March 6, 2020

Horiba ABX SAS
Caroline Ferrer
Regulatory Affairs Manager
Parc Euromedecine, Rue Du Caducee BP 7290
Montpellier Cedex 4, 341184
France

Re: K191562
    Trade/Device Name: Yumizen C1200 Ferritin, Yumizen C1200 Transferrin, Yumizen C1200
                        Rheumatoid Factor
    Regulation Number: 21 CFR 866.5340
    Regulation Name: Ferritin immunological test system
    Regulatory Class: Class II
    Product Code: DBF, DDG, DHR
    Dated: June 11, 2019
    Received: June 13, 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,

Carolina Kagan, M.Sc.
Acting Chief
Division of Immunology
  and Hematology Devices
OHT7: Office of In Vitro Diagnostics
   and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number *(if known)*
k191562

Device Name
Yumizen C1200 Ferritin
Yumizen C1200 Transferrin
Yumizen C1200 Rheumatoid Factor

Indications for Use *(Describe)*
Yumizen C1200 Ferritin reagent is intended for the quantitative in vitro diagnostic determination of Ferritin in human serum by latex-enhanced immunoturbidimetric assay. Measurements of ferritin aid in the diagnosis of diseases affecting iron metabolism, hemochromatosis (iron overload) and iron deficiency anemia.

Yumizen C1200 Transferrin reagent is intended for the quantitative in vitro diagnostic determination of transferrin in human serum and lithium heparin plasma by turbidimetry.
Measurement of transferrin levels aids in the diagnosis of malnutrition, acute inflammation, infection, and iron deficiency anemia.

Yumizen C1200 Rheumatoid Factor reagent is intended for the quantitative in vitro diagnostic determination of rheumatoid factor in human serum by latex-enhanced immunoturbidimetric assay.
Measurement of rheumatoid factor may aid in the diagnosis of rheumatoid arthritis.

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.

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.

![HORIBA Medical logo]

1- **Date of Summary**
   Date submitted : 5th March, 2020

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 Ferritin (1300023880)
   Yumizen C1200 Transferrin (1300023889)
   Yumizen C1200 Rheumatoid Factor (1300023888)

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 Ferritin	Yumizen C1200 Ferritin reagent is intended for the quantitative in vitro diagnostic determination of Ferritin in human serum by latex-enhanced immunoturbidimetric assay. Measurements of ferritin aid in the diagnosis of diseases affecting iron metabolism, hemochromatosis (iron overload) and iron deficiency anemia.
Yumizen C1200 Transferrin	Yumizen C1200 Transferrin reagent is intended for the quantitative in vitro diagnostic determination of Transferrin in human serum and lithium heparin plasma by turbidimetry. Measurement of transferrin levels aids in the diagnosis of malnutrition, acute inflammation, infection, and iron deficiency anemia.
Yumizen C1200 Rheumatoid Factor	Yumizen C1200 Rheumatoid Factor reagent is intended for the quantitative in vitro diagnostic determination of rheumatoid factor in human serum by latex-enhanced immunoturbidimetric assay. Measurement of rheumatoid factor may aid in the diagnosis of rheumatoid arthritis.

Trade/Proprietary Name: Yumizen C1200 Ferritin
Device Class: Class II / 510(k) required
Classification Name: §866.5340: Ferritin immunological test system
Product Code: DBF
Panel: Immunology (82)

Trade/Proprietary Name: Yumizen C1200 Transferrin
Device Class: Class II / 510(k) required
Classification Name: §866.5880: Transferrin immunological test system
Product Code: DDG
Panel: Immunology (82)

Trade/Proprietary Name: Yumizen C1200 Rheumatoid Factor
Device Class: Class II / 510(k) required
Classification Name: §866.5775: Rheumatoid factor immunological test system
Product Code: DHR
Panel: Immunology (82)

- This submission allows to evaluate the functionality of the Yumizen C1200 analyzer for immunology analytes (ie.immunoturbidimetry).

