510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K242170

B Applicant

Kamiya Biomedical Company, LLC

C Proprietary and Established Names

K-*ASSAY* CRP (Ver.2)

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 (CRP)

C Type of Test:

Latex-enhanced immunoturbidimetric assay, quantitative

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

K-*ASSAY* CRP (Ver.2) is intended to be used for the quantitative determination of C-reactive protein (CRP) in human serum and plasma (potassium-EDTA or lithium-heparin) by immunoturbidimetric assay. Measurement of CRP aids in the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases. FOR IN VITRO DIAGNOSTIC USE.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Abbott Architect c8000 analyzer

IV Device/System Characteristics:

A Device Description:

The device consists of two liquid reagents (ready to use):

Reagent 1 (R1): 1 x 20 mL, Buffer reagent
Reagent 2 (R2): 1 x 20 mL, Latex suspension (Latex particles coated with goat anti-human CRP polyclonal antibody)

Materials required but not supplied

K-*ASSAY* CRP Calibrator (Ver.2): Calibrator A-F Human CRP (6 x 2 mL), pooled human serum with assigned values for the specific serum protein CRP (0.0, 10.0, 50.0, 150.0, 300.0 and 400.0 mg/L), ready to use.

B Principle of Operation:

The K-*ASSAY* CRP (Ver.2) assay uses immunoturbidimetry techniques to quantify CRP. Latex particles coated with polyclonal antibody specific to human CRP aggregate in the presence of CRP from the sample, forming immune complexes. The immune complexes cause an increase in light scattering, which is in proportion to the concentration of CRP in the sample. The light scattering is measured by reading turbidity at 570 nm. The sample CRP concentration is determined based on the calibration curve prepared using a series of CRP calibrators of known CRP concentrations.

V Substantial Equivalence Information:

A Predicate Device Name(s):

K-*ASSAY* CRP (3)

B Predicate 510(k) Number(s):

K023828

C Comparison with Predicate(s):

Device & Predicate Device(s):	K242170	K023828
Device Trade Name	**K-*ASSAY* CRP (Ver.2)**	**K-*ASSAY* CRP (3)**
General Device Characteristic Similarities		
Intended Use/ Indications For Use	K-*ASSAY* CRP (Ver.2) is intended to be used for the quantitative determination of C-reactive protein (CRP) in human serum and plasma (potassium-EDTA or lithium-heparin) by immunoturbidimetric assay. Measurement of CRP aids in the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases. FOR IN VITRO DIAGNOSTIC USE.	K-ASSAY CRP (3) is intended to be used as a high-sensitive assay for the quantitative determination of CRP in serum and plasma by immunoturbidimetric assay. Measurement of C-Reactive Protein aids in the detection and evaluation of tissue injury, inflammatory disorders, and related diseases.
Assay	Latex-enhanced (immuno)turbidimetric assay	Same
General Device Characteristic Differences		
Antibody	Goat anti-human CRP antibody	Rabbit anti-human CRP antibody
Range	5 – 400.0 mg/L	0.2 – 480 mg/L
Calibrator Levels	6 levels (0.0, 10.0, 50.0, 150.0, 300.0, 400.0 mg/L)	Multi-point calibrators E, D and F; 5 levels for each calibrator set
Traceability/ Standardization	Standardized against the ERM-DA474/IFCC	Standardized against CRM 470

VI Standards/Guidance Documents Referenced:

The following Clinical and Laboratory Standards Institute (CLSI) guidelines and FDA guidance were used:

- CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition
- CLSI EP06-Ed2, Evaluation of the Linearity of Quantitative Measurement Procedures – Second Edition
- CLSI EP07-A3, Interference Testing in Clinical Chemistry – Third Edition
- CLSI EP37, Supplemental Tables for Interference Testing in Clinical Chemistry – First Edition
- CLSI EP09c, 3rd Ed., Measurement Procedure Comparison and Bias Estimation Using Patient Samples
- CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP25- Ed2, Evaluation of Stability of *In Vitro* Medical Laboratory Test Reagents; Approved Guideline
- CLSI EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition
- 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. September 2005.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision of the K-*ASSAY* CRP (Ver.2) was evaluated according to CLSI EP05-A3.

