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

A. 510(k) Number:
k072018

B. Purpose for Submission:
New submission for glucose, sodium, potassium and chloride on a new analyzer

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-200 Chemistry Analyzer, Mode BS-200

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-200 Chemistry Analyzer is 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. 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-200 Chemistry Analyzer

I. Device Description:

The BS-200 is an automated chemistry analyzer 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) 4000U/L, G6PDH (Leuconostoc mesenteroides) 4000U/L, ATP 6.0mM, NAD 3.0mM, Buffer pH 7.5 ± 0.1, Nonreactive stabilizers, and sodium azide (0.1%) as preservative. The reagent is manufactured by Point Scientific for Shenzhen Mindray Bio-Medical.

The ISE module consists of ion selective electrodes for sodium, potassium, and chloride, a reference electrode and accessory reagents. The module is manufactured for Midray by Medica. The electrodes and accessory reagents were also previously cleared as the Medica Easyelectrolyte Analyzer and Rapidlyte Analyzer (k000926).

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Roche, Hitachi 911 analyzer
   Point Scientific Glucose reagent
   Medica Easyelectrolyte Analyzer and Rapidlyte Analyzer
2. Predicate 510(k) number(s):
   k953239
   k002199
3. k000926

Comparison with predicate:

Comparison Section	BS-200	Boehringer Mannheim/Hitachi 917 analyzer	EasyElectroLyte/RapidLyte Na/K/Cl Analyzer
510(K) Number	Pending	k953239	k000926
Intended use	The BS-200 Chemistry Analyzer is 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. Additionally, other various chemistry assays may be adaptable to the analyzer depending on the reagent used to induce a photometric reaction.	The Boehringer Mannheim/Hitachi 917 analyzer is intended for the quantitative and qualitative measurement of analytes in body fluids.	EasyElectroLyte/Rapid Lyte Na/K/Cl Analyzer is designed for clinical laboratory use by laboratory professionals to assess the levels of Na+ (sodium), K+ (potassium), and Cl- (chloride) found in whole blood, serum, plasma, and urine of patients. The analysis is performed in-vitro, and neither the analyzer nor any of its components come in contact with the patient.
Parameter	Glucose	**Glucose**	None
	ISE (K,Na,Cl)	ISE(K,Na,Cl)	**ISE (K,Na,Cl)**

BS-200 and (Roche) Boehringer Mannheim/Hitachi 917 analyzer

	Feature	BS-200	Boehringer Mannheim/Hitachi 917 analyzer	S/D
	510(K)	Pending	510(k) Number k953239	/
1	**Standards**			
		IEC 61010-1	IEC 61010-1	**S**
2	**System Function**			
	System Control	Automatic, microprocessor controlled	Automatic, microprocessor controlled	**S**
	LIS external connectivity capability	Yes	Yes	**S**
	Calibration/QC	Automatic and Manual calibration/QC	Automatic and Manual calibration/QC	**S**
	Barcode	Yes	Yes	**S**
3	**Throughput (Max)**			
		200 photometric tests per hour 330 tests per hour with ISE	800 photometric tests per hour 1200 tests per hour with ISE	**D**

	Feature	BS-200	Boehringer Mannheim/Hitachi 917 analyzer	**S/ D**
	510(K)	Pending	510(k) Number k953239	**/**
4	**Configuration**			
		Analytical unit, Operational Unit	Analytical unit, Operational Unit	**S**
5	**Principle of Analysis**			
	Mode of detection	Photometric	Photometric	**S**
	Analytical methods	Endpoint with sample blanking Fixed-time Kinetic	Endpoint with sample blanking Endpoint Kinetics	**S**
	Calibration methods	Linear calibration and nonlinear calibration	Linear calibration and nonlinear calibration	**S**
6	**Optical Measurement Unit**			
	Measurement Modes	Absorbance	Absorbance	**S**
	Optical Modes	Monochromatic, Bichromatic	Monochromatic, Bichromatic	**S**
	Wavelength	340nm, 405nm, 450nm, 510nm, 546nm, 578nm, 630nm, 670nm	340nm, 376 nm, 415 nm, 450 nm, 505 nm, 546 nm, 570 nm, 600 nm, 660 nm, 700 nm, 800 nm	**D**
	Linear absorbance range	0.0000-4.0000 absorbance	0.0000-2.5000 absorbance	**D**
	Light Source	Tungsten halogen lamp	Tungsten halogen lamp	**S**
	Detector	Photodiode	Photodiode	**S**
7	**Reaction Unit**			
	Reaction cuvettes	Plastics, 80 disposable	Plastics, 160 semi-disposable	**D**
	Reaction volume	180~500uL	180~380uL	**D**
	Path length	5mm	5mm	**S**
	Reaction temperature	37°C	37°C	**S**
8	**Sample and Reagent System**			
	Sample tube/ reagent bottle positions	40 sample tube positions on the outer circle and 40 reagent bottle positions on the inner circle	110 positions on sample disk 1, 60 positions on sample disk 2; 45 positions on reagent disk 1(R1), 44 positions on reagent disk 2(R2)	**D**
	Pipettor System	Positive displacement stepper motor driven	Positive displacement stepper motor driven	**S**
	Refrigerator temperature	4-15°C	2-12°C	**D**
	Sample Dispense	3µl -45µl	2-35µl	**D**
	Reagent Dispense	30µl-450µl	20-270µl	**D**
9	**POWER**			
	Input	100-130V～,50/60±1 Hz	115V±10v AC, 60±0.5 Hz	**D**
	Consumption	1000 VA (max.)	3kVA	**D**
10	**Operating environmental conditions**			
	Temperature	+15ºC to +30ºC	+15ºC to +32ºC	**D**
	Humidity	35% to 80%, non-condensing	45% to 85% relative humidity	**D**

