510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
   k050944
B. Purpose for Submission:
   New Device
C. Measurand:
   Ferritin
D. Type of Test:
   Quntitative, latex-enhanced immunoturbidimetric assay
E. Applicant:
   Kamiya Biomedical Company
F. Proprietary and Established Names:
   K-*ASSAY*® Ferritin (2) and K-*ASSAY*® Ferritin Calibrator Set
G. Regulatory Information:
   1. Regulation section:
      21 CFR §866.5340, Ferritin Immunological Test System
      21 CFR 862.1150, Calibrator
   2. Classification:
      Class II
   3. Product code:
      DBF, Ferritin immunological test system
      JIT, Calibrator, Secondary
   4. Panel:
      Immunology (82), assay
      Chemistry (75), Calibrator
H. Intended Use:
   1. Intended use(s):
      The **K-*ASSAY*®** Ferritin (2) assay is an *in vitro* diagnostic reagent for the quantitative determination of ferritin (an iron-storing protein) in human serum and plasma by immunoturbidimetric assay on the Roche/Hitachi 917 analyzer. Measurements of ferritin aid in the diagnosis of diseases affecting iron overload and iron deficiency anemia. For *in vitro* diagnostic use.

      The **K-*ASSAY*®** Ferritin Calibrator Set is an *in vitro* diagnostic reagent for calibration of the **K-*ASSAY*®** Ferritin (2) Assay. For *in vitro* diagnostic use.
   2. Indication(s) for use:
      Same as Intended use.
   3. Special conditions for use statement(s):
      The device is for prescription use only.
   4. Special instrument requirements:
      Roche/Hitachi 917 analyzer
I. Device Description:
   The device **K-*ASSAY*®** Ferritin (2) assay is a latex enhanced immunoturbidimetric

assay for the quantitative in vitro diagnostic determination of ferritin levels in serum and plasma (EDTA and sodium heparin) samples. The reagent kit contains 2 reagents, reagent 1 (1x18 mL) and reagent 2 (1x18 mL). Reagent 1 is a buffer and reagent 2 is the latex suspension with rabbit anti-human ferritin antibody.

The **K-*ASSAY* ®** Ferritin Calibrator contains four calibrators (A through D) each with a specific assigned value. Calibrator A: 100 ng/mL, Calibrator B: 200 ng/mL, Calibrator C: 500 ng/mL and Calibrator D: 1000 ng/mL

J. Substantial Equivalence Information:
  1. Predicate device name(s):
     Roche Tina-quant® (a) Ferritin
  2. Predicate 510(k) number(s):
     k964282
  3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	K-*ASSAY* ® Ferritin (2) assay	Roche Tina-quant® (a) Ferritin
Intended Use	Quantitative *in vitro* diagnostic determination of ferritin	Same
Methodology	latex Enhanced Immunoturbidimetry	Same
Uses calibration curve to determine the ferritin levels	Yes	Yes
Reagents	Reaction buffer and Latex particles coated with rabbit anti-human ferritin antibodies	Same

Differences		
Item	Device	Predicate
Sample type	Serum, and Plasma (Sodium EDTA or Sodium Heparin)	Serum, Plasma (Li-Heparin, citrated or EDTA)
Instrument	Hitachi 917	Roche/Hitachi 717/902, 904/911/912/917/MODULAR
Range of the assay	2 to 1000 ng/mL	15 to 800 ng/mL
Limit of detection	2 ng/mL	3 ng/mL (with automatic re-run)
Calibration	K-Assay® Ferritin Calibrator	c.f.a.s proteins
Calibrators	liquid	lyophilized

Differences		
Item	Device	Predicate
Calibration	Five point calibration curve	Six-point calibration curve
Quality Control	Each laboratory is encouraged to run their own controls (normal and abnormal samples)	Control materials are recommended

K. Standard/Guidance Document Referenced (if applicable):

M29-A2 and H3-A2 (NCCLS documents)

L. Test Principle:

The **K-*ASSAY*®** Ferritin (2) assay is a latex enhanced immunoturbidimetric assay. When a sample containing ferritin is mixed with the reagent 2 which is a suspension of latex particles sensitized with rabbit anti-human ferritin antibody, a clear agglutination occurs. This agglutination is measured by turbidimetry and 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 of ferritin is then determined by interpolation from a calibration curve prepared from calibrators of known ferritin concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:
      i. Precision:
         Precision was performed on Hitachi 917 using three samples. The samples were low, medium and high controls (Immuno Q sera II from Denka Seiken, Japan). For calculating within-run precision, the samples were assayed twenty one times on the same day. For calculating between-day precision, samples were assayed in duplicate over twenty different days. The precision study met the acceptance criteria for all three samples which was < 7% CV.

Within-Run	Mean (ng/mL)	Low (ng/mL)	High (ng/mL)	SD	CV (%)
Low control	14.9	13.8	15.9	0.600	4.03
Medium control	100.0	98.7	101.2	0.647	0.65
High Control	431.1	427.6	435.5	2.203	0.51

Between-day	Mean (ng/mL)	Low (ng/mL)	High (ng/mL)	SD	CV (%)	Total Precision (%)
Low control	16.5	15.4	18.1	0.733	4.45	3.44
Medium	105.2	102.7	107.6	1.522	1.45	1.54
High Control	428.7	421.0	432.6	2.510	0.59	0.83

ii. Lot to lot reproducibility:

Lot to lot reproducibility was performed using three different lots of reagents. The samples were assayed in duplicate over twenty different days. The acceptance criteria for 10-50 ng/mL and 51-1000 ng/mL are %CV $\leq$ 15% and $\leq$ 10% respectively.

