K141143

JUL 17 2014

510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set

Date prepared: July 14th, 2014

Purpose of submission

Roche Diagnostics hereby submits this 510(k) to provide FDA with notification of intent to market a new device named Tina-quant Cystatin C Gen. 2 reagent.

This candidate device is a new reagent that was developed by Roche Diagnostics. The Diazyme Cystatin C Assay was cleared in 510(k) k093680 and serves as the predicate device. The candidate reagent uses the same calibrator that was cleared in k080811 and the new Cystatin C Control Set. The new Control Set Gen.2 has three levels compared to the two levels control set which previous cleared in k080811. The Mid level is the only difference between this control set and the one that was cleared in k080811. This submission presents data to support clearance of this new reagent and control.

All data in this submission was generated on the **cobas c** 501 analyzer.

Measurand

Cystatin C

Type of test

Quantitative turbidimetric method

Applicant

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Candidate device names

Proprietary name:
cobas c Tina-quant Cystatin C Gen. 2
Common name:
Cystatin C Gen. 2

510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Regulatory information

Product Code	Classification	Regulation	Panel
NDY	Class II	21 CFR 862.1225 (Cystatin C test system)	Clinical Chemistry
JIT	Class II	21 CFR 862.1150, (Calibrator, secondary)	Clinical Chemistry
JJX	Class I	21 CFR 862.1660, (Single (specified) analyte controls (assayed and unassayed))	Clinical Chemistry

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Intended use	In vitro test for the quantitative determination of cystatin C in human serum and plasma on Roche/Hitachi **cobas c** systems.
Indications for use	Tina-quant Cystatin C Gen. 2 assay: The Tina-quant Cystatin C Gen. 2 is an in vitro test for the quantitative determination of cystatin C in human serum and plasma on Roche/Hitachi **cobas c** systems. Cystatin C measurements are used as an aid in the diagnosis and treatment of renal diseases. C.f.a.s. Cystatin C: The C.f.a.s. Cystatin C is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets. Cystatin C Control Set Gen.2: The Cystatin C Control Set is for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.
Special conditions for use	For prescription use only
Special instrument requirements	For use on Roche/Hitachi cobas c systems
Candidate device description	Roche Tina-quant Cystatin C Gen. 2 reagent provides quantitative measurement of the cystatin C that is present in human serum and plasma. Assay: Reagents are packaged in a cassette with two bottles labeled with their instrument positioning, R1 (Reagent 1) and R2 (Reagent 2). R1 contains solution of polymers in MOPS-buffered saline; preservative, stabilizers. R2 is latex particles in glycine buffer coated with anti-Cystatin C antibodies (rabbit); preservative, stabilizers.

Calibrator:
C.f.a.s. Cystatin C is a liquid, ready-to-use calibrator based on pooled delipidated human serum enriched with recombinant human Cystatin C produced in E. Coli. Single level calibrators with lot specific values are diluted on board the analyzer to create a 6-point calibration curve.

Control:
Cystatin C Control Set contains 3 controls based on pooled delipidated human serum enriched with human recombinant Cystatin C produced in E. Coli.

Predicate device

Diazyme Cystatin C Assay was cleared in k093680 on the Hitachi 917 analyzer for the quantitative determination of Cystatin C in serum or plasma by latex enhanced immunoturbidimetric method. The measurement of Cystatin C is used as an aid in the diagnosis and treatment of renal disease. C.f.a.s Cystatin C calibrator and Cystatin C Control Set were cleared in k080811 on Hitachi 917, MODULAR P, cobas c 501.

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Substantial equivalence - similarities

The following table compares the identical features of the candidate device to the predicate device that was cleared in 510(k) k093680 and k080811.

Feature	Predicate Device: Diazyme Cystatin C	Candidate Device: Tina-Quant Cystatin C Gen. 2
Intended Use	The Diazyme Cystatin C Assay is an in-vitro diagnostic test for the quantitative determination of Cystatin C in serum or plasma by latex enhanced immunoturbidimetric method. The measurement of Cystatin C is used as an aid in the diagnosis and treatment of renal disease.	The Tina-Quant Cystatin C Gen.2 is an in vitro test for the quantitative determination of Cystatin C in human serum and lithium-heparin plasma on Roche automated clinical chemistry analyzers. Cystatin C measurements are used as an aid in the diagnosis and treatment of renal diseases.
Sample Types	Serum and plasma	Same
Permissible Anticoagulants	Li-heparin plasma K_2-EDTA plasma	Li-heparin plasma K_2-EDTA, K_3-EDTA plasma
Reference Method	colorimetric method	Same
Calibrator	5 Levels Cystatin C Calibrators and saline as the zero calibrator.	C.f.a.s. (Calibrator for automated systems), single level and use water as the zero calibrator. (C.f.a.s. cleared for use with Cystatin C assay in 510(k) k080811)
Calibration Stability	Any calibration frequency is dependent on instrument used. Additionally, that assay should be recalibrated and controls run with each new lot of reagent.	After reagent lot change and as required following quality control procedures.
Reagent Shelf Life Stability	Unopened: 2-8 °C until expiration date On-board in use: 4 weeks	Unopened: 2-8 °C until expiration date On-board in use: 8 weeks
Calibration Mode	6-point; Spine	Same

