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

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number
K191562

B Applicant
Horiba ABX SAS

C Proprietary and Established Names
Yumizen C1200 Ferritin, Yumizen C1200 Transferrin, Yumizen C1200 Rheumatoid Factor

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DBF	Class II	21 CFR 866.5340 - Ferritin Immunological Test System	IM - Immunology
DDG	Class II	21 CFR 866.5880 - Transferrin immunological test system	IM - Immunology
DHR	Class II	21 CFR 866.5775 - Rheumatoid factor immunological test system	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:
New assays

B Measurand:
Ferritin
Transferrin
Rheumatoid Factor (RF)

C Type of Test:
Quantitative immunoturbidmetric assays

III Intended Use/Indications for Use:

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

B Indication(s) for Use:
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.

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

D Special Instrument Requirements:
For the Yumizen C1200 (K183375 and K191993) only

IV Device/System Characteristics:

A Device Description:
Yumizen C1200 Ferritin:
- Reagent 1: Glycine buffer solution
- Reagent 2: Suspension of latex particles bound to rabbit anti-ferritin antibodies

Yumizen C1200 Transferrin:
- Reagent 1: TRIS buffer solution
- Reagent 2: Goat anti-human transferrin antibodies in TRIS buffer

Yumizen C1200 Rheumatoid Factor:
- Reagent 1: Glycine buffer solution
- Reagent 2: Suspension of latex particles sensitized with denatured human IgG

All assays' calibrators and control materials are sold separately.

B Principle of Operation:
Yumizen C1200 Ferritin:
When an antigen-antibody reaction occurs between ferritin in a sample and rabbit anti-ferritin-antibodies coated on latex particles, agglutination results. This agglutination is detected as an

absorbance change, with the magnitude of the change being proportional to the quantity of ferritin in the sample. The actual concentration is calculated from a calibration curve.

Immune complexes formed in solution scatter light in proportion to their size, shape, and concentration. Turbidimeters measure the reduction of incidence light due to reflection, absorption or scatter. In this procedure, the measurement of the rate of decrease in light intensity transmitted (increase in absorbance) through particles suspended in solution is the result of complexes formed during the immunological reaction between the analyte in the patient sample and rabbit anti-ferritin-antibodies coated on latex particles.

Yumizen C1200 Transferrin:
The immunoturbidimetric assay measures increasing sample turbidity caused by the formation of insoluble immune complexes when goat anti-human transferrin antibodies are bound to added to the transferrin sample in the sample. The transferrin concentration is proportional to the amount of turbidity formed.

Yumizen C1200 Rheumatoid Factor:
When an antigen-antibody reaction occurs between RF in a sample and denatured human IgG which has been attached to latex particles, agglutination results. This agglutination is detected as an absorbance change, with the magnitude of the change being proportional to the quantity of RF in the sample. The actual concentration is calculated from a calibration curve.

V Substantial Equivalence Information:

A Predicate Device Name(s): Beckman Coulter Ferritin Reagent, Model: OSR61203
Roche TINA-QUANT TRANSFERRIN VER.2
Olympus RF Latex Reagent

B Predicate 510(k) Number(s):
K092505
K012393
K060201

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device K191562	Predicate K092505
Device Trade Name	Yumizen C1200 Ferritin	Beckman Coulter Ferritin Reagent, Model: OSR61203
General Device Characteristic Similarities		
Intended Use/ Indications for Use	Yumizen C1200 Ferritin reagent is intended for the quantitative in vitro diagnostic determination of ferritin in human serum by latex-enhanced immunoturbidimetric	The Ferritin Reagent is for the determination of ferritin concentrations in human serum and plasma on the Beckman Coulter family of clinical

