October 3, 2019

Horiba ABX SAS
Caroline Ferrer
Regulatory Affairs Manager
Parc Euromédecine, Rue du Caducée - BP7290
34184 Montpellier Cedex 4
France

Re: K191993
Trade/Device Name: Yumizen C1200 CRP
Regulation Number: 21 CFR 866.5270
Regulation Name: C-reactive protein immunological test system
Regulatory Class: Class II
Product Code: DCK
Dated: July 24, 2019
Received: July 25, 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,

For: 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)*
K191993

Device Name
Yumizen C1200 CRP

Indications for Use *(Describe)*
Yumizen C1200 CRP reagent is intended for use as a high sensitive assay for the quantitative in vitro diagnostic determination of the C-reactive protein in human serum and plasma based on an immunoturbidimetric assay. CRP is used to evaluate conditions thought to be associated with inflammation in otherwise healthy individuals.

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.

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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 : K191993

1- Date of Summary

Date submitted : 25th September, 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
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4- Product Name

Yumizen C1200 CRP

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 CRP	**Yumizen C1200 CRP** reagent is intended for use as a high sensitive assay for the quantitative in vitro diagnostic determination of the C-reactive protein in human serum and plasma based on an immunoturbidimetric assay. CRP is used to evaluate conditions thought to be associated with inflammation in otherwise healthy individuals.

Trade/Proprietary Name:	Yumizen C1200 CRP
Device Class:	Class II / 510(k) required
Classification Name:	§866.5270: C-reactive protein immunological test system
Product Code:	DCK
Panel:	Immunology (82)

- In this submission, HORIBA Medical presents Yumizen C1200 CRP with the **H**igh **s**ensitive application.

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 CRP	VITROS Chemistry Products hsCRP Reagent	Ortho-Clinical Diagnostics, Inc.	K160712

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 CRP

i. Comparison with predicate Device : Similarities

Item	Predicate K160712	Candidate
Device Name	**VITROS Chemistry Products hsCRP Reagent**	Yumizen C1200 CRP
Intended Use	VITROS Chemistry Products hsCRP Reagent is used on the VITROS 5,1 FS Chemistry System, the VITROS 4600 Chemistry System and the VITROS 5600 Integrated System to quantitatively measure C-reactive protein (CRP) in human serum and plasma. CRP is used to evaluate conditions thought to be associated with inflammation in otherwise healthy individuals.	**Yumizen C1200 CRP** reagent is intended for use as a high sensitive assay for the quantitative in vitro diagnostic determination of the C-reactive protein in human serum and plasma based on an immunoturbidimetric assay. CRP is used to evaluate conditions thought to be associated with inflammation in otherwise healthy individuals.
Reagent format	Liquid	Same
Method	Immunoturbidimetry	Same
Measurement	Quantitative	Same
Product code	DCK	DCK
Sample type	Serum, and Lithium heparin plasma	Serum, and Lithium heparin plasma

ii. Comparison with predicate Device: Differences

Item	Predicate K160712	Candidate
Device Name	**VITROS Chemistry Products hsCRP Reagent**	Yumizen C1200 CRP
Instrument	VITROS 4,1 FS/4600 Chemistry	Yumizen C1200 Clinical chemistry Analyzer
Manufactured by	Ortho-Clinical Diagnostics, Inc.	HORIBA ABX SAS
Calibrators	VITROS Chemistry Products Calibrator Kit 17 VITROS Chemistry Products FS Calibrator 1 VITROS Chemistry Products FS Diluent Pack 2 (BSA/Saline) (for calibration only)	Yumizen C1200 CRPhs Cal (1300071246)
Controls	VITROS Chemistry Products hsCRP Performance Verifier I, II and III	Yumizen C1200 Level 1 CRPhs Control (1300071247) Yumizen C1200 Level 2 CRPhs Control (1300071248)
Analytical Range	0.10 to 15.00 mg/L	0.2 to 10 mg/L
Reagent On board Stability	≤ 4 weeks	8 weeks
Shelf-life	Stable until the expiration date printed on the label when stored at 2-8°C	Stable up to expiry date on the label if stored at 2-10°C
Discussion on the analysis differences : 1. Instrument : Yumizen C1200 CRP is used on Yumizen C1200 analyzer. And Yumizen C1200 CRP is manufactured by HORIBA ABX SAS. 2. Calibrators&Controls : Yumizen C1200 CRP uses Yumizen C1200 CRPhs Cal and 2 Levels of controls : Yumizen C1200 Level 1 CRPhs Control and Yumizen C1200 Level 2 CRPhs Control. on Yumizen C1200 whereas the predicate uses VITROS Chemistry Products calibrator Kit 17. 3. Analytical range: The measuring range for Yumizen C1200 CRP is different. Concerning low value, it is similar but slightly lower than the predicate value. Concerning high value, it is lower than the predicate value.		

Item	Predicate K160712	Candidate
4.On board stability: The on board stability of Yumizen C1200CRP is longer. Stability depends on the reagent composition and cassette capacity. 5.Shelf-life Yumizen C1200 CRP has a reagent stability up to the expiration date when unopened and stored in 2-10°C.		

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
- Guidance for Industry and FDA Staff : Review Criteria for Assessment of C-Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein (cCRP Assays) – Document issued on : September 22, 2005

c. Others Guidances followed

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

8- Analytical Performance Characteristics

8.1 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 range is appropriate.

- Results :

	Limit of detection	Limit of quantitation	Linearity	Measuring range
Serum	0.13 mg/L	0.16 mg/L	0.03 to 11.53 mg/L.	0.2 to 10 mg/L

For hsCRP with 1:5 dilution, the EMI is 10-50 mg/L.