a. *Within-Laboratory Precision:*

Five pooled human serum samples covering the measuring range were analyzed using three lots of reagents on one Architect c8000 analyzer. Each sample was analyzed in two replicates per run, two runs per day for 20 days, resulting N=80 per sample per lot. The repeatability, between-run, within-day, between-day, and within-laboratory were calculated (CV% and SD) for each lot. The results from one representative lot are summarized in the table below:

Sample	Mean (mg/L)	N	Within-Run		Between-Run		Within-Day		Between-Day		Within-Laboratory	
			SD	CV %	SD	CV %	SD	CV %	SD	CV %	SD	CV %
1	5.4	80	0.10	1.8	0.00	0.0	0.10	1.8	0.05	0.9	0.11	2.1
2	11.2	80	0.10	0.9	0.09	0.8	0.14	1.2	0.07	0.6	0.15	1.4
3	45.0	80	0.30	0.7	0.41	0.9	0.51	1.1	0.00	0.0	0.51	1.1
4	196.8	80	1.66	0.8	1.65	0.8	2.34	1.2	0.00	0.0	2.34	1.2
5	330.7	80	3.50	1.1	4.48	1.4	5.69	1.7	2.03	0.6	6.04	1.8

b. *Lot-to-Lot Precision:*

Based on the data generated from the study described above, the lot-to-lot imprecision was evaluated based on the total of 240 datapoints for each sample. The results are presented in the table below:

Sample	Mean (mg/L)	N	Within-Run		Between-Run		Between-Lot		Total	
			SD	CV %	SD	CV %	SD	CV %	SD	CV %
1	5.4	240	0.12	2.2	0.00	0.0	0.06	1.2	0.12	2.3
2	11.1	240	0.14	1.2	0.06	0.5	0.03	0.3	0.15	1.3
3	45.0	240	0.36	0.8	0.25	0.6	0.05	0.1	0.40	0.9
4	196.5	240	1.81	0.9	0.76	0.4	0.79	0.4	1.94	1.0
5	330.7	240	4.56	1.4	1.34	0.4	0.00	0.0	4.67	1.4

c. *Multi-site/Analyzer Precision:*

The study was performed using five serum samples using one lot of reagent on three different Architect c8000 analyzers (each analyzer from a different site). Each sample was analyzed in replicates of five per run, one run per day for five days, resulting a total of 75 datapoint per sample. The data was analyzed for within-run, between-run and between-site. The results are summarized in the table below:

Sample	Mean (mg/L)	N	Within-Run		Between-Run		Between-Day		Between-Site/Analyzer		Reproducibility	
			SD	CV %	SD	CV %	SD	CV %	SD	CV %	SD	CV %
1	5.4	75	0.07	1.2	0.00	0.0	0.07	1.2	0.06	1.1	0.09	1.6
2	11.1	75	0.11	1.0	0.00	0.0	0.11	1.0	0.20	1.8	0.23	2.0
3	45.0	75	0.23	0.5	0.17	0.4	0.29	0.6	0.39	0.9	0.48	1.1
4	200.6	75	1.31	0.7	1.68	0.8	2.13	1.1	1.93	1.0	2.87	1.4
5	344.5	75	5.08	1.5	3.69	1.1	6.28	1.8	5.83	1.7	8.57	2.5

2. Linearity:

The linearity of the K-*ASSAY* CRP (Ver.2) was evaluated in accordance with CLSI EP06-Ed2. A dilution series composed of 17 levels distributed across a range from 4.6 mg/L to 441.2 mg/L was prepared by mixing a native high serum sample and a CRP-negative serum sample. The series covered a range from 4.6 mg/L to 441.2 mg/L. Measurements were made in replicates of five per level on Architect c8000 analyzer. The data was analyzed and results are summarized in the following table:

Dilution Range	Slope (95% CI)	Intercept (95% CI)	R^2	% Deviation
4.6 – 441.2 mg/L	0.971 (0.964 – 0.978)	-1.095 (-2.494 – 0.2755)	0.999	-4.09 – 3.83%

The study supports the linear range of 4.6 – 441.2 mg/L for the K-*ASSAY* CRP (Ver.2), with a deviation from linearity within 10%. The results support the linearity throughout the analytical measuring interval of 5.0 – 400 mg/L.