Device & Predicate Device(s):	Device K191562	Predicate K092505
Device Trade Name	Yumizen C1200 Ferritin	Beckman Coulter Ferritin Reagent, Model: OSR61203
	assay. Measurements of ferritin aid in the diagnosis of diseases affecting iron metabolism, hemochromatosis (iron overload) and iron deficiency anemia.	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.
Assay Method	Latex enhanced immuno-turbidimetry	Same
Assay Type	Quantitative, competitive	Same
Reagent Format	Liquid	Same
Traceability/ Standardization	3rd International Standard for Ferritin, Recombinant NIBSC Code: 94/572	Same
General Device Characteristic Differences		
Instrument Platform	Yumizen C1200	Beckman Coulter AU400
Measuring Range	10–450 ng/mL	8.0–450 ng/mL
Sample Matrices	Serum	Serum, Li-heparin plasma, and EDTA plasma

Device & Predicate Device(s):	Device K191562	Predicate K012393
Device Trade Name	Yumizen C1200 Transferrin	Roche TINA-QUANT TRANSFERRIN VER.2
General Device Characteristic Similarities		
Intended Use/ Indications for Use	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.	The cassette COBAS Integra Tina-quant Transferrin ver.2 contains an in vitro diagnostic reagent system intended for use on COBAS Integra systems for the quantitative immunological determination of human transferring in serum and plasma. A transferrin immunological test system is a device that consists of the reagents used to measure by immunochemical techniques the

Device & Predicate Device(s):	Device K191562	Predicate K012393
Device Trade Name	Yumizen C1200 Transferrin	Roche TINA-QUANT TRANSFERRIN VER.2
		transferrin (an iron-binding and transporting serum protein) in serum and plasma. Measurement of transferrin levels aids in the diagnosis of malnutrition, acute inflammation, infection, and red blood cell disorders, such as iron deficiency anemia.
Assay Method	Quantitative immunoturbidimetry	Same
Measuring Range	10–520 mg/dL	Same
Sample Matrix	Serum, Li-heparin plasma	Serum, plasma
Reagent Format	Liquid	Same
Traceability/ Standardization	ERM-DA470k/IFCC	Same
General Device Characteristic Differences		
Instrument Platform	Yumizen C1200	Cobas C701

Device & Predicate Device(s):	Device K191562	Predicate K060201
Device Trade Name	Yumizen C1200 Rheumatoid Factor	Olympus RF Latex Reagent
General Device Characteristic Similarities		
Intended Use/ Indications for Use	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.	Olympus RF Latex System Reagent for the quantitative determination of Rheumatoid Factor (RF) in human serum and plasma on OLYMPUS Analyzers. Measurement of rheumatoid factor may aid in the diagnosis of rheumatoid arthritis.
Assay Method	Latex enhanced immuno-turbidimetry	Same
Assay Type	Quantitative, competitive	Same
Assay Cut-off	14 IU/mL	Same
Traceability/ Standardization	WHO/NIBSC Rheumatoid Arthritis Serum (64/002)	Same
Reagent Format	Liquid	Same
General Device Characteristic Differences		

Device & Predicate Device(s):	Device K191562	Predicate K060201
Device Trade Name	Yumizen C1200 Rheumatoid Factor	Olympus RF Latex Reagent
Instrument Platform	Yumizen C1200	Olympus/Beckman Coulter AU400
Sample Matrices	Serum	Serum; lithium heparin plasma; and K2+ EDTA plasma
Measuring Range	10–120 IU/mL	5–120 IU/mL

VI Standards/Guidance Documents Referenced:

- **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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Yumizen C1200 Ferritin:
The precision of the Yumizen C1200 Ferritin assay was evaluated on three Yumizen C1200 immunoassay analyzers with one reagent lot. Five human sera samples and two levels of Yumizen C1200 Protein Control were tested with two replicates per run, two runs per day for 20 days on each analyzer (n=240 per sample). The results are summarized below:

		Repeatability		**Between Run**		**Between Day**		**Between Instrument**		**Total**	
Sample	**Mean (ng/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sera 1	**29.6**	1.6	**5.5**	0.7	**2.2**	0.7	**2.2**	1.4	**4.7**	2.3	**7.9**
Sera 2	**50.9**	2.1	**4.1**	1.0	**1.9**	0	**0**	1.2	**2.4**	2.6	**5.1**
Sera 3	**172.6**	2.4	**1.4**	0.4	**0.3**	1.0	**0.6**	1.8	**1.1**	3.2	**1.9**
Sera 4	**328.6**	4.2	**1.3**	11.8	**3.6**	6.6	**2.0**	0	**0**	14.2	**4.3**
Sera 5	**403.2**	3.9	**1.0**	2.6	**0.6**	2.2	**0.6**	1.8	**0.4**	5.5	**1.4**

		Repeatability		Between Run		Between Day		Between Instrument		Total	
Sample	**Mean (ng/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Control 1	**47.6**	1.7	**3.6**	0	**0**	0.7	**1.5**	1.5	**3.1**	2.4	**4.9**
Control 2	**279.3**	3.2	**1.1**	0	**0**	4.6	**1.6**	2.2	**0.8**	6.0	**2.1**

The reproducibility of the Yumizen C1200 Ferritin assay was evaluated on one analyzer with three reagent lots. Five human sera samples and two levels of Yumizen C1200 Protein Control were tested in triplicates per run, two runs per day for five days on each lot (n=90 per sample). The results are summarized below:

		Repeatability		Between Day		Within-Lot		Between Lot		Total	
Sample	**Mean (ng/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sera 1	**19.1**	1.7	**8.8**	0.9	**4.8**	1.9	**10.0**	1.2	**6.3**	2.2	**11.8**
Sera 2	**34.0**	2.2	**6.5**	0	**0**	2.2	**6.5**	0.2	**0.5**	2.2	**6.5**
Sera 3	**51.5**	1.8	**0**	0	**0**	1.8	**3.6**	0.6	**1.1**	1.9	**3.8**
Sera 4	**192.3**	2.6	**1.4**	0	**0**	2.6	**1.4**	4.8	**2.5**	5.5	**2.8**
Sera 5	**407.4**	3.8	**0.9**	0	**0**	3.8	**0.9**	4.2	**1.0**	5.7	**1.4**
Control 1	**52.8**	2.4	**4.6**	2.4	**4.5**	3.4	**6.4**	0	**0**	3.4	**6.4**
Control 2	**281.9**	2.6	**0.9**	2.0	**0.7**	3.2	**1.1**	3.3	**1.2**	4.6	**1.6**

Yumizen C1200 Transferrin:

The precision of the Yumizen C1200 Transferrin assay was evaluated on three Yumizen C1200 immunoassay analyzers with one reagent lot. Four human sera samples and two levels of Yumizen C1200 Protein Control were tested with two replicates per run, two runs per day for 20 days on each analyzer (n=240 per sample). The results are summarized below:

		Repeatability		Between Run		Between Day		Between Instrument		Total	
Sample	**Mean (mg/dL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sera 1	**78**	0.8	**1.0**	0.4	**0.5**	1.8	**2.3**	2.0	**3.7**	3.5	**4.5**
Sera 2	**102**	1.2	**1.2**	0.3	**0.3**	1.7	**1.7**	2.5	**2.5**	3.3	**3.2**
Sera 3	**183**	2.3	**1.3**	0.8	**0.5**	2.3	**1.3**	2.4	**1.3**	4.1	**2.3**
Sera 4	**378**	5.6	**1.5**	2.2	**0.6**	4.3	**1.1**	7.3	**1.9**	10.4	**2.7**
Control 1	**124**	1.5	**1.2**	8.0	**0.7**	2.6	**2.1**	3.2	**2.5**	4.4	**3.6**
Control 2	**335**	5.1	**1.5**	2.1	**0.6**	4.7	**1.4**	7.3	**2.8**	12.0	**3.6**

The reproducibility of the Yumizen C1200 Transferrin assay was evaluated on one analyzer with three reagent lots. Four human sera sample and two levels of Yumizen C1200 Protein Control were tested in triplicates per run, two runs per day for five days on each lot (n=90 per sample). The results are summarized below:

