February 21, 2020

Roche Diagnostics Operations (RDO)
Barbara McWhorter
Regulatory Affairs Program Manager
9115 Hague Road
Indianapolis, Indiana 46250

Re: K192072
Trade/Device Name: Tina-quant C-Reactive Protein IV
Regulation Number: 21 CFR 866.5270
Regulation Name: C-reactive protein immunological test system
Regulatory Class: Class II
Product Code: DCN
Dated: August 20, 2019
Received: August 22, 2019

Dear Barbara McWhorter:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Carolina Kagan
Acting Chief, IMFB
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K192072

Device Name
Tina-quant® C-Reactive Protein IV

Indications for Use *(Describe)*
Tina-quant® C-Reactive Protein IV is an immunoturbidimetric assay for the in vitro quantitative determination of CRP in human serum and plasma on cobas c systems.

A C-reactive protein immunological test system is a device that consists of the reagents used to measure by immunochemical techniques the C-reactive protein in serum and plasma. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues.

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.

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Tina-quant® C-Reactive Protein IV
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 510(k).

The purpose of this Traditional 510(k) Premarket Notification is to obtain FDA review and clearance for the Tina-quant® C-Reactive Protein IV.

Submitter Name	Roche Diagnostics
Address	9115 Hague Road P.O. Box 50416 Indianapolis, IN 46250-0457
Contact	Barbara Ann McWhorter Phone: (317) 521-2336 FAX: (317) 521-2324 Email: barbara.mcwhorter@roche.com
Date Prepared	January 10, 2020
Proprietary Name	Tina-quant® C-Reactive Protein IV
Common Name	C-Reactive Protein
Classification Name	C-reactive protein immunological test system
Product Codes, Regulation Numbers	DCN, 21 CFR § 866.5270
Predicate Devices	Roche Diagnostics C-Reactive Protein Gen.3
Establishment Registration	Roche Diagnostics GmbH Mannheim, Germany: 9610126 Roche Diagnostics GmbH in Penzberg, Germany: 9610529 Roche Diagnostics Indianapolis IN, United States: 1823260

1. DEVICE DESCRIPTION

The Tina-quant® C-Reactive Protein IV reagent will be a liquid ready to use 2 component particle enhanced immunoturbidimetric assay.

Reagents - working solutions

R1: TRIS* buffer with bovine serum albumin; preservatives

R2 Latex particles coated with anti-CRP (mouse) in glycine buffer; immunoglobulins (mouse); preservative

* TRIS= Tris(hydroxymethyl)-aminomethane

The Tina-quant® C-Reactive Protein IV assay will be based on the DUREL technology (dual radius enhanced latex - technology) which is also used in C-Reactive Protein Gen.3 predicate method. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The aggregates are determined turbidimetrically.

2. INDICATIONS FOR USE

Tina-quant® C-Reactive Protein IV is an immunoturbidimetric assay for the in vitro quantitative determination of CRP in human serum and plasma on **cobas c** systems.

A C-reactive protein immunological test system is a device that consists of the reagents used to measure by immunochemical techniques the C-reactive protein in serum and plasma. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues.

3. TECHNOLOGICAL CHARACTERISTICS

Table 1: Tina-quant® C-Reactive Protein IV Technical Characteristics

Feature	Predicate C-Reactive Protein Gen.3 k083444	Candidate Device Tina-quant® C-Reactive Protein IV k192072
Intended Use	Immunoturbidometric assay for the in vitro quantitative determination of CRP in human serum and plasma on Roche automated clinical chemistry analyzers.	Tina-quant® C-Reactive Protein IV is an immunoturbidimetric assay for the in vitro quantitative determination of CRP in human serum and plasma on **cobas c** systems.

Feature	Predicate C-Reactive Protein Gen.3 k083444	Candidate Device Tina-quant® C-Reactive Protein IV k192072
Indications for Use	Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues.	A C-reactive protein immunological test system is a device that consists of the reagents used to measure by immunochemical techniques the C-reactive protein in serum and plasma. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues.
Assay Method	Particle enhanced immunoturbidimetric assay	Same
Detection Method	turbidimetric	Same
Instrument Platform	Roche automated clinical chemistry analyzers	**cobas c** 501 analyzer
Sample Type/Matrix	Serum Plasma: K2- or K3-EDTA, lithium heparin	Same
Calibrator	Calibrator f.a.s. Proteins	Same
Calibration Method	6-point spline	Same
Calibration Interval	After reagent lot change As required following quality control procedures	- after reagent lot change - after 3 weeks on-board the analyzer - after 6 months when using a single reagent lot - as required following quality control procedures
Controls	Precinorm Protein Precipath Protein PreciControl ClinChem Multi 1 PreciControl ClinChem Multi 2	Precinorm Protein Precipath Protein PreciControl ClinChem Multi 1 PreciControl ClinChem Multi 2
Traceability/Standardization	Standardized against an internal method traceable to CRM 470 (RPPHS - Reference Preparation for Proteins in Human Serum).	Standardized against the certified reference material in human serum of the IRMM (Institute for Reference Materials and Measurements) ERM-DA474/IFCC.
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: 12 weeks	Same
Measuring Range	0.3 to 350 mg/L	3 to 350 mg/L