	Mean (ng/mL)	Low (ng/mL)	High (ng/mL)	SD	CV (%)
Low control	16.91	15.1	18.4	0.867	5.12
Medium control	105.79	103.0	108.6	1.573	1.49
High Control	431.05	425.2	435.0	2.538	0.59

b. *Linearity/assay reportable range:*

Linearity testing was performed using serially diluted in-house controls made from spiked serum pool (Denka Seiken, Japan) with ferritin in low, medium and high range. The acceptance criteria for linearity is $\pm$ 10% of theoretical value and R $\geq$ 0.99

To calculate the 'low range' linearity, a sample with 98 ng/mL ferritin was diluted down to zero. The theoretical measurements of the different levels of dilutions were 88.2, 78.4, 68.6, 58.8, 49, 39.2, 29.4, 19.6, 9.8 and 0.0 ng/mL. The regression equation for this measurement is y=0.9858x-0.0591 with an R=0.9997.

To calculate the 'medium range' linearity, a sample with 630 ng/mL ferritin was diluted down to zero. The theoretical measurements of the different levels of dilutions were 567, 504, 441, 378, 315, 252, 189, 126, 63 and 0.0 ng/mL. For this measurement, y=0.9888x + 3.1818 with an R=0.9998.

To calculate the 'high range' linearity, a sample with 1000 ng/mL ferritin was diluted down to zero. The theoretical measurements of the different levels of dilutions were 900, 800, 700, 600, 500, 400, 300, 200, 100 and 0.0 ng/mL. For this measurement, y=0.9513x + 18.377 with an R=0.9993.

The linear assay range is from 2-1000 ng/mL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The reference standard for Ferritin calibrator is the 1st WHO International reference Preparation Human Ferritin, established in 1984 (BIBSC code 80/602).

Calibrator: Secondary calibrators (In-house master standards) are produced from commercially available human ferritin prepared from human liver and value assigned to the WHO reference standard. The secondary calibrators are used to assign values to the product calibrators. The unopened calibrators are stable for one year from the date of manufacturing and Opened reagents are

found to be stable for 2 months if tightly capped and stored at 2-10°C. The stability of the calibration curve is found to be at least 4 weeks.

   d. *Detection limit:*
   The lower limit of detection was determined by assaying the absorbance of serial dilutions of diluted Ferritin Calibrator A (10 ng/mL Ferritin) with saline. The lower detection limit is claimed as 2 ng/mL. This was found to be the lowest level of ferritin that had an absorbance range (mean +2 standard deviation (SD)) above the absorbance range (mean +2 SD) of saline. The 2 ng/mL sample has a within run precision (n=10) of CV = 2.9%. Using a clinical acceptance criteria of CV ≤ 20% at the lower limit of detection, the 2 ng/mL lower limit of detection meets the clinical acceptance criteria.

   e. *Analytical specificity:*
   Interference testing was preformed by adding the interfering substances at highest concentration to the base serum. These preparations were diluted serially with saline. Ferritin was measured in these diluted samples and the percent recovery calculated based on ferritin concentration of the serum diluent. The acceptance criterion for the percent recovery is within ± 10% of serum diluent. Based on the acceptance criterion, no significant interference was found with hemoglobin up to 1040 mg/dL, bilirubin F up to 62 mg/dL, bilirubin C up to 62 mg/dL, intra-fat (which contains 10% soybean oil) up to 3% and intra-lipid (which contains 10% soybean oil, different manufacturer) up to 5%. No interference with rheumatoid factor (RF) up to 520 IU/mL.

   f. *Assay cut-off:*
   No assay cut off was provided.

2. Comparison studies:
   a. *Method comparison with predicate device:*
   The Method Comparison study was performed with 64 patient serum samples on the new device and the predicate device, Roche Tina-Quant, both on Roche/Hitachi 917 analyzer. The samples were obtained from clinical laboratories by the manufacturer. The samples were from Asian patients. The samples covered a range from 11.2 to 766.8 ng/mL. The required specification was R value ≥ 0.95. Linear regression analysis showed a slope of 0.89 (95% CI: 0.872 to 0.907) and an intercept of -9.4 (95%CI: -15.846 to -2.96). The correlation coefficient was 0.9969.

   b. *Matrix comparison:*
   Matrix comparison was generated for serum, EDTA and sodium heparin, with 20 samples. The samples covered a range from 7.5 to 161 ng/mL. The required specification was R value ≥ 0.99. Linear regression analysis (serum vs. Na EDTA plasma) showed a slope of 0.989 and an intercept of 0.21 and the correlation coefficient was 0.997. Linear regression analysis (serum vs. Na heparin plasma) showed slope of 1.0612 and an intercept of -0.5524 and the correlation coefficient was 0.998.

3. Clinical studies:
   a. *Clinical Sensitivity:*
   Not provided
   b. *Clinical specificity:*

Not provided
   c. *Other clinical supportive data (when a. and b. are not applicable):*
       Not applicable
   4. Clinical cut-off:
      Not provided
   5. Expected values/Reference range:
      The package insert provides the reference range which was determined at the manufacturer's site using real samples. Two hundred and twenty six normal male serum samples and two hundred and five normal female serum samples were assayed for ferritin. The reference range for male was found to be 7-253 ng/mL. The reference range for the female was found to be 2-110 ng/mL. Each laboratory is recommended to establish its own expected range.

N. Proposed Labeling:
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

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