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

A. 510(k) Number:

k140690

B. Purpose for Submission:

Adding previously cleared assays on new instrument platforms (BS-480 / BS-490 / CLC720i Chemistry Analyzers)

C. Measurand:

Sodium, Potassium, Chloride, and Urea Nitrogen

D. Type of Test:

Quantitative Photometric and Ion Selective Electrodes

E. **Applicant**:

Shenzhen Mindray Bio-Medical Electronics Co., Ltd

F. Proprietary and Established Names:
BS-480 Chemistry Analyzer
BS-490 Chemistry Analyzer
CLC720i Chemistry Analyzer

G. Regulatory Information:

Product Code	Regulation Name	Classification	Regulation Section	Panel
CDQ	Urea Nitrogen test system	II	21 CFR 862.1770	Chemistry (75)
JGS	Sodium test system	II	21 CFR 862.1665	Chemistry (75)
CEM	Potassium test system	II	21 CFR 862.1600	Chemistry (75)
CGZ	Chloride test system	II	21 CFR 862.1170	Chemistry (75)
JJE	Discrete photometric chemistry analyzer for clinical use	I, exempt	21 CFR 862.2160	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indication(s) for use below

2. Indication(s) for use:

   The BS-480 / BS-490 / CLC720i Chemistry Analyzer is designed for clinical chemistry laboratory use, making direct quantitative measurements of Na^+(sodium), K^+ (potassium), Cl^- (chloride) in serum, plasma and urine samples, and Urea Nitrogen in serum samples. Additionally, other various chemistry tests may be adaptable to the analyzer depending on the reagent used to induce a photometric reaction.

   Sodium measurements monitor electrolyte balance and in the diagnosis and treatment of diseases involving electrolyte imbalance.

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

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

   Urea Nitrogen (BUN) measurements are used to aid in the determination of liver and kidney function and other diseases associated with protein catabolism.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   BS-480 Chemistry Analyzer, BS-490 Chemistry Analyzer, and CLC720i Chemistry Analyzer

I. Device Description:

The BS-480, BS-490, and CLC720i are automated chemistry analyzers containing an automated reagent probe, sample probe, mixers, reagent carousel, reaction carousel, wash station 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 devices are composed of a photometric module and an Ion Selective Electrode module for measuring sodium, potassium, and chloride. All three analyzers are the exact same analyzer except for the model names.

The Urea Nitrogen reagent is a previously cleared (k971309) liquid ready to use reagent

composed of Urease (jack bean), 30,000 U/L, GLDH (bovine liver), 200 U/L, α-KG, 9.5 mmol/L, NADH (yeast), 0.28 mmol/L, buffer, and stabilizer. The ISE module is the same module as the one cleared on the BS-200 analyzer k072018) and consists of ion selective electrodes for sodium, potassium, chloride, and reference electrodes along with pump, tubes, connectors, and accessory reagents.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Shenzhen Mindray Bio-Medical Electronics BS-400/CLC 720 Chemistry Analyzer, ISE Derma Media Lab Urea Nitrogen

2. Predicate 510(k) number(s):
   k112377
   k971309

3. Comparison with predicate:

BS-480 Chemistry Analyzer/ISE

Similarities / Differences		
Item	BS-480 Chemistry Analyzer k140690 (Candidate Device)	BS-400 Chemistry Analyzer k112377 (Predicate Device)
Intended use	The BS-480 Chemistry Analyzer is an automated chemistry analyzer for in vitro diagnostic use in clinical laboratories. The analyzer is designed for the in vitro quantitative determination of clinical chemistries in serum, plasma or urine sample	The BS-400 Chemistry Analyzer is an automated chemistry analyzer for in vitro diagnostic use in clinical laboratories. The analyzer is designed for the in vitro quantitative determination of clinical chemistries in serum, plasma, urine, or cerebral spinal fluid samples.
System Function		
System Control	Automatic computer control	Same
LIS external connectivity capability	Yes	Same
Calibration/QC	Automatic and Manual calibration/QC	Same
Barcode	Yes	Same
Throughput (Max)	400 photometric test per hour	Same
Configuration	Analytical unit, Operational Unit	Same
Principle of Analysis		
Mode of detection	Photometric	Same

Similarities / Differences		
Item	BS-480 Chemistry Analyzer k140690 (Candidate Device)	BS-400 Chemistry Analyzer k112377 (Predicate Device)
Analytical methods	Endpoint Fixed-time Kinetic	Same
Calibration methods	Linear calibration and nonlinear calibration	Same
Optical Measurement Unit		
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	Same
Linear absorbance	0 – 3.3 absorbance	0 – 3.0 absorbance
Light Source	Tungsten halogen lamp	Same
Detector	Photodiode	Same
Reaction Unit		
Reaction cuvettes	Glass 90 non-disposable	Plastic or Glass 90 non-disposable
Reaction Volume	120 ~ 360 µL	150 ~ 360 µL
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.	Same
Reagent disk	80 positions, 40 positions respectively for inner and outer circles.	Same
Pipettor System	Positive displacement stepper motor driven	Same
Refrigerator temperature	2 - 10°C	Same
Sample Dispense	1.5µL - 45µL	2µL - 45µL
Reagent Dispense	10µL - 350µL	20µL - 350µL
Power		
Input	110/115V~, 60Hz	Same
Operational environment conditions		
Temperature	15°C - 30°C	Same

Similarities / Differences		
Item	BS-480 Chemistry Analyzer k140690 (Candidate Device)	BS-400 Chemistry Analyzer k112377 (Predicate Device)
Humidity	35% - 85% non-condensing	Same
ISE Module		
Principle	ISE (ion selective electrode)	Same
Sample type	Serum, plasma, or diluted urine	Same
Test	Na^+, K^+, Cl^-	Same
Sample Size	70µL Serum, plasma mode; 140µL Urine mode	Same
ISE Calibration	Two-point and single-point calibrations	Same

BUN

Similarities / Differences		
Item	Shenzhen-Mindray BUN Reagent (Candidate Device)	Derma Media Lab BUN (k971309) (Predicate Device)
Intended Use	Measurements are used to aid in the determination of liver and kidney functions and other diseases associated with protein catabolism.	Same
Sample type	Serum	Same
Assay method	Photometric	Same
Reagent format	Liquid, ready to use	Same
Calibration frequency	Every 14 days	Same
Instrument platform	BS 480 chemistry analyzer	Olympus Chemistry Analyzer.

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

CLSI-Evaluation of Precision Performance of Clinical Chemistry Devices-EP05-A2

CLSI-Evaluation of Linearity of Quantitative Analytical Methods-EP06-A

CLSI-Interference Testