K072638

OCT 19 2007

510(k) Summary – Roche/Hitachi Urinary/CSF Protein

Introduction and purpose of submission

Roche Diagnostics Corporation hereby submits this Special 510(k): Device Modification to provide notification of modifications to our Urine/CSF Protein test system. The reagent was originally cleared as an endpoint, turbidimetric assay for use as Roche/Hitachi Urinary/CSF Protein via K913615. Subsequent to this filing, a rate (kinetic) application was developed, in addition to the original endpoint assay, and applied to the Hitachi family of analyzers. This additional rate application did not involve any changes to the reagent formulation, and is the sole purpose of this Special 510(k).

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510(k) Summary – Roche/Hitachi Urinary/CSF Protein,
Continued

Submitter name, address, contact

Roche Diagnostics
9115 Hague Rd
Indianapolis IN 46250
(317) 521-7637

Contact person: Kerwin Kaufman

Date prepared: September 17, 2007

Device Name

Proprietary name: Roche/Hitachi Urinary/CSF Protein
Common name: Total Protein
Classification name: Total Protein test system

Classification

The FDA has classified Total protein test system in Class II.

Panel	Classification Number	Classification Name	Regulation Citation
75 Clinical Chemistry	JGQ	Total Protein test system	21 CFR 862.1635

Establishment registration

The establishment registration number for Roche Diagnostics GmbH Penzberg is 9610529.

The establishment registration number for Roche Diagnostics Corporation Indianapolis is 1823260.

Device Description

The Roche/Hitachi Urinary/CSF Protein reagent is an in vitro test for the quantitative determination of protein in urine and cerebrospinal fluid on Roche automated clinical chemistry analyzers.

The modified device includes both the original endpoint assay and the additional rate assay. The new rate assay was developed to provide absorbance limits that will flag high protein samples with high absorbance, thus eliminating the need for prescreening samples for high protein levels. The endpoint assay still requires sample prescreening or inspection of the Reaction Monitor display after completion of the reaction to ensure that high samples are detected and appropriately diluted for rerun. The attached labeling provides a more complete description of this potential high sample / prozone effect.

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510(k) Summary – Roche/Hitachi Urinary/CSF Protein, Continued

Intended use and Summary

Intended Use

The Roche/Hitachi Urinary/CSF Protein reagent is an in vitro test for the quantitative determination of protein in urine and cerebrospinal fluid on Roche automated clinical chemistry analyzers.

Summary

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 diagnosis and treatment of disease conditions such as meningitis, brain tumors and infections of the central nervous systems.

Predicate Device

We claim substantial equivalence to the Hitachi Urinary/CSF Protein test system cleared as K913615.

Substantial equivalency – Similarities

The table below indicates the similarities and differences between the modified Urinary/CSF Protein reagent and the predicate device.

Continued on next page

510(k) Summary – Roche/Hitachi Urinary/CSF Protein,
Continued

Feature	Predicate device: Roche/Hitachi Urinary/CSF Protein K913615	Modified device: Roche/Hitachi Urinary/CSF Protein, Additional RATE Application
General		
Intended Use	For the quantitative determination of protein in urine (U) and cerebrospinal fluid (CSF).	In vitro test for the quantitative determination of protein in urine and cerebrospinal fluid on Roche automated clinical chemistry analyzers.
Specimen	Urine and CSF	Same
Application	Endpoint assay	Endpoint and Rate application
Instrument Platforms	Roche/Hitachi analyzers	Same
Test Principle		
Reference method	Turbidimetric	Same
Reagent information		
Reagent composition	R1: Sodium hydroxide 530 mmol/L, EDTA sodium, 74 mmol/L R2: Benzethonium chloride 32 mmol/L	Same
Stability - shelf life and on-board	20-25 °C until expiration date R1: 3 weeks on board at 2-12 °C R2: 3 weeks on board at 2-12 °C	15-25 °C until expiration date R1: 21 days on board and refrigerated on the analyzer R2: 21 days on board and refrigerated on the analyzer
Calibrator	Preciset U/CSF Protein 5 levels: 10, 20, 40, 80, 200 mg/dL 0.9 % NaCl used for a 0 mg/dL level	Same
Quality control	Commercially available urine and CSF protein controls	Same
Traceability	This method has been standardized against the National Bureau of Standards Reference Material SRM 927a using the biuret method for the quantitation of protein.	Same

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Substantial equivalency – Similarities

<table>
<tr><th>Feature</th><th>Predicate device:
Roche/Hitachi Urinary/CSF Protein
K913615</th><th>Modified device:
Roche/Hitachi Urinary/CSF Protein,
Additional RATE Application</th></tr>
<tr><td colspan="3">Performance characteristics</td></tr>
<tr><td>Precision</td><td>Urine: (data from K913615 labeling, page 33)