8.2 Accuracy and Precision

- Repeatability (within-run precision) and Reproducibility (total precision) – Serum samples

Within run : CV limits, for the low, middle and high level are respectively 9.0 %, 4.5 % and 3.8 %.
Total precision: CV limits, for the low, middle and high level are respectively 12.0 %, 6.0 % and 5.0 %.

Results with calibration every week (previous study):

Sample	N	Mean (mg/L)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Low CRP Control (internal control)	240	**1.50**	**1.5**	1.8	1.9	0.0	**3.0**
Sample 1	240	**0.34**	**4.7**	2.8	2.3	0.1	**5.9**
Sample 2	240	**0.83**	**1.6**	2.6	0.9	2.1	**3.8**
Sample 3	240	**4.13**	**0.6**	1.7	1.7	1.9	**3.1**
Sample 4	240	**8.73**	**0.8**	2.5	1.2	1.0	**3.1**

Results with calibration only at the beginning of the study (new study):

Sample	N	Mean (mg/L)	Within-Run (%CV)	Between-Run (%CV)	Between-Day (%CV)	Between-Instrument (%CV)	Total (%CV)
Low CRP Control (internal control)	240	**1.50**	**1.3**	0.4	1.0	1.1	**2.0**
Sample 1	240	**0.39**	**4.8**	0.0	1.6	3.7	**6.2**
Sample 2	240	**1.27**	**3.3**	1.7	1.7	2.1	**4.6**
Sample 3	240	**3.00**	**1.3**	1.4	0.7	0.6	**2.1**
Sample 4	240	**8.81**	**0.8**	0.4	1.6	1.5	**2.4**

The results are within the specifications.

- Repeatability (within-run precision) for Heparin-Lithium sample

Study materials:
Anonymous remnants of human Heparin-Lithium specimens collected from routine clinical laboratory.The within-run precision is performed using one lot of reagent, one instrument in a single run.

Description:
6 specimens (sample low, mid, high) were tested 20 times in a single run for each sample.

Within run : CV limits, for the low (1 mg/L), middle (5 mg/L) and high level (9 mg/L) are respectively 9.0 %, 4.5 % and 3.8 %.

Sample	N	Mean (mg/L)	Within-Run (%CV)	SD (mg/L)
Sample 1	20	**0.35**	**2.17**	**0.01**
Sample 2	20	**0.51**	**2.11**	**0.01**
Sample 3	20	**1.25**	**1.00**	**0.01**
Sample 4	20	**4.75**	**2.27**	**0.11**
Sample 5	20	**7.77**	**1.31**	**0.10**
Sample 6	20	**9.31**	**0.69**	**0.06**

The results are within the specifications.

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.

Serum		
Hemoglobin	290 µmol/L	500 mg/dL
Triglycerides	3.19 mmol/l	279 mg/dL
Total Bilirubin	472 µmol/	27.61 mg/dL
Direct Bilirubin	520 µmol/L	30.41 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	Up to 400 IU/mL	

Concerning Triglycerides Interferences :
At 395 mg/dL triglycerides, there was a deviation of -11.2% per sample with a concentration of 4.15 mg/L CRP, and at 517 mg/dL triglycerides, there was a deviation of -10.5% per sample with a concentration of 0.83 mg/L CRP.

Concerning Rheumatoid Factor Interferences :
"No significant influence is observed up to 400 IU/mL when tested at ~5 mg/L and ~9 mg/L CRP."

This information is included in the reagent Instruction for use.

8.4 Matrix comparison

- **Matrix comparison serum vs heparin-lithium on Yumizen C1200**

Study materials :

Anticoagulant : heparin-lithium

Samples: individual donors from blood bank (in serum and plasma for each donor)

Description of Test Procedure/Method

54 samples were evaluated on Yumizen C1200 analyzer using Yumizen C1200 CRP reagent. For this study, each sample came from single donor. Samples was collected both in serum and heparin-lithium tube.

Passing Bablok	N	Min	Max	Intercept	Slope	Correlation
CRP (mg/L)	54	0.210	9.180	-0.003012	0.9787	0.998

Conclusion :

The results show there is no significant difference between Serum and Heparin-Lithium specimens for the method in evaluation.

8.5 Method comparison with a comparator device

Comparator :

Yumizen C1200 CRP	CRP reagent model : CRP LATEX REAGENT OSR6199 on Olympus AU400 Clinical Chemistry Analyzer	BECKMAN COULTER	K051564

This study has been carried out using recommendations found in the NCCLS (CLSI) EP-9A3guidance.
Samples: Anonymous remnants of human serum specimens collected from routine clinical laboratory. These samples are in the candidate measuring range and comparator measuring range.
138 native 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
CRP (mg/L)	138	0.200	9.570	-0.06852	0.9987	0.995

8.6 Reagent Stability

8.2.1 Closed stability

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

Stability before opening:

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

- **CRP**

The Shelf Life of Yumizen C1200 CRP is correct at 24 months.

8.6.2 Open stability

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

On board reagent Stability:

The stability claim after opening, on-Board, is 8 weeks.

8.7 Reference range

Serum / Plasma

≤ 1 mg/L

Reference :

Raifai N, Ridker PM. Population Distributions of C- reactive Protein in Aparently Healthy Men and Women in the United States: Implication for Clinical Interpretation. Clin Chem (2003) **49**: 666-669.

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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 this device is substantially equivalent to its predicate device.