DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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ROCHE DIAGNOSTICS OPERATIONS (RDO)
PATRICK STIMART
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December 9, 2014

Re: K141925
Trade/Device Name: TPUC3 Total Protein Urine/CSF Gen.3
Regulation Number: 21 CFR 862.1645
Regulation Name: Urinary protein or albumin (nonquantitative) test system
Regulatory Class: I exempt, meets limitations of exemptions per 862.9 (c)(1)(4)
Product Code: JIQ
Dated: November 7, 2014
Received: November 10, 2014

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)*
k141925

Device Name
Total Protein Urine/CSF Gen.3

Indications for Use *(Describe)*
In vitro test for the quantitative determination of the total protein concentration in urine and cerebral spinal fluid.

Protein measurements in urine are used in the diagnosis and treatment of disease conditions such as renal or heart diseases, or thyroid disorders.
CSF protein measurements are used in the diagnosis and treatment of conditions such as meningitis, brain tumors, and infections of the central nervous systems.

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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510(k) Summary for Total Protein Urine/CSF Gen.3

Introduction

The following information provides sufficient detail to understand the basis for a determination of substantial equivalence according to the requirements of 21 CFR 807.92.
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.

Applicant

This Special 510(k) premarket notification was prepared by Patrick Stimart from Roche Professional Diagnostics Regulatory Affairs and submitted on July 15, 2014.

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Candidate device

Proprietary name: TPUC3 Total Protein Urine/CSF Gen.3
Common name: Total Protein Urine/CSF

Measurand

Total Protein

Predicate device

The candidate device is a modification of the predicate device. The device name, TPUC3 Total Protein Urine/CSF Gen.3, is unchanged from how it was cleared in 510(k) K071239.

Regulatory classification of device

Table 1: Regulatory Classification of Candidate Device

Device Classification Name	Urinary protein or albumin test system
Produce Code	JIQ
Device Class	I*
Regulation	862.1645
Panel	Clinical Chemistry

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510(k) Summary for Total Protein Urine/CSF Gen.3,
Continued

Regulatory classification of device (Continued)	*Although the regulation for this assay lists it as Class I, exempt from 510(k) requirements, a 510(k) submission is required because the Total Protein Urine/CSF Gen.3 assay meets the limitations for exemption found in 21 CFR 862.9 (c) 1 and 4.
Device description	The Total Protein Urine/CSF assay provides quantitative measurement of total protein that is present in human urine and cerebral spinal fluid (CSF). Measurement is accomplished using a turbidimetric method. Reagents for the COBAS Integra 400 plus analyzer are packaged in a **cobas c** pack with two bottles labeled with their instrument positioning, Reagent R1 in position B and Reagent SR in position C. R1 contains Sodium Hydroxide: 677 mmol/L; EDTA-Na: 74 mmol/L SR contains Benzethonium chloride: 32 mmol/L
Intended use/indications for use	In vitro test for the quantitative determination of the total protein concentration in urine and cerebral spinal fluid. Protein measurements in urine are used in the diagnosis and treatment of disease conditions such as renal or heart diseases, or thyroid disorders. CSF protein measurements are used in the diagnosis and treatment of conditions such as meningitis, brain tumors and infections of the central nervous systems. Note: The intended use of the modified device, as described in its labeling, has not changed as a result of the modification.
Special conditions for use	For prescription use only
Special instruments required	For use on the Roche COBAS Integra 400 plus analyzer

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Device modification

The candidate device, Total Protein Urine/CSF Gen.3, has been modified from the predicate device with the addition of the following information to the Limitations-interferences section of the labeling:

- Patient samples containing greater than 6.4 g/L of organically bound iodine from Radiopaque media (e.g. Hexabrix) may have falsely elevated results.
- High levels of homogentisic acid can be found in the urine of patients with the rare genetic disorder Alkaptonuria[10]. Homogentisic acid in urine samples at concentration greater than 1.2 mmol/L can cause falsely elevated results.
- There is no high dose hook effect at protein concentrations up to 100 g/L.

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Similarities

The table compares features of the candidate device to the predicate device that was cleared in K071239.

