510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number
K192727

B Applicant
Kamiya Biomedical Company

C Proprietary and Established Names
K-ASSAY RF (Ver.2)
K-ASSAY RF Calibrator (Ver.2)

D Regulatory Information:

Product Code(s)	Classification	Regulation Section	Panel
DHR	Class II	21 CFR 866.5775 - Rheumatoid Factor Immunological Test System	IM - Immunology
JIS	Class II Exempt	862.1150 - Calibrator	Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:
New assay

B Measurand:
Rheumatoid Factor (RF)

C Type of Test:
Quantitative latex turbidimetric assay

III Intended Use/Indications for Use:

A Intended Use(s):

The K-ASSAY RF (Ver.2) assay is for the quantitative determination of human IgG rheumatoid factor antibodies in patient serum or plasma (citric acid, EDTA or lithium heparin) based on immunoturbidimetric assay. The presence of IgG RF antibodies, in conjunction with clinical findings and other laboratory tests, is an aid in the diagnosis of rheumatoid arthritis (RA). FOR IN VITRO DIAGNOSTIC USE.

The K-ASSAY® RF Calibrator (Ver.2) is intended to be used to calibrate the K-ASSAY® RF (Ver.2) immunoturbidimetric assay. FOR IN VITRO DIAGNOSTIC USE.

B Indication(s) for Use:
See Intended Use above

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

D Special Instrument Requirements:
Clinical Chemistry Analyzer

IV Device/System Characteristics:

A Device Description:
The K-ASSAY RF (Ver.2) assay is comprised of the following reagents:
(a) R1: Buffer Reagent (Phosphate Buffer)
(b) R2: Latex Reagent (suspension of latex particles sensitized with human γ globulin and Phosphate Buffer)

The K-ASSAY® RF Calibrator (Ver.2) is comprised of six calibrators: A, B, C, D, E, and F. Calibrator A contains sodium chloride and sodium azide; Calibrator B-F contain pooled human serum with assigned values for the rheumatoid factor and sodium azide. The K-ASSAY® RF Calibrator (Ver.2) is sold separately.

B Principle of Operation:
The K-ASSAY RF (Ver.2) quantifies the rheumatoid factor in the patient's serum based on latex-enhanced immunoturbidimetric assay. Calibrators, controls, and patient samples are pipetted into sample cups. Microvolumes of samples and reagent diluent are automatically pipetted into individual cuvettes.

Following an initial incubation and measurement of sample solution, gamma globulin containing aggregated human IgG is added to the cuvettes. The patient sample (autoantibodies) solution and gamma globulin reagent (antigen) are then mixed in the reaction cuvettes. Insoluble antigen-antibody (immune) complexes form. The immune complexes cause an increase in light scattering, which correlates with the concentration of rheumatoid factor. Following an incubation period lasting approximately 5 minutes, the absorbance change of the solution is measured. A calibration curve is generated by assaying a series of calibrators with known concentrations of proteins and using the instrument’s data reduction capability or manually plotting the change in absorbance versus concentration. Concentration of the controls and patient samples are interpolated from the calibration curve.

The K-ASSAY RF (Ver.2) should be run using the K-ASSAY RF Calibrator (Ver.2). These six calibrators are used to prepare a calibration curve for quantifying the levels of rheumatoid factor present in the patient's serum or plasma sample.

V Substantial Equivalence Information:

A Predicate Device Name(s):
K-ASSAY Rheumatoid Factor

B Predicate 510(k) Number(s):
K991409

C Comparison with Predicate(s):

Assay:

Device & Predicate Device(s):	Device K192727	Predicate K991409
Device Trade Name	K-ASSAY RF (Ver.2)	K-ASSAY RF
General Device Characteristic Similarities		
Antigen	Polyclonal IgG RF antibody	Same
Expected value	<11.0 IU/mL	Same
General Device Characteristic Differences		
Intended Use/ Indications For Use	The K-ASSAY RF (Ver.2) assay is for the quantitative determination of human IgG rheumatoid factor antibodies in patient serum or plasma (citric acid, EDTA or lithium heparin) based on immunoturbidimetric assay. The presence of IgG RF antibodies, in conjunction with clinical findings and other laboratory tests, is an aid in the diagnosis of rheumatoid arthritis (RA). For in vitro diagnostic use.	The K-ASSAY RF assay is for the quantitative determination of human rheumatoid factor antibodies, in patient serum based on immunoturbidimetric assay. For in vitro diagnostic use.
Method	Latex-enhanced immunoturbidimetric	Immunoturbidimetric
Sample type	Serum and Plasma (citric acid, EDTA and lithium	Serum

