510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY

A. 510(k) Number:

k120369

B. Purpose for Submission:

New device

C. Measurand:

Glucose

D. Type of Test:

Quantitative Photometric

E. Applicant:

Hitachi Chemical Diagnostics, Inc

F. Proprietary and Established Names:

Hitachi Clinical Analyzer S TEST Reagent Cartridge for Glucose

G. Regulatory Information:

1. Regulation section:
   21 CFR § 862.1345- glucose test system

2. Classification:
   Class II

3. Product code:

   CFR

4. Panel:
   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) for use:

   The S TEST reagent cartridge for glucose is intended for the quantitative measurement of glucose in serum, lithium heparin plasma, K3 EDTA plasma, and sodium citrate plasma on the Hitachi Clinical Analyzer. The test system is intended for use in clinical laboratories or physician office laboratories. For *in vitro* diagnostic use only. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus and idiopathic hypoglycemia.

3. Special conditions for use statement(s):
   Prescription use only

4. Special instrument requirements:
   Hitachi Clinical Analyzer(previously cleared in k111753)

I. 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 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, 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).

GLU Reagent (1):

- Hexokinase (Yeast) 4.0 U/mL
- Nicotinamide adenine dinucleotide phosphate (oxidized form) 3.0 g/L
- Glucose-6-phosphate dehydrogenase (E.coli) 2.0 U/mL
- 2-Amino-2-hydroxymethyl-1,3-propanediol Buffer (pH7.2) 0.1 mol/L

GLU Reagent (2):

- 2'-Deoxyadenosine-5'-triphosphate sodium salt 5.0 mmol/L
- 2-Amino-2-hydroxymethyl-1,3-propanediol Buffer (pH8.4) 0.1 mol/L

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Roche cobas 8000

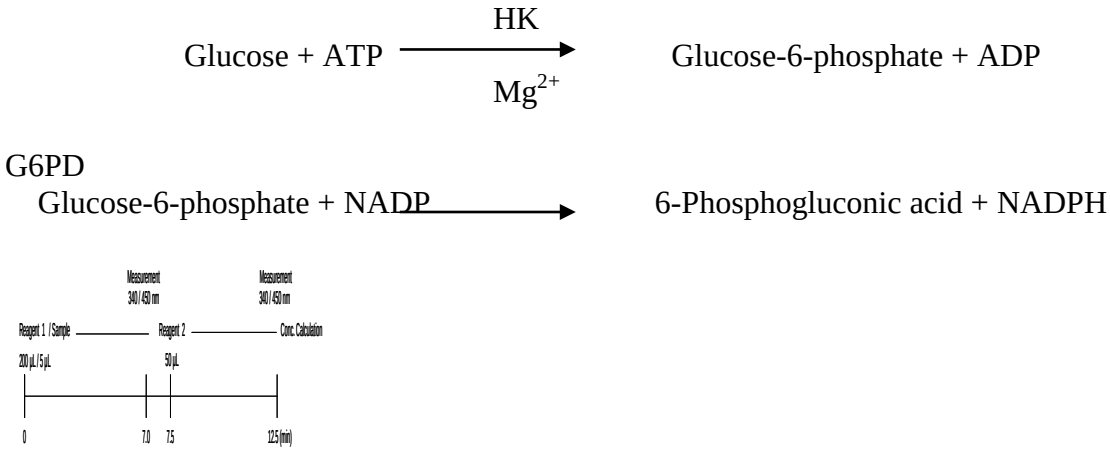
2. Predicate 510(k) number(s):
   k100853

3. Comparison with predicate:

Characteristic	Hitachi S TEST Systems	PREDICATE(S)
Glucose Test System	K number- k120369	Roche K number- k100853
Intended Use	Quantitative determination of glucose	Same
Testing Environment	Physician office or clinical lab	Clinical lab- cobas
Test Principle	Enzymatic method (Hexokinase method)	UV Test- enzymatic reference method with hexokinase
Specimen Type	Human serum or plasma	Human serum, plasma, CSF, or urine
Reportable Range	5 to 500 mg/dL	2 to 750 mg/dL
Detection Wavelength	340/450 nm	700/340 nm
Detection Limit	5 mg/dL	2 mg/dL
Linearity	5 to 500 mg/dL	2 to 750 mg/dL
Precision	%CVs ranged from 2.1% to 3.9%	%CVs range from 0.7% to 1.3% (from product labeling)

