

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY ONLY TEMPLATE**

**A. 510(k) Number:**

k093137

**B. Purpose for Submission:**

New device

**C. Measurand:**

Cystatin C

**D. Type of Test:**

Quantitative immunoturbidimetric assay

**E. Applicant:**

Kamiya Biomedical Company

**F. Proprietary and Established Names:**

K-ASSAY Cystatin C Reagent  
K-ASSAY Cystatin C Calibrator  
K-ASSAY Cystatin C Control

**G. Regulatory Information:**

<b>Device</b>	<b>Regulation</b>	<b>Classification</b>	<b>Product Code</b>	<b>Panel</b>
K-ASSAY Cystatin C Reagent	21 CFR 862.1225	II	NDY	75 (Clinical Chemistry)
K-ASSAY Cystatin C Calibrator	21 CFR 862.1150	II	JIT	75 (Clinical Chemistry)
K-ASSAY Cystatin C Control	21 CFR 862.1660	I, reserved	JJX	75 (Clinical Chemistry)

## H. Intended Use:

1. Intended use(s):

Refer to indications for use below.

2. Indication(s) for use:

K-ASSAY Cystatin C Reagent: The K-ASSAY Cystatin C Assay is for the quantitative determination of human cystatin C in serum, EDTA plasma, or lithium heparin plasma by immunoturbidimetric assay. Cystatin C measurements are used as an aid in the diagnosis and treatment of renal diseases. For *in vitro* diagnostic use.

K-ASSAY Cystatin C Calibrator: The K-ASSAY Cystatin C Calibrator is intended to be used for the calibration of the K-ASSAY Cystatin C Assay. For *in vitro* diagnostic use.

K-ASSAY Cystatin C Control: The K-ASSAY Cystatin C Control is intended for use as an assayed quality control material for monitoring the performance of cystatin C assays.

3. Special conditions for use statement(s):

For prescription use only.

For *in vitro* diagnostic use only.

4. Special instrument requirements:

Testing for device was performed on the Roche/Hitachi 917 (k953239).

## I. Device Description:

1. K-ASSAY Cystatin C Reagent: The K-ASSAY Cystatin C reagent consists of two reagents: Reagent 1 contains buffer reagent and Reagent 2 contains a solution of latex suspension with goat anti-human cystatin C antibodies.

2. K-ASSAY Cystatin C Calibrator: The K-ASSAY Cystatin C calibrators are liquid stable products consisting of buffered aqueous solutions containing known quantities of human cystatin C at six different levels. The calibrator contains sodium azide as a preservative.

3. K-ASSAY Cystatin C Control: The K-ASSAY Cystatin C controls are liquid stable products consisting of buffered aqueous solutions containing known

quantities of human cystatin C at two different levels. The control contains sodium azide as a preservative.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

DakoCytomation Cystatin C Assay

2. Predicate 510(k) number(s):

k041627

3. Comparison with predicate:

<b>Comparison Table: K-ASSAY Cystatin C Reagent</b>		
<b>Item</b>	<b>Device (k093137)</b>	<b>Predicate (k041627)</b>
Indications for Use	For the quantitative determination of human cystatin C in serum, EDTA plasma, or lithium heparin plasma by immunoturbidimetric assay. Cystatin C measurements are used as an aid in the diagnosis and treatment of renal diseases. For <i>in vitro</i> diagnostic use.	Same
Assay Reaction Principle	Latex suspension with goat anti-human cystatin C antibodies is mixed with sample. The resulting immune complexes are measured by turbidimetry.	Cystatin C immunoparticles are mixed with sample. The resulting immune complexes are measured by turbidimetry or nephelometry.
Sample Type	Human serum, EDTA and Lithium Heparin plasma	same
Instrument(s)	Two-reagent clinical chemistry analyzers capable of accurate absorbance reading at 570 nm	Commercially available nephelometer or turbidimeter
Calibration Interval	Every month on Roche/Hitachi 917	Every 90 days on Roche/Hitachi 917
Reagent Stability	Unopened: 2-8°C - 12 months Opened: 2-8°C - 1 month On-board (37°C) - 30 days	2-8°C - until expiration date printed on label. 37°C, on-board analyzers - 90 days
Calibrator	K-ASSAY Cystatin C Calibrator	DakoCytomation Cystatin C Calibrator
Controls	K-ASSAY Cystatin C Control	DakoCytomation Cystatin C Control
Measuring	0.4-8.0 mg/L	0.4-7.5 mg/L