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 Ferritin	Ferritin (OSR61203)	BECKMAN COULTER	K092505
Yumizen C1200 Transferrin	Transferrin Model :TRSF2	Roche Diagnostics	K012393
Yumizen C1200 Rheumatoid Factor	Olympus RF Latex reagent (OSR61105)	Olympus America, Inc.	K060201

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 Ferritin

i. Comparison with predicate Device : Similarities

Item	Predicate K092505	Candidate
Device Name	Ferritin (OSR61203)	Yumizen C1200 Ferritin (1300023880)
Intended Use	The Ferritin Reagent is for the determination of ferritin concentrations in human serum and plasma on the Beckman Coulter AU clinical chemistry analyzers. Serum ferritin is an indicator of body iron stores: it has been shown to correlate with stainable bone marrow iron. Measurements of ferritin aid in the diagnosis of diseases affecting iron metabolism, such as hemochromatosis (iron overload) and iron deficiency anemia.	Yumizen C1200 Ferritin reagent is intended for the quantitative in vitro diagnostic determination of Ferritin in human serum by latex-enhanced immunoturbidimetric assay. Measurements of ferritin aid in the diagnosis of diseases affecting iron metabolism, hemochromatosis (iron overload) and iron deficiency anemia.
Reagent format	Liquid	Same
Measurement	Quantitative	Same
Method	Latex-enhanced immuno-turbidimetric method	Same
Product code	DBF	Same
On board Stability	Once opened, the reagent cassette placed in the refrigerator compartment is stable for **60 days**	Once opened, the reagent cassette placed in the refrigerator compartment is stable for **2 months (or 60 days).**
Calibration Stability	The frequency of calibration for the Ferritin procedure is every 30 days.	The reagent is calibrated on Day 0. The calibration stability is checked by testing 2 control specimens. The calibration stability is 1 month (or 30 days)

ii. Comparison with predicate Device: Differences

Item	Predicate K092505	Candidate
Device Name	Ferritin (OSR61203)	Yumizen C1200 Ferritin (1300023880)
Instrument	Beckman Coulter AU400 Clinical Chemistry Analyzer	Yumizen C1200 Clinical chemistry analyzer
Manufactured by	BECKMAN COULTER	HORIBA ABX SAS
Sample type	Serum, Li-heparin plasma and EDTA plasma samples	Serum
Packaging	Cassette of : R1= 4 x 24 mL R2= 4 x 12 mL	Cassette of : R1: 6 x 11 mL R2: 6 x 7 mL
Shelf-life	Unopened, up to the stated expiry date when stored at 2-8°C.	Stable up to the expiration date if stored at 2-10°C.
Analytical Range	**Measuring Range** 8.0 – 450.0 ng/mL	**Measuring Range** 10 -450 ng/mL
Reference range	Women: 10 – 158 ng/mL Men: 16 – 243 ng/mL	Adults : Women: 10 - 120 ng/mL (µg/L) Men: 20 - 250 ng/mL (µg/L)

Discussion on the analysis differences :
1. Instrument: Yumizen C1200 Ferritin is used on Yumizen C1200
2. Packaging: Packaging is different; depends on cassette capacity.
3. Reagent stability/ Shelf-life:storage temperature is different.
4. Analytical range: the measuring range for Yumizen C1200 Ferritin is slightly higher on the lower end
5. Reference range: Yumizen C1200 Ferritin has tighter reference range on the upper end for Women and slightly larger reference range on the upper end for Men.
6. Sample type: Yumizen C1200 Ferritin uses serum.

c. **Yumizen C1200 Transferrin (1300023889)**

i. **Comparison with predicate Device : Similarities**

Item	Predicate k012393	Candidate
Device Name	Transferrin Model :TRSF2	Yumizen C1200 Transferrin (1300023889)
Intended Use	In vitro test for the quantitative determination of transferrin in human serum and plasma in Roche/Hitachi cobas c systems.	Yumizen C1200 Transferrin reagent is intended for the quantitative in vitro diagnostic determination of Transferrin in human and lithium heparin plasma by turbidimetry. Measurement of transferrin levels aids in the diagnosis of malnutrition, acute inflammation, infection, and iron deficiency anemia.
Sample type	Serum plasma	Serum plasma
Reagent format	Liquid	Same
Measurement	Quantitative	Same
Method	Turbidimetry	Same
Product code	DDG	Same
Shelf-life	**2-8°C,** See expiration date on label	Stable up to the expiry date on the label **if stored at 2-8°C.**
Analytical Range	**Measuring Range** 0.1-5.2 g/L	**Measuring Range** 0.10-5.20 g/L
Reference range	200-360 mg/dL	200-360 mg/dL