K. Standard/Guidance Document Referenced (if applicable):
CLSI - Protocols for Determination of Limits of Detection and Limits of Quantitation - EP17-A
CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices - EP05-A2
CLSI - Interference Testing in Clinical Chemistry - EP07-A2

L. Test Principle:
Glucose is phosphorylated to glucose-6-phosphate by hexokinase (HK) in the presence of ATP. When the glucose-6-phosphate is converted into 6-phosphogluconic acid by glucose-6-phosphate dehydrogenase (G6PD), NADP is converted into NADPH with an increase in absorbance at 340 nm. The concentration of glucose can be determined by measuring the amount of change in absorbance of NADPH.



M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:
   Three levels of serum samples (low, middle, and high levels of GLU) were tested in duplicate with 2 cartridges, twice a day, for 20 days, for a total of 80 results per level to assess in-house precision. The precision estimates are described below.

GLU- Low, Level 1, Summary

GLU	Within-Run	Total
Mean (mg/L)	73.0	73.0
SD (mg/L)	2.86	2.88
%CV	3.9%	3.9%

GLU- Middle, Level 2, Summary

GLU	Within-Run	Total
Mean (mg/dL)	213.8	213.8
SD (mg/dL)	3.11	4.49
%CV	1.5%	2.1%

GLU- High, Level 3, Summary

GLU	Within-Run	Total
Mean (mg/L)	306.1	306.1
SD (mg/L)	3.33	9.20
%CV	1.1%	3.0%

Three levels of serum samples (A= low, B= medium, and C= high) were tested at three POL sites, six times a day for five days. The precision estimates are described below.

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

Site	Sample	Mean	Within-run Precision		Total Precision	
			SD (mg/dL)	%CV	SD (mg/dL)	%CV
Site 1	A	59.3	2.6	4.5%	2.8	4.6%
Site 2	A	59.1	0.7	1.1%	1.0	1.7%
Site 3	A	59.1	1.2	2.1%	1.4	2.3%
Site 1	B	117.3	4.0	3.4%	4.4	3.7%
Site 2	B	117.7	0.9	0.8%	1.3	1.1%
Site 3	B	114.9	1.6	1.4%	1.7	1.7%
Site 1	C	358.7	11.5	3.2%	12.8	3.6%
Site 2	C	354.8	3.5	1.0%	6.8	1.9%
Site 3	C	343.9	7.1	2.1%	10.2	3.0%

b. Linearity/assay reportable range:

11 serum samples (0, 1.5, 4.0, 6.5, 8.0, 15.0, 29.0, 132, 251, 468, 690 mg/dL were assigned their reference values arithmetically and were tested in duplicate by the Hitachi Clinical Analyzer, and the mean Hitachi results (y-axis) were plotted against the assigned values (x-axis).

	Linearity (assigned)	Regression analysis	reportable range (within linearity)
GLU	2 mg/dL and 655 mg/dL	y = 1.038x-0.4173 R^2 = 0.9992	5 mg/dL and 500 mg/dL

The data supported the sponsor's claimed range of the device (5-500 mg/dL).

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Glucose S Test cartridge lot is calibrated using standard material traceable to ReCCS (Reference Material Institute for Clinical Chemistry Standards) standard serum JCCRM 521.

Shelf life/ stability of the cartridge:

Real-time, shelf-life stability studies for the GLU reagent cartridge were performed. A two-level control set, (92 and 212 mg/dL, respectively) was tested in replicates of

five with three lots of cartridges across six analyzers according to standard procedure.

