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510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K132462.

807.92 (a)(1): Name: Hitachi Chemical Diagnostics
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OCT 2 8 2013

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Consultant to Hitachi Chemical Diagnostics, Inc.

807.92 (a)(2): Device name- trade name and common name, and classification

Trade name:
S TEST Reagent Cartridge Blood Urea Nitrogen (BUN)
S TEST Reagent Cartridge Creatinine (CRE)

Common Name: Routine chemistry analyzer for blood urea nitrogen (BUN)
Routine chemistry analyzer for creatinine (CRE)

Classification: Class II, 21 CFR § 862.1770- BUN test system (BUN)
Class II, 21 CFR § 862.1225- creatinine test system (CRE)

807.92 (a)(3): Identification of the legally marketed predicate devices
Cobas c systems UREAL (Roche Diagnostics, Inc., Indianapolis, IN)- K100853
Cobas c systems CREJ2 (Roche Diagnostics, Inc., Indianapolis, IN)- K100853

807.92 (a)(4): Device Description
The Hitachi Clinical Analyzer is an automatic, bench-top, wet chemistry system intended for use in clinical laboratories or physician office laboratories. The instrument consists of a desktop analyzer unit, an operations screen that prompts the user for operation input and displays data, a printer, and a unit cover. The analyzer unit includes a single probe, an incubation rotor, carousels for sample cups and reagent cartridges, and a multi-wavelength photometer. The single-use reagent cartridges may be placed in any configuration on the carousel, allowing the user to develop any test panel where the reagent cartridges are available.

The S TEST reagent cartridges are made of plastic and include two small reservoirs capable of holding two separate reagents (R1 and R2), separated by a reaction cell/photometric cuvette. The cartridges also include a dot code label that contains all chemistry parameters,

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calibration factors, and other production-related information, e.g., expiration dating. The dimensions of the reagent cartridges are: 13.5 mm (W) × 28 mm (D) × 20.2 mm (H).

System operation: After the sample cup is placed into the carousel, the analyzer pipettes the sample, pipettes the reagent, and mixes (stirs) the sample and reagent together. After the sample and reagent react in the incubator bath, the analyzer measures the absorbance of the sample, and based on the absorbance of the reactions, it calculates the concentration of analyte in the sample. The test system can measure analytes in serum or plasma and results are available in approximately 15 minutes per test. This submission is for reagent cartridge test systems for glucose.

Chemistry reactions (BUN):
Urea is degraded by urease into ammonia. When glutamate dehydrogenase (GLD) reacts with ammonia and alfa-ketoglutaric acid to produce glutamic acid, NADPH is converted into NADP with a decrease of absorbance at 340 nm. The concentration of urea nitrogen can be determined by measuring the amount of change in absorbance.

$$\text{Urea} \xrightarrow{\text{Urease}} NH_3 + CO_2$$

$$NH_3 + \text{Alfa-ketoglutaric acid} + \text{NADPH} \xrightarrow{\text{GLD}} \text{Glutamic acid} + H_2O + \text{NADP}$$

Chemistry reactions (CRE):
As the first reaction, creatine in samples is decomposed into water and oxygen by the action of creatinase, sarcosine oxidase, and catalase. Subsequently, as the second reaction, creatinine in samples is converted into creatine by the action of creatininase, and then sarcosine is formed by creatinase. Then, the quinone pigment is formed by oxidation condensation between N,N-Bis (4-sulfobutyl)-3-methylaniline disodium salt (TODB) and 4-aminoantipyrine in the presence of peroxidase (POD) and hydrogen peroxide is by sarcosine oxidase. The concentration of creatinine is determined by measuring the absorbance of the resulting quinone pigment (purple-red).