		Repeatability		Between Day		Within-Lot		Between Lot		Total	
Sample	**Mean (mg/dL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sera 1	**77**	3.3	**4.2**	2.1	**2.7**	3.9	**5.0**	1.6	**2.0**	4.2	**5.4**
Sera 2	**108**	1.6	**1.5**	0.9	**0.9**	1.9	**1.7**	3.0	**2.8**	3.5	**3.3**
Sera 3	**196**	2.5	**1.3**	0.4	**0.2**	2.5	**1.3**	6.3	**3.2**	6.7	**3.4**
Sera 4	**354**	9.2	**2.6**	2.6	**0.7**	9.6	**2.7**	7.4	**2.1**	12.1	**3.4**
Control 1	**129**	4.5	**3.5**	6.8	**5.3**	8.2	**6.3**	2.2	**1.7**	8.5	**6.6**
Control 2	**341**	5.7	**1.7**	4.1	**1.2**	7.0	**2.1**	7.5	**2.2**	10.3	**3.0**

Yumizen C1200 Rheumatoid Factor:

The precision of the Yumizen C1200 Rheumatoid Factor assay was evaluated on three Yumizen C1200 immunoassay analyzers with one reagent lot. Five human sera samples and two levels of Yumizen C1200 Protein Control were tested with two replicates per run, two runs per day for 20 days on each analyzer (n=240 per sample). The results are summarized below:

		Repeatability		Between Run		Between Day		Between Instrument		Total	
Sample	**Mean (IU/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sera 1	**22.2**	0.3	**1.2**	0.2	**0.9**	0.2	**0.9**	0.4	**1.0**	0.4	**2.0**
Sera 2	**34.3**	0.3	**0.8**	0.4	**1.3**	0.4	**1.3**	0.3	**0.9**	0.8	**2.2**
Sera 3	**49.4**	0.2	**0.5**	0.5	**1.0**	0.6	**0.5**	0.7	**1.3**	0.9	**1.8**
Sera 4	**70.2**	0.4	**0.5**	0.3	**0.4**	0.5	**0.8**	0.7	**1.3**	1.1	**1.6**
Sera 5	**103.4**	0.9	**0.8**	0.6	**0.6**	0.7	**0.7**	0.6	**0.5**	1.4	**1.4**
Control 1	**41.0**	0.2	**0.5**	0.2	**0.4**	0.5	**1.2**	0.7	**1.7**	0.9	**2.2**
Control 2	**63.9**	0.3	**0.4**	0.4	**0.6**	1.0	**1.6**	1.1	**1.8**	1.6	**2.5**

The reproducibility of the Yumizen C1200 Rheumatoid Factor assay was evaluated on one analyzer with three reagent lots. Five human sera samples and two levels of Yumizen C1200 Protein Control were tested in triplicates per run, two runs per day for five days on each lot (n=90 per sample).

		Repeatability		Between Day		Within-Lot		Between Lot		Total	
Sample	**Mean (IU/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sera 1	**17.3**	0.5	**2.9**	0.1	**0.7**	0.5	**3.0**	0.1	**0.8**	0.5	**3.1**
Sera 2	**30.9**	0.4	**1.4**	0.2	**0.6**	0.5	**1.6**	0.3	**0.9**	0.6	**1.8**
Sera 3	**53.1**	0.7	**1.4**	0.5	**0.9**	0.9	**1.6**	1.5	**2.7**	1.7	**3.2**
Sera 4	**70.2**	0.8	**1.1**	0.5	**0.8**	0.9	**1.3**	0	**0**	0.9	**1.3**
Sera 5	**102.1**	1.1	**1.0**	0.4	**0.4**	1.2	**1.1**	1.5	**1.4**	1.9	**1.8**
Control 1	**41.7**	0.7	**1.8**	0.1	**0.3**	0.8	**1.8**	0.3	**0.6**	0.8	**1.9**
Control 2	**67.0**	0.9	**1.4**	0.3	**0.5**	1.0	**1.5**	1.1	**1.6**	1.5	**2.2**

