k130685

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SECTION 8
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 K130685.

807.92 (a)(1): Name: Hitachi Chemical Diagnostics
Address: 630 Clyde Court
Mountain View, CA 94043

AUG 09 2013

Contact: Erika Ammirati, Ammirati Regulatory Consulting
Consultant to Hitachi Chemical Diagnostics, Inc.
Address: 575 Shirlynn Court
Los Altos, CA 94022
Phone: (650) 949-2768
FAX: (650) 949-5347

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

Trade name:
S TEST Reagent Cartridge Lactate Dehydrogenase (LD)
S TEST Reagent Cartridge Amylase (AMY)

Common Name: Routine chemistry analyzer for LD
Routine chemistry analyzer for AMY

Classifications: 21 CFR § 862.1440 Lactate Dehydrogenase (LD)
21 CFR § 862.1070 Amylase (AMY)

807.92 (a)(3): Identification of the legally marketed predicate devices
Cobas c systems LDHI2 (Roche Diagnostics, Inc., Indianapolis, IN)- K100853
Cobas c systems AMYL2 (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.

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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, 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 ALP.

Chemistry reactions: (LD) Lactate dehydrogenase in samples catalyzes the reaction of converting lactic acid to pyruvic acid. During this reaction, NAD is converted into NADH with an increase in absorbance at 340 nm. The LD activity can be determined by measuring the production rate of the resulting NADH.

(AMY) Amylase in blood samples reacts with the substrate alfa-2-chloro-4-nitrophenyl-galactopyranosylmaltoside (Gal-G2-CNP), and the substrate is cleaved into 4-galactopyranosylmaltose (Gal-G2) and 2-chloro-4-nitrophenol (CNP). Amylase activity is determined by measuring the production rate of CNP (yellow).

807.92 (a)(5): Intended Use

The S TEST Reagent Cartridge Lactate Dehydrogenase (LD) is intended for the quantitative determination of LD in serum and plasma using the HITACHI Clinical Analyzer E40. The S TEST Reagent Cartridge Lactate Dehydrogenase (LD) is intended for use in clinical laboratories or physician office laboratories. For in vitro diagnostic use only.

Measurements of LD are used in the diagnosis and treatment of heart, liver, kidney, and blood diseases.

The S TEST Reagent Cartridge Amylase (AMY) is intended for the quantitative determination of AMY in serum and plasma using the HITACHI Clinical Analyzer E40. The S TEST Reagent Cartridge Amylase (AMY) is intended for use in clinical laboratories or physician office laboratories. For in vitro diagnostic use only.

Measurements of AMY are mainly used in the diagnosis and treatment of pancreatic diseases.

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630 Clyde Court, Mountain View, CA 94043-2239 Tel: 800 233 6278 Fax: 650 969 2745
www.hcdiagnostics.com

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

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

Characteristic	Hitachi S TEST Systems	PREDICATE
Instrument Platform	Hitachi Clinical Analyzer (originally cleared under K111753)	Roche cobas c systems – K100853
Lactate Dehydrogenase (LD)	K number- K130685	Roche K number- K100853
Device Class, Regulation Code	Class II, Reserved, 21 CFR 862.1440	Same, except Exempt (not POC)
Classification Product Code	CFJ	CFJ
Intended Use	Quantitative determination of LD	Same
Testing Environment	Physician office or clinical lab	Clinical lab
Test Principle	LD in the sample catalyzes the conversion of lactic acid to pyruvic acid. NAD is converted to NADH with an increase in absorbance.	UV assay- LD catalyzes the conversion of L-lactate to pyruvate (pyruvic acid); NAD is reduced to NADH in the process.
Specimen Type	Human serum or plasma	Same
Reportable Range	10 to 1,000 U/L	Same
Detection Wavelength	340/546 nm	700/340 nm
Detection Limit	10 U/L	Same
Linearity	10 to 1,000 U/L	Same
Precision	%CVs range from 5.4% to 6.3%	%CVs range from 0.4% to 2.7% (from product labeling)