ii. Comparison with predicate Device: Differences

Item	Predicate k012393	Candidate
Device Name	Transferrin Model :TRSF2	Yumizen C1200 Transferrin (1300023889)
Instrument	Roche analyzer (Cobas C701)	Yumizen C1200 Clinical chemistry analyzer
Manufactured by	ROCHE	HORIBA ABX SAS
On board Stability	4 weeks	Once opened, the reagent cassette placed in the refrigerated compartment is stable for **6 weeks.**
Discussion on the analysis differences : 1. Instrument & Manufacturer: Yumizen C1200 Transferrin is used on Yumizen C1200. Yumizen C1200 Transferrin is manufactured by HORIBA ABX SAS. 2. Reagent stability: the on board stability of Yumizen C1200 Transferrin is longer. Stability depends on the reagent composition and cassette capacity.		

d. **Yumizen C1200 Rheumatoid Factor**

i. **Comparison with predicate Device : Similarities**

Item	Predicate K060201	Candidate
Device Name	Rheumatoid Factor reagent model : OSR61105	Yumizen C1200 Rheumatoid Factor (1300023888)
Intended Use	Olympus RF Latex System reagent for the quantitative determination of Rheumatoid Factor (RF) in human serum and plasma on Olympus AU analyzers. Measurement of rheumatoid factor may aid in the diagnosis of rheumatoid arthritis	Yumizen C1200 Rheumatoid Factor reagent is intended for the quantitative in vitro diagnostic determination of rheumatoid factor in human serum by latex-enhanced immunoturbidimetric assay. Measurement of rheumatoid factor may aid in the diagnosis of rheumatoid arthritis.
Manufactured by	OLYMPUS AMERICA, INC	HORIBA ABX SAS
Measurement	Quantitative	Quantitative
Method	Latex-enhanced Immunoturbidimetry	Same
Product code	DHR	Same
Calibration Stability	The frequency of calibration for the RF Latex procedure is every **30 days.**	The calibration stability is **1 month (or 30 days)**
Reference range	Adult ≤ 14 IU/mL	Same

ii. Comparison with predicate Device: Differences

Item	Predicate K060201	Candidate
Device Name	Rheumatoid Factor reagent model : OSR61105	Yumizen C1200 Rheumatoid Factor (1300023888)
Instrument	Olympus AU400 Clinical Chemistry Analyzer	Yumizen C1200 Clinical chemistry analyzer
Sample type	Serum, plasma	Serum
Reagent format	Liquid	Same
Packaging	Cassette of : R1= 4 x 24 mL R2= 4 x 8mL	Cassette of : R1: 6 x 13 mL R2: 6 x 6 mL
Analytical range	**Measuring range :** 5-120 IU/mL	**Measuring range :** 10 - 120 IU/mL
Shelf-life	Until expiration date on label **(+2-8 °C)**	Stable up to expiration date **if stored at 2-10°C**
On board Stability	Once opened, the reagent is stable **for 60 days** in refrigerated compartment of analyzer.	Once opened, the reagent cassette placed in the refrigerator compartment is stable for 1 month **(or 30 days)**

Discussion on the analysis differences :
1. Instrument: Yumizen C1200 Rheumatoid Factor is used on Yumizen C1200
3. Packaging: Packaging is different; depends on cassette capacity.
4. Reagent stability: the on board stability Yumizen C1200 Rheumatoid Factor is shorter. The Shelf life is different. Stability depend on reagent composition and cassette capacity.
5.Analytical range: the measuring range for serum for Yumizen C1200 Rheumatoid factor is slightly tighter on the lower end
6. Sample type: Yumizen C1200 RF uses serum only.

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 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

c. Other reference cited

- Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745)
- CLSI EP09-A3 : Measurement Procedure Comparison and Bias Estimation Using Patient Samples - Third Edition - August 2013

8- Analytical Performance Characteristics

8.1 Measuring Range

- **Yumizen C1200 Ferritin**

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 evaluated	Measuring range
Serum	6.30 ng/mL	9.39 ng/mL	13.3 - 426.6 ng/mL	10 to 450 ng/mL
Serum Post-dilution	NA	NA	NA	until 2250 ng/mL

- **Yumizen C1200 Transferrin**

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 evaluated	Measuring range
Serum/ Plasma	0.002 g/L	0.07 g/L	0.15 - 4.61 g/L	0.10 to 5.20 g/L
Serum/ Plasma Post-dilution	NA	NA	NA	15.60 until g/L

- **<u>Yumizen C1200 Rheumatoid Factor</u>**

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.