2. Linearity:

Yumizen C1200 Ferritin:
Linearity of the Yumizen C1200 Ferritin assay was assessed according to CLSI EP06-A. A high concentration ferritin-spiked human serum sample and a ferritin-depleted human serum were used to create a dilution series covering the measuring range were measured. Sample dilutions were assayed in quadruplicate within a single run and samples within the measuring range were used to determine linearity:

Dilution Range (ng/mL)	Regression Equation	Slope (95% CI)	Intercept (95% CI)	R^2
13.3–426.6	y=0.99x+3.16	0.98–1.00	1.15–5.18	0.999

Auto-rerun validation study: An auto-rerun study was performed to evaluate the accuracy of the analyzer's auto dilution function to obtain results for ferritin samples with analyte concentrations above the primary measuring range (450 ng/mL). Seven samples were used for the study, ranging from 470–2166 ng/mL. Each sample was manually diluted with a 1:5 ratio. The automatic instrument dilutions and the manual dilutions were measured in quadruplicates. The results of the auto-rerun study support the claim that samples having concentrations up to 2250 ng/mL can be run via the rerun function which uses a 1:5 dilution.

Prozone effect: The potential for a prozone effect was evaluated for the ferritin assay. Testing elevated samples did not indicate a prozone effect with concentrations up to 5043 ng/mL. A prozone alarm will flag samples ≥5043 ng/mL.

Yumizen C1200 Transferrin:
Linearity of the Yumizen C1200 Transferrin assay was assessed according to CLSI EP06-A. A high concentration transferrin-spiked human serum sample and a transferrin-depleted human serum were used to create a dilution series covering the measuring range. Sample dilutions were assayed in quadruplicate within a single run and samples within the measuring range were used to determine linearity. The results are summarized below:

Dilution Range (mg/dL)	Regression Equation	Slope (95% CI)	Intercept (95% CI)	R^2
15.4–461.3	y=1.05x-5.46	1.04–1.07	-10.24 – -0.68	0.998

Auto-rerun validation study: An auto-rerun study was performed to evaluate the accuracy of the analyzer's auto dilution function to obtain results for transferrin samples with analyte concentrations above the primary measuring range (520 mg/dL). Seven samples were used for the study, ranging from 540–1450 mg/dL. Each sample was manually diluted with a 1:3 ratio. The automatic instrument dilutions and the manual dilutions were measured in quadruplicates. The results of the auto-rerun study support the claim that samples having higher concentrations up to 1560 mg/dL can be run via the rerun function which uses a 1:3 dilution.

Prozone effect: The potential for a prozone effect was evaluated for this assay with spiked native serum samples. Testing elevated samples did not indicate a prozone effect with concentrations up to 4000 mg/dL.

Yumizen C1200 Rheumatoid Factor:
Linearity of the Yumizen C1200 Rheumatoid Factor assay was assessed according to CLSI EP06-A. A high concentration RF-spiked human serum sample and diluent was used to create a dilution series covering the measuring range were measured. Sample dilutions were assayed in quadruplicate within a single run and samples within the measuring range were used to determine linearity. The results are summarized below:

Dilution Range (IU/mL)	Regression Equation	Slope (95% CI)	Intercept (95% CI)	R^2
13.2–118.8	y=0.92x+4.78	0.91–0.93	3.95–5.60	0.999

Auto-rerun validation study: An auto-rerun study was performed to evaluate the accuracy of the analyzer's auto dilution functions to obtain results for RF-positive samples with analyte concentrations above the primary measuring range (120 IU/mL). The Yumizen C1200 Rheumatoid Factor assay includes two flags in the instrument method: an "alarm H" corresponding to a sample that is higher than 120 IU/mL and an "alarm P" corresponding to a prozone effect (see below) if the samples is higher than 229 IU/mL. A 1:4 post-dilution factor will be used if the alarm H is triggered; a 1:10 post-dilution factor will be used if the alarm P is triggered.