Testing occurred at Time 0 (baseline), and again at approximately, 6, 9, 11, 12 and 13 months; the storage condition was refrigerated (2 to 8 ºC). The studies supported the sponsor's claimed shelf life of 12 months at 2 to 8 ºC.

d. Detection limit:

Per CLSI EP17-A, blank samples for each reagent system were assayed 20 times per day for three days for a total of 60 replicate results to determine LOB and LOD. Low samples were assayed 20 times with the specific reagent cartridges to determine the detection limit below:

LoD for GLU: 0.3 mg/dL
LoB for Glu : (mean of the 57^{th} and 58 point) -0.28

LoQ study was performed as follows: three clinical samples were diluted to target 5.5 mg/dL glucose. Each sample was tested with one lot of cartridges 6x/day on 3 different days with three different analyzers for a total of 54 replicate results per sample. From these data, the means, standard deviations (SDs), and percent coefficients of variation (%CVs) were calculated. The % CVs ranged from 14.5 to 17.5 % with all three < 20 %. The data supported the sponsor's claimed LoQ of 5 mg/dL.

e. Analytical specificity:

The studies followed CLSI EP7-A2. The data demonstrated that GLU was not affected by the following substances at the levels noted below. No significant interference is defined by the sponsor as the highest level of interferent that is within 10% of the neat sample.

The interference studies demonstrated that the S TEST for GLU was resistant to high levels of ascorbic acid (up to 50mg/dL), hemoglobin up to 500 mg/dL for low (50mg/dL) glucose levels and 1000 mg/dL for high (200 mg/dL) glucose levels, unconjugated bilirubin up to 6.25 mg/dL for low (50mg.dL) glucose levels and 50 mg/dL for high (50mg.dL) glucose levels, and triglycerides (up to 800 mg/dL).

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The in-house method comparison study evaluated 100 serum samples; matched aliquots

were assayed with both the Hitachi Clinical Analyzer with S TEST GLU reagent cartridge and the Roche/Hitachi cobas 6000. The data were analyzed by least squares linear regression (Hitachi = y-axis), and the results were as follows:

Glucose (mg/dL)
n= 100
y= 0.99x -2.7
correlation coefficient (r) = 0.999
95% confidence interval of the slope = 0.98 to 1.02; 95% confidence interval of the y-intercept = -5.5 to 0.8
Range (serum) = 12 to 441 mg/dL

Method comparison at POL sites:

Site #	n	Range (mg/dL)	Regression equation	CI slope	CI intercept	r
1	53	75 to 375	y = 1.01x – 1.1	0.99 to 1.02	-2.7 to 0.6	0.99
2	52	69 to 361	y = 0.97x -0.1	0.96 to 0.99	-2.1 to 1.9	0.99
3	51	75 to 399	y = 1.05x – 2.5	1.03 to 1.07	1.03 to 1.07	0.99

b. Matrix comparison:

Serum/Plasma Comparison Study

A study was performed to validate the use of sodium citrate (Na citrate), lithium heparinized, and K3 EDTA plasma as alternatives to serum for the Hitachi Clinical Analyzer with S TEST GLU reagent cartridges Thirty-eight (38) matched serum/plasma samples that spanned the glucose dynamic range were assayed in singleton and the results were compared using least squares liner regression (plasma = y-axis). The performance characteristics were as follows.

N = 38
Range (serum) = 12 to 441 mg/dL

	Na Citrate Plasma	Heparinized Plasma	K3 EDTA Plasma
Slope (95% CIs)	0.98 (0.96 to 1.00)	1.00 (0.98 to 1.02)	1.00 (0.99 to 1.02)
y-intercept (95% CIs)	-4.6 (-8.2 to -0.8)	-2.1 (-5.8 to 1.6)	-0.3 (-3.1 to 2.6)
r	0.99	0.99	0.99

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

*b. Clinical specificity**:***

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

None

4. Clinical cut-off**:**
   Not applicable

5. Expected values/Reference range:
   Reportable range: 5 - 500 mg/dL
   Reference range (US, fasting serum): 60 – 95 mg/dL*
   It is recommended that each laboratory determine the expected values for its particular population.

   ** Tietz, Tietz Fundamentals of Clinical Chemistry, 4th Edition, WB Saunders Company, (1996*

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.