BS-200 and Easy Electrolytes

	Feature	BS-200	EasyElectroLyte/RapidLyte Na/K/Cl Analyzer	S/ D
	510(K)	Pending	510(k) Number K000926	/
1	**Principle**			
		ISE (ion selective electrode technology)	ISE (ion selective electrode technology)	**S**
2	**Sample Type**			
		Serum, plasma, or diluted urine	Serum, plasma, or diluted urine	**S**
3	**Test**			
		Na^+, K^+, Cl^-	Na^+, K^+, Cl^-	**S**
4	**Sample Size**			
		70 µL Serum, plasma mode; 140 µL Urine mode	55 µL Serum, plasma mode; 300 µL Urine mode	**D**
5	**ISE Calibration**			
		Two-point and single-point calibrations	Two-point and single-point calibrations	**S**

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

- IEC 61010-1 - Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use - Part 1
- ISO14971 - Medical devices — Application of risk management to medical devices
- 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

This method uses hexokinase and glucose-6-phosphate-dehydrogenase to catalyze the reaction:

$$\text{Glucose} + \text{ATP} \xrightarrow{\text{HK}} \text{G6P} + \text{ADP}$$

$$\text{G6P} + \text{NAD} \xrightarrow{\text{G6PDH}} \text{6-Phosphogluconate} + \text{NADH} + \text{H}^+$$

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):

1. Analytical performance:

a. Precision/Reproducibility:

Glucose

Precision studies were performed using control serum samples at low, middle and high concentration. The studies were conducted for 20 days with two runs per day and duplicates per run according to CLSI EP5-A2 document.

Within-Run			
Mean	**S.D.**	**C.V.%**	**N**
56	0.5	0.9	80
122	0.7	0.6	80
296	1.3	0.5	80

Between-day			
Mean	**S.D.**	**C.V.%**	**N**
56	1.1	2.0	80
122	2.0	1.6	80
296	4.9	1.7	80

ISE Serum Mode

Precision studies were performed following a modification of the guidelines contained in CLSI document EP5-A2. The testing was conducted in duplicate for 20 days with two runs per day. The results are summarized in the tables below.

Within-run precision

Item	Level I			Level II		
	Mean	SD	CV%	Mean	SD	CV%
K mmol/L	4.11	0.03	0.7%	6.77	0.05	0.8%
Na mmol/L	136.13	0.61	0.4%	146.74	0.72	0.5%
Cl mmol/L	99.59	0.73	0.7%	115.68	0.52	0.5%

Day-to-Day precision

Item	Level I			Level II		
	Mean	SD	CV%	Mean	SD	CV%
K mmol/L	4.11	0.07	1.6%	6.77	0.06	1.0%
Na mmol/L	136.13	2.12	1.6%	146.74	1.66	1.1%
CL mmol/L	99.59	1.78	1.8%	115.68	1.13	1.0%

ISE Urine Mode

Within-run precision

Item	Level I			Level II		
	Mean	SD	CV%	Mean	SD	CV%
K mmol/L	37.09	0.46	1.2%	67.49	0.63	0.9%
Na mmol/L	99.23	1.13	1.1%	170.84	1.36	0.8%
CL mmol/L	82.90	1.36	1.6%	132.16	1.24	0.9%

Day-to-Day precision

Item	Level I			Level II		
	Mean	SD	CV%	Mean	SD	CV%
K mmol/L	37.09	0.48	1.3%	67.49	0.70	1.0%
Na mmol/L	99.23	1.68	1.7%	170.84	2.41	1.4%
CL mmol/L	82.90	1.50	1.8%	132.16	2.12	1.6%

b. Linearity/assay reportable range:

The reportable ranges of the assays are as follows:

Glucose = 1– 600 mg/dl
Potassium = 1.1 – 8.6 mmol/L
Sodium = 113 – 194 mmol/L
Chloride = 53 – 154 mmol/L

ISE Urine mode
Potassium = 13 – 184 mmol/L
Sodium = 27 – 372 mmol/L
Chloride = 42 – 442 mmol/L

Linearity studies were performed to validate the measuring range of the assays. The samples were prepared with 11 concentrations with the range from lowest to the highest concentration. They analyzed each of levels for 4 times, and then calculated the linear deviation and linearity range in accordance with CLSI EP6-A document.

