

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

k112377

B. Purpose for Submission:

New submission for the BS-400/CLC 720 using previously cleared Glucose Reagent (k971467) and the same ISE module cleared under Mindray's BS-200 Chemistry Analyzer (k072018)

C. Measurand:

Glucose, Sodium, Potassium, Chloride

D. Type of Test:

Quantitative, Photometric and Ion Selective Electrode

E. Applicant:

Shenzhen Mindray Bio-Medical Electronics Co., Ltd

F. Proprietary and Established Names:

BS-400/CLC 720

G. Regulatory Information:

1. Regulation section:

21CFR Sec.-862.1345 Glucose test system

21CFR Sec.-862.1665 Sodium test system

21CFR Sec.-862.1600 Potassium test system

21CFR Sec.-862.1170 Chloride test system

21CFR Sec.-862.2160-Discrete photometric chemistry analyzer for clinical use

2. Classification:

Class II for assays

Class I for analyzer (reviewed as part of Class II test systems)

3. Product code:

CFR - hexokinase, glucose

JGS - electrode, ion specific, sodium

CEM - electrode, ion specific, potassium

CGZ - electrode, ion-specific, chloride

JJE - analyzer, chemistry (photometric, discrete), for clinical use

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):
See indications for use below
2. Indication(s) for use:
The BS-400/CLC 720 Chemistry Analyzers are designed for clinical laboratory use, making direct quantitative measurements of Na⁺ (sodium), K⁺ (potassium), Cl⁻ (chloride) in serum, plasma and urine samples and Glucose in serum samples plasma and urine samples. Additionally, other various chemistry assays may be adaptable to the analyzer depending on the reagent used to induce a photometric reaction.

Sodium measurements are used in the diagnosis and treatment diseases involving electrolyte imbalance.

Potassium measurements monitor electrolyte balance and in the diagnosis and treatment of diseases conditions characterized by low or high blood potassium levels.

Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders.

Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

3. Special conditions for use statement(s):
Prescription use
4. Special instrument requirements:
BS-400/CLC 720 Chemistry Analyzers

I. Device Description:

The BS-400/CLC 720 are automated chemistry analyzers for in vitro diagnostic use in clinical laboratories and designed for in vitro quantitative determination of clinical chemistries in serum, plasma and urine samples. The device is composed of a photometric module and an Ion Selective Electrode module.

The Glucose reagent is ready to use and the composition is Liquid Glucose (Hexokinase) Reagent: Hexokinase (yeast) 2000U/L, G6PDH (Leuconostoc mesenteroides) 4000U/L, ATP 1.1 mmol/L, NAD 2.7mmol/L, magnesium 2mmol/L, preservative and stabilizers. The reagent is manufactured by Carolina Liquid Chemistries for use on the BS-400/CLC 720 Chemistry Analyzers.

The ISE module is the same module as the one cleared on the BS- 200 analyzer and consists of ion selective electrodes for sodium, potassium, and chloride, a reference electrode and accessory reagents.

J. Substantial Equivalence Information:

1. Predicate device name(s):
BS-200 Chemistry Analyzer
2. Predicate 510(k) number(s):
k072018
3. Comparison with predicate:

BS-400 and BS-200

Feature	BS-400	BS-200
Indications	The BS-400/CLC 720 Chemistry Analyzers are designed for clinical laboratory use, making direct quantitative measurements of Na+ (sodium), K+ (potassium), Cl- (chloride) in serum, plasma and urine samples and Glucose in serum samples plasma and urine samples. Additionally, other various chemistry assays may be adaptable to the analyzer depending on the reagent used to induce a photometric reaction.	Same
System Function		
System Control	Automatic, computer controlled	same
LIS external connectivity capability	Yes	same
Calibration/QC	Automatic and Manual calibration/QC	same
Barcode	Yes	same
Throughput (Max)		
	400 photometric tests per hour	200 photometric tests per hour
Configuration		
	Analytical unit, Operational Unit	same
Principle of Analysis		
Mode of detection	Photometric	same
Analytical methods	Endpoint Fixed-time Kinetic	same
Calibration methods	Linear calibration and nonlinear calibration	same
Optical Measurement Unit		