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

Characteristic	Hitachi S TEST Systems	PREDICATE
Instrument Platform	Hitachi Clinical Analyzer (originally cleared under K111753)	Roche cobas c systems – K100853
Amylase (AMY)	K number- K130685	Roche K number- K100853
Device Class, Regulation Code	Class II, 21 CFR 862.1070	Same
Classification Product Code	JFJ	Same
Intended Use	Quantitative determination of AMY	Same
Testing Environment	Physician office or clinical lab	Clinical lab
Test Principle	Alpha amylases in blood samples react with the substrate alfa-2-chloro-4-nitrophenyl-galactopyranosylmaltoside (Gal-G2-CNP), and the substrate is cleaved into 4-galactopyranosylmaltose (Gal-G2) and 2-chloro-4-nitrophenol (CNP). Amylase activity is determined by measuring the production rate of CNP (yellow)	Defined oligosaccharides are cleaved under the catalytic action of alpha amylases. The fragments formed are completely hydrolyzed to p-nitrophenol (p-NP) and glucose by alpha-glucosidase. The color intensity of the p-NP formed is directly proportional to the amylase activity and is determined by measuring the increase in absorbance
Specimen Type	Human serum or plasma	Human serum, plasma, or urine
Reportable Range	4 to 1,500 U/L	3 to 1,500 U/L
Detection Wavelength	405/546 nm	700/415 nm
Detection Limit	4 U/L	3 U/L
Linearity	3 to 1,700 U/L	3 to 1,500 U/L
Precision	%CVs range from 2.7% to 3.7%	%CVs range from 0.7% to 2.4% (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 each analyte: 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 types.

Analytical Sensitivity (Limits of Detection)- LD

The study followed CLSI EP17-A, and the limit of detection was found to be 7.9 U/L. The quantitation limit was found to be 10 U/L.

Analytical Sensitivity (Limits of Detection)- AMY

The study followed CLSI EP17-A, and the limit of detection was found to be 2.2 U/L. The quantitation limit was found to be 4 U/L.

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Linearity- LD
The study followed CLSI EP-6A, and the range of linearity was 3 U/L to 1,196 U/L. The reportable range is 10 U/L to 1,000 U/L.

Linearity- AMY
The study followed CLSI EP-6A, and the range of linearity was 3 U/L to 1,700 U/L. The reportable range is 4 U/L to 1,500 U/L.

20-day In-house Precision- LD
The studies followed CLSI EP5-A2, where three levels of samples were each tested in two runs, twice a day, for 20 days. The results were as follows:

Precision Summary:

LD- Low, Level 1, Summary

LD	Within-Run	Total
Mean (U/L)	108.2	108.2
SD (U/L)	5.24	6.82
%CV	4.8%	6.3%

LD- Middle, Level 2, Summary

LD	Within-Run	Total
Mean (U/L)	159.3	159.3
SD (U/L)	9.15	8.85
%CV	5.7%	5.6%

LD- High, Level 3, Summary

LD	Within-Run	Total
Mean (U/L)	628.0	628.0
SD (U/L)	20.0	33.8
%CV	3.2%	5.4%

20-day In-house Precision- AMY
The studies followed CLSI EP5-A2, where three levels of samples were each tested in two runs, twice a day, for 20 days. The results were as follows:

Precision Summary:

AMY- Low, Level 1, Summary

AMY	Within-Run	Total
Mean (U/L)	54.1	54.1
SD (U/L)	0.94	1.45
%CV	1.7%	2.7%

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AMY- Middle, Level 2, Summary

AMY	Within-Run	Total
Mean (U/L)	188.5	188.5
SD (U/L)	1.50	6.99
%CV	0.8%	3.7%

AMY- High, Level 3, Summary

AMY	Within-Run	Total
Mean (U/L)	1126.8	1126.8
SD (U/L)	8.85	39.5
%CV	0.8%	3.5.%

Interference Testing (per CLSI EP7-A2)
The data demonstrated that the **LD** test system was not affected by high levels of the following substances at the levels noted:

Unconjugated bilirubin: no interference up to 50 mg/dL
Lipemia: no interference up to 1,000 mg/dL
Ascorbic acid: no interference up to 50 mg/dL
Hemoglobin: Positive interference (increase in concentration) from hemolysis occurred at levels as low as 31mg/dL hemoglobin. Any level of hemolysis may cause interference. Do not use hemolyzed specimens.

Lack of interference was defined as recoveries between 90% and 110% of the neat value, and assay performance claims were established on the HITACHI Clinical Analyzer by testing two serum pools containing approximately 100 and 350 U/L LD.