Device & Predicate Device(s):	Device K192727	Predicate K991409
	heparin)	
Analytical Measuring Range	6.65 – 600 IU/mL	5 – 320 IU/mL
Calibrators	Six calibrator-set: 0, 15, 75, 150, 300, 600 IU/mL	Three calibrator-set: 50, 150, 300 IU/mL (saline blank is also needed, resulting in four levels)
Traceability	NIBSC Rheumatoid Arthritis serum 64/002	None specified

Calibrators:

Device & Predicate Device(s):	Device K192727	Predicate K991409
Device Trade Name	K-ASSAY RF Calibrator (Ver.2)	K-ASSAY RF
General Device Characteristic Similarities		
Form	Liquid	Same
Matrix	Human serum based	Same
Units	IU/mL	Same
General Device Characteristic Differences		
Intended Use/ Indications For Use	The K-ASSAY® RF Calibrator (Ver.2) is intended to be used to calibrate the K-ASSAY® RF (Ver.2) immunoturbidimetric assay. for in vitro diagnostic use.	RF Calibrator was part of the cleared RF Kit and the PI listed it as required but not supplied; it had no separate IU

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition

CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP07 3rd Edition, Interference Testing in Clinical Chemistry; Approved Guideline - Third Edition

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

All studies were performed on Abbott c8000 instruments.

1. Precision/Reproducibility:

Precision – single site evaluation study: The single site precision of the RF (Ver.2) assay was evaluated according to CLSI EP05-A3 by running eight clinical samples across the assay ranges and two commercial controls. Samples were run in duplicates, twice a day, for 20 days and one calibrator lot (total of n = 80 per sample). Three lots were evaluated independently and the results are summarized in the tables below:

Lot 1:

			Repeatability		Between-Run		Within-Day		Between-Day		Within-Laboratory	
Sample	**Mean (IU/mL)**	**N**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**
Control Level 1	43.38	80	0.6%	0.28	0.0%	0	0.6%	0.28	0.5%	0.23	0.8%	0.36
Control Level 2	91.46	80	0.3%	0.27	0.5%	0.45	0.6%	0.52	0.0%	0	0.6%	0.52
Sample 1	13.65	80	4.3%	0.59	1.2%	0.17	4.5%	0.61	0.0%	0	4.5%	0.61
Sample 2	21.92	80	2.0%	0.45	0.8%	0.18	2.2%	0.48	1.4%	0.31	2.6%	0.58
Sample 3	99.17	80	0.3%	0.34	0.6%	0.61	0.7%	0.70	0.7%	0.70	1.0%	0.9
Sample 4	250.94	80	0.5%	1.30	0.3%	0.78	0.6%	1.52	0.5%	1.21	0.8%	1.94
Sample 5	285.02	80	0.6%	1.57	0.6%	1.71	0.8%	2.32	0.2%	0.60	0.8%	2.40
Sample 6	313.93	80	0.6%	1.88	0.0%	0	0.6%	1.88	0.2%	0.73	0.6%	2.02
Sample 7	349.20	80	0.6%	2.21	0.1%	0.50	0.6%	2.27	0.2%	0.85	0.7%	2.42
Sample 8	521.95	80	0.6%	3.33	0.0%	0	0.6%	3.33	0.5%	2.42	0.8%	4.11

Lot 2:

			Repeatability		Between-Run		Within-Day		Between-Day		Within-Laboratory	
Sample	**Mean (IU/mL)**	**N**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**
Control Level 1	43.38	80	0.6%	0.28	0.0%	0	0.6%	0.28	0.5%	0.23	0.8%	0.36
Control Level 2	91.46	80	0.3%	0.27	0.5%	0.45	0.6%	0.52	0.0%	0	0.6%	0.52
Sample 1	13.65	80	4.3%	0.59	1.2%	0.17	4.5%	0.61	0.0%	0	4.5%	0.61
Sample 2	21.92	80	2.0%	0.45	0.8%	0.18	2.2%	0.48	1.4%	0.31	2.6%	0.58
Sample 3	99.17	80	0.3%	0.34	0.6%	0.61	0.7%	0.70	0.7%	0.70	1.0%	0.99
Sample 4	250.94	80	0.5%	1.30	0.3%	0.78	0.6%	1.52	0.5%	1.21	0.8%	1.94
Sample 5	285.02	80	0.6%	1.58	0.6%	1.71	0.8%	2.32	0.2%	0.60	0.8%	2.40
Sample 6	313.93	80	0.6%	1.88	0.0%	0	0.6%	1.88	0.2%	0.73	0.6%	2.02
Sample 7	349.20	80	0.6%	2.21	0.1%	0.50	0.6%	2.27	0.2%	0.85	0.7%	2.42
Sample 8	521.95	80	0.6%	3.33	0.0%	0	0.6%	3.33	0.5%	2.42	0.8%	4.11