The first reaction:

$$\text{Creatine} + H_2O \xrightarrow{\text{Creatinase}} \text{Sarcosine} + \text{Urea}$$

$$\text{Sarcosine} + O_2 + H_2O \xrightarrow{\text{Sarcosine oxidase}} \text{Glycine} + HCHO + H_2O_2$$

$$2H_2O_2 \xrightarrow{\text{Catalase}} O_2 + 2H_2O$$

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The second reaction:

$$\text{Creatinine} + H_2O \xrightarrow{\text{Creatininase}} \text{Creatine}$$

$$\text{Creatine} + H_2O \xrightarrow{\text{Creatinase}} \text{Sarcosine} + \text{Urea}$$

$$\text{Sarcosine} + O_2 + H_2O \xrightarrow{\text{Sarcosine oxidase}} \text{Glycine} + HCHO + H_2O_2$$

$$H_2O_2 + \text{TODB} + \text{4-aminoantipyrine} \xrightarrow{\text{POD}} \text{Quinone pigment (purple-red)}$$

807.92 (a)(5): Intended Use (BUN and CRE)

The S TEST Reagent Cartridge Blood Urea Nitrogen (BUN) is intended for the quantitative measurement of BUN in serum, lithium heparin plasma, K3 EDTA plasma, and sodium citrate plasma on the Hitachi Clinical Analyzer E40. The test system is intended for use in clinical laboratories or physician office laboratories. For *in vitro* diagnostic use only. BUN measurements are used in the diagnosis and treatment of certain renal and metabolic diseases.

The S TEST reagent cartridge Creatinine (CRE) is intended for the quantitative measurement of creatinine in serum, lithium heparin plasma, K3 EDTA plasma, and sodium citrate plasma on the Hitachi Clinical Analyzer E40. The test system is intended for use in clinical laboratories or physician office laboratories. For *in vitro* diagnostic use only. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

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807.92 (a)(6): Technological Similarities and Differences to the Predicate

The following chart describes similarities and differences between the two test systems.

Characteristic	Hitachi S TEST Systems	PREDICATE(S)
Instrument Platform	Hitachi Clinical Analyzer	Roche cobas 8000 – K100853
BUN Test System	K number- pending	Roche K number- K100853
Device Class, Regulation Code	Class II, 21 CFR 862.1770	Same
Classification Product Code	CDN	Same
Intended Use	Quantitative measurement of BUN	Same
Testing Environment	Physician office or clinical lab	Clinical lab
Test Principle	Kinetic test (UV rate) with urease and glutamate dehydrogenase	Kinetic test with urease and glutamate dehydrogenase
Specimen Type	Human serum or plasma	Human serum, plasma, or urine
Reportable Range	1.5 to 80.0 mg/dL	1.4 to 112 mg/dL
Detection Wavelength	340/546 nm (main/sub)	700/340 nm (sub/main)
Detection Limit	0.8 mg/dL	1.4 mg/dL
Linearity	0.9 to 110 mg/dL	1.4 to 112 mg/dL
Precision	%CVs range from 2.3% to 5.0%	%CVs range from 0.9% to 1.3% (from product labeling)
CRE Test System	K number- pending	Roche K number- K100853
Device Class, Regulation Code	Class II, 21 CFR 862.1225	Same
Classification Product Code	CGX	Same
Intended Use	Quantitative measurement of CRE	Same
Testing Environment	Physician office or clinical lab	Clinical lab- cobas
Test Principle	Enzymatic with creatinase and formation of quinone pigment	Kinetic colorimetric assay based on Jaffe method
Specimen Type	Human serum or plasma	Human serum, plasma, or urine
Reportable Range	0.1 to 25.0 mg/dL	0.2 to 24.9 mg/dL
Detection Wavelength	546/700 nm (main/sub)	570/505 nm (sub/main)
Detection Limit	0.1 mg/dL	0.2 mg/dL
Linearity	0.1 to 31.3 mg/dL	0.2 to 24.9 mg/dL
Precision	%CVs range from 1.4% to 8.5%	%CVs range from 1.1% to 5.0% (from product labeling)

807.92 (b)(1): Brief Description of Nonclinical Data

A series of studies were performed that evaluated the following nonclinical performance characteristics for glucose: analytical sensitivity (limits of detection), linearity, 20-day in-house precision, interference testing, in-house method comparisons, and matrices comparison between serum and various plasma options.