Three samples, ranging from 131–364 IU/mL, were used to test the accuracy between manual dilutions and automated dilutions triggered by alarm H. Each sample was manually diluted with a 1:4 ratio. The automatic instrument dilutions and the manual dilutions were measured in quadruplicates. The results of the auto-rerun study support the claim that samples having higher concentrations can be run via the rerun function when the alarm H function is triggered.

Four samples, ranging from 503–1180 IU/mL, were used to test the accuracy between manual dilutions and automated dilutions triggered by alarm P. Each sample was manually diluted with a 1:10 ratio. The automatic instrument dilutions and the manual dilutions were measured in quadruplicates. The results of the auto-rerun study support the claim that samples having higher concentrations up to 1200 IU/mL can be run via the rerun function when the alarm P function is triggered.

Prozone effect: The potential for a prozone effect was evaluated for the Yumizen C1200 Rheumatoid Factor assay. There was a prozone effect with concentrations higher than 143 IU/mL. Samples with a concentration >229 IU/mL have reaction kinetics that could be interpreted by the instrument as a result within the calibration range of the assay (although still very elevated). The prozone alarm will flag samples with a concentration >229 IU/mL and will be rerun automatically. The package insert describes the prozone flag.

3. Analytical Specificity/Interference:
For all three assays, the effect of the presence of endogenous and exogenous interferents in samples was evaluated by testing native unmodified serum pools at two analyte levels with a

range of concentration of the substances listed below. Each sample was tested at four concentrations of interferent and with an interferent-free control in four replicates each. The percent recovery for each sample spiked with the interference substance was calculated by comparing its result to that of the corresponding reference sample spiked with an equal volume of the solvent without the interferent. No interference was observed up to the following concentrations for each assay. The results are summarized in the tables below:

Yumizen C1200 Ferritin:

Endogenous		Exogenous (mg/dL)			
Direct Bilirubin	25.9 mg/dL	Acetaminophen	20.0	Diltiazem	0.4
Total Bilirubin	29.5 mg/dL	Acetylsalicylic Acid	65.2	Ferrous Sulfate	15.2
Hemoglobin	500 mg/dL	Ampicillin	8.7	Ibuprofen	50.1
Triglycerides	270.4 mg/dL	Ascorbic Acid	6.0	Methotrexate	136.0
Rheumatoid Factor	500 IU/mL	Azithromycin	1.5	Prednisone	17.9
		Deferoxamine	22.4	Rifampicin	8.2
				Simvastatin	0.4

Yumizen C1200 Transferrin:

Endogenous		Exogenous (mg/dL)	
Direct Bilirubin	23.9 mg/dL	Acetaminophen	20.0
Total Bilirubin	43.8 mg/dL	Acetylsalicylic Acid	65.2
Hemoglobin	500 mg/dL	Ascorbic Acid	6.0
Triglycerides	353.3 mg/dL	Ibuprofen	50.1
Rheumatoid Factor	400 IU/mL		

Yumizen C1200 Rheumatoid Factor:

Endogenous		Exogenous (mg/dL)	
Direct Bilirubin	25.4 mg/dL	Acetaminophen	20.0
Total Bilirubin	31.3 mg/dL	Acetylsalicylic Acid	65.2
Hemoglobin	500 mg/dL	Ascorbic Acid	6.0
Triglycerides	526.8 mg/dL	Ibuprofen	50.1

4. Assay Reportable Range:

Yumizen C1200 Ferritin:
The claimed measuring range is from 10 ng/mL to 450 ng/mL.

Yumizen C1200 Transferrin:
The claimed measuring range is from 10 mg/dL to 520 mg/dL.

Yumizen C1200 Rheumatoid Factor:
The claimed measuring range is 10 mg/L to 120 IU/L.

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

Traceability:
Yumizen C1200 Ferritin:
The Ferritin assay is traceable to the 3rd International Standard for Ferritin, Recombinant NIBSC Code: 94/572.