Lot 3:

			Repeatability		Between-Run		Within-Day		Between-Day		Within-Laboratory	
Sample	**Mean (IU/mL)**	**N**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**
Control Level 1	42.00	80	0.8%	0.34	0.4%	0.17	0.9%	0.38	0.5%	0.19	1.0%	0.42
Control Level 2	89.31	80	0.3%	0.28	0.6%	0.50	0.6%	0.58	0.6%	0.52	0.9%	0.78
Sample 1	13.48	80	3.7%	0.50	0.0%	0	3.7%	0.50	2.1%	0.28	4.2%	0.57
Sample 2	21.67	80	1.9%	0.42	0.0%	0	1.9%	0.42	1.5%	0.32	2.4%	0.53
Sample 3	99.08	80	0.5%	0.50	0.2%	0.16	0.5%	0.53	0.8%	0.80	1.0%	0.96
Sample 4	249.19	80	0.8%	1.90	0.4%	1.07	0.9%	2.18	0.9%	2.28	1.3%	3.16
Sample 5	283.26	80	1.5%	4.17	0.0%	0	1.5%	4.17	1.4%	4.02	2.0%	5.80
Sample 6	313.12	80	0.7%	2.06	0.4%	1.26	0.8%	2.42	1.2%	3.72	1.4%	4.44
Sample 7	349.03	80	0.6%	2.07	0.6%	2.02	0.8%	2.90	1.1%	3.73	1.4%	4.72
Sample 8	515.85	80	0.5%	2.65	0.0%	0	0.5%	2.65	0.9%	4.90	1.1%	5.57

Precision – multiple site evaluation study:
The multiple site precision of the RF (Ver.2) assay was evaluated according to CLSI EP05-A3 by running five clinical samples and two commercial controls across the assay range. Samples were run in five replicates/sample, once a day, for 5 days using one reagent lot, one calibrator lot on three Abbott Architect c8000 instruments (total of n = 525). The results of multiple site precision on one lot are summarized in the table below:

			Repeatability		Between-Run		Within-Laboratory		Between-Laboratory		Reproducibility	
Sample	**Mean**	**N**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**
Control Level 1	38.41	75	1.5%	0.59	1.2%	0.47	2.0%	0.76	0.0%	0	2.0%	0.76
Control Level 2	86.40	75	0.8%	0.66	0.4%	0.35	0.9%	0.75	0.8%	0.70	1.2%	1.03
Sample 1	14.13	75	4.5%	0.64	5.6%	0.79	7.2%	1.02	0.0%	0	7.2%	1.02
Sample 2	21.24	75	2.5%	0.54	4.1%	0.88	4.9%	1.03	0.0%	0	4.9%	1.03
Sample 3	101.69	75	0.7%	0.75	1.4%	1.42	1.6%	1.61	0.0%	0	1.6%	1.61
Sample 4	302.35	75	1.4%	4.16	2.2%	6.68	2.6%	7.86	0.4%	1.25	2.6%	7.96
Sample 5	532.83	75	0.8%	4.44	1.2%	6.15	1.4%	7.58	0.4%	2.05	1.5%	7.86

2. Linearity:
The linearity of K-Assay RF (Ver.2) Assay was evaluated by a study performed according to CLSI EP6-A. The linearity was evaluated using a high human serum samples and an analyte-depleted serum to create a dilution series to cover the range of 6.65–600.0 IU/mL. Each dilution was tested in triplicate. The regression equation for the linear range was: $y = 0.992x + 2.41$ IU/mL with an r value of 0.999. The assay claimed reportable range/linear range is 6.65–600 IU/mL.

Hook effect was evaluated, and no hook effect was observed up to 1700 IU/mL.

3. Analytical Specificity/Interference:
The interference studies were performed according to CLSI EP07-3rd Ed. Four serum specimens (below the LoQ sample: ~10 IU/mL, low positive: ~15 IU/mL, middle: ~100 IU/mL and high positive: ~300 IU/mL) were aliquoted. Interfering substances at different concentrations were spiked into aliquots and compared results to the unspiked aliquot containing no interferent (control). The highest concentration tested with no interference is shown in the following table:

Endogenous Interferent	Concentration		Exogenous Interferent	Concentration
Bilirubin C	20 mg/dL		Ascorbic Acid	50 mg/dL
Bilirubin F	20 mg/dL			
Chyle	1500 FTU			
Hemoglobin	500 mg/dL			
Total Cholesterol	400 mg/dL			
Total Triglyceride	1000 mg/dL			

4. Assay Reportable Range:
The claimed measuring range is 6.65–600 IU/mL.

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

Traceability: The in-house RF secondary standards are traceable to the NISBC – Rheumatoid Arthritis Serum (NIBSC code: 64/002).