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Analytical Sensitivity (Limits of Detection)
The study followed CLSI EP17-A2. The sensitivity/limit of detection (LoD) for BUN was calculated to be 0.8 mg/dL, and the LoD for CRE was calculated to be 0.1 mg/dL.

Linearity/Reportable Range
The study followed CLSI EP-6A. The BUN test is linear between 0.9 mg/dL and 110 mg/dL, and the CRE test is linear between 0.1 mg/dL and 31.3 mg/dL. The reportable range for BUN is 1.5 mg/dL to 80 mg/dL, and the reportable range for CRE is 0.1 mg/dL to 25 mg/dL.

20-day In-house Precision
The studies followed CLSI EP5-A2, where three (BUN) or four (CRE) levels of samples were each tested four times a day for 20 days. The results were as follows:

Precision Summary:

		Mean (mg/dL)	Within-Run %CV	Total %CV
BUN	Level 1	7.24	3.0	5.0
n= 80 per level	Level 2	14.07	1.6	2.7
	Level 3	49.05	1.2	2.3
CRE	Level 1	0.59	6.8	8.5
n= 80 per level	Level 2	1.75	2.3	3.4
	Level 3	6.55	1.2	2.9
	Level 4	20.34	0.9	1.4

Interference Testing
The studies followed CLSI EP7-A2. Two serum pools per analyte were spiked with increasingly high concentrations of substances. The data demonstrated that the BUN and CRE systems were not affected by high levels of the following substances at the levels noted. Non interference was defined as spiked samples quantitating within 10% of the neat samples.

BUN (serum pools: ~12 mg/dL and 30 mg/dL)
- Hemoglobin: no interference up to 1,000 mg/dL
- Unconjugated bilirubin: no interference up to 50 mg/dL
- Lipemia (Intralipid ®): no interference up to 1,000 mg/dL
- Ascorbic acid: no interference up to 50 mg/dL

CRE (serum pools: ~1.5 mg/dL and 5.7 mg/dL)
- Hemoglobin: no interference up to 250 mg/dL
- Unconjugated bilirubin no interference up to 25 mg/dL
- Lipemia (Intralipid ®): no interference up to 1,000 mg/dL
- Ascorbic acid: no interference up to 25 mg/dL

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Method Comparison - **BUN**

A total of 162 clinical specimens spanning the dynamic range (2.4 to 78.5 mg/dL), were assayed in singleton and in a blinded fashion by both the Hitachi E40 system (y-axis) and a standard laboratory system (x-axis). The comparative data were analyzed by linear regression and are shown below. (CI = confidence interval)

BUN Regression Statistics:

n	r	Slope (95% CI)	y-intercept (95% CI)	X mean	Y mean
162	0.997	0.96 (0.95 to 0.97)	-0.27 (-0.64 to 0.10)	27.2 mg/dL	25.8 mg/dL

Method Comparison - **CRE**

A total of 100 clinical specimens spanning the dynamic range (0.5 to 24.7 mg/dL) were assayed in singleton and in a blinded fashion by both the Hitachi E40 system (y-axis) and a standard laboratory system (x-axis). The comparative data were analyzed by linear regression and are shown below. (CI = confidence interval)

CRE Regression Statistics:

n	r	Slope (95% CI)	y-intercept (95% CI)	X mean	Y mean
100	0.999	0.99 (0.98 to 1.00)	-0.13 (-0.18 to -0.07)	4.26 mg/dL	4.09 mg/dL

Matrices Comparisons- BUN

A study was performed to validate the use of three plasma types as an alternative to serum for S TEST Reagent Cartridge BUN. The plasma types were lithium heparin, K3 EDTA, and sodium citrate. Thirty-six (36) matched serum/plasma samples that spanned the dynamic range (2.4 to 75.3 mg/dL) were assayed in singleton and the results were compared using linear regression (plasma = y-axis, each type). The performance characteristics were as follows.