<table>
<tr><th>Urine</th><th colspan="3">Within-run (n = 120)</th></tr>
<tr><td>Sample</td><td>Mean
mg/dL</td><td>SD
mg/dL</td><td>CV
%</td></tr>
<tr><td>Control 1</td><td>8.2</td><td>0.53</td><td>6.4</td></tr>
<tr><td>Control 2</td><td>22.4</td><td>0.30</td><td>1.4</td></tr>
<tr><td>Control 3</td><td>182.4</td><td>0.90</td><td>0.5</td></tr>
</table>

<table>
<tr><th>Urine</th><th colspan="3">Total (n = 120)</th></tr>
<tr><td>Sample</td><td>Mean
mg/dL</td><td>SD
mg/dL</td><td>CV
%</td></tr>
<tr><td>Control 1</td><td>8.2</td><td>0.65</td><td>7.9</td></tr>
<tr><td>Control 2</td><td>22.4</td><td>0.55</td><td>2.5</td></tr>
<tr><td>Control 3</td><td>182.4</td><td>1.60</td><td>0.9</td></tr>
</table>

CSF: (data from K913615 labeling, page 33)

<table>
<tr><th>CSF</th><th colspan="3">Within-run</th></tr>
<tr><td>Sample</td><td>Mean
mg/dL</td><td>SD
mg/dL</td><td>CV
%</td></tr>
<tr><td>Control 1 (n=120)</td><td>11.4</td><td>0.42</td><td>3.7</td></tr>
<tr><td>Control 2 (n=119)</td><td>23.8</td><td>0.31</td><td>1.3</td></tr>
<tr><td>Control 3 (n=119)</td><td>81.0</td><td>0.60</td><td>0.7</td></tr>
</table>

<table>
<tr><th>CSF</th><th colspan="3">Total</th></tr>
<tr><td>Sample</td><td>Mean
mg/dL</td><td>SD
mg/dL</td><td>CV
%</td></tr>
<tr><td>Control 1 (n=120)</td><td>11.4</td><td>0.59</td><td>5.1</td></tr>
<tr><td>Control 2 (n=119)</td><td>23.8</td><td>0.49</td><td>2.0</td></tr>
<tr><td>Control 3 (n=119)</td><td>81.0</td><td>0.74</td><td>0.9</td></tr>
</table></td><td>Urine:
Within run and Between run:

<table>
<tr><th>Urine</th><th colspan="3">Within-run (n = 21)</th><th colspan="3">Between-run (n = 10)</th></tr>
<tr><td>Sample</td><td>Mean
mg/dL</td><td>SD
mg/dL</td><td>CV
%</td><td>Mean
mg/dL</td><td>SD
mg/dL</td><td>CV
%</td></tr>
<tr><td>Human urine</td><td>10.0</td><td>0.52</td><td>5.2</td><td>12.0</td><td>0.46</td><td>3.8</td></tr>
<tr><td>Control 1</td><td>21.7</td><td>0.42</td><td>1.9</td><td>34.5</td><td>0.60</td><td>1.7</td></tr>
<tr><td>Control 2</td><td>67.3</td><td>0.66</td><td>1.0</td><td>114.37</td><td>1.30</td><td>1.1</td></tr>
</table>

CSF:
Within run and Between run:

<table>
<tr><th>CSF</th><th colspan="3">Within-run (n = 20)</th><th colspan="3">Between-run (n = 10)</th></tr>
<tr><td>Sample</td><td>Mean
mg/dL</td><td>SD
mg/dL</td><td>CV
%</td><td>Mean
mg/dL</td><td>SD
mg/dL</td><td>CV
%</td></tr>
<tr><td>Control 1</td><td>23.1</td><td>0.20</td><td>0.9</td><td>29.3</td><td>0.30</td><td>1.0</td></tr>
<tr><td>Control 2</td><td>53.6</td><td>0.36</td><td>0.7</td><td>90.2</td><td>0.56</td><td>0.6</td></tr>
</table></td></tr>
</table>

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Substantial equivalency – Similarities (continued)

Feature	Predicate device: Roche/Hitachi Urinary/CSF Protein K913615	Modified device: Roche/Hitachi Urinary/CSF Protein, Additional RATE Application
Measuring range	Endpoint Assay: 2-200 mg/dL If results exceed the upper limit of the measuring range, dilute the specimen with isotonic saline and repeat the assay.	Endpoint Assay: 2-200 mg/dL Rate Assay: 6-200 mg/dL Determine samples with U/CSF protein concentrations > 200 mg/dl (2000 mg/L) via the rerun function. On instruments without rerun function, manually dilute samples with 0.9% NaCl. Multiply the result by the appropriate dilution factor.
Lower detection limit	2 mg/dL	Endpoint Assay: 2 mg/dL Rate Assay 6 mg/dL
Expected values (literature reference)	Urine Random: < 12 mg/dL Urine 24h: < 150 mg/day CSF: 15-45 mg/dL	Urine 24h: < 150 mg/day CSF: 15-45 mg/dL
Endogenous interferences **	Hemolysis or RBC contamination interferes with the assay Reference to Young et al and Friedman et al	Icterus: No significant interference up to an I index of 36 (approximate conjugated concentration: 36 mg/dL or 615 µmol/L). Hemolysis: Hemoglobin interferes.