The data demonstrated that the **AMY** test system was not affected by high levels of the following substances at the levels noted:

Hemoglobin: no interference up to 500 mg/dL
Unconjugated bilirubin: no interference up to 50 mg/dL
Lipemia: no interference up to 2,000 mg/dL
Ascorbic acid: no interference up to 50 mg/dL

Lack of interference was defined as recoveries between 90% and 110% of the neat value, and assay performance claims were established on the HITACHI Clinical Analyzer by testing two serum pools containing approximately 150 and 300 U/L AMY.

Method Comparison - **LD**
A total of 106 clinical specimens spanning the dynamic range (13 to 959 U/L), were assayed in singleton and in a blinded fashion by both the Hitachi E40 system and a standard

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laboratory system. The comparative data were analyzed by linear regression and are shown below. (CI = confidence interval)

LD Regression Statistics:

n	r	Slope (95% CI)	y-intercept (95% CI)	X mean	Y mean
106	0.991	1.01 (0.99 to 1.04)	5.4 (-3.8 to 14.6)	288 U/L	297 U/L

Method Comparison - **AMY**

A total of 105 clinical specimens spanning the dynamic range (5 to 1,443 U/L), were assayed in singleton and in a blinded fashion by both the Hitachi E40 system and a standard laboratory system. The comparative data were analyzed by linear regression and are shown below. (CI = confidence interval)

AMY Regression Statistics:

n	r	Slope (95% CI)	y-intercept (95% CI)	X mean	Y mean
105	0.997	1.08 (1.06 to 1.10)	-3.3 (-8.7 to 2.1)	218 U/L	232 U/L

Matrices Comparisons- LD

A study was performed to validate the use of two plasma types as an alternative to serum for the Hitachi Clinical Analyzer with S TEST Reagent Cartridge LD. The plasma types were K3 EDTA and lithium heparin. Thirty-nine (39) matched serum/plasma samples that spanned the dynamic range (13 to 967) were assayed in singleton and the results were compared using linear regression (plasma = y-axis, each type). The performance characteristics were as follows.

N = 39
Range (serum) = 32 to 804 U/L

LD	Heparinized Plasma	K3 EDTA Plasma
Slope (95% CIs)	0.99 (0.97 to 1.01)	0.97 (0.94 to 1.00)
y-intercept (95% CIs)	-5.5(-10.7 to -0.3)	0.1 (-8.9 to 9.0)
r	0.998	0.994

Matrices Comparisons- AMY

A study was performed to validate the use of two plasma types as an alternative to serum for the Hitachi Clinical Analyzer with S TEST Reagent Cartridge AMY. The plasma types were K3 EDTA and lithium heparin. Approximately 43matched serum/plasma samples that spanned the dynamic range (5 to 1,494) were assayed in singleton and the results were compared using linear regression (plasma = y-axis, each type). The performance characteristics were as follows.

N = 43 (serum)
Range (serum) = 5 to 1,494 U/L

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AMY	Heparinized Plasma	K3 EDTA Plasma
Slope (95% CIs)	1.02 (1.00 to 1.04)	0.97 (0.95 to 0.99)
y-intercept (95% CIs)	-8.4 (-17.2 to 0.3)	-6.6 (-14.3 to 1.0)
r	0.998	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 LD and AMY 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 LD or AMY. Each sample was assayed six times per day for five days, reporting 30 results per level. Precision estimates for total precision were as follows:

LD (U/L)
n = 30 replicates per sample per site

Site	Sample	Mean	Within-run Precision		Total Precision	
			SD (U/L)	%CV	SD (U/L)	%CV
Site 1	Low	47.3	3.83	8.1	4.42	9.3
Site 2	Low	49.8	3.00	6.0	3.20	6.4
Site 3	Low	45.7	3.69	8.1	3.82	8.4
Site 1	Middle	161.9	5.60	3.5	6.45	4.0
Site 2	Middle	161.6	6.01	3.7	6.25	3.9
Site 3	Middle	155.7	8.90	5.7	9.63	6.2
Site 1	High	498.1	12.70	2.6	15.10	3.0
Site 2	High	488.5	20.29	4.2	35.20	7.2
Site 3	High	497.0	14.71	3.0	20.55	4.1

