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

A. 510(k) Number:

k063647

B. Purpose for Submission:

New Device

C. Measurand:

Cystatin C

D. Type of Test:

Quantitative

E. Applicant:

Thermo Fisher Oy

F. Proprietary and Established Names:

Cystatin C

Cystatin C Calibrator

Cystatin C Control and Cystatin C Control High

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
NDY	II	21 CFR 862.1225	Clinical Chemistry
JIT	II	21 CFR 862.1150	Clinical Toxicology
JJX	I	21 CFR 862.1660	Clinical Toxicology

H. Intended Use:

1. Intended use(s):

See indications for use statements below.

2. Indication(s) for use:
   Cystatin C is intended for quantitative in-vitro diagnostic determination of
   Cystatin C in human serum or Li-heparin plasma and EDTA plasma by
   turbidimetry using T60 Clinical Chemistry Analyzers.
   Cystatin C measurements in serum and plasma are used as an aid in the diagnosis
   and treatment of renal diseases.

   Cystatin C Calibrator is intended for in vitro diagnostic use on T60 analyzer.
   Cystatin C Calibrator is used as a calibrator for quantification of Cystatin C in
   serum and plasma by immunoturbidimetry using methods defined by Thermo
   Electron Oy.

   Cystatin C control is intended for in vitro diagnostic use on T60 analyzer.
   Cystatin C control is used as a quality control to monitor precision of the Cystatin
   C test using method defined by Thermo Electron Oy.

   Cystatin C Control High is intended for in vitro diagnostic use on T60 analyzer.
   Cystatin C Control High is used a quality control serum to monitor precision of
   the Cystatin C test using methods defined by Thermo Electron Oy.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   T60 clinical chemistry analyzers.

I. Device Description:

The Cystatin C has reagents (2 vials), buffer (2 vials) and diluent (1 vial). The
Cystatin C reagent is comprised of microparticles coated with rabbit anti-human
Cystatin C. Cystatin C Buffer is a solution of polymers in MPOS buffered saline and
the diluent is PBS and NaN^3.

The Cystatin C Calibrator contains 2 vials of delipidated human serum liquid pools
enriched with recombinant human Cystatin C produced in *E. coli*.

The Cystatin C controls contains 3 vials of delipidated human serum liquid pools
enriched with recombinant human Cystatin C produced in *E. coli*. The Cystatin C
controls is a bi-level control with levels of approximately 1.06 and 4.27.

This product has been tested, and found negative for HBsAg and for antibodies to
HIV 1/2 and HCV. The tests used were cleared for in vitro use in the EU (Directive
98/79/EC, Annex II).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Cystatin C Immunoparticles

   Cystatin C Calibrator

   Cystatin C Control Set

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

   k041627

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Indications for Use	In vitro diagnostic determination of Cystatin C in human serum or Li-heparin plasma and EDTA plasma. Cystatin C measurements in serum and plasma are used as an aid in the diagnosis and treatment of renal diseases.	Intended for the quantitative determination of Cystatin C in human serum, heparinized plasma and EDTA plasma by turbidimetry and nephelometry. Cystatin C measurements are used as an aid in diagnosis and treatment of renal diseases.
Method	Particle enhanced immunoturbidimetric	Particle enhanced immunoturbidimetric.
Matrix	Human serum, Li-Heparin Plasma and EDTA Plasma	Human Serum, Heparinized Plasma and EDTA Plasma

Differences		
Item	Device	Predicate
Instrument	T60 clinical chemistry analyzers	Hitachi 911, 917 and Cobas Mira Plus and IMMAGE
Measuring Range	0.44 – 7.0 mg/L	0.4 – 7.5 mg/L

K. Standard/Guidance Document Referenced (if applicable):
   CLSI EP5-A Evaluation of Precision Performance of Clinical Chemistry Devices;
   CLSI EP6-P2 Evaluation of the Linearity of Quantitative Analytical Methods;
   CLSI EP9-A Method Comparison and Bias Estimation Using Patient Samples;

L. Test Principle:

The Cystatin C assay uses a method based on measurement of immunoprecipitation at 540 nm. Microparticles coated with anti-human Cystatin C are added to buffered samples. The increase in absorbance caused by immunoprecipitation is recorded after a fixed timing. The amount of immunoprecipitate is proportional to the Cystatin C concentration in the solution.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

      Within run, between run and total precision was conducted according to CLSI EP5-A. Four samples (2 controls levels and 2 serum pools) were run on the T60 in duplicate, twice a day for twenty days. The results are summarized below.

Precision								
	Low Control mean 1.03 mg/L		High Control mean 4.59 mg/L		Low Pool mean 0.70 mg/L		High Pool mean 1.49 mg/L	
	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Within run	0.027	2.7	0.054	1.2	0.010	1.4	0.039	2.6
Between run	0.032	3.1	0.038	0.8	0.011	1.5	0.006	0.4
Total	0.044	4.2	0.074	1.6	0.016	2.3	0.038	2.6

   b. *Linearity/assay reportable range:*
      Linearity was assessed according to CLSI EP6-A. Serum samples diluted with saline were run in triplicate. Linear regression results (expected vs. observed values) are summarized in the chart below.

	n	**Range** mg/L	**Slope** mg/L	**Intercept** mg/L
Cystatin C	10	0.577- 5.80	1.02	-0.018

An antigen excess study (hook effect) was conducted through a dilution study of de-lipidated human serum enriched with human recombinant Cystatin C. The measured signal was plotted against the concentration of Cystatin C for each dilution. The antigen excess was defined as the concentration range between the highest standard point and the critical concentration where the signal becomes lower than the signal of the highest standard point. There was no hook effect/antigen excess found up to a Cystatin C concentration of 37.4 mg/L.