BUN: n = 36, range (serum) = 2.4 to 75.3 mg/dL

	Heparinized Plasma	EDTA Plasma	Na Citrate Plasma
Slope (95% CIs)	1.01 (1.00 to 1.03)	1.01(1.00 to 1.03)	0.99 (0.97 to 1.01)
y-intercept (95% CIs)	-0.56 (-0.84 to -0.28)	-0.61 (-0.94 to -0.27)	-0.98 (-1.42 to -0.54)
r	0.999	0.999	0.998

Matrices Comparisons- CRE

A study was performed to validate the use of three plasma types as an alternative to serum for S TEST Reagent Cartridge CRE. The plasma types were lithium heparin, K3 EDTA, and sodium citrate. Thirty-nine (39) matched serum/plasma samples that spanned the dynamic range (0.1 to 24.5 mg/dL) were assayed in singleton and the results were compared using linear regression (plasma = y-axis, each type). The performance characteristics were as follows.

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CRE: n = 39, range (serum) = 0.1 to 24.5 mg/dL

	Heparinized Plasma	EDTA Plasma	Na Citrate Plasma
Slope (95% CIs)	0.99 (0.98 to 1.00)	1.01 (1.00 to 1.02)	1.00 (0.99 to 1.02)
y-intercept (95% CIs)	-0.02 (-0.08 to 0.05)	-0.06 (-0.15 to 0.03)	-0.05 (-0.14 to 0.05)
r	0.999	0.999	0.999

807.92 (b)(2): Brief Description of Clinical Data

Studies for precision and method comparison (accuracy) were performed at three external POL-type sites to evaluate the Hitachi E40 Clinical Analyzer with S TEST Reagent Cartridges for BUN and CRE in one of its targeted intended use environments, the physician's office laboratory.

For the external site precision study, each site received three blinded serum samples (the Precision Panel, labeled A, B, and C) that were chosen to represent low, middle, and high concentrations of BUN or CRE. Each sample was assayed six times per day for five days, reporting 30 results per level. Precision estimates for total precision were as follows:

BUN (mg/dL)
n = 30 replicates per sample per site

Site #	Sample	Mean (mg/dL)	Within-run Precision		Total Precision	
			SD (mg/dL)	%CV	SD (mg/dL)	%CV
1	A	12.04	0.13	1.1	0.22	1.8
2	A	10.92	0.26	2.3	0.39	3.6
3	A	11.68	0.24	2.0	0.23	2.0
1	B	46.94	0.37	0.8	0.69	1.5
2	B	45.40	0.48	1.1	0.65	1.4
3	B	46.40	0.48	1.0	0.66	1.4
1	C	75.68	0.71	0.9	0.69	0.9
2	C	74.29	0.60	0.8	0.85	1.2
3	C	75.23	0.41	0.5	0.47	0.6

CRE (mg/dL)
n = 30 replicates per sample per site

Site #	Sample	Mean (mg/dL)	Within-run Precision		Total Precision	
			SD (mg/dL)	%CV	SD (mg/dL)	%CV
1	A	0.58	0.03	5.0	0.04	6.8
2	A	0.60	0.00	0.0	0.00	0.0
3	A	0.51	0.03	6.7	0.03	6.7
1	B	1.80	0.03	1.8	0.07	3.8
2	B	1.80	0.03	1.8	0.07	3.8
3	B	1.61	0.03	2.0	0.07	4.4
1	C	6.52	0.05	0.7	0.13	2.1
2	C	6.38	0.05	0.8	0.08	1.2
3	C	5.95	0.07	1.2	0.31	5.2

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For the BUN external method comparison studies, a series of approximately 75 serum specimens with BUN values ranging from 5.7 mg/dL to 73.6 mg/dL, were assayed on the Hitachi Clinical Analyzer E40 at three sites using S TEST Reagent Cartridge BUN (y) and a comparative method as the reference method (x). The same study design was used for the S TEST Reagent CRE, using approximately 45 serum specimens ranging from 0.6 mg/dL to 24.1 mg/dL CRE. Linear regression analyses (least squares) yielded the following results.

