent (Predicate device).

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation
Calcium (mmol/L)	108	1.080	4.010	0.1159	+0.9423	0.997

- **Yumizen C1200 Creatinine Jaffé**

Study materials :

Anticoagulant : heparin-lithium
Samples: individual donors from blood bank

Description:

69 plasma samples were evaluated on Yumizen C1200 analyzer using Yumizen C1200 Creatinine Jaffé reagent and with the Horiba Pentra C400 analyzer with Horiba Pentra reagent (Predicate device).

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation
Calcium (µmol)	69	51.400	1618.880	-7.102	+1.087	0.999

Conclusion :

This study shows that heparin lithium plasma samples are validated for these applications.

8.5 Method comparison with a predicate device

- **Yumizen C1200 Calcium AS**

Serum/Plasma :

This study has been carried out using recommendations found in the CLSI EP-9A3 guidance.
Correlation of Calcium measurement with the Yumizen C1200 Calcium AS reagent on Yumizen C1200.
166 native serum samples have been assayed in duplicate, in ascendant order and descendant order on 6 working days.
The equation for the regression line using Passing Bablok was obtained.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation – r^2
Calcium (mmol/L)	166	1.56	4.47	0.06	1	0.976

Urine :

This study has been carried out using recommendations found in the CLSI EP-9A3 guidance.
Correlation of Calcium measurement with the Yumizen C1200 Calcium AS reagent on Yumizen C1200.
105 native serum samples have been assayed in duplicate, in ascendant order and descendant order on 5 working days.
The equation for the regression line using Passing Bablok was obtained.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation – r^2
Calcium (mmol/L)	105	0.27	4.3	+0.1381	0.9436	0.995

- **Yumizen C1200 Creatinine Jaffé**

Serum/Plasma :

This study has been carried out using recommendations found in the CLSI EP-9A3 guidance.
Correlation of Creatinine assay with the Yumizen C1200 Creatinine Jaffé reagent on Yumizen C1200.
131 native samples have been assayed in duplicate, in ascendant order and descendant order on 5 working days.
The equation for the regression line using Passing Bablok was obtained.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation – r^2
(µmol/L)	131	28.57	1233.70	9.158	0.9633	0.995

Urine :

This study has been carried out using recommendations found in the CLSI EP-9A3 guidance.
Correlation of Creatinine assay with the Yumizen C1200 Creatinine Jaffé reagent on Yumizen C1200.
148 native samples have been assayed in duplicate, in ascendant order and descendant order on 5 working days.
The equation for the regression line using Passing Bablok was obtained.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation – r^2
(mmol/L)	148	436.57	22858.07	-41.4	+09483	0.997

8.6 Reagent Stability

8.2.1 Closed stability

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

- **Calcium :**

Stability before opening:
Stable up to the expiry date on the label if stored at 2-8°C.

The shelf life claim for HORIBA Medical reagent will be 24 months.

- **Creatinine Jaffé :**

Stability before opening:
Stable up to the expiry date on the label if stored at 2-8°C. Store protected from light.

The shelf life claim for HORIBA Medical reagent will be 24 months in Yumizen C1200 container.

8.6.2 Open stability

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

On board reagent Stability:

- The reagent stability claim for the Yumizen C1200 Calcium AS is 6 weeks
- The reagent on Board stability claim for Yumizen C1200 Creatinine Jaffé is 7 days.

8.7 Reference range

The Reference Range was determined according to the CLSI guideline EP28-A3.

- **Calcium :**

Serum/Plasma:

40 “normal samples” from blood bank have been assayed with the method in evaluation. Each sample is assayed in duplicates.
Study performed on 2 different working days: 20 samples / day.

The mean of the duplicate results for each subject was compared against reference ranges cited in literature. The verification studies support in the following reference ranges which were established through literature

Normal range – Calcium
Adults: 2.15 – 2.55 mmol/L / 8.6 – 10.2 mg/dL.

Reference:
Roberts WL, McMillin GA, Burtis CA, Bruns DE. Reference Information for the Clinical Laboratory, TIETZ Textbook of Clinical Chemistry and Molecular Diagnostics. 4th Ed; Burtis CA, Ashwood ER, Bruns
DE, (Elsevier Saunders eds. St Louis, USA), (2006): 2258.

Urine :

Normal range Calcium
Women < 250 mg/24 h (6.24 mmol/24 h)
Men < 300 mg/24 h (7.49 mmol/24 h)

Reference:
Thomas L. Clinical Laboratory Diagnostics. 1st ed. Frankfurt: TH-Books Verlagsgesellschaft; 1998. p. 231–241

- **Creatinine Jaffé :**

Serum/Plasma :

- Men :

35 “normal samples” from blood bank have been assayed with the method in evaluation. Each sample is assayed in duplicates.
Study performed on 2 different working days.

The mean of the duplicate results for each subject was compared against reference ranges cited in literature. The verification studies support in the following reference ranges which were established through literature

62 -106 µmol/L / 7 -12 mg/dL.

Reference:
Mazzachi BC, Peake MJ, Ehrhard V. Reference range and method comparison studies for enzymatic and Jaffe creatinine assays in plasma and serum and early morning urine. Clin. Lab. (2000) 46: 53-55.

- Women :

25 “normal samples” from blood bank have been assayed with the method in evaluation. Each sample is assayed in duplicates.
Study performed on 2 different working days.

The mean of the duplicate results for each subject was compared against reference ranges cited in literature. The verification studies support in the following reference ranges which were established through literature

44 -80 µmol/L / 5 -9 mg/dL.

Reference:
Mazzachi BC, Peake MJ, Ehrhard V. Reference range and method comparison studies for enzymatic and Jaffe creatinine assays in plasma and serum and early morning urine. Clin. Lab. (2000) 46: 53-55.

Urine :

Normal range Creatinine - Urine (24 hours):

Men	Women
14 - 26 mg/kg/day	11 - 20 mg/kg/day
124 - 230 µmol/kg/day	97 - 177 µmol/kg/day

Reference :

Roberts WL, McMillin GA, Burtis CA, Bruns DE. Reference Information for the Clinical Laboratory, TIETZ Textbook of Clinical Chemistry and Molecular Diagnostics. 4th Ed; Burtis CA, Ashwood ER, Bruns DE, (Elsevier Saunders eds. St Louis, USA), (2006): 2264.

8.8 Proposed Labeling

The labeling is written as per the recommendations given in standard EN18113-2.
It takes into account the requirements of 21 CFR Part 809.10.

8.9 Conclusions for Performance Testing

The performance testing data conclude that the safety and effectiveness of the devices are not compromised, and that they met all acceptance criteria, demonstrating that each device is substantially equivalent to its predicate device.