510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K192028

B Applicant

Horiba ABX SAS

C Proprietary and Established Names

Yumizen C1200 CRP

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DCK	Class II	21 CFR 866.5270 - C-Reactive Protein Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

C-reactive protein

C Type of Test:

Quantitative, Immunoturbidimetric

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
Yumizen C1200 CRP reagent is intended for the quantitative in vitro diagnostic determination of the C-reactive protein in human serum and lithium heparin plasma based on an immunoturbidimetric assay. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues and for evaluation of infections, tissue injury and inflammatory disorders. This test should be used in conjunction with other laboratory and clinical findings.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

Yumizen C1200 Clinical Chemistry Analyzer (cleared under K183375)

IV Device/System Characteristics:

A Device Description:
The composition of Yumizen C1200 CRP is as follows:

- Reagent 1: Buffer solution: Glycine buffer solution
- Reagent 2: Latex suspension: 0.20% w/v suspension of latex particles sensitized with anti-CRP antibodies (rabbit)

Additional materials and equipment (not supplied):

- Automated clinical chemistry analyzer: Yumizen C1200
- Calibrators: Yumizen C1200 CRP Cal (1300023899)
- Controls: Yumizen C1200 Level 1 Protein Control (1300023944)
  Yumizen C1200 Level 2 Protein Control (1300023945)
- Distilled or deionized water
- Standard laboratory equipment

B Principle of Operation:
Yumizen C1200 CRP is a latex-enhanced immunoturbidimetric assay to measure CRP levels in serum and plasma samples for conventional CRP ranges. When an antigen-antibody reaction occurs between CRP in a sample and anti-CRP antibody which has been sensitized to latex particles, agglutination occurs. This agglutination is detected as an absorbance change, with the magnitude of the change being proportional to the quantity of CRP in the sample. The actual concentration is then determined by interpolation from a calibration curve prepared from calibrators of known concentration.

V Substantial Equivalence Information:

A Predicate Device Name(s):
QuikRead go CRP, QuikRead go CRP Verification Set, QuikRead go CRP Control Set, and QuikRead go Instrument

B Predicate 510(k) Number(s):
K142993

C Comparison with Predicate(s):

Device & Predicate Device(s):	K192028	K142993
Device Trade Name	Yumizen C1200 CRP	QuikRead Go CRP
General Device Characteristic Similarities		
Intended Use/Indications For Use	Yumizen C1200 CRP reagent is intended for the quantitative in vitro diagnostic determination of the C-reactive protein in human serum and lithium heparin plasma based on an immunoturbidimetric assay. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues and for evaluation of infections, tissue injury and inflammatory disorders. This test should be used in conjunction with other laboratory and clinical findings.	The QuikRead go CRP test is an immunoturbidimetric assay for the in vitro quantitative determination of C-reactive protein (CRP) in K2-EDTA and lithium heparin whole blood, K2-EDTA and lithium heparin plasma and in serum samples. The test is carried out by means of the QuikRead go instrument. Measurement of C-reactive protein aids in the evaluation of injury to body tissues, and infection and inflammatory disorders. The instrument and assay are for use by trained professionals in the clinical laboratory. For in vitro diagnostic use only. Not for point-of-care use.
Technology	Immunoturbidimetry	Same
Assay Type	Quantitative	Same
Product Code	DCK	Same
Limit of Quantitation	5 mg/L	Same
Reference Range	< 5 mg/L	Same

General Device Characteristic Differences		
Instrument	Yumizen C1200 Clinical chemistry Analyzer	QuikRead go Analyzer
Test	Latex particles	Microparticles
Antibody	Rabbit anti-CRP antibodies	Anti-human CRP F(ab)2 fragment
Sample Type	Serum, plasma (lithium heparin)	Serum, plasma (Li-Heparin, K2-EDTA), whole blood (Li-heparin, K2-EDTA)
Analytical Measuring Range	5 to 160 mg/L	5 to 200 mg/L: serum and plasma 5 to150 mg/L: whole blood
Traceability	IRMM/ERM-DA472/IFCC	ERM-DA 474