3. Prozone Effect (Hook Effect):

The prozone effect of the K-*ASSAY* CRP (Ver.2) was evaluated using one serum sample (pooled) with CRP level at 980 mg/L. This high-level sample was serially diluted using either saline or CRP-negative serum. Each dilution was tested in quintuplicate on one Architect c8000 analyzer. All samples with concentrations above 400 mg/L were correctly reported as out of assay range for both saline dilution samples and CRP-negative serum dilution samples. No hook effect or prozone effect was observed up to 980 mg/L.

4. Analytical Specificity/Interference:

The effect of the K-*ASSAY* CRP (Ver.2) in the presence of potential interference substances was evaluated per CLSI EP07–A3. Three pooled serum samples with CRP concentrations of approximately 5, 10, and 50 mg/L were used in the study. For each potential interference substance, test sample was prepared by spiking the interferent to the samples, and the corresponding controls were samples without interferents. All samples were tested in replicates of ten. The mean of the test sample was compared to the mean of corresponding control sample. No significant interference (defined as <±10% difference of test samples from the control sample for all three CRP levels) was observed for the tested substances up to the concentration listed in the table below:

Interfering Substances	**Test concentration**
Endogenous Substances	
Bilirubin C	40 mg/dL
Bilirubin F	40 mg/dL
Cholesterol	300 mg/dL
Hemoglobin	1,000 mg/dL
Intralipids	500 mg/dL
Rheumatoid Factor	1,000 IU/mL
Triglycerides	1,000 mg/dL
Exogenous Substances	
Acetaminophen	1.5 mM
Amoxicillin	400 µmol/L
Aspirin (Acetylsalicylic Acid)	3.6 mM
Cephalexin	360 µmol/L
Fluconazole	480 µmol/L
Ibuprofen	2.5 mg/dL
Methotrexate	1,400 µmol/L
Prednisolone	2 µmol/L
Vitamin C (Ascorbic Acid)	500 mg/L

5. Assay Reportable Range:

The assay reportable range for the K-*ASSAY* CRP (Ver.2) is the same as the claimed analytical measuring interval (AMI): 5.0 – 400.0 mg/L.

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

a. Traceability:

The K-*ASSAY* CRP (Ver.2) determine the CRP concentration based on a multi-point calibration curve generated by the K-*ASSAY* CRP Calibrator (Ver.2) which are traceable to the ERM-DA474 reference material.

b. Stability:

The stability of the K-*ASSAY* CRP (Ver.2) under three storage conditions: unopened reagents, opened reagents, and onboard reagents, were evaluated per CLSI EP25-Ed2.

Reagent Stability (Shelf-Life)
Three lots of the K-*ASSAY* CRP (Ver.2) reagents were stored at 2–8°C and tested monthly using four clinical serum pools with concentrations of 10, 25, 100, and 300 mg/L. At each testing point, the results were compared to the value from Day 0. The results support that the reagents of the K-*ASSAY* CRP (Ver.2) are stable at least 18 months (i.e., deviation within ±10% of the Day 0 value) if stored at 2–8°C.

Opened (in-use) Reagent Stability
Three lots of the K-*ASSAY* CRP (Ver.2) reagents were opened and stored at 2–8°C and tested over time using four levels of clinical serum sample pools of 10, 25, 100, and 300 mg/L. The results from each testing point were compared to the values from Day 0. The results support opened reagents stability of the K-*ASSAY* CRP (Ver.2) up to 14 days (i.e., deviation within ±10% of the Day 0 value) when kept at 2–8°C.