AMY (U/L)
n = 30 replicates per sample per site

Site	Sample	Mean	Within-run Precision		Total Precision	
			SD (U/L)	%CV	SD (U/L)	%CV
Site 1	Low	53.2	2.43	4.6	2.44	4.6
Site 2	Low	50.4	1.44	2.8	1.74	3.5
Site 3	Low	51.2	2.08	4.1	1.93	3.8
Site 1	Middle	116.9	1.58	1.4	1.65	1.4
Site 2	Middle	111.5	1.73	1.6	2.11	1.9
Site 3	Middle	113.3	2.29	2.0	3.51	3.1

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Site 1	High	1527.4	7.19	0.5	15.51	1.0
Site 2	High	1428.6	16.06	1.1	29.24	2.0
Site 3	High	1465.4	13.51	0.9	19.10	1.3

For the external method comparison studies, a series of approximately 70-80 serum specimens with LD values ranging from 16 to 938 U/L, and AMY values ranging from 27 to 1,146 U/L, were assayed on the Hitachi E40 Clinical Analyzer at three sites using S TEST Reagent Cartridges LD and AMY (y) and a comparative method as the reference method (x). Linear regression analyses (least squares) yielded the following results:

POL ACCURACY DATA SUMMARY- LD (U/L)

Site #	n	Range (U/L)	Regression Equation	"r"	CI* Slope	CI Intercept
1	87	16 to 938	y = 0.96x + 2.5	0.997	0.94 to 0.97	-2.3 to 7.4
2	78	23 to 877	y = 0.96x + 4.7	0.998	0.94 to 0.97	0.6 to 8.9
3	86	17 to 914	y = 0.91x +13.5	0.999	0.90 to 0.93	9.6 to 17.4

*95% Confidence Interval

POL ACCURACY DATA SUMMARY- AMY (U/L)

Site #	n	Range (U/L)	Regression Equation	"r"	CI* Slope	CI* Intercept
1	76	29 to 1134	y = 1.05x -1.2	0.999	1.04 to 1.06	-4.6 to 2.2
2	69	27 to 1146	y = 1.00x -0.5	0.995	0.98 to 1.03	-6.6 to 5.7
3	71	29 to 1112	y = 0.98x + 3.3	0.995	0.95 to 1.00	-3.2 to 9.8

*95% Confidence Interval

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

Nonclinical and clinical testing was performed for the Hitachi E40 Clinical Analyzer with the S TEST Reagent Cartridge Lactate Dehydrogenase (LD) and the S TEST Reagent Cartridge Amylase (AMY). The test systems were shown to be safe and effective for their intended uses.

Hitachi Chemical Diagnostics, Inc.
630 Clyde Court, Mountain View, CA 94043-2239 Tel: 800 233 6278 Fax: 650 968 2745
www.hcdiagnostics.com

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

August 9, 2013

Hitachi Chemical Diagnostics, Inc.
C/O Erika Ammirati
President, Ammirati Regulatory Consulting
575 Shirlynn Court
LOS ALTOS CA 94022

Re: K130685
Trade/Device Name: S TEST Reagent Cartridge Amylase (AMY)
S TEST Reagent Cartridge Lactate Dehydrogenase (LD)
Regulation Number: 21 CFR 862.1070
Regulation Name: Amylase test system
Regulatory Class: II
Product Code: JFJ, CFJ
Dated: July 29, 2013
Received: July 30, 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 Part 801); 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 regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. 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 C. 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): k130685

Device Name:
S TEST Reagent Cartridge Lactate Dehydrogenase (LD)

S TEST Reagent Cartridge Amylase (AMY)

Indications for Use:

The S TEST Reagent Cartridge Lactate Dehydrogenase (LD) is intended for the quantitative determination of LD in serum and plasma using the HITACHI Clinical Analyzer E40. The S TEST Reagent Cartridge Lactate Dehydrogenase (LD) is intended for use in clinical laboratories or physician office laboratories. For in vitro diagnostic use only. Measurements of LD are used in the diagnosis and treatment of liver and cardiac diseases.

The S TEST Reagent Cartridge Amylase (AMY) is intended for the quantitative determination of AMY in serum and plasma using the HITACHI Clinical Analyzer E40. The S TEST Reagent Cartridge Amylase (AMY) is intended for use in clinical laboratories or physician office laboratories. For in vitro diagnostic use only. Measurements of AMY are mainly used in the diagnosis and treatment of pancreatic diseases.

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

Yung-Wo Chan -S

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

510(k) k130685