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures– Third Edition - October 2014
- CLSI EP06-A: Evaluation of the Linearity of Quantitative measurement Procedures A Statistical Approach – First Edition – April 2003
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures – Second Edition - June 2012
- 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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   Precision: The study was performed based on CLSI guideline EP05-A3, where five serum samples were tested in duplicates per run, two runs per day for 20 days using three reagent lots on three analyzers. Each reagent lot was tested on each analyzer to generate a total of 240 test results per sample (2 replicates x 2 runs x 20 days x 3 lot/analyzer = 240). The total SD and CV% calculation was based on the within-run, between-run, between-day, and between-instrument data. The results are shown in the table below.

Sample	N	Mean (mg/L)	Within-run		Between-run		Between-day		Between-instrument		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	240	5.1	0.0	0.8	0.1	1.0	0.1	2.5	0.0	0.7	0.2	2.9
2	240	9.8	0.1	0.8	0.1	0.8	0.1	0.8	0.1	0.5	0.1	1.5
3	240	27.6	0.2	0.8	0.4	1.4	0.6	2.3	0.0	0	0.8	2.8
4	240	65.3	0.6	0.9	0.6	0.9	0.9	1.4	0.3	0.5	1.3	2.0
5	240	141.3	2.6	1.8	0.0	0	2.4	1.7	1.0	0.7	3.6	2.6
Control 1	240	16.6	0.1	0.8	0.2	1.4	0.3	2.0	0.0	0	0.4	2.6
Control 2	240	74.9	0.6	0.9	0.9	1.2	0.9	1.1	0.6	0.8	1.5	2.0

Between-Lot Imprecision: The study was done using six serum samples with different CRP concentrations across the measuring interval. Within-run, between-day, within-lot, between-lot, and total SDs and %CVs were calculated based on 90 determinations per sample performed with three replicates per run, two runs per day, for five different days, using three reagent lots (3 replicates x 2 runs x 5 days x 3 lots = 90). The results are shown in the table below.

Sample	N	Mean (mg/L)	Within-run		Between-day		Within-lot		Between-lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	90	5.2	0.1	1.1	0.1	1.2	0.1	1.6	0.1	1.5	0.1	2.2
2	90	9.7	0.1	1.2	0.0	0.2	0.1	1.2	0.2	1.8	0.2	2.2
3	90	24.7	0.3	1.1	0.2	0.8	0.3	1.4	0.3	1.1	0.4	1.8
4	90	71.7	0.7	1.0	1.1	1.6	1.3	1.9	1.5	2.1	2.0	2.8
5	90	95.7	0.9	1.0	1.2	1.3	1.6	1.6	0.6	0.6	1.7	1.7
6	90	139.4	1.8	1.3	1.6	1.1	2.4	1.7	1.2	0.8	2.7	1.9
Control 1	90	14.0	0.1	0.9	0.2	1.3	0.2	1.6	0.1	0.8	0.3	1.8
Control 2	90	72.8	1.0	1.3	1.0	1.4	1.4	1.9	1.3	1.7	1.9	2.6

Between-Instrument Imprecision: The study was done using six serum samples with different CRP concentrations across the measuring interval. Within-run, between-day, within-lot, between-lot, and total SDs and %CVs were calculated based on 90 determinations per sample performed with three replicates per run, two runs per day for five different days, using three reagent lots (3 replicates x 2 runs x 5 days x 3 instruments = 90). The results are shown in the table below.