On-board Stability
Three lots of the K-*ASSAY* CRP (Ver.2) were stored on the Abbott Architect c8000 analyzer at 2–8°C. Four clinical serum sample pools of 10, 25, 100, and 300 mg/L, and controls were tested in replicates of five at each testing points and the values were compared to the values from Day 0. The results showed the K-*ASSAY* CRP (Ver.2) is stable (i.e., deviation within ±10% of the Day 0 value) for 14 days when placed on-board of the Architect c8000 analyzer.

7. Detection Limit:

The detection limits of the K-*ASSAY* CRP (Ver.2) assay were evaluated following CLSI EP17-A2.

For the Limit of Blank (LoB) determination, the study used three reagent lots on a single Abbott Architect c8000 analyzer. Five CRP-negative serum samples were tested in quadruplicate per run, one run per day, over three days, resulting in 60 measurements per lot. The LoB was determined to be 0.3 mg/L, which was the highest observed LoB across the three reagent lots.

For the Limit of Detection (LoD) determination, five low-concentration serum samples, diluted with CRP-negative serum, were tested using the same protocol as the LoB on three

lots of the K-*ASSAY* CRP (Ver.2) reagents. The LoD was determined to be 0.5 mg/L, which was the highest observed LoD across the three reagent lots.

For the Limit of Quantitation (LoQ) determination, five low CRP serum samples, diluted with CRP-negative serum to concentrations between 0.5 mg/L to 5.0 mg/L, were tested in quintuplicate per run, one run per day for over five days using three reagent lots on a single Abbott Architect c8000 instrument, resulting in 75 measurements per sample across all reagent lots. The LoQ was determined as the value meeting the within-laboratory precision ≤ 20% CV for each of the three reagent lots. The maximum observed LoQ value was of 1.0 mg/L. The claimed LoQ for the K-*ASSAY* CRP (Ver.2) is 5.0 mg/L.

8. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was conducted by testing a total of 175 native serum samples using the K-*ASSAY* CRP (Ver.2) and the predicate device, K-ASSAY CRP (3) on the same Abbott Architect c8000 analyzer. The samples covered measuring ranges for both devices. Weighted Deming regression analysis was performed to assess the equivalency of the K-*ASSAY* CRP (Ver.2) (y) and the predicate device (x). The results are summarized in the table below:

N	Range (mg/L)*	Slope (95% CI)	Intercept (95% CI)	r
175	5.4 – 409.5	1.01 (0.99 – 1.01)	-0.00 (-0.26 – 0.26)	0.999

*Tested by predicate

2. Matrix Comparison:

The effect on quantitation of CRP in the presence of different anticoagulants (i.e., serum, K2-EDTA plasma, and Li-Heparin plasma) using the K-*ASSAY* CRP (Ver.2) was determined by testing 42 paired samples on one Abbott Architect c8000 analyzer. Analytical comparison between the results obtained from each plasma sample type (y) and the results from serum (x) was evaluated using linear regression analyses. The results are summarized in the table below:

	N	Range (mg/L)*	Slope (95% CI)	Intercept (95% CI)	r
Li-heparin vs. Serum	42	5.1 – 399.1	0.97 (0.95 – 0.99)	0.07 (-0.08 – 0.23)	0.999
K2-EDTA vs. Serum	42	5.1 – 399.1	1.01 (0.99 – 1.02)	-0.14 (-0.32 – 0.03)	0.999

*Measured in serum

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:

The reference range of the K-*ASSAY* CRP (Ver.2) was verified per CLSI EP28-A3. A total of 168 serum samples taken from apparently healthy individuals in the U.S. were tested using the K-*ASSAY* CRP (Ver.2) on one Abbott Architect c8000 analyzer. The results showed that 4 out of the 168 samples were >5.0 mg/L (2.4%).

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.