<table>
<tr><th>Feature</th><th>Predicate C-Reactive Protein Gen.3 k083444</th><th>Candidate Device Tina-quant® C-Reactive Protein IV k192072</th></tr>
<tr><td rowspan="4">Precision</td><td>Repeatability
<table><tr><th></th><th>Mean (mg/L)</th><th>SD (mg/L)</th><th>CV%</th></tr><tr><td>CRP T Control N</td><td>3.35</td><td>0.04</td><td>1.2</td></tr><tr><td>Precipath Protein</td><td>44.4</td><td>0.6</td><td>1.3</td></tr><tr><td>Human Serum 1</td><td>0.57</td><td>0.02</td><td>3.6</td></tr><tr><td>Human Serum 2</td><td>1.56</td><td>0.03</td><td>1.6</td></tr><tr><td>Human Serum 3</td><td>43.2</td><td>0.5</td><td>1.2</td></tr></table></td><td>Repeatability
<table><tr><th></th><th>Mean (mg/L)</th><th>SD (mg/L)</th><th>CV%</th></tr><tr><td>Precinorm Protein</td><td>9.69</td><td>0.128</td><td>1.3</td></tr><tr><td>Precipath Protein</td><td>55.2</td><td>0.859</td><td>1.6</td></tr><tr><td>Human Serum 2</td><td>4.55</td><td>0.0702</td><td>1.5</td></tr><tr><td>Human Serum 3</td><td>10.6</td><td>0.167</td><td>1.6</td></tr><tr><td>Human Serum 4</td><td>82.4</td><td>1.82</td><td>2.2</td></tr><tr><td>Human Serum 5</td><td>186</td><td>3.76</td><td>2.0</td></tr><tr><td>Human Serum 6</td><td>331</td><td>4.40</td><td>1.3</td></tr></table></td></tr>
<tr><td>Intermediate Precision
<table><tr><th></th><th>Mean (mg/L)</th><th>SD (mg/L)</th><th>CV%</th></tr><tr><td>CRP T Control N</td><td>3.06</td><td>0.09</td><td>2.9</td></tr><tr><td>Precipath Protein</td><td>43.6</td><td>0.8</td><td>1.9</td></tr><tr><td>Human Serum 1</td><td>0.51</td><td>0.06</td><td>11.1</td></tr><tr><td>Human Serum 2</td><td>1.44</td><td>0.06</td><td>3.9</td></tr><tr><td>Human Serum 3</td><td>41.3</td><td>0.7</td><td>1.7</td></tr></table></td><td>Intermediate Precision
<table><tr><th></th><th>Mean (mg/L)</th><th>SD (mg/L)</th><th>CV%</th></tr><tr><td>Precinorm Protein</td><td>9.69</td><td>0.142</td><td>1.5</td></tr><tr><td>Precipath Protein</td><td>55.2</td><td>1.04</td><td>1.9</td></tr><tr><td>Human Serum 2</td><td>4.55</td><td>0.0735</td><td>1.6</td></tr><tr><td>Human Serum 3</td><td>10.6</td><td>0.206</td><td>1.9</td></tr><tr><td>Human Serum 4</td><td>82.4</td><td>1.97</td><td>2.4</td></tr><tr><td>Human Serum 5</td><td>186</td><td>4.39</td><td>2.4</td></tr><tr><td>Human Serum 6</td><td>331</td><td>5.80</td><td>1.8</td></tr></table></td></tr>
<tr><td>LoB</td><td>0.2 mg/L</td><td>Same</td></tr>
<tr><td>LoD</td><td>0.3 mg/L</td><td>Same</td></tr>
<tr><td>LoQ</td><td>0.6 mg/L</td><td>3 mg/L</td></tr>
</table>

Feature	Predicate C-Reactive Protein Gen.3 k083444	Candidate Device Tina-quant® C-Reactive Protein IV k192072
Method Comparison: Predicate vs Candidate	Passing Bablok: Y=0.985x+0.278 R=0.999 N=110 Min=3.06/Max=347 mg/L	
Interferences:	Serum Index: I=60 mg/dL H=1000 mg/dL L=1000 RH: no interference up to 1200 IU/mL Immunoglobulins: no interference up to 50 g/L	Same

4. NON-CLINICAL PERFORMANCE EVALUATION

The following performance data were provided in support of the substantial equivalence determination:

Precision according to CLSI EP5-A3

Detection Limit: LoB, LoD and LoQ according to CLSI EP17-A2

Linearity according to CLSI EP6-A

Interferences- L, H and I Indices

Interferences – Albumin, Immunoglobulin (IgG) and Rheumatoid Factors

Interference - Drugs

Matrix Comparison - Anticoagulants

Method Comparison to Predicate

All performance specifications were met.

4.1. Precision: Repeatability and Intermediate Precision (CLSI EP05-A3)

Precision measurements were conducted to evaluate repeatability (within-run precision) and the intermediate precision (within-laboratory precision) according the CLSI guideline EP05-A3.

The Tina-quant® C-Reactive Protein IV reagent was evaluated on a single **cobas c** 501 analyzer according to CLSI guideline EP05-A3. The protocol consisted of 4 human serum samples along with 2 controls (Precinorm Protein and Precipath Protein) which were analyzed in 2 parts for 21 days. Two aliquots of each sample were randomized and then analyzed on 3 lots of reagents. One operator performed all analysis along with utilizing 1 calibration throughout the 21-day study period.

Table 2: Repeatability Summary

Specimen	Mean (mg/L)	SD (mg/L)	CV %
Precinorm Protein	9.69	0.128	1.3
Precipath Protein	55.2	0.859	1.6
Serum 2	4.55	0.0702	1.5
Serum 3	10.6	0.167	1.6
Serum 4	82.4	1.82	2.2
Serum 5	186	3.76	2.0
Serum 6	331	4.40	1.3

Table 3: Intermediate/Within Lab Precision Summary

Specimen	Mean (mg/L)	SD (mg/L)	CV %
Precinorm Protein	9.69	0.142	1.5
Precipath Protein	55.2	1.04	1.9
Serum 2	4.55	0.0735	1.6
Serum 3	10.6	0.206	1.9
Serum 4	82.4	1.97	2.4
Serum 5	186	4.39	2.4
Serum 6	331	5.80	1.8

4.2. Analytical Sensitivity (CLSI EP17-A2)

4.2.1. Limit of Blank (LoB)

LoB of the Tina-quant® C-Reactive Protein IV assay was tested on 3 reagent lots. Ten aliquots of analyte free saline were analyzed on 1 Roche **cobas c** 501 analyzer in 6 runs over 3 days, for a total of N=60 determinations per lot.

Table 4: LoB

Claimed LoB [mg/L]	Observed LoB [mg/L]
0.2	0.0700

4.2.2. Limit of Detection (LoD)

LoD of the Tina-quant® C-Reactive Protein IV assay was tested on 3 reagent lots. Five samples of low analyte level human serum were analyzed, each with 2 aliquots, on 1 Roche **cobas c** 501 analyzer, in 6 runs, over 3 days, for a total of N=60 determinations per lot.

Table 5: LoD

Claimed LoD [mg/L]	Observed LoD [mg/L]
0.3	0.137

4.2.3. Limit of Quantitation (LoQ)

The LoQ of Tina-quant® C-Reactive Protein IV assay was tested on 3 reagent lots. Nine low concentration human serum samples (in the range from LoB up to approximately 2 times the specified LoQ) were analyzed on 1 Roche **cobas c** 501 analyzer, in 5 runs, with 5 aliquots of each sample for a total of N=25 determinations per sample per lot.

Table 6: LoQ

Claimed LoQ [mg/L]	Observed LoQ [mg/L]
3	0.313

4.3. Linearity/Assay Reportable Range (CLSI EP06-A)

The dilution series was prepared from native unmodified human serum sample pools and then analyzed on using Tina-quant® C-Reactive Protein IV reagent. The dilution series was prepared resulting in 15 levels (including the high and low concentration pools). The diluted samples spanned the measuring range including a non-zero sample below the low end of measuring range and a sample over the high end of measuring range. Each dilution level was measured in triplicate ($n \geq 3$).

Table 7: Linearity

Sample type	Linear Regression	Claimed Measuring Range
Serum	y=1.002x-0.0169 Pearson correlation coefficient (R)=0.9994	3 to 350 mg/L

4.4. Endogenous Interference

4.4.1. L, H, and I Indices

The effect on quantitation of Tina-quant® C-Reactive Protein IV in the presence of lipemia, hemolysis and bilirubin were determined at 2 levels, 5-10 mg/L and 35-100 mg/L c-reactive protein, utilizing a dilution set of the added interfering substances. Eleven level serial dilution sets were prepared. Each of the 11 interferent levels were measured in triplicate from low to high concentration. All dilution levels for each interferent were measured in 1 run. The mean concentration of the 3 replicates at each level was used to calculate recovery to the known c-reactive protein concentration.