POL ACCURACY DATA SUMMARY- BUN (mg/dL)

Site #	n	Range (mg/dL)	Regression Equation	"r"	CI* Slope	CI* Intercept
1	75	6.0 to 73.6	y = 0.98x – 0.23	0.999	0.96 to 0.99	-0.59 to 0.13
2	74	5.7 to 69.3	y = 0.94x – 0.24	0.999	0.93 to 0.95	-0.50 to 0.01
3	73	5.7 to 70.8	y = 0.95x – 0.05	0.999	0.93 to 0.96	-0.41 to 0.32

*95% Confidence Interval

POL ACCURACY DATA SUMMARY- CRE (mg/dL)

Site #	n	Range (mg/dL)	Regression Equation	"r"	CI* Slope	CI* Intercept
1	45	0.6 to 23.5	y = 0.97x – 0.06	0.999	0.96 to 0.98	-0.13 to 0.02
2	44	0.6 to 24.1	y = 0.98x – 0.09	0.999	0.96 to 0.99	-0.19 to 0.02
3	47	0.6 to 22.8	y= 0.96x – 0.04	0.999	0.95 to 0.96	-0.10 to 0.02

*95% Confidence Interval

807.92 (b)(3): Conclusions from Nonclinical and Clinical Testing

Nonclinical and clinical testing was performed for the S TEST Reagent Cartridge BUN and CRE. The test system was shown to be safe and effective for its intended use.

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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

October 28, 2013

Hitachi Chemical Diagnostics, Inc.
c/o Erika Ammirati
Ammirati Regulatory Consulting
575 Shirlynn Court
LOS ALTOS CA 94022

Re: K132462
Trade/Device Name: S TEST Reagent Cartridge Blood Urea Nitrogen (BUN)
S TEST Reagent Cartridge Creatinine (CRE)
Regulation Number: 21 CFR 862.1770
Regulation Name: Urea nitrogen test system
Regulatory Class: II
Product Code: CDN, CGX
Dated: August 6, 2013
Received: August 12, 2013

Dear Ms. Ammirati:

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 Small Manufacturers, International and Consumer Assistance 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" (21CFR 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 Small Manufacturers, International and Consumer Assistance 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,

Carol E. Benson -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

INDICATIONS FOR USE

510(k) Number (if Known): k132462

Device Name:
S TEST Reagent Cartridge Blood Urea Nitrogen (BUN)
S TEST Reagent Cartridge Creatinine (CRE)

Indications for Use:

The S TEST Reagent Cartridge Blood Urea Nitrogen (BUN) is intended for the quantitative measurement of BUN in serum, lithium heparin plasma, K3 EDTA plasma, and sodium citrate plasma on the Hitachi Clinical Analyzer E40. The test system is intended for use in clinical laboratories or physician office laboratories. For *in vitro* diagnostic use only. BUN measurements are used in the diagnosis and treatment of certain renal and metabolic diseases.

The S TEST Reagent Cartridge Creatinine (CRE) is intended for the quantitative measurement of creatinine in serum, lithium heparin plasma, K3 EDTA plasma, and sodium citrate plasma on the Hitachi Clinical Analyzer E40. The test system is intended for use in clinical laboratories or physician office laboratories. For *in vitro* diagnostic use only. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

Prescription Use ___X___ And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Ruth A. Chesler -S

Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health (OIR)

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