Traceability	Standardized against the Doumas manual reference method	**Assay:** This method has been standardized against ERM-DA471/IFCC reference material. **Calibrator**: The Cystatin C calibrator is traceable to ERM-DA471/IFCC reference material. The value assignment was carried out by turbidimetry on Hitachi 917 analyzer. **Control**: The Cystatin C control is traceable to ERM-DA471/IFCC reference material. The value assignment was carried out by turbidimetry on Hitachi 917 analyzer.
Instrument Platform	Hitachi 917 analyzer	**cobas c** 501 analyzer

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Substantial equivalence - differences

The following table compares the different features of the candidate device to the predicate device that was cleared in 510(k) k093680 and k080811.

Feature	Predicate Device: Diazyme Cystatin C	Candidate Device: Tina-Quant Cystatin C Gen. 2
Reagent Composition	R1: 100 mM Tris-buffer Solution R2: Suspension of anti-human Cystatin C chicken polyclonal antibody coated latex particles (< 0.5%).	R1: Solution of polymers in MOPS-buffered saline; preservative, stabilizers R2: Latex particles in glycine buffer coated with anti-Cystatin C antibodies (rabbit); preservative, stabilizers
Reagent On-Board Stability	on-board in use and refrigerated on the analyzers: 4 weeks	on-board in use and refrigerated on the analyzers: 8 weeks
Controls	Cystatin C Control	Cystatin C Control Set (3 levels) These two level control set was cleared for use with Cystatin C in k080811.

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Substantial equivalence - differences continued

Feature	Predicate Device: Diazyme Cystatin C	Candidate Device: Tina-Quant Cystatin C Gen. 2
Measuring Range	0.2 – 8.0 mg/L	0.40 – 6.80 mg/L
Expected Values	Age 18-55 0.62-1.16 mg/L	Age 21-77 0.61-0.95 mg/L
Hook Effect	Not tested	No hook effect up to 20 mg/L
Lower Limits of Measurement□	LoB: 0.04 mg/L LoD: 0.07 mg/L LoQ: 0.19 mg/L	LoB: 0.30 mg/L LoD: 0.40 mg/L LoQ: 0.40 mg/L

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Test principle

Tina-quant Cystatin C Gen.2 measures cystatin C in human serum and plasma on Roche automated clinical analyzer by turbidimetric method. The human cystatin C agglutinates with latex particles coated with anti-cystatin C antibodies. The aggregate is determined turbidimetrically at 546 nm.

Precision/ reproducibility

Precision was determined according to CLSI EP5-A2. The study included three human serum samples (0.56, 2.80, and 6.39 mg/L) and three control samples in two aliquots per run and two runs per day for 21 days.

Here are summaries of the repeatability and intermediate precision data.

Repeatability Summary

Specimen	Control 1	Control 2	Control 3	Human Serum 1	Human Serum 2	Human Serum 3
Total Mean (mg/L)	**1.00**	**1.84**	**4.12**	**0.560**	**2.80**	**6.39**
Within Run Imprecision SD (mg/L)	**0.02**	**0.02**	**0.03**	**0.010**	**0.02**	**0.04**
Within Run Imprecision CV%	**1.7**	**0.9**	**0.7**	**1.8**	**0.6**	**0.6**
Min (mg/L)	0.88	1.76	4.01	0.530	2.73	6.25
Max (mg/L)	1.04	1.89	4.22	0.590	2.88	6.55

Intermediate Precision

Specimen	Control 1	Control 2	Control 3	Human Serum 1	Human Serum 2	Human Serum 3
Total Mean (mg/L)	**1.00**	**1.84**	**4.12**	**0.560**	**2.80**	**6.39**
Total Imprecision SD (mg/L)	**0.02**	**0.03**	**0.06**	**0.011**	**0.04**	**0.07**
Total Imprecision CV%	**2.2**	**1.4**	**1.4**	**2.0**	**1.3**	**1.1**
Min (mg/L)	0.88	1.76	4.01	0.530	2.73	6.25
Max (mg/L)	1.04	1.89	4.22	0.590	2.88	6.55

Values that appear in bold type also appear in the labeling.