Feature	BS-400	BS-200
Measurement Modes	Absorbance	same
Optical Modes	Monochromatic, Bichromatic	same
Photometer	Multi-wavelength diffraction grating spectrophotometer	same
Wavelength	340nm, 380nm, 412nm, 450nm, 505nm, 546nm, 570nm, 605nm, 660nm, 700nm, 740nm and 800nm	340nm, 405nm, 450nm, 410nm, 546nm, 578nm, 630nm, 670nm
Linear absorbance range	0-3.0 absorbance	0-4.0 absorbance
Light Source	Tungsten halogen lamp	same
Detector	Photodiode	same
Reaction Unit		
Reaction cuvettes	Plastic or Glass 90 non-disposable	Plastics, 80 disposable
Reaction volume	150~360 μ L	180~500uL
Path length	5mm	same
Reaction temperature	37°C	same
Sample and Reagent System		
Sample disk	90 positions. 30 positions respectively for inner, middle and outer circles.	40 sample tube positions on the outer circle
Reagent disk	80 positions. 40 positions respectively for inner and outer circles	40 reagent bottle positions on the inner circle of the sample disk
Pipettor System	Positive displacement stepper motor driven	same
Refrigerator temperature	2-10°C	4-15°C
Sample Dispense	2 μ L -45 μ L	3 μ l -45 μ l
Reagent Dispense	20 μ L-350 μ L	30 μ l-450 μ l
POWER		
Input	110/115V~, 60Hz	100-130V ,50/60 \pm 1 Hz
Operating environmental conditions		

Feature	BS-400	BS-200
Temperature	15°C to 30°C	same
Humidity	35% to 80%, non-condensing	Same
	ISE (ion selective electrode technology)	same
Sample Type		
	Serum, plasma, or diluted urine	same
Test		
	Na+, K+, Cl	same
Sample Size		
	70 µL Serum, plasma mode; 140 µL Urine mode	same
ISE Calibration		
	Two-point and single-point calibrations	same

K. Standard/Guidance Document Referenced (if applicable):

CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices - EP05-A2
 CLSI - Evaluation of the Linearity of Quantitative Analytical Methods - EP06-A
 CLSI - Interference Testing in Clinical Chemistry - EP07-A2
 CLSI - Method Comparison and Bias Estimation Using Patient Samples - EP09-A2
 CLSI - Protocols for Determination of Limits of Detection and Limits of Quantitation - EP17-A

L. Test Principle:

Glucose is phosphorylated with adenosine triphosphate (ATP) in the reaction catalyzed by hexokinase (HK). The product, glucose-6-phosphate (G6P) is then oxidized with the concomitant reduction of nicotinamide adenine dinucleotide (NAD) to NADH in the reaction catalyzed by glucose-6-phosphate-dehydrogenase (G6PDH). The formation of NADH causes an increase in absorbance at 340nm. The increase is directly proportional to the amount of glucose in the sample.

The ion selective electrodes develop a voltage that varies with the concentration of the ion (Na+, K+, Cl-) to which they are specific. The relationship between the voltage developed and the concentration of the sensed ion is logarithmic and calculated by the Nernst equation.

M. Performance Characteristics (if/when applicable):

These studies are intended to verify use of photometric and ISE technology on the analyzer.

1. Analytical performance:

a. *Precision/Reproducibility:*

Repeatability and within device imprecision for both serum/control and urine specimens are shown through the replicate assay of specimen pools and control materials over twenty days as described in CLSI document EP5-A2

Imprecision statistics are summarized below.

Imprecision of Glucose Measurements (in mg/dL)

Specimen	Sample	n	mean	Repeatability		Within Device Imprecision	
				SD	%CV	SD	%CV
Serum	Control pool 1	120	56.3	0.57	1.0%	0.88	1.6%
	Serum Pool	120	117.0	0.83	0.7%	1.74	1.5%
	Control pool 2	120	561.6	3.42	0.6%	6.84	1.2%
Urine	Urine pool 1	117	14.9	0.26	1.7%	0.32	2.1%
	Urine pool 2	117	194.3	1.08	0.6%	1.91	1.0%
	Urine pool 3	120	330.0	1.80	0.5%	2.95	0.9%

ISE within-run precision

Item	Level I			Level II		
	Mean	SD	CV%	Mean	SD	CV%
Serum K+ (mmol/L)	3.49	0.02	0.54%	6.21	0.03	0.43%
Serum Na+ (mmol/L)	128.1	0.63	0.49%	150.8	0.50	0.33%
Serum Cl- (mmol/L)	84.8	0.95	1.12%	117.9	0.51	0.44%
	Urine Level I			Urine Level II		
Urine K+ (mmol/L)	21	0.51	2.48%	44	0.00	0.00%
Urine Na+ (mmol/L)	65	1.60	2.46%	124	1.81	1.47%
Urine CL- (mmol/L)	53	1.08	2.03%	106	1.15	1.08%

ISE Total precision

Item	Level I			Level II		
	Mean	SD	CV%	Mean	SD	CV%
Serum K+ (mmol/L)	3.48	0.03	0.78	6.17	0.04	0.64
Serum Na+ (mmol/L)	129.1	1.00	0.78	150.4	0.89	0.59
Serum Cl- (mmol/L)	85.1	1.10	1.29	117.1	0.96	0.82
	Urine Level I			Urine Level II		
Urine K+ (mmol/L)	21	0.47	2.23	44	0.24	0.56
Urine Na+ (mmol/L)	67	3.19	4.75	126	3.45	2.74
Urine CL- (mmol/L)	56	2.13	3.83	108	2.02	1.87

b. *Linearity/assay reportable range:*

Linearity claims for both the serum and urine applications are validated using procedures based on CLSI document EP06-A

Glucose

A first set of 0, 5, 25, 50, 100, 200, 300, 400, 500, 600 and 700 mg/dL glucose (NIST SRM 917c) in a matrix of 7 g/dL BSA, 0.85% sodium chloride, and an inert preservative for the serum/plasma application.

A second, analogous set of standards was similarly prepared in an aqueous matrix without BSA for the urine application.

ISE

Linearity samples were prepared by using low and high samples with serial dilution schemes to cover 11 points in the test range.

Measuring Range		
Glucose mg/dL Serum/Plasma Based on LOQ and Linearity $y = 0.999x + 0.777$ $R^2 = 1$	5	700
Glucose Urine mg/dL Based on LOQ and Linearity $y = 1.002x + 0.610$ $R^2 = 1$	2	700
ISE Based on Linearity and supported by LOQ		
K (mmol/L) serum(ISE) $y = 1.0007x - 0.0051$ $R^2 = 0.9998$	0.94	8.2
Na (mmol/L) serum(ISE) $y = 1.0001x - 0.0038$ $R^2 = 0.9998$	71	232.3
CL (mmol/L) serum(ISE) $y = 1.0001x - 0.015$ $R^2 = 0.9999$	50	198
K (mmol/L) Urine(ISE) $y = 0.9998x + 0.0203$ $R^2 = 0.9987$	3.5	209.3
Na (mmol/L) Urine(ISE) $y = 1.0000x - 0.0024$ $R^2 = 0.9999$	9.25	725.5
CL (mmol/L) Urine(ISE) $y = 0.9999x + 0.0129$ $R^2 = 0.9986$	7.25	693.3

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

Cleared under Point Multi-Analyte Chemistry Calibrator (k070207)
Cleared under Medica EasyElectroLyte/RapidLyte Na/K/Cl Analyzer (k000926)

d. *Detection limit:*

The limits of blank (LoB) and detection (LoD) are listed below with the number of determinations they are based on. These limits were determined consistent with the guidelines of CLSI protocol EP17-A with proportions of false positives less than 5% and false negatives less than 5%.