Table 8: Interference – L, H and I Indices

Interferent	Claim No interference up to
Lipemia	1000 L Index
Hemolysis	1000 H Index
Bilirubin	60 I Index
Ditauro Bilirubin	60 I Index

4.4.2. Albumin, Immunoglobulin (IgG) and Rheumatoid Factors Interference

The effect on quantitation of Tina-quant® C-Reactive Protein IV in the presence of albumin, IgG and rheumatoid factors were determined at 2 levels, 5-10 mg/L and 35-100 mg/L c-reactive protein, utilizing a dilution set of the added interfering substances. Eleven level serial dilution sets were prepared. Each of the eleven interferent levels were measured in triplicate from low to high concentration. All dilution levels for each interferent were measured in 1 run. The median

concentration of the 3 replicates at each level was used to calculate recovery to the known c-reactive protein concentration.

Table 9: Interference – Albumin, Immunoglobulin (IgG) and Rheumatoid Factors

Interferent	Claim No interference up to
Albumin	60 g/L
IgG	50 g/L
RF Factor	1200 IU/mL

4.5. Exogenous Interferences – Drugs

The effect on quantitation of Tina-quant® C-Reactive Protein IV in the presence of potentially interfering drugs were determined at 2 levels, 5-10 mg/L and 35-100 mg/L c-reactive protein. One portion of each pool was spiked with the respective amount of drug and the other portion of the pool with solvent used to dissolve the drug, which was used for the baseline reference c-reactive protein concentration. The c-reactive protein mean concentration of both portions was determined in N=5 results. The mean % Recovery was calculated when comparing the drug spiked portions to the c-reactive protein baseline reference mean concentration.

Table 10: Exogenous Interference - Drugs

Drug	Tested Up To With No Interference (mg/L)
N-Acetylcysteine	1660
Ampicillin-Na	1000
Ascorbic acid	300
Cefoxitin	6600
Heparin	5000 IU/L
Levodopa	20
Methyldopa + 1.5	22.5
Metronidazole	200
Doxycyclin	50
Acetylsalicylic acid	1000
Rifampicin	60
Ticarcillin	225
Penicillamin	24

Phenylbutazone	400
Cyclosporine	5
Acetaminophen	200
Ibuprofen	500
Theophylline	100

4.6. Sample Matrix Comparison

The effect on quantitation of c-reactive protein in the presence of anticoagulants with the Tina-quant® C-Reactive Protein IV reagent was determined on the **cobas c** 501 analyzer by comparing values obtained from native samples (single donors) drawn into serum, Li-Heparin, K2- and K3-EDTA plasma primary tubes.

Table 11: Sample Matrix Comparison

Anticoagulant	Linear Regression	Range Tested [mg/L]
Serum vs. Li-Heparin	y = 1.029x -0.192, r = 0.999	3.34 to 344
Serum vs. K2-EDTA	y = 1.024x – 0.201, r = 0.999	3.34 to 344
Serum vs. K3-EDTA	y = 1.024x – 0.258, r = 0.999	3.34 to 344

4.7. Method Comparison to Predicate

A method comparison of the Tina-quant® C-Reactive Protein IV on the **cobas c** 501 analyzer versus the predicate device, Roche Diagnostics C-Reactive Protein Gen.3 was completed. One hundred ten native, unaltered serum samples, were tested in 1 run on 1 **cobas c** 501 analyzer in singlet using 1 lot of reagent. All samples were also testing for icteric, lipemic and hemolytic interference via analyzer serum indices. Statistics were created using Passing/Bablok and weighted Deming regression analysis.

	Passing/Bablok Regression	Weighted Deming Regression
Slope	0.985	0.979
Intercept	+0.278	+0.296
Correlation (Pearson)	0.999	0.999

4.8. Stability

The stability studies and acceptance criteria have been reviewed and found to be acceptable. The stability data supports Roche Diagnostic's claims as reported on the package labeling.

5. FDA GUIDANCE

FDA Guidance for Industry and FDA Staff: Review Criteria for Assessment of C-Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein (cCRP) Assays was followed in this 510(k) submission.

6. ADDITIONAL INFORMATION

Other Devices Required But Not Provided:

- Calibrator f.a.s Proteins, k133330
- Precinorm Protein, k133330
- Precipath Protein, k133330
- PreciControl ClinChem Multi 1, k133330
- PreciControl ClinChem Multi 2, k133330

There have been no changes to these items marketed with the new Tina-quant® C-Reactive Protein IV.