<b>Comparison Table: K-ASSAY Cystatin C Reagent</b>		
Item	Device (k093137)	Predicate (k041627)
Range		
Hook Effect	≥50 mg/L	NA
Limit of Blank	0.012 mg/L	NA
Limit of Detection	0.024 mg/L	0.03 mg/L

<b>Comparison Table: K-ASSAY Cystatin C Calibrator</b>		
Item	Device (k093137)	Predicate (k041627)
Indications for Use	Intended to be used for the calibration of the assay.	Same
Format	Liquid, buffered aqueous solution containing human cystatin C	Liquid pool of delipidated human serum enriched with human cystatin C
Analyte Constituents	Cystatin C	Same
Levels	Six	Same
Stability	Unopened: 2-8°C - 12 months Opened: 2-8°C – 2 weeks	2-8°C - until expiration date printed on label
Volume	2 mL	1 mL

<b>Comparison Table: K-ASSAY Cystatin C Control</b>		
Device (k093137)	Device (k093137)	Device (k093137)
Intended Use	Intended for use as an assayed quality control material for monitoring the performance of cystatin C assays.	Same
Format	Liquid, buffered aqueous solution containing human cystatin C	Liquid pool of delipidated human serum enriched with human cystatin C
Analyte Constituents	Cystatin C	Cystatin C
Levels	Two	Two
Stability	Unopened: 2-8°C - 12 months Opened: 2-8°C - 2 weeks	2-8°C - until expiration date printed on label
Volume	2 mL	1 mL

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

1. CLSI EP5-A2 – Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline (2004)
2. CLSI EP6-A – Evaluation of the Linearity of Quantitative Measurement

- Procedures: A Statistical Approach; Approved Guideline (2003)
3. CLSI EP7-A2 – Interference Testing in Clinical Chemistry; Approved Guideline (2005)
  4. CLSI EP9-A2 – Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (2002)
  5. CLSI EP17-A – Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (2004)

**L. Test Principle:**

Human serum or plasma is mixed with a suspension of latex particles coated with purified goat anti-human cystatin C polyclonal antibodies. The resulting immune complexes are measured by turbidimetry. The signal generated is correlated with the concentration of cystatin C in the sample. By interpolation on a standard curve, the concentration of cystatin C in the sample is calculated. The K-ASSAY Cystatin C assay is analyzed using a two-reagent clinical chemistry analyzer.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

*a. Precision/Reproducibility:*

Precision studies were conducted using the Roche/Hitachi 917 chemistry analyzer following CLSI EP5-A2 guidelines. Three control samples and one human serum specimen containing cystatin C at various levels were evaluated in duplicate twice a day for twenty days. Calculated means, standard deviations, and coefficients of variation (CV) are shown below:

Precision: K-ASSAY Cystatin C on Roche/Hitachi 917								
Sample	Mean Concentration (mg/L)	n	Within Run		Between Run		Total Precision	
			SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)
1-Control	0.968	80	0.007	0.712	0.024	2.496	0.024	2.462
2-Control	1.999	80	0.013	0.640	0.019	0.960	0.027	1.353
3-Control	4.389	80	0.030	0.690	0.079	1.811	0.088	2.008
4-Human Specimen	0.511	80	0.006	1.094	0.005	1.066	0.007	1.421

*b. Linearity/assay reportable range:*

Linearity of the K-ASSAY Cystatin C assay was evaluated with 18 test concentrations of analyte in human serum samples prepared using a normal human serum spiked with human cystatin C and a cystatin C depleted normal

human serum. The linearity test was performed following CLSI EP6-A guidelines. The calculated cystatin C concentrations ranged from 0.05 to 8.0 mg/L. Samples were measured in quadruplicate on the Roche/Hitachi 917 chemistry analyzer using one reagent lot. Least-square regression analysis resulted in a linear correlation of  $Y=1.017X - 0.008$  and a correlation coefficient (r) of 1.0. Nonlinearity was further assessed based on CLSI EP6-A guidelines by comparison to a pre-defined goal of 10% deviation. The K-ASSAY Cystatin C assay was demonstrated to be linear throughout the claimed measuring range of 0.4-8.0 mg/L.