Glucose Linearity Percent Difference

Ranks	*Assigned* (mg/dl)	*% of high Std. with saline*	*mean of 4 rep.*	*% diff. from assigned*
1	0	0	0	0.00%
2	1	0.15%	1	0.00%
3	4	0.60%	4	0.00%
4	17	2.50%	17.25	1.47%
5	34	5%	34.5	1.47%
6	68	10%	68.25	0.37%
7	136	20%	140	2.94%
8	204	30%	211	3.43%
9	340	50%	342.5	0.74%
10	473	70%	479	1.27%
11	680	100%	686.25	0.92%

$$y = 1.003x + 1.8864$$
$$r^2=0.9998$$

Serum Potassium Linearity Percent Difference

Ranks	*Assigned* (mg/dl)	*ratio of high to low std.*	*mean of 4 rep.*	*% diff. from assigned*
1	1.08	0:1	1.075	0.00%
2	1.84	1:9	1.875	1.90%
3	2.6	2:8	2.600	0.00%
4	3.36	3:7	3.200	-4.76%
5	4.12	4:6	4.300	4.37%
6	4.88	5:5	4.925	0.92%
7	5.64	6:4	5.700	1.06%
8	6.4	7:3	6.225	-2.73%
9	7.16	8:2	7.025	-1.89%
10	7.92	9:1	7.925	0.06%
11	8.68	1:0	8.675	-0.06%

$y = 0.9919x + 0.0253$
$r^2 = 0.9981$

Serum Sodium Linearity Percent Difference

Ranks	*Assigned* (mg/dl)	*ratio of high to low std.*	*mean of 4 rep.*	*% diff. from assigned*
1	114	0:1	114.00	0.00%
2	122.2	1:9	122.75	0.45%
3	130.4	2:8	129.50	-0.69%
4	138.5	3:7	135.50	-2.17%
5	146.7	4:6	148.25	1.06%
6	154.9	5:5	154.75	-0.10%
7	163.1	6:4	163.25	0.09%
8	171.2	7:3	168.25	-1.72%
9	179.4	8:2	178.00	-0.78%
10	187.6	9:1	187.25	-0.19%
11	195	1:0	195.75	0.38%

$y = 0.9969x - 0.0461$
$r^2 = 0.9967$

Serum Chloride Linearity Percent Difference

Ranks	*Assigned* (mg/dl)	*ratio of high to low std.*	*mean of 4 rep.*	*% diff. from assigned*
1	52.8	0:1	52.75	0.00%
2	63	1:9	64.00	1.59%
3	73.2	2:8	72.00	-1.64%
4	83.4	3:7	80.25	-3.78%
5	93.7	4:6	95.50	1.92%
6	103.9	5:5	104.25	0.34%
7	114.1	6:4	114.75	0.57%
8	124.3	7:3	122.25	-1.65%
9	134.6	8:2	133.25	-1.00%
10	144.8	9:1	144.25	-0.38%
11	155	1:0	155.00	0.00%

$y = 0.9953x + 0.0785$
$r^2 = 0.9974$

Urine Potassium Linearity Percent Difference

Ranks	*Assigned* (mg/dl)	*ratio of high to low std.*	*mean of 4 rep.*	*% diff. from assigned*
1	11	0:1	11.00	0.00%
2	28.21	1:9	29.40	4.22%
3	45.41	2:8	47.15	3.83%
4	62.62	3:7	65.25	4.20%
5	79.82	4:6	82.20	2.98%
6	97.03	5:5	99.50	2.55%
7	114.23	6:4	115.88	1.44%
8	131.44	7:3	132.90	1.11%
9	148.64	8:2	149.93	0.86%
10	165.84	9:1	165.23	-0.37%
11	183.05	1:0	183.05	0.00%

$$y = 0.9938\,x - 1.8873$$
$$r^2 = 0.9994$$

Urine Sodium Linearity Percent Difference

Ranks	*Assigned* (mg/dl)	*ratio of high to low std.*	*mean of 4 rep.*	*% diff. from assigned*
1	21	0:1	21.00	0.00%
2	55.9	1:9	61.25	9.57%
3	90.8	2:8	96.75	6.55%
4	125.8	3:7	132.75	5.52%
5	160.7	4:6	166.50	3.61%
6	195.6	5:5	202.25	3.40%
7	230.6	6:4	236.50	2.56%
8	265.5	7:3	268.50	1.13%
9	300.4	8:2	301.00	0.20%
10	335.3	9:1	335.75	0.13%
11	370.3	1:0	370.25	-0.01%