➢ <u>Results :</u>

	Limit of detection	Limit of quantitation	Linearity evaluated	Measuring range
Serum	4.07 IU/mL	7.41 IU/mL	13.2 - 118.8 IU/mL	10 to 120 IU/mL
SerumPost -dilution	NA	NA	NA	until 1200 IU/mL

8.2 <u>Accuracy and Precision</u>

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

- **<u>Yumizen C1200 Ferritin</u>**

  ➢ *Total Precision : analyzer variability - 20x2x2 study*

<u>Within Run :</u> CV limits, for the low, middle and high level are respectively 8.0 %, 6.0% and 6.0% for serum
<u>Total Precision :</u> CV limits, for the low, middle and high level are respectively 10.0 %, 8.0 % and 8.0 % for serum.

Sample	N	Mean (ng/mL)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Yumizen C1200 Level 1 Protein Control	240	47.58	3.6	0.0	1.5	3.1	4.9
Yumizen C1200 Level 2 Protein Control	240	279.31	1.1	0.0	1.6	0.8	2.1
Sample 1	240	29.56	5.5	2.2	2.2	4.7	7.9
Sample 2	240	50.87	4.1	1.9	0.0	2.4	5.1
Sample 3	240	172.63	1.4	0.3	0.6	1.1	1.9
Sample 4	240	328.60	1.3	3.6	2.0	0.0	4.3
Sample 5	240	403.21	1.0	0.6	0.6	0.4	1.4

The results are within the specifications.

➢ *Lot to Lot variability : 3x5x2x3*

<u>Within Run :</u> CV limits, for the low, middle and high level are respectively 8.0 %, 6.0 % and 6.0 % for serum

<u>Total Precision :</u> CV limits, for the low, middle and high level are respectively 10.0 %, 8.0 % and 8.0 % for serum.

Sample	N	Mean (ng/mL)	Within-Run (%CV)	Between-Day (%CV)	Within-Batch (%CV)	Between-Batch (%CV)	Total (%CV)
Yumizen C1200 Level 1 Protein Control	90	52.84	4.6	4.5	6.4	0.0	6.4
Yumizen C1200 Level 2 Protein Control	90	281.87	0.9	0.7	1.1	1.2	1.6
Sample 1	90	19.09	8.8	4.8	10.0	6.3	11.8
Sample 2	90	34.05	6.5	0.0	6.5	0.5	6.5
Sample 3	90	51.53	3.6	0.0	3.6	1.1	3.8
Sample 4	90	192.31	1.4	0.0	1.4	2.5	2.8
Sample 5	90	407.38	0.9	0.0	0.9	1.0	1.4

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

The results are within the specifications.

- **<u>Yumizen C1200 Transferrin</u>**

  ➢ *Total Precision : analyzer variability - 20x2x2 study*

<u>Within Run :</u> CV limits, for the low, middle and high level are respectively 6.0 %, 4.5 % and 3.8 % for serum and plasma
<u>Total Precision :</u> CV limits, for the low, middle and high level are respectively 8.0 %, 6.0 % and 5.0 % for serum and plasma.

Sample	N	Mean (g/L)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Yumizen C1200 Level 1 Protein Control	240	**1.24**	**1.2**	0.7	2.1	2.5	**3.6**
Yumizen C1200 Level 2 Protein Control	240	**3.35**	**1.5**	0.6	1.4	2.8	**3.6**
Sample 1	240	**0.78**	**1.0**	0.5	2.3	3.7	**4.5**
Sample 2	240	**1.02**	**1.2**	0.3	1.7	2.5	**3.2**
Sample 3	240	**1.83**	**1.3**	0.5	1.3	1.3	**2.3**
Sample 4	240	**3.78**	**1.5**	0.6	1.1	1.9	**2.7**

The results are within the specifications.

➢ *Lot to Lot variability : 3x5x2x3*

<u>Within Run :</u> CV limits, for the low, middle and high level are respectively 6.0 %, 4.5 % and 3.8 % for serum and plasma

<u>Total Precision :</u> CV limits, for the low, middle and high level are respectively 8.0 %, 6.0 % and 5.0 % for serum and plasma.

Sample	N	Mean (g/L)	Within-Run (%CV)	Between-Day (%CV)	Within-Batch (%CV)	Between-Batch (%CV)	Total (%CV)
Yumizen C1200 Level 1 Protein Control	90	1.29	3.5	5.3	6.3	1.7	6.6
Yumizen C1200 Level 2 Protein Control	90	3.41	1.7	1.2	2.1	2.2	3.0
Sample 1	90	0.77	4.2	2.7	5.0	2.0	5.4
Sample 2	90	1.08	1.5	0.9	1.7	2.8	3.3
Sample 3	90	1.96	1.3	0.2	1.3	3.2	3.4
Sample 4	90	3.54	2.6	0.7	2.7	2.1	3.4

The results are within the specifications.

- **Yumizen C1200 Rheumatoid Factor**

  ➢ *Total Precision : analyzer variability - 20x2x2 study*

Within Run : CV limits, for the low, middle and high level are respectively 6.0 %, 4.5 % and 3.8 % for serum
Total Precision : CV limits, for the low, middle and high level are respectively 8.0 %, 6.0 % and 5.0 % for serum.

Sample	N	Mean (IU/mL)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Yumizen C1200 Level 1 Protein Control	240	**40.99**	**0.5**	0.4	1.2	1.7	**2.2**
Yumizen C1200 Level 2 Protein Control	240	**63.93**	**0.4**	0.6	1.6	1.8	**2.5**
Sample 1	240	**22.24**	**1.2**	0.9	0.9	1.0	**2.0**
Sample 2	240	**34.28**	**0.8**	1.3	1.3	0.9	**2.2**
Sample 3	240	**49.41**	**0.5**	1.0	0.5	1.3	**1.8**
Sample 4	240	**70.16**	**0.5**	0.4	0.8	1.3	**1.6**
Sample 5	240	**103.42**	**0.8**	0.6	0.7	0.5	**1.4**

The results are within the specifications.

> *Lot to Lot variability : 3x5x2x3*

Within Run : CV limits, for the low, middle and high level are respectively 6.0 %, 4.5 % and 3.8 % for serum

Total Precision : CV limits, for the low, middle and high level are respectively 8.0 %, 6.0 % and 5.0 % for serum.

Sample	N	Mean (IU/mL)	Within-Run (%CV)	Between-Day (%CV)	Within-Batch (%CV)	Between-Batch (%CV)	Total (%CV)
Yumizen C1200 Level 1 Protein Control	90	**41.70**	**1.8**	0.3	1.8	0.6	**1.9**
Yumizen C1200 Level 2 Protein Control	90	**67.05**	**1.4**	0.5	1.5	1.6	**2.2**
Sample 1	90	**17.30**	**2.9**	0.7	3.0	0.8	**3.1**
Sample 2	90	**30.88**	**1.4**	0.6	1.6	0.9	**1.8**
Sample 3	90	**53.08**	**1.4**	0.9	1.6	2.7	**3.2**
Sample 4	90	**70.24**	**1.1**	0.8	1.3	0.0	**1.3**
Sample 5	90	**102.14**	**1.0**	0.4	1.1	1.4	**1.8**

The results are within the specifications.

8.3 <u>Interferences</u>

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.

- **<u>Yumizen C1200 Ferritin</u>**

Serum		
Hemoglobin	290 µmol/L	500 mg/dL
Triglycerides	3.09 mmol/L	270.42 mg/dL
Total Bilirubin	504 µmol/l	29.5 mg/dL
Direct Bilirubin	442 µmol/l	25.87 mg/dL
Ascorbic Acid	340 µmol/L	5.98 mg/dL
Acetylsalicylic Acid	3.62 mmol/L	65.16 mg/dL
Ibuprofen	2.43 mmol/L	50.10 mg/dL
Acetaminophen	1324 µmol/L	20 mg/dL
Rheumatoid Factor	500 IU/mL	
Deferoxamine	400 µmol/L	22.43 mg/dL
Prednisone	500 µmol/L	17.92 mg/dL
Methotrexate	3000 µmol/L	136 mg/dL
Ferrous Sulfate	1 mmol/L	15.19 mg/dL
Ampicillin	250 µmol/L	8.7 mg/dL
Azithromycin	20 µmol/L	1.49 mg/dL
Rifampicin	100 µmol/L	8.20 mg/dL
Diltiazem	10 µmol/L	0.41 mg/dL
Simvastatin	10 µmol/L	0.42 mg/dL

- **Yumizen C1200 Transferrin**

Serum/Plasma		
Hemoglobin	290 µmol/L	500 mg/dL
Triglycerides	4.04 mmol/L	353.28 mg/dL
Total Bilirubin	749 µmol/l	43.84 mg/dL
Direct Bilirubin	408 µmol/l	23.86 mg/dL
Ascorbic Acid	340 µmol/L	5.98 mg/dL
Acetylsalicylic Acid	3.62 mmol/L	65.16 mg/dL
Ibuprofen	2.43 mmol/L	50.10 mg/dL
Acetaminophen	1324 µmol/L	20 mg/dL
Rheumatoid Factor	400 IU/mL	

- **Yumizen C1200 Rheumatoid Factor**

Serum		
Hemoglobin	290 µmol/l	500 mg/dL
Triglycerides	6.02 mmol/l	526.75 mg/dL
Total Bilirubin	535 µmol/l	31.32 mg/dL
Direct Bilirubin	433 µmol/l	25.34 mg/dL
Ascorbic Acid	340 µmol/L	5.98 mg/dL
Acetylsalicylic Acid	3.62 mmol/L	65.16 mg/dL
Ibuprofen	2.43 mmol/L	50.10 mg/dL
Acetaminophen	1324 µmol/L	20 mg/dL

8.4 Yumizen C1200 Transferrin : Anticoagulant study

Study materials :
       Anticoagulant : heparin-lithium
       Samples: single donors

59 paired serum/ plasma samples were evaluated on Yumizen C1200 analyser using Yumizen C1200 Transferrin reagent.
For this study, each paired samples (sera and heparinized plasma) has been obtained from single donor.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation
Transferrin: serum sample (g/L)	59	1.933	3.786			
Transferrin: Heparin sample (g/L)	59	1.901	3.724	0.04833	0.9691	0.995

Conclusion :
The results show there is not significative difference between serum and plasma with heparin specimens
-> coagulation does not have an impact on Transferrin determination.

8.5 Prozone / Antigen excess effect

For each analyte, a range of high concentration samples is prepared in order to identify a high dose hook effect.

- **Yumizen C1200 Ferritin**

An antigen excess effect is observed for samples with a concentration higher than 5043 ng/mL, as they have a rate which could be inside the calibration range and the assay could give underestimated results, but remaining inside the pathological range.
For such samples, a prozone alarm will flag the samples having concentration higher than 5043 ng/mL. The flagged sample will be automatically rerun by the analyzer.

- **Yumizen C1200 Transferrin**

No antigen excess has been detected up to a concentration of 40 g/L.

- **Yumizen C1200 Rheumatoid Factor**

An antigen excess effect is observed for samples with a concentration higher than 229 IU/mL, as they have a rate which could be inside the calibration range and the assay could give underestimated results, but remaining inside the pathological range.
For such samples, a prozone alarm will flag the samples having concentration higher than 229 IU/mL. The flagged sample will be automatically rerun by the analyzer.

8.6 Method comparison with a predicate device

- **Yumizen C1200 Ferritin**

This study has been carried out using recommendations found in the CLSI EP-9A3 guidance.
Samples: Anonymous remnants of human serum specimens collected from blood bank. These samples are in the candidate measuring range and predicate measuring range.
103 native sera samples have been assayed in duplicate, in ascendant order and descendant order on 6 working days.
Only the first replicate of each method will be used for the data analysis reported below.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation – r^2
(ng/mL)	103	16.74	413.00	2.105	0.9142	0.999

- **Yumizen C1200 Transferrin**

This study has been carried out using recommendations found in the CLSI EP-9A3 guidance.
Samples: Anonymous remnants of human serum specimens collected from CHU Nîmes (University Hospital Center).
115 native samples have been assayed in duplicate, in ascendant order and descendant order on 5 working days.
Only the first replicate of each method will be used for the data analysis reported below.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation – r^2
(g/L)	115	0.37	4.81	0.006364	0.9455	0.993