Table 2: Similarities between Predicate and Candidate Devices

Feature	**Predicate Device** Total Protein Urine/CSF Gen.3	**Candidate Device** Total Protein Urine/CSF Gen.3
Intended use/indications for use	In vitro test for the quantitative determination of the total protein concentration in urine and cerebrospinal fluid on COBAS INTEGRA systems. Protein measurements in urine are used in the diagnosis and treatment of disease conditions such as renal or heart diseases, or thyroid disorders, which are characterized by proteinuria or albuminuria. CSF protein measurements are used in the diagnosis and treatment of conditions such as meningitis, brain tumors and infections of the central nervous systems.	same
Test principle	Turbidimetric method	same
Sample volume	10 µL	same
Sample types	Urine and cerebral spinal fluid (CSF)	same
Reagents	R1: Sodium hydroxide 677 mmol/L; EDTA-Na 74 mmol/L SR: Benzethonium chloride 32 mmol/L	same

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Similarities, continued

Table 4: Similarities between Predicate and Candidate Devices

Feature	**Predicate Device** Total Protein Urine/CSF Gen.3	**Candidate Device** Total Protein Urine/CSF Gen.3
Calibration interval	COBAS INTEGRA 400 plus system: ▪ each **cobas c** pack ▪ every 43 days ▪ as required following quality control procedures	same
Traceability	Traceability: This method has been standardized against the National Bureau of Standards Reference Material SRM-927 using the biuret method for the quantitation of protein.	same
Reagent stability	Shelf life at 15-25 °C See expiration date on **cobas c** pack label COBAS INTEGRA 400 plus system On-board in use at 10-15 °C 12 weeks	same
Measuring range	40-2000 mg/L (4-200mg/dL)	same
Lower detection limit	40 mg/L (4 mg/dL)	same
Expected values	Urine: 24h: < 150 mg/24 h CSF: 150-450 mg/L (15-45 mg/dL) Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.	same

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Differences

Table 5: Differences between Predicate and Candidate Devices

Feature	**Predicate Device** Total Protein Urine/CSF Gen.3	**Candidate Device** Total Protein Urine/CSF Gen.3
Instrument platform	COBAS Integra 400/400+/700/800	COBAS Integra 400+
Calibrator	C.f.a.s. TPUC 200	C.f.a.s. PUC
Controls	Use commercially available urine and CSF protein controls or other suitable control material.	Precinorm PUC, Precipath PUC In addition, other suitable control material can be used.
Limitations – interference	See predicate method sheet	Same as predicate except for the following additions: Patient samples containing greater than 6.4 g/L of organically bound iodine from Radiopaque media (e.g. Hexabrix) may have falsely elevated results. High levels of homogentisic acid can be found in the urine of patients with the rare genetic disorder Alkaptonuria[10]. Homogentisic acid in urine samples at concentration greater than 1.2 mmol/L can cause falsely elevated results. There is no high dose hook effect at protein concentrations up to 100 g/L.

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Summary of performance data	Based on the risk analysis, the modifications to the Total Protein Urine/CSF Gen.3 did not introduce any new risks to the performance of the assay. To address the modifications, performance data from verification and validation testing demonstrated that all of the acceptance criteria were met.
Testing of interference by radiopaque media	Testing is performed in pooled human urine samples at two different total protein levels on the Integra 400 plus analyzer. Each level is spiked with varying levels of the radiopaque media Hexabrix containing organically bound iodine (10 dilution steps per level) which were tested in triplicate and the median value was used to calculate % deviation from expected concentration. Acceptance criterion: Deviation ≤ ± 10 % Results: At an organically bound Iodine concentration of 6.4 g/L; Deviation = 5.6 % at level 1 (92.5 mg/L total protein) Deviation = 9.7 % at level 2 (961 mg/L total protein) The results meet the criterion of ≤ ± 10 % deviation at all concentrations tested up to and including 6.4 g/L of organically bound iodine, and thus support the claim of no interference up to 6.4 g/L of organically bound iodine from Radiopaque media.
Testing of interference by Homogentisic acid	The same protocol as described for radiopaque media above except that human urine samples were spiked with homogentisic acid instead of Hexabrix. Acceptance criterion: Deviation ≤ ± 10 % Results: At a homogentisic acid concentration of 1.2 mmol/L; Deviation = 6.8 % at level 1 (107 mg/L total protein) Deviation = 6.9 % at level 2 (1180 mg/L total protein) The results meet the criterion of ≤ ± 10 % deviation at all concentrations tested up to and including 1.2 mmol/L of homogentisic acid, and thus support the claim of no interference up to 1.2 mmol/L of homogentisic acid.

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Testing for high dose hook effect

A pooled human urine sample was spiked with human Albumin up to a total protein concentration of 100 g/L. A dilution series was prepared by diluting the sample with un-spiked pooled human urine sample. The samples were tested in triplicate. The median was calculated.

Acceptance criterion:
No false result reported up to a protein concentration 100 g/L.
All samples above the measuring range are flagged.

Results: No false result reported up to a protein concentration up to100 g/L.
All samples above the measuring range are flagged as either being above the measuring range or above the absorbance limit.

The results meet the criterion of no false result reported up to a protein concentration 100 g/L, and thus support the claim that there is no high dose hook effect at protein concentrations up to 100 g/L.

Conclusion

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