DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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ROCHE DIAGNOSTICS OPERATIONS (RDO)
PATRICK STIMART
REGULATORY AFFAIRS CONSULTANT
9115 HAGUE ROAD
INDIANAPOLIS IN 46250

July 27, 2016

Re: K161817
Trade/Device Name: Tina-quant Cystatin C Gen.2
Regulation Number: 21 CFR 862.1225
Regulation Name: Creatinine test system
Regulatory Class: II
Product Code: NDY
Dated: June 27, 2016
Received: July 1, 2016

Dear Mr. Patrick Stimart:

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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k161817

Device Name
Tina-quant Cystatin C Gen.2

Indications for Use *(Describe)*
Tina-quant Cystatin 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.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Tina-quant Cystatin C Gen.2
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

In accordance with 21 CFR 807.87, Roche Diagnostics hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification Special 510(k).

The purpose of this Special 510(k) Premarket Notification is to inform FDA of the proposed modifications to the Tina-quant Cystatin C Gen.2 labeling and provide sufficient detail to support a determination of substantial equivalence. The primary change is the addition and expansion of sample stability claims. Other changes that will also be addressed are a reduction in the hook effect interference level claim and the addition of a warning against testing of patient samples containing human anti-rabbit antibodies (HARA).

Note: There were no prior submissions for this device for which FDA provided feedback related to the data or information needed to support substantial equivalence.

Submitter Name	Roche Diagnostics
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Date Prepared	June 24, 2016
Proprietary Name	Tina-quant Cystatin C Gen.2
Common Name	Cystatin C Gen.2
Classification Name	Cystatin C test system (21CFR862.1225, Class 2 device)
Product Codes	NDY
Predicate Devices	The candidate device is a modification of the predicate device. The device name, Tina-quant Cystatin C Gen.2, is unchanged from how it was cleared in 510(k) K141143
Establishment Registration	For the Tina-quant Cystatin C Gen.2, the establishment registration number for Roche Diagnostics GmbH in Mannheim, Germany is 9610126, and for Penzberg, Germany, 9610529. The establishment registration number for Roche Diagnostics in the United States is 1823260.

1. DEVICE DESCRIPTION

The Roche Tina-quant Cystatin C Gen.2 assay provides quantitative measurement of the cystatin C that is present in human serum and plasma. The reagents are packaged in a cassette with two bottles labeled with their instrument positioning, R1 (Reagent 1) and R2 (Reagent 2).

R1 contains a solution of polymers in MOPS-buffered saline with preservative and stabilizers. R2 is latex particles coated with anti-cystatin C antibodies (rabbit) in glycine buffer with preservatives and stabilizers.

Human cystatin C agglutinates with the antibody coated latex particles. The aggregate is determined turbidimetrically.

Note: Since Tina-quant Cystatin C Gen.2 is a reagent, drawings, schematics, illustrations, photos and figures are not pertinent to describe the device and therefore are not present in this submission.

2. INDICATIONS FOR USE

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.

Note: The intended use of the modified device, as described in its labeling, has not changed as a result of the modification.

3. TECHNOLOGICAL CHARACTERISTICS

The candidate device, Tina-quant Cystatin C Gen.2, has been modified from the predicated device with the addition of the following information to the assay method sheet.

- Added new room temperature and refrigerated serum and plasma sample stability information to the Specimen collection and preparation section.
- Added a warning to the Limitations and interference section regarding elevated cystatin C results in patient samples containing human anti-rabbit antibodies (HARA)
- In the Limitations and interference section, the Hook-effect limit was changed from 20 mg/L to a more conservative 12 mg/L.

The following tables compare the Tina-quant Cystatin C Gen.2 with its predicate device, Tina-quant Cystatin C Gen.2 (k141143).