Sample	N	Mean (mg/L)	Within-day		Between-day		Within-instrument		Between-instrument		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	90	5.2	0.1	1.1	0.1	1.3	0.1	1.7	0.1	2.0	0.1	2.6
2	90	9.8	0.1	0.9	0.1	0.5	0.1	1.0	0.1	1.0	0.1	1.4
3	90	25.4	0.3	1.1	0.2	0.7	0.3	1.3	0.7	2.6	0.7	2.9
4	90	71.3	0.9	1.3	1.1	1.5	1.4	2.0	0.9	1.2	1.7	2.4
5	90	94.8	1.2	1.3	0.7	0.8	1.4	1.5	1.1	1.1	1.8	1.9
6	90	139.0	2.1	1.5	0.8	0.6	2.2	1.6	1.8	1.3	2.9	2.1
Control 1	90	14.3	0.2	1.1	0.2	1.4	0.3	1.8	0.3	2.2	0.4	2.9
Control 2	90	71.5	1.0	1.4	1.2	1.7	1.6	2.3	1.2	1.7	2.0	2.8

2. Linearity:
The linearity was evaluated using a series of pooled human serum samples prepared to evenly cover the CRP concentration range of 0.00 to 188.48 mg/L. Each sample dilution was measured in one run with three replicates; the mean of the three replicates was calculated for each sample. Linear regression analysis of observed CRP value vs. expected value was performed to determine whether the sample set exhibits linearity based on the CLSI guideline EP06-A. The linear regression results for nine samples within the measuring interval are shown in the table below.

Range (mg/L)	Slope (95%CI)	Intercept (95% CI)	R^2
9.42 – 150.78	1.03 (1.01 – 1.05)	-1.33 (-3.23 – 0.58)	1.00

Prozone Effect: The prozone effect was evaluated for the Yumizen C1200 CRP on the Yumizen C1200 analyzer using native human serum samples spiked with a high CRP stock solution. Theoretical concentration and the concentration measured of the study samples and the calibrators was compared. A prozone effect was determined if the slope of the sample and the calibrator over the theoretical concentration curve was inverted. A security range was calculated corresponding to 110% of the rate of the highest calibration point. No prozone effect was found for the CRP level up to 360 mg/L.

Dilution Study: The study was done using a total of seven serum samples with CRP concentrations above the measuring interval and ranging from 162.73 to 737.40 mg/L. Each sample was diluted at a 1:5 dilution manually and automatically on the Yumizen C1200 analyzer. Each dilution was tested in four replicates and the mean was calculated. The difference in the test results between manual and automatic dilution for each dilution sample was shown to be <10% up to 737.40 mg/L using 1:5 sample dilution.

3. Analytical Specificity/Interference:
To investigate the test performance with presence of potential endogenous and exogenous interferents, two pooled human serum samples with various CRP concentrations (72 and 110 mg/L for testing rheumatoid factor; ~ 11 and ~ 26 mg/L for testing all other potential interferents) were prepared and spiked with potential interfering substances at four different levels. The CRP level in the test samples was measured in four replicates and the recovery in relation to the unspiked sample without interferent was calculated. The acceptance criterion was < 10% in the mean bias for the individual recovery. No significant interference was observed up to the concentration of the potential interfering substances as shown in the table below.

Endogenous Interferent	Concentration
Hemoglobin	500 mg/dL
Triglycerides	504 mg/dL
Total Bilirubin	35.53 mg/dL
Direct Bilirubin	22.97 mg/dL
Rheumatoid Factor	400 IU/mL

Exogenous Interferent	Concentration
Ascorbic Acid	5.98 mg/dL
Acetylsalicylic Acid	65.16 mg/dL
Ibuprofen	50.10 mg/dL
Acetaminophen	20 mg/dL
Erythromycin	14.71 mg/dL
Gentamycin	3.11 mg/dL
Ampicillin	8.7 mg/dL
Prednisone	0.018 mg/dL
Methotrexate	136 mg/dL
Etanercept	0.75 mg/dL
Simvastatin	0.21 mg/dL
Omeprazole	0.86 mg/dL

4. Assay Reportable Range:

   The analytical measuring range of Yumizen C1200 CRP is 5 to 160 mg/L.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   a. Traceability: The calibrators are traceable against IRMM/ERM-DA472/IFCC.