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Linearity/ assay reportable range

Linearity was assessed according to CLSI EP6-A with one batch of reagent, in one run, and with samples measured in triplicate. Two separate dilution series differing by sample type (serum and plasma) were prepared with thirteen levels for the plasma series and twenty one levels for the serum series. Lithium-heparin was used to prepare the plasma sample series. The highest concentration samples exceed the desired measuring range. Human Serum sample pool with high concentration of Cystatin C, spiked with recombinant Cystatin C. Human Plasma sample pool with high concentration of Cystatin C, spiked with recombinant Cystatin C

Measuring Ranges that are Supported by the Linearity Data (mg/L)

	Plasma	Serum
Range tested	0.046 – 8.893	0.0 – 7.578
Range found	0.0 – 8.893	0.00 – 7.578
Recommended measuring range	**0.40 – 6.80**	**0.40 – 6.80**

The first order (linear) regression is significant for both sample types.

Linear Regression Equation for Serum
$Y = 1.001x - 0.0057$ $R^2 = 0.999$
Linear Regression Equation for Plasma
$Y = 1.000x + 0.0000$ $R^2 = 0.999$

Traceability and stability

This method has been standardized against the ERM-DA471/IFCC reference material.

The reagent has been evaluated for transport, shelf-life, and open on-board stability.

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Detection Limit

LoB, LoD, and LoQ studies were performed based upon CLSI EP17-A2.

LoB Protocol: One blank sample was tested in n=5 with two analyzers with three reagent batches for six runs per day across three days.

LoD Protocol: Five low-analyte samples were measured in singlicate on two analyzers with three reagent batches for six runs per day across three days.

LoQ Protocol: A low Level Sample Set was prepared by diluting 5 human serum samples with an analyte free diluent (0.9% NaCl). The Low level Sample Set was tested in 2 replicates per sample on 5 days, one runs per day on one **cobas c** 501 analyzers. The mean concentration is plotted versus the % CV. The concentration at % CV of 13.3 is the LoQ.

The LoB, LoD, and LoQ claims represent the specifications for each.

LoB claim = 0.30 mg/L
LoD claim = 0.40 mg/L
LoQ claim = 0.40 mg/L at % CV of 13.3

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Analytical specificity - interference from endogenous substances

The reagent was evaluated with four endogenous substances, Hemoglobin, Lipemia, Bilirubin and Rheumatoid factor for potential interference with the measurement of Cystatin C.

One pool of human serum was spiked with the interferent. A second pool of human serum contained none. The two pools were mixed in different ratios to yield a dilution series with varying concentrations of the interferent.

The endogenous interference data are summarized in the table. Interference was tested at two levels of Cystatin C.

	no interference up to	Claim as it appears in the labeling.
Lipemia Level 1	2334 L index	No significant interference up to an L index of 1000.
Lipemia Level 2	2364 L index	
Hemolysis Level 1	1313 H index	No significant interference up to an H index of 1000.
Hemolysis Level 2	1461 H index	
Unconjugated Bilirubin Level 1	77 H index	No significant interference up to an I index of 60.
Unconjugated Bilirubin Level 2	73 H index	
Rheumatoid factor Level 1	1301 mg/L	Rheumatoid factor < 1200 IU/mL do not interfere
Rheumatoid factor Level 2	1216 mg/L	

All data passed the following acceptance criteria:

Recovery within ± 0.100 mg/L of initial values for samples ≤ 1.00 mg/L and within ± 10% for sample > 1.00mg/L.

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Analytical specificity - interference from common drugs

Seventeen commonly used drugs were examined for potential interference on measurement with **cobas c** Tina-Quant Cystatin C Gen. 2 reagent.

Two sample pools, containing a low and high concentration of Cystatin C are used. These sample pools are divided into an appropriate number of aliquots. One aliquot is not spiked with the drugs and it is used as the reference sample for Cystatin C concentration. The Cystatin C concentration in the sample is determined with n = 3 measurements on a **cobas c** 501 analyzer.

The other sample aliquots, with either the high or low Cystatin C concentrations, are spiked with the respective amount of drug. The Cystatin C concentration of the spiked aliquots are determined in triplicate and the mean of the triplicate determinations is compared to the Cystatin C concentration determined for the reference aliquot (mean of n=3).