Glucose				
Specimen	n	LoB	LoD	LOQ
Serum	80	2.2	2.6	5.0 mg/dL
Urine	60	0.6	0.9	1.0 mg/dL

ISE

Item	n	LoB	LoD	LoQ
Serum				
K (mmol/L)	60	0.06	0.08	0.48
Na (mmol/L)	60	0.92	1.41	3.27
CL (mmol/L)	60	1.12	1.94	5.04
Urine				
K (mmol/L)	60	1.50	1.76	3.01
Na (mmol/L)	60	3.50	6.88	11.22
CL (mmol/L)	60	1.00	2.96	5.55

e. Analytical specificity:

Glucose

Effects of potentially interfering substances are shown by spiking serum pools with increasing amounts of interferent and measuring the effect of the additions on results. Bilirubin, hemoglobin, and Intralipid® 20% Emulsion are used to estimate icterus, hemolysis, and lipemia interference.

Interferent	Glucose Concentration	Interferent Concentration	Change in Glucose Result
Ascorbic acid	76 mg/dL	30 mg/L†	-0.1 mg/dL*
	140 mg/dL	30 mg/L†	-0.8 mg/dL*
Bilirubin	78 mg/dL	4.8 mg/dL	-2.6 mg/dL
		8.0 mg/dL	-4.0 mg/dL
	138 mg/dL	8.0 mg/dL	-3.3 mg/dL
Hemoglobin		16.0 mg/dL	-6.9 mg/dL
	74 mg/dL	400 mg/dL†	-2.0 mg/dL
	134 mg/dL	400 mg/dL†	-3.8 mg/dL
Triglycerides (non-turbid)	69 mg/dL	728 mg/dL	+2.3 mg/dL
		910 mg/dL	+3.0 mg/dL
	115 mg/dL	742 mg/dL	+2.2 mg/dL
Metronidazole		927 mg/dL†	+2.7 mg/dL
	75 mg/dL	24 mg/L	+2.6 mg/dL
		48 mg/L	+5.6 mg/dL
	137 mg/dL	24 mg/L	+3.1 mg/dL
		48 mg/L	+5.1 mg/dL

Tetracycline	76 mg/dL	15 mg/L†	-1.5 mg/dL
	140 mg/dL	15 mg/L†	-1.5 mg/dL
EDTA	76 mg/dL	8 mg/mL†	+0.2 mg/dL*
	145 mg/dL	8 mg/mL†	-0.1 mg/dL*
Potassium oxalate	76 mg/dL	8 mg/dL†	+0.0 mg/dL*
	146 mg/dL	8 mg/dL†	-0.8 mg/dL*
Sodium citrate	76 mg/dL	140 mg/dL†	-1.1 mg/dL
	145 mg/dL	140 mg/dL†	-2.8 mg/dL
Sodium fluoride	77 mg/dL	10 mg/dL†	+0.1 mg/dL*
	145 mg/dL	10 mg/dL†	+0.9 mg/dL*

* Result is statistically insignificant at p=0.05.

† Highest level tested.

Serum pools containing 73 mg/dL and 121 mg/dL glucose and respectively spiked with 50 mg/dL and 60 mg/dL Intralipid® give lipemia index values of 47.1 and 54.9. Both pools appear moderately lipemic.

Visibly lipemic specimens with lipemic index values greater than 47 may produce elevated results. Assay these specimens using the Glucose (Blanked) Application.

ISE

Interference: Interference studies were performed based on CLSI document EP7-A2, the test results are showing below with no interference up to the amounts tested.