- **Yumizen C1200 Rheumatoid Factor**

This study has been carried out using recommendations found in the CLSI EP-9A3 guidance.
Samples: Anonymous remnants of human serum specimens collected from blood bank. These samples are in the candidate measuring range and predicate measuring range.
113 native samples have been assayed in duplicate, in ascendant order and descendant order on 6 working days.
Only the first replicate of each method will be used for the data analysis reported below.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation – r^2
(IU/mL)	113	16.7900	118.8100	-1.11	1.014	0.992

8.7 <u>Reagent Stability</u>

8.7.1   Closed stability

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

- **<u>Yumizen C1200 Ferritin</u>**

Stability before opening:
Stable up to the expiry date on the label if stored at 2-10°C. Store protected from light.

The shelf life claim for HORIBA Medical reagent is 18 months.

- **<u>Yumizen C1200 Transferrin</u>**

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 is 24 months.

- **<u>Yumizen C1200 Rheumatoid Factor</u>**

Stability before opening:
Stable up to the expiry date on the label if stored at 2-10°C.

The shelf life claim for HORIBA Medical reagent is 18 months.

8.7.2 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 Ferritin is 2 months.
- The reagent stability claim for the Yumizen C1200 Transferrin is 6 weeks.
- The reagent stability claim for the Yumizen C1200 Rheumatoid Factor is 1 month.

8.8 <u>Reference range</u>

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

- **<u>Yumizen C1200 Ferritin</u>**

  ➢ <u>Adults data (bibliographic reference and study- see below)</u>

  ▪ <u>Women :</u>
50 "normal samples" from blood bank have been assayed with the method in evaluation. Each sample is assayed in duplicates.
Only the first replicate of each method will be used for the data analysis reported below.

Only the first replicate result 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.

Women :   10 - 120 ng/ml (µg/l)

Reference:
Roberts W.L., McMillin G.A., Burtis C.A., Bruns D.E., Reference Information for the Clinical Laboratory, TIETZ Textbook of Clinical Chemistry and Molecular Diagnostics. 4ème Ed; Burtis C.A., Ashwood E.R., Bruns D.E., (Elsevier Saunders eds. St Louis, USA); 2006, 2269.

  ▪ <u>Men :</u>

95 "normal samples" from blood bank have been assayed with the method in evaluation. Each sample is assayed in duplicates.
Only the first replicate of each method will be used for the data analysis reported below.

Only the first replicate result 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.

Men: 20 - 250 ng/ml (µg/l)

Reference:
Roberts W.L., McMillin G.A., Burtis C.A., Bruns D.E., Reference Information for the Clinical Laboratory, TIETZ Textbook of Clinical Chemistry and Molecular Diagnostics. 4ème Ed; Burtis C.A., Ashwood E.R., Bruns D.E., (Elsevier Saunders eds. St Louis, USA); 2006, 2269.

- **<u>Yumizen C1200 Transferrin</u>**

85 "normal samples" (28 women + 57 men) from blood bank have been assayed with the method in evaluation. Each sample is assayed in duplicates.
Only the first replicate of each method will be used for the data analysis reported below.

Only the first replicate result 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 Transferrin – Serum

2 - 3.6 g/l (200 - 360 mg/dl) based on CRM 470.

Reference:
Dati F., Schumann G, Thomas L, Aguzzi F, Baudner S. Bienvenu J. et al. Consensus of a group of professional societies and diagnostic companies on guidelines for interim reference ranges for 14 proteins in serum based on the standardization against IFCC/BCR/CAP Reference Material (CRM 470). Eur. J Clin Chem. Cli Biochem. 1996; 34: 517-20.

- **<u>Yumizen C1200 Rheumatoid Factor</u>**

60 "normal samples" from blood bank have been assayed with the method in evaluation. Each sample is assayed in duplicates.
Only the first replicate of each method will be used for the data analysis reported below.

Only the first replicate result 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 Rhumatoid Factor
        Adult < 14 IU/ml

Reference:
Tietz NW, editor. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia: WB Saunders Company, 1990.

8.9 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.

8.10   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.