The table below summarizes the common drug interferences data:

	Drug	Highest Concentration Shown Not to Interfere with Cystatin C (drug concentrations in mg/L)
1	Acetylcystein	150
2	Ampicillin - Na	1000
3	Ascorbic acid	300
4	Cyclosporine	5
5	Cefoxitin	2500
6	Heparin	5000U
7	Intralipid	10000
8	Levodopa	20
9	Methyldopa + 1.5	20
10	Metronidazole	200
11	Phenylbutazone	400
12	Doxycyclin	50
13	Acetylsalycilic acid	1000
14	Rifampicin	60
15	Acetaminophen	200
16	Ibubrofen	500
17	Theophylline	100

All data passed the following acceptance criteria:

Difference in recovery to the reference sample: $\leq \pm 10\%$

510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Method comparison with predicate device

A total of 103 human serum samples were tested in singlicate with the Cystatin C reagent from Diazyme on one Modular P and the CYSC2 reagent on one **cobas c** 501 analyzer.

Cystatin C values for n=103 human sera adult samples were obtained using the candidate reagent (y-axis) to the predicate reagent (x-axis) on the Roche/Hitachi **cobas c** 501 analyzer. Candidate sample concentrations ranged from 0.500 to 6.67 mg/L, and they were tested in singlicate. The values were regressed using the Passing/Bablok model to produce the following equation.

Passing/Bablok	Linear regression
Y = 0.997x – 0.064 mg/L	y = 1.031x – 0.153 mg/L
T = 0.937	r = 0.988

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Matrix comparison

Lithium-heparin, K_2-EDTA and K_3-EDTA are permissible anticoagulants for use with this reagent because they do not interfere with recovery of Cystatin C. In an internal study, a total of 57 tubes were collected per anticoagulant. Plasma results were compared to serum results and percent recovery was determined. In terms of % recovery. All data passed the following criteria: For sample concentrations ≤ 0.1 mg/L, the deviation must be $\leq \pm 10$ mg/L. For sample concentrations > 0.1 mg/L, the deviation must be $\leq \pm 10\%$.

anticoagulants	Sample concentration range tested (mg/L)	Claimed Measuring Range (mg/L)
Li-Heparin (full)	0.560 - 6.63	0.40 - 6.80
Li-Heparin (half)	0.650 - 5.04	
K_2-EDTA (full)	0.550 - 6.67	
K_2-EDTA (half)	0.630 - 5.05	
K_3-EDTA (full)	0.580 - 6.72	
K_3-EDTA (half)	0.620 - 4.89	
Gel Separation Tube	0.510 - 6.55	

In addition, method comparisons with plasma vs. serum were calculated with the following results:

Serum vs. Li-heparin P/B: $y = 1.010x + 0.020$, $r = 1.000$

Serum vs. K_2-EDTA P/B: $y = 1.020x - 0.010$, $r = 1.000$

Serum vs. K_3-EDTA P/B: $y = 1.030x + 0.000$, $r = 1.000$

Serum vs. Gel Separation P/B: $y = 1.000x - 0.010$, $r = 1.000$

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510(k) Summary for Tina-quant Cystatin C Test System, Calibrator and Control Set, Continued

Expected values/ reference range	Age 21-77 0.61 - 0.95 mg/L Samples of subjects from US panel of healthy subjects were used as a reference population (n=273) measured with Roche Tina-quant Cystatin C Gen.2. They were evenly distributed across gender and age between 21 and 77 years. The analysis of the data with the 2.5% and the 97.5 % percentile gave a Cystatin C range for from 0.61 mg/L to 0.95 mg/L.
Conclusion	The submitted information in this premarket notification supports a substantial equivalence decision.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

ROCHE DIAGNOSTICS
KHOA TRAN
REGULATORY AFFAIRS CONSULTANT
9115 HAGUE ROAD
INDIANAPOLIS IN 46250-0416

July 17,2014

Re: K141143
Trade/Device Name: Tina-quant Cystatin C Gen.2 Assay, C.f.a.s (Calibrator for automated systems) Cystatin C, Cystatin C Control Set Gen. 2
Regulation Number: 21 CFR 862.1225
Regulation Name: Creatinine test system
Regulatory Class: II
Product Code: NDY, JIT, JJX
Dated: May 1, 2014
Received: May 2, 2014

Dear Mr. Khoa Tran:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano
-S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
k141143

Device Name
Tina-quant Cystatin C Gen.2 Assay, C.f.a.s (Calibrator for automated systems) Cystatin C, Cystatin C Control Set Gen.2

Indications for Use *(Describe)*

The Tina-quant Cystatin C Gen.2 is an in vitro test for the quantitative determination of cystatin C in human serum and plasma on Roche/Hitachi cobas c systems. Cystatin C measurements are used as an aid in the diagnosis and treatment of renal diseases.

Calibrator:

The C.f.a.s. (Calibrator for automated systems) Cystatin C is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.

Control:

The Cystatin C Control Set Gen.2 is for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 807 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Ruth A. Chesler -S

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