** Data on interferences applies to both the endpoint and the *additional* rate application

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510(k) Summary – Roche/Hitachi Urinary/CSF Protein, Continued

Substantial equivalency – Similarities (continued)

Feature	Predicate device: Roche/Hitachi Urinary/CSF Protein K913615	Modified device: Roche/Hitachi Urinary/CSF Protein, Additional RATE Application
Exogenous interferences **	There is no significant interference from the following substances: Ascorbic Acid, Creatinine, Glucose, Phosphorus, Urea, Magnesium, Sodium Citrate, Caffeine, Cefazolin Sodium, Chlorpromazine, Calcium L-Dopa, Gentamicin Sulfate, Sodium Oxalate and Uric Acid	No significant interference from: Ascorbic Acid, Creatinine, Glucose, Phosphorus, Urea, Magnesium, Sodium Citrate, Caffeine, Cefazolin Sodium, Chlorpromazine, Calcium L-Dopa, Gentamicin Sulfate, Sodium Oxalate and Uric Acid Therapeutic concentrations of Ca-dobesilate, levodopa and phenazopyridine interfere with the assay. The administration of gelatin-based plasma replacements can lead to increased urine protein values. In very rare cases gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.

** Data on interferences applies to both the endpoint and the *additional* rate application

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510(k) Summary – Roche/Hitachi Urinary/CSF Protein,
Continued

Substantial equivalency – Similarities (continued)

Feature	Predicate device: Roche/Hitachi Urinary/CSF Protein K913615	Modified device: Roche/Hitachi Urinary/CSF Protein, Additional RATE Application
Method comparison	A comparison of this method on the Hitachi 717 analyzer using the DuPont ACA method as the reference resulted in the following linear regression statistics: Urine samples: y= 1.051x +2.78 r = 0.996 n=34 CSF samples: y = 0.992x – 0.957 r = 0.982 n=59	A comparison of the U/CSF Protein determination with Roche Diagnostics U/CSF Protein reagent using the rate application (y) with the same reagent using the endpoint application (x) gave the following correlations (mg/dL): Urine samples: Passing/Bablok y = 0.988x - 0.434 r = 1.000 Number of samples measured: 60 The sample concentrations were between 1.7 and 3286.5 mg/dL. Statistics include all results (diluted and undiluted). CSF samples: Passing/Bablok y = 0.984x + 0.480 r = 1.000 Number of samples measured: 50 The sample concentrations were between 5.8 and 110.2 mg/dL.

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510(k) Summary – Roche/Hitachi Urinary/CSF Protein,
Continued

Proposed Labeling

Proposed labeling sufficient to describe the device, its intended use, and the directions for use are included. We believe the proposed version of the device labeling presented contains all of the technical information required per 21 CFR 809.10.

Validation and Design Control

Development activities were conducted under appropriate design control procedures and the overall product specifications were met. The Declaration of Conformity with Design Controls and Results of Risk Analysis are provided.

Closing

The modification of the Roche/Hitachi Urinary/CSF Protein reagent described above does not affect the intended use or indications for use of the device as described in the labeling, nor does it alter the fundamental scientific technology of the device. Therefore, we trust the information provided in this Special 510(k) will support a decision of substantial equivalence of the Roche/Hitachi Urinary/CSF Protein with the Rate application to its predicate.

If you have any questions or require further information, please do not hesitate to contact this office.

Kerwin Kaufman, MBA, MT(ASCP)

Regulatory Affairs Principal
Roche Diagnostics
- Phone: (317) 521-7637
- FAX: (317) 521-2324
- email: Kerwin.Kaufman@roche.com

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

OCT 19 2007

Roche Diagnostics Corp.
c/o Mr. Kerwin L. Kaufman
Regulatory Affairs Principal
9115 Hague Road
Indianapolis, IN 46250-0416

Re: k072638
Trade/Device Name: Roche/Hitachi Urinary/CSF Protein
Regulation Number: 21 CFR 862.1635
Regulation Name: Total Protein test system.
Regulatory Class: Class II
Product Code: JGQ
Dated: September 17, 2007
Received: September 18, 2007

Dear Mr. Kaufman:

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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0490. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address at http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Jean M. Cooper, M.S., D.V.M.

Jean M. Cooper, M.S., D.V.M.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): **K072638**

Device Name: **Roche/Hitachi Urinary/CSF Protein**

Indications For Use:

In vitro test for the quantitative determination of protein in urine and cerebrospinal fluid on Roche automated clinical chemistry analyzers.

Measurements obtained by this device are used in the diagnosis and treatment of a variety of diseases involving the liver, kidney or bone marrow as well as metabolic or nutritional disorders.

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 diagnosis and treatment of conditions such as meningitis, brain tumors and infections of the central nervous systems.

Prescription Use XXX AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Carol C. Benson
ion Sign-Off

ffice of In Vitro Diagnostic Device
valuation and Safety

K072638