*c. Traceability, Stability, Expected values (controls, calibrators, or methods):*

There is no internationally recognized reference standard for cystatin C. The K-ASSAY Cystatin C assay is traceable to an in-house standard that was developed from purified human recombinant cystatin C. The cystatin C concentration of this standard was determined by its optical density at 280 nm and its individual extinction coefficient. The cystatin C value assignment for the calibrators is performed by testing serial dilutions of source material and evaluating linearity and recovery against the in-house standard. The cystatin C value assignment for the controls is carried out using the K-ASSAY Cystatin C reagent and calibrators using the Roche/Hitachi 917 chemistry analyzer. After calibration, controls are assayed in two runs per day on two separate days. The levels of cystatin C are assigned to each control based on the average of all runs.

The stability of the K-ASSAY Cystatin C reagent, calibrator, and control were demonstrated with real-time stability studies. The unopened shelf life is twelve months for the reagent, twelve months for the calibrator, and twelve months for the controls when stored at the recommended temperature of 2 to 8°C. The open-vial stability is one month for the reagent, two weeks for the calibrator, and two weeks for the controls when stored at the recommended temperature of 2 to 8°C. An on-board stability study confirmed that the reagent is stable for thirty days on-board the Roche/Hitachi 917 analyzer.

*d. Detection limit:*

Limits of Blank (LoB) and Limits of Detection (LoD) for the K-ASSAY Cystatin C assay were evaluated using CLSI EP17-A guideline. Studies were performed on the Roche/Hitachi 917 analyzer.

<b>Detection Limits: K-ASSAY Cystatin C on Roche/Hitachi 917</b>		
<b>Limit</b>	<b>Protocol</b>	<b>Claimed Value</b>
LOB	Sixty replicates of saline blank were tested in twelve runs per day for five days.	0.012 mg/L

LOD	Six normal human serum samples at cystatin C levels from 0.01 to 0.06 mg/L were tested in four runs per day over five days.	0.024 mg/L
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e. *Analytical specificity:*

Two serum samples containing cystatin C at concentrations of 0.8 and 2.2 mg/L were evaluated with the K-ASSAY Cystatin C assay on the Roche/Hitachi 917 analyzer for the effect of interferences based on CLSI EP7-A2 guidelines. The following substances demonstrated no significant interference based on acceptance criteria:  $\pm 10\%$  deviation from control value:

<b>Interferences: K-ASSAY Cystatin C on Roche/Hitachi 917</b>	
<b>Substance</b>	<b>No Interference at Listed Level</b>
Bilirubin, Conjugated	60 mg/dL
Bilirubin, Unconjugated	60 mg/dL
Hemoglobin	900 mg/dL
Intralipid	11 g/L
Rheumatoid Factor	1000 IU/L
Triglycerides	1500 mg/dL

The sponsor included the results from this interference study in the labeling.

A high dose (hook effect) study was conducted to determine if high doses of cystatin C interfere with the assay. Based on the results of the study, the sponsor claimed that there is no high dose effect for concentrations up to 50 mg/L

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

A total of 50 unaltered human serum samples containing cystatin C concentrations ranging from 0.4 to 7.4 mg/L were tested with the K-ASSAY Cystatin C assay and the predicate device on the Roche/Hitachi 917 analyzer according to CLSI EP9-A2 guidelines. Least-square regression analysis resulted in the following correlation  $Y = 1.0093X - 0.0411$  with a correlation coefficient (r) of 0.9983.

b. *Matrix comparison:*

A matrix comparison study was performed by splitting 57 human samples containing cystatin C concentrations ranging from 0.4 to 7.9 mg/L into three aliquots (serum, EDTA plasma, lithium-heparinized plasma) and testing with the K-ASSAY Cystatin C assay on the Roche/Hitachi 917 analyzer. A total of 7 samples were diluted or spiked to obtain low and high cystatin C concentrations. Results from the EDTA plasma and lithium-heparin plasma aliquots were individually compared to the results obtained with the serum aliquot. Least-square regression analysis yielded the following results:

<b>Matrix Comparison: K-ASSAY Cystatin C on Roche/Hitachi 917</b>				
<b>Matrix</b>	<b>n</b>	<b>Slope</b>	<b>Intercept</b>	<b>r</b>
EDTA Plasma vs. Serum	57	0.993	0.040	0.999
Li-Heparin vs. Serum	57	0.987	0.059	0.998

The sponsor included serum or plasma (sodium EDTA or lithium heparin) in the labeling as acceptable assay specimens.

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable

b. *Clinical specificity:*

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The sponsor claims an expected value of 0.5 to 1.0 mg/L based on the following reference: Tietz, N.W. Clinical Guide to Laboratory Tests, 4<sup>th</sup> ed., 2005. The following statement is included in the labeling, “Due to population differences, each laboratory should establish its own expected values using this kit.”

**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.