Item	Interference materials		
	Hemoglobin	Bilirubin	Lipemia Intralipids®
K (mmol/L)	500 mg/dL	40 mg/dL	1000 mg/dL
Na (mmol/L)	500 mg/dL	40 mg/dL	1000 mg/dL
CL (mmol/L)	500 mg/dL	40 mg/dL	1000 mg/dL

Note: Hemolysis: Hemoglobin had no interference to serum K⁺ due to Hemoglobin used not having K⁺, but Hemolysis will interfere with K⁺ due to the high K⁺ concentration in erythrocytes.

f. Assay cut-off:
Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Method comparison using 110 serum and 108 plasma samples (vs. Beckman

Synchron CX7)

Item	Specimen	N	r ²	Slope	Intercept	Range
GLU (mg/dL)	Serum + Plasma	218	0.999	0.989	1.31	38 – 672
GLU (mg/dL)	Serum	110	1.000	0.992	1.40	38 – 672
GLU (mg/dL)	Plasma	108	0.999	0.986	1.22	42 – 672

Method comparison using urine samples (vs. Beckman Synchron CX7)

Item	N	r ²	Slope	Intercept	Range
GLU (mg/dL)	108	1.000	1.001	1.36	2 – 660

ISE analysis (vs. BS-200 Chemistry Analyzer)

Item (mmol/L)	Regression Slope	Regression Intercept	Correlation coefficient square R ²	Analyze Range of BS-400 (mmol/L)	Sample numbers
Serum K ⁺	1.0097	0.0591	0.997	0.93~8.18	40
Serum Na ⁺	1.0092	-0.7885	0.9975	70.7~232.3	40
Serum Cl ⁻ (mmol/L)	0.9763	1.3848	0.9946	49.5~198.0	40
Urine K ⁺	0.9718	1.7022	0.9996	4~210	40
Urine Na ⁺	1.0249	-13.487	0.9994	12~725	40
Urine Cl ⁻	0.9984	2.1591	0.9996	7~690	40

b. *Matrix comparison:*

See 2.a method comparison above for glucose plasma and urine and ISE urine claim. The plasma claim for the ISE electrodes was previously cleared under the Medica EasyElectroLyte/RapidLyte Na/K/Cl Analyzer (k000926).

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):

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

Glucose

Sample _____ Conventional Units SI Units _____

Serum/Plasma	74 to 100 mg/dL	4.1 to 5.1 mmol/L
Urine, Random	1 to 15 mg/dL	0.1 to 0.8 mmol/L
Urine, 24 hour	< 0.5 g/day	< 2.87 mmol/day

Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. Elsevier Inc., St. Louis, MO, 2006.

Sodium – serum: 136-145 mmol/L, 24 hour urine: 40-220 mmol/L
 Potassium – serum: 3.5-5.1 mmol/L, 24 hour urine: 25-125 mmol/L
 Chloride – serum: 98-107 mmol/L, 24 hour urine: 110-250 mmol/L

Tietz, N.W., Clinical Guide to Laboratory Tests, Philadelphia, W.B. Saunders, 1990

N. Instrument Name:

BS-400/CLC 720 Chemistry Analyzer

O. System Descriptions:

1. Modes of Operation:

Random access instrument with ISE module

Does the applicant’s device contain the ability to transmit data to a computer, webserver, or mobile device?:

Yes X or No _____

Does the applicant’s device transmit data to a computer, webserver, or mobile device using wireless transmission?:

Yes _____ or No X

2. Software:

FDA has reviewed applicant’s Hazard Analysis and software development processes for this line of product types:

Yes X or No _____

3. Specimen Identification:

Sample bar code option

4. Specimen Sampling and Handling:

Random access and stat mode operation Samples are loaded on sample disk

5. Calibration:

Linear calibration and nonlinear calibration

6. Quality Control:

Includes quality control program

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

None

Q. Proposed Labeling:

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

R. Conclusion:

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