Yumizen C1200 Transferrin:
The Transferrin assay is traceable to ERM-DA470k/IFCC.

Yumizen C1200 Rheumatoid Factor:
The RF assay is traceable to WHO/NIBSC Rheumatoid Arthritis Serum (64/002).

Stability:
Real-time shelf-life stability testing supports a shelf-life for unopened reagents stored at the labeling recommendation [2–10°C (ferritin and RF) or 2–8°C (transferrin)]. On-board reagent stability studies support the on-board storage claims of the Yumizen C1200. The results are summarized below:

Stability Claims	Ferritin (ng/mL)	Transferrin (mg/dL)	RF (IU/mL)
Reagent Shelf-life if stored as recommended	18 months	24 months	18 months
Reagent On-board	2 months	6 weeks	1 month
Serum Sample*	7 days at 20–25°C 7 days at 2–8°C 1 year at-20°C	8 days at 20–25°C 8 days at 4–8°C 6 months at -20°C	1 day at 20–25°C - 8 days at 4–8°C -3 months at -20°C
*Sample stability claims in the package insert cite published references.			

6. Detection Limit:
The detection limits of all three assays were performed according to CLSI EP17-A2. The Limit of Blank (LoB) corresponds to the concentration below which analyte-free samples are found with a probability of 95%. The Limit of Detection (LoD) is determined based on the limit of blank and the standard deviation of low concentration samples. The limit of detection corresponds to the lowest analyte concentration which can be detected (value above the limit of blank with a probability of 95%). The Limit of Quantitation (LoQ) was defined as the lowest analyte concentration which can be quantified with a total error of ≤ 20%.

Yumizen C1200 Ferritin:
LoB:
The LoB of the Ferritin assay was determined by assaying one ferritin-depleted serum sample in five replicates per day for four days on three Yumizen instruments. A total of 60 data points per lot were generated; two lots were tested. The LoB for each lot was calculated separately and the higher value determined the LoB. The LoB was defined as 4.21 ng/mL.

LoD:
The LoD of the Ferritin assay was determined by testing four low analyte serum samples in quadruplicate for four days on one instrument. A total of 64 data points per lot were generated; two lots were tested. The LoD for each lot was calculated separately and the higher value determined the LoD. The LoD was defined as 6.30 ng/mL.

LoQ:
The LoQ of the Ferritin assay was determined by testing nine low native serum samples in quadruplicate per run, two runs per day, for five days on one instrument. A total of 360 data points per lot were generated; two lots were tested. The LoQ for each lot was calculated separately and the higher value determined the LoQ. The LoQ was defined as 9.39 ng/mL.

Yumizen C1200 Transferrin:
LoB:
The LoB of the Transferrin assay was determined by assaying one blank (PBS+BSA) sample in five replicates per day for four days on three Yumizen instruments. A total of 60 data points per lot were generated; two lots were tested. The LoB for each lot was calculated separately and the higher value determined the LoB. The LoB was defined as 0.10 mg/dL.

LoD:
The LoD of the Transferrin assay was determined by testing four low analyte samples in quadruplicate for four days on one instrument. A total of 64 data points per lot were generated; two lots were tested. The LoD for each lot was calculated separately and the higher value determined the LoD. The LoD was defined as 0.20 mg/dL.

LoQ:
The LoQ of the Transferrin assay was determined by testing five low native samples in quadruplicate per run, two runs per day, for five days on one instrument. A total of 200 data points per lot were generated; two lots were tested. The LoQ for each lot was calculated separately and the higher value determined the LoQ. The LoQ was defined as 7.00 mg/dL.

Yumizen C1200 Rheumatoid Factor:
LoB:
The LoB of the RF assay was determined by testing one diluent sample in five replicates per day for four days on three Yumizen instruments. A total of 60 data points per lot were generated; two lots were tested. The LoB for each lot was calculated separately and the higher value determined the LoB. The LoB was defined as 1.50 IU/mL.