   b. Reagent Shelf-Life Stability: The reagent shelf-life was previously evaluated under K061138 on ABX PENTRA 400 Clinical Chemistry Analyzer. The reagent shelf-life tested on Yumizen C1200 analyzer was verified up to 6 months at 2–10°C. Further verification for a longer-term shelf-life stability on Yumizen C1200 analyzer is ongoing.

   c. On-board Stability: The on-board stability was evaluated by testing samples with CRP concentrations at 22.9, 64.8, and 139.2 mg/L, and two controls at 1, 36, 46, 53, and 62 days using reagents stored on the Yumizen C1200 analyzer. The Yumizen C1200 CRP reagent is stable on-board for up to 62 days.

   d. Calibration Stability: Stability of the calibration on the Yumizen C1200 analyzer was evaluated by testing samples at different CRP concentrations (22.7, 65.1, and 139.1 mg/L) and two controls at 0, 8, 13, 19, 25, 35, and 36 days after an initial calibration. The Yumizen C1200 CRP calibration is stable on-board for up to 4 weeks.

   e. Sample Stability: The sample is stable for 11 days at 20–25°C, 2 months at 4–8°C, and 3 years at -20°C. (Reference: Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2. 2002, p28.)

6. Detection Limit:

   For limit of blank (LoB), a set of four analyte depleted serum samples was investigated using two reagent lots. Each sample was tested in four replicates per run, one run per day for four days to reach a total of 64 measurements per reagent lot. LoB was determined per CLSI EP17-A2. The higher value from both lots was taken for the LoB at 0.14 mg/L.

For limit of detection (LoD), a set of four low level serum samples in the range below the measuring interval was investigated using two reagent lots. Each sample was tested in four replicates per run, one run per day for four days to reach a total of 64 measurements per reagent lot. The LoD was determined per CLSI EP17-A2. The higher value from both lots was taken for the LoD at 0.23 mg/L.

For limit of quantitation (LoQ), a set of five low measurand content serum samples from the lower end of the measuring interval was investigated. Each sample was tested in two replicates per run, four runs per day for five days using two lots to reach a total of 80 measurements. The LoQ was determined as 0.47 mg/L following CLSI EP17-A2, the sample with the highest value for the %CV in accordance with the specification for both reagent lots (<20%). The claimed LoQ is 5 mg/L.

7. Assay Cut-Off:

   See below for Expected Values/Reference Range

B Comparison Studies:

1. Method Comparison with Predicate Device:
   A total of 102 serum samples spanning the assay measuring interval were tested by both the Yumizen C1200 CRP and a comparator. Measurement comparison between these two assays was evaluated using Passing-Bablok regression analysis and the result is shown in the table below. At the medical decision point of 5.0 mg/L, the calculated bias was 0.8%.

Sample (N)	Range (mg/L)	Slope (95%CI)	Intercept (95% CI)	R
102	5. 25 – 144.48	0.98 (0.97 – 1.00)	0.13 (-0.14 – 0.63)	1.00

2. Matrix Comparison:
   The usability of plasma in the Yumizen C1200 CRP was investigated using 38 matched serum and lithium-heparin plasma samples collected from 38 individuals. The samples cover CRP levels across the measuring interval of the assay. Passing-Bablok regression analysis was performed for the comparison of matched plasma and serum samples. The results are shown in the table below.

Sample (N)	Range (mg/L)	Slope (95%CI)	Intercept (95% CI)	R
38	5.09 – 133.86	0.94 (0.90 – 1.01)	0.34 (-0.16 – 0.65)	1.00

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable

2. Clinical Specificity:

   Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   See below for Expected Values/Reference Range

D Clinical Cut-Off:

See Expected Values/Reference range.

E Expected Values/Reference Range:

The expected value in the normal population aged 20 to 60 years is < 5mg/L per literature (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 (2006): 2263).

This reference range was verified by testing 80 normal healthy subjects (44 female and 36 male) aged 20 to 60 years. Seventy-six (76) of 80 samples (95%) tested had concentrations within the consensus reference interval taken from the literature reference.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.