Stability:
RF Reagent (Ver,2), RF Calibrator stability (unopened): The real-time and accelerated stability of each kit was tested using three lots of kits (i.e., with three different lots of RF reagent, one lot of calibrator, and one lot of each control sample 1 and control sample 2). The real-time stability testing supports the reagent claim of 13 months at stability for unopened reagent kits and 10 months of unopened calibrator and controls stored at 2–8°C.

Opened RF Reagent (Ver.2): To establish the in-use stability of the reagent, three reagent lots were tested with two RF control samples at two levels. The samples were tested at 0, 7, 14, 21, 28, 35, 42, 49, 56, and 63 days. The opened RF (Ver.2) reagent stability supports the claim for 63 days stored at 2–8°C.

Opened RF Calibrator stability
To establish the in-use stability of the calibrator, one lot of calibrator was tested with two RF control samples. The samples were tested at 0, 7, 14, 21, 28, 35, 42, 49, and 56 days. The opened RF Calibrator stability supports the claim for 56 days stored at 2–8°C.

Calibration curve stability: To establish the calibration curve stability, calibration was performed only on day zero. Two levels of control were measured using this single calibration curve every 2–3 days for up to 43 days. Reagent was stored at 2–8°C and the same bottles were used for all 43 days. On day zero, the controls were prepared and then aliquoted. Aliquots were frozen at -80°C for future use. For each new day of testing, a new aliquot was thawed and used. The calibration curve stability study met the acceptance criteria that the daily mean of each control is within ±10% from the day zero mean. The calibration curve stability claim is 43 days.

Sample stability: The following claims are cited from literature reference: "Use of Anticoagulants in Diagnostic Laboratory Investigations and Stability of Blood, Plasma and Serum Samples", WHO/DIL/LAB/99.1 Rev.2:41 WHO reference by Ehret W. et. al (p. 41):

- 20–25 °C: 1 day
- 4–8 °C: 8 days
- –20 °C: 3 months (and no repeat freeze–thaw)

6. Detection Limit:
Limit of Blank study (LoB):
The LoB of the RF assay was determined by assaying five blank samples in four replicates per day for three days with three reagent lots. Sixty data points were generated for each lot. The calculation was as follows: $\alpha=\beta=0.05$ for Type I and Type II error risks for LoB and LoD. The LoB for each lot was calculated separately. The claimed LoB value was defined by the highest calculated value, 2.21 IU/mL.

Limit of Detection study (LoD):
The LoD of RF assay was determined by assaying five low-level samples with RF tested in four replicates over three days on three reagent lots. Sixty data points were generated for each lot. The LoD for each lot was calculated separately. The claimed LoD was defined as the highest calculated value, 4.29 IU/mL.

Limit of Quantitation study (LoQ):
The accuracy goal of the LoQ of the assay was defined as a 10% CV. The LoQ of the RF assays was determined by testing seven low-level samples run in two replicates per day, two runs per day and tested for 20 days on two reagent lots. For both lots, the percent CV (%CV) for each sample was calculated and a precision profile curve was plotted. The claimed RF LoQ is 6.65 IU/mL.

7. Assay Cut-Off:
   The assay cut-off was determined as <11 IU/mL through the verification of the predicate's <11 IU/mL expected values which studied 125 normal U.S. serum samples taken from apparently healthy individuals (77% of samples were Caucasian and/ or Hispanic, 13% were African American and 10% Asian American).

B Comparison Studies:

1. Method Comparison with Predicate Device:
   To show comparison between the K-Assay RF (Ver.2) and the predicate K-ASSAY RF, a total of 178 clinical samples were with sample ranges were from 5.10–558.8 IU/mL. The regression equation is as follows: $y = 1.001x + 1.331$ with an $r = 0.989$.

2. Matrix Comparison:
   A total of 59 patient samples were collected; each sample was processed to make four samples — serum, citric acid plasma, Li-heparin plasma, and EDTA plasma. Each processed sample from each patient was tested; the plasma sample results were compared to the serum results and the regression equation are as follows:
   - Serum vs. citric acid plasma: $y = 0.9854x – 0.4601$ with an $R^2 = 0.9929$
   - Serum vs. Li-heparin plasma: $y = 0.9897x + 1.4617$ with an $R^2 = 0.9985$
   - Serum vs. EDTA plasma: $y = 0.9971x – 0.2719$ with an $R^2 = 0.9985$

C Clinical Studies:

1. Clinical Sensitivity/Specificity:
   Not applicable

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

D Clinical Cut-Off:
Same as assay cut-off

E Expected Values/Reference Range:

Same as assay cut-off

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.