LoD:
The LoD of the RF assay was determined by testing four low analyte serum samples in quadruplicate for four days on one instrument. A total of 64 data points per lot were generated; two lots were tested. The LoD for each lot was calculated separately and the higher value determined the LoD. The LoD was defined as 4.07 IU/mL.

LoQ:
The LoQ of the RF assay was determined by testing five low native samples in quadruplicate per run, two runs per day, for five days on one instrument. A total of 200 data points per lot were generated; two lots were tested. The LoQ for each lot was calculated separately and the higher value determined the LoQ. The LoQ was defined as 7.41 IU/mL.

Detection Limit Summary:

	Ferritin (ng/mL)	Transferrin (mg/dL)	RF (IU/mL)
LoB	4.21	0.10	1.50
LoD	6.30	0.20	4.07
LoQ	9.39	7.00	7.41

7. Assay Cut-Off:
Not applicable for Ferritin and Transferrin.
RF is expected to be negative in normal healthy population. See Expected Value/Reference Range Section below.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Yumizen C1200 Ferritin:
The sponsor conducted a method comparison of the Yumizen C1200 Ferritin (candidate device) assay and the predicate device. A total of 103 remnant clinical samples covering the measuring range were tested and compared using the Passing-Bablok method. The results are summarized below:

Parameter	Result
Range (ng/mL)	12.2–440.7 ng/mL (Predicate, X) 16.7–413.0 ng/mL (Assay, Y)
Slope (95th CI)	0.91 (0.91–0.92)
Intercept (95th CI)	2.10 (0.98–3.30)
Correlation Coefficient	0.999

Yumizen C1200 Transferrin:
The sponsor conducted a method comparison of the Yumizen C1200 Transferrin (candidate device) assay and the predicate device. A total of 115 remnant clinical samples covering the measuring range were tested and compared using the Passing-Bablok method. The results are summarized below:

Parameter	Result
Range (mg/dL)	43–500 mg/dL (Predicate, X) 37–481 mg/dL (Candidate, Y)
Slope	0.946

Parameter	Result
(95th CI)	(0.926–0.964)
Intercept (95th CI)	0.006 (-0.023–0.055)
Correlation Coefficient	0.993

Yumizen C1200 Rheumatoid Factor:
The sponsor conducted a method comparison of the Yumizen C1200 Rheumatoid Factor (candidate device) assay and the predicate device. A total of 113 anonymous samples collected from a blood bank covering the entire measuring range were tested and compared using the Passing-Bablok method:

Parameter	Result
Range (mg/dL)	16.9–119.0 IU/mL (Predicate, X) 16.8–118.8 IU/mL (Candidate, Y)
Slope (95th CI)	1.01 (1.00–1.03)
Intercept (95th CI)	-1.11 (-1.70 – -0.23)
Correlation Coefficient	0.992

2. Matrix Comparison:
Only serum is indicated for the Yumizen C1200 Ferritin and Rheumatoid Factor assays.

For the Yumizen C1200 Transferrin assay, a study comparing 59 paired serum and lithium heparin plasma samples demonstrated equivalence between the matrices:

	N	**Range (mg/dL)**	**Slope (95% CI)**	**Intercept (95% CI)**	**Pearson r**
Li-heparin vs. Serum	59	193–379	0.97 (0.93–0.99)	0.05 (-0.02– 0.14)	0.995

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):
Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Yumizen C1200 Ferritin:

The sponsor validated female and male ferritin reference ranges cited in a reference[1]. Samples from a blood bank were used: 50 female samples and 95 male samples to validate a reference range of 10–120 ng/mL for women and 20–250 ng/mL for men.

Yumizen C1200 Transferrin:

The sponsor validated transferrin reference ranges cited in a reference[2]. Samples (n=85, 28 female and 57 males) from a blood bank were used and validate a reference range of 200–360 mg/dL.

Yumizen C1200 Rheumatoid Factor:

The sponsor validated RF reference ranges cited in a reference[3]. Sixty samples from a blood bank were used and validate a reference range of <14 IU/mL.

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.

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

[2] 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.

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