Table 1 Assay Comparison, General Assay Features

Feature	Predicate Device Tina-quant Cystatin C Gen.2 (K141143)	Candidate Device Tina-quant Cystatin C Gen.2
Intended use / Indications for use	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.	same
Test principle	Particle enhanced immunoturbidimetric assay	same
Instrument	Roche/Hitachi cobas c 501	same
Sample type	Serum, Li-heparin, K2-, and K3- EDTA plasma	same
Calibrator	C.f.a.s. Cystatin C	same
Calibration frequency	After reagent lot change and after 90 days	same
Controls	Cystatin C Control Set Gen.2	same
Traceability/Standardization	This method has been standardized against ERM-DA471/IFCC	same
Reagent stability	Shelf life at 2-8°C: See expiration date on cobas c pack label On-board in use and refrigerated on the analyzer: 8 weeks	same

Table 2: Assay Comparison, Labeled Performance Characteristics

Feature	Predicate Device Tina-quant Cystatin C Gen.2 (K141143)	Candidate Device Tina-quant Cystatin C Gen.2
Measuring Range	0.40 - 6.80 mg/L	Same
Precision	See predicate method sheet	Same
LoB	0.30 mg/L	Same
LoD	0.40 mg/L	Same
LoQ	0.40 mg/L	Same
Hook effect	No false result occurs up to a cystatin C concentration of 20 mg/L.	No false result occurs up to a cystatin C concentration of 12 mg/L.
Method Comparison	See predicate method sheet	Same
Limitations - interference	See predicate method sheet	Same as predicate except for the following change and addition: "High dose hook-effect: No false result occurs up to a cystatin C concentration of 20 mg/L " was changed to "High dose hook-effect: No false result occurs up to a cystatin C concentration of 12 mg/L" The warning statement "In very rare cases falsely elevated results for Cystatin C will be obtained from samples taken from patients who have been treated with rabbit antibodies or have developed anti-rabbit antibodies." was added along with the supporting reference number 33 Kricka LH. Human Anti-Animal Antibody Interferences in Immunological Assays. Clin Chem 1999;45(7):942-956.

4. NON-CLINICAL PERFORMANCE EVALUATION

Based on the risk analysis, the modifications to the Tina-quant Cystatin C Gen.2 method sheet did not introduce any new risks to the performance of the assay.

To address the modifications, verification and validation activities, which are summarized below, demonstrated that all of the acceptance criteria were met.

4.1. Sample stability

Human serum and plasma (Li-heparin, K2-EDTA, K3-EDTA) patient samples are adjusted with cystatin C to cover the Tina-quant Cystatin C Gen.2 assay reportable measuring range. These samples are split into two sets, one set stored at 15-25 °C and the other at 2-8 °C. The samples are tested in triplicate on a **cobas c** 501 analyzer, and the median value is used to calculate the % difference from the result of the fresh sample at time zero.

4.2. High dose hook-effect

A human serum pool is adjusted to obtain a cystatin C concentration of > 24 mg/L. A 18 step dilution series is prepared by diluting with 0.9 % saline. These samples are tested on the **cobas c** 501 analyzer and the known concentration is compared to the result reported by the analyzer.

4.3. HARA interference

A customer inquiry made Roche aware of the potential for interference with Tina-quant Cystatin C Gen.2 assay test results in patient samples containing human anti rabbit antibodies (HARA). Internal testing was done at Roche to confirm the customer results.

This testing, customer information, and the information presented in the peer reviewed and published literature reference cited in the method sheet, support the addition of a warning statement, regarding the use of patient samples containing HARA, to the Limitations and interference section of the method sheet.

5. ADDITIONAL INFORMATION

The Tina-quant Cystatin C Gen.2 assay will continue to use the current C.f.a.s. Cystatin C (k080811) for calibration, and the Cystatin C Control Set Gen.2 (K141143) for quality control. There have been no changes to the C.f.a.s. Cystatin C and the Cystatin C Control Set Gen.2.

6. CONCLUSIONS

The submitted information in this premarket notification supports a substantial equivalence decision. The differences between predicated and candidate do not impact the indications for use or technological characteristics.