The sponsor recommends dilution of samplesabove the assay range up to15 mg/L. They conducted a study to assess the linearity of the assay above 7 mg/L with human serum samples spiked with recombinant Cystatin C. Linear regression results are summarized in the chart below.

	n	Range mg/L	Slope mg/L	Intercept mg/L
Cystatin C	10	1.26- 15.91	1.045	-0.360

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

Traceability

The Cystatin C calibrator is traceable to a pure recombinant human Cystatin C reference preparation. The Cystatin C concentration was established by a dry mass determination.

Stability

An accelerated stability study was conducted on two lots of the reagents at 30° C for 65 days. Real time reagent stability studies are ongoing.

Real time stability studies were conducted for the Cystatin C calibrators and controls (low and high). Three lots of each were stored at 4-8°C and were tested with two levels of frozen serum pools at 3 month intervals. The Cystatin C test was calibrated with the calibrator and controls and the serum pools were measured. The sponsors' recovery acceptance criteria were +/- 15% or 0.1 mg/L. The results support the sponsor's open vial and closed vial stability of 12 months.

Value Assignment

A Cystatin C primary calibrator is prepared gravimetrically. The assay calibrator values are assigned by multiple runs on assays calibrated using the primary calibrator. The Cystatin C controls were value assigned from multiple runs on assays calibrated by the Cystatin C calibrators.

d. Detection limit:

The detection limit was determined as the lowest concentration that gave a signal higher than the signal of the blank plus 3 SD. The results support the claimed detection limit of 0.18 mg/L.

e. Analytical specificity:

Interference studies were conducted with 3 serum pools with low, medium and high Cystatin C concentrations. Varying concentrations of interferents were added and samples were analyzed in triplicate. The sponsor defined "no interference" as deviations less than or equal to +/- 10% of initial value or +/- 0.1 mg/L of initial value.

Interfering substance		Cystatin C (mg/L)					
		Low Cystatin C	Dev. (%)	Medium Cystatin C	Dev. (%)	High Cystatin C	Dev. (%)
Hemoglobin	0 mg/dL	0.68	-	1.66	-	5.63	-
	500 mg/dL	0.66	-3.9	1.60	-3.8	5.65	0.4
	1000 mg/dL	0.62	-9.3	1.58	-4.6	5.70	1.4
Bilirubin conjugated	0 mg/dL	0.73	-	1.44	-	5.88	-
	30 mg/dL	0.74	0.9	1.44	0.5	6.00	2.0
	60 mg/dL	0.73	0.0	1.40	-2.6	5.94	1.0
Bilirubin nonconjugated	0 mg/dL	0.72	-	1.38	-	5.91	-
	30 mg/dL	0.67	-7.0	1.34	-2.9	5.85	-1.0
	60 mg/dL	0.69	-3.7	1.33	-3.6	5.88	-0.5
Rheumatoid factor	0 IU/mL	0.70	-	1.20	-	5.81	-
	600 IU/mL	0.70	0.0	1.20	0.3	5.74	-1.1
	1200 IU/mL	0.77	10.0	1.24	3.3	5.85	0.7
Triglyceride	0 mg/dL	0.64	-	1.40	-	5.69	-
	750 mg/dL	0.63	-0.5	1.26	-9.8	5.70	0.1
	1500 mg/dL	0.60	-5.2	1.37	-1.7	5.61	-1.4
Intralipid®	0 mg/dL	0.71	-	1.17	-	5.99	-
	500 mg/dL	0.67	-5.2	1.14	-2.6	5.68	-5.2
	800 mg/dL	0.68	-4.7	1.12	-4.3	5.66	-5.6

The sponsor claims no interference for:
Hemoglobin up to 1000 mg/dL
Bilirubin conjugated and nonconjugated up to 58.5 mg/dL
Rheumatoid factor up to 1200 IU/mL
Triglyceride up to 1500 mg/dL
Intralipid® up to 800 mg/dL

f. Assay cut-off:

Not applicable.

2. Comparison studies:

   a. *Method comparison with predicate device:*

   The sponsor conducted a method comparison study according to CLSI EP9-A.
   Fifty-four serum samples were analyzed with Cystatin C test on the T60 and
   the predicate Dako Cystatin C reagents on the Hitachi 917.   The samples
   were run in singlets on a single day with a new calibration for each run. The
   results were recalculated using EP Evaluator version 7 method comparison
   CLSI EP 9 module and the Deming regression equation was determined.

	n	Range mg/L	Equation mg/L	Correlation Coefficient
Cystatin C	54	0.25-6.17	y = 1.06x – 0.1	.999

   b. *Matrix comparison:*

   The sponsor conducted a comparison study of serum samples paired with
   lithium heparin and EDTA plasma samples. Thirty paired serum samples,
   lithium heparin and EDTA plasma samples were analyzed in duplicate using
   deming regression. Six of the thirty paired samples were spiked with
   recombinant Cystatin C.

n	Serum mean (mg/L)	EDTA mean (mg/L)	% Deviation	Range (mg/L)	Regression Equation	r
30	1.55	1.59	1.9	0.68 to 7.03	Y= 1.03x + 0	0.998
n	Serum mean (mg/L)	Lithium Heparin mean (mg/L)	% Deviation	Range (mg/L)	Regression Equation	r
30	1.55	1.43	-6.4	0.68 to 6.75	Y=0.88x + 0.06	0.998

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:

    From a study of apparently healthy individuals, the sponsor reports the following expected values:

    For individuals 1-50 years: 0.55-1.15 mg/L

    For individuals > 50 years: 0.63 – 1.44 mg/L

    The sponsor recommends that these values should serve as a guide only and that each laboratory should verify the range or derive a reference interval for its own population.

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 substantial equivalence decision.