$$y = 0.9886x + 5.9159$$
$$r^2 = 0.9994$$

Urine Chloride Linearity Percent Difference

Ranks	*Assigned* (mg/dl)	*ratio of high to low std.*	*mean of 4 rep.*	*% diff. from assigned*
1	5	0:1	5.00	0.00%
2	47	1:9	44.75	-4.79%
3	88.9	2:8	84.00	-5.51%
4	130.8	3:7	122.75	-6.15%
5	172.8	4:6	166.25	-3.79%
6	214.8	5:5	209.25	-2.58%
7	256.7	6:4	251.00	-2.22%
8	298.6	7:3	294.25	-1.46%
9	340.6	8:2	338.25	-0.69%
10	382.6	9:1	383.50	0.24%
11	424.5	1:0	424.50	0.00%

$y = 1.0062 – 4.8541$

$r^2 = 0.9995$

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

The applicant is not making a claim for a glucose calibrator or control but is recommending the use of an NIST-traceable Glucose Standard (100mg/dl) or serum calibrator. The glucose studies were conducted using the calibrator cleared under k810674.

Cleared under Medica EasyElectroLyte/RapidLyte Na/K/Cl Analyzer (k000926)

d. *Detection limit:*

Glucose

The lower limit of the reportable range is 1.0 mg/dl, which was defined by the sponsor as the lowest measurable analyte level with a CV less then or equal to 20%. The studies were conducted for 10 days with two runs per day using serum sample containing the analyte at 1mg/dl concentration.

The lower limit of the measuring range for the ISE assays was determined from the linear range study above.

e. Analytical specificity:

The applicant references Young, et al (Young, D.S., et al, Clin. Chem. 21:1D (1975)) for drugs and substances that may affect glucose values.

The applicant has tested glucose for the following:

Bilirubin to the level of 18 mg/dl has been found to exhibit ≤10% interference in this assay. Hemoglobin to the level of 250 mg/dl has been found to exhibit ≤10% interference in this assay. Intralipid has been found to exhibit ≤10% interference in this assay to a level of 300 mg/dl.

The applicant has tested all the ISE assays for the following:

Bilirubin to the level of 20 mg/dl has been found to exhibit ≤10% interference in this assay. Hemoglobin* to the level of 500 mg/dl has been found to exhibit ≤10% interference in this assay. Intralipid has been found to exhibit ≤10% interference in this assay to a level of 1000 mg/dl.

* Hemolysis: Hemoglobin had no interference with K^+ due to the nature of the commercial Hemoglobin product having no K^+ ion. However, hemolysis will interfere with K^+ due to the high K^+ concentration in erythrocytes. The sponsor has listed this interference in the PI.

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison using serum samples (vs. Hitachi 917)

Item	N	r	Slope	Intercept	Range
GLU (mg/dL)	60	0.9992	1.015	-0.0288	27-593

Method comparison using serum samples (vs. EasyElectrolytes K/Na/Cl)

Item	N	r	Slope	Intercept	Range
K (mmol/L)	40	0.9983	0.986	0.124	2.9-6.9
Na (mmol/L)	40	0.9868	1.007	-1.1	129.3-176.4
CL (mmol/L)	40	0.9894	0.973	4.35	75.6-129.8

Method comparison using diluted urine samples (vs. EasyElectrolytes K/Na/Cl)

Item	N	r	Slope	Intercept	Range
K (mmol/L)	40	0.9992	0.967	0.34	11-84.4
Na (mmol/L)	40	0.9974	0.949	-4.2	21-218
CL (mmol/L)	40	0.9895	0.997	-6.5	62-286

b. Matrix comparison:
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 Normal range - 74-106 mg/dl
   (as referenced by Tietz, N.W., Text Book of Clinical Chemistry, Philadelphia, W.B. Saunders, p.782 (1999))

   ISE normal ranges
   Chloride – serum: 98-107 mmol/L, 24 hour urine: 110-250 mmol/L
   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
   (as referenced by Tietz, N.W., Clinical Guide to Laboratory Tests, Philadelphia, W.B. Saunders, (1990))

N. Instrument Name:

Mindray, BS 200 Chemistry Analyzer

O. System Descriptions:

1. Modes of Operation:

   Random access instrument with ISE module

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 reagent wheel

5. Calibration:
   Endpoint with sample blanking
   Fixed-time
   Kinetic
   Linear calibration and nonlinear calibration methods

6. Quality Control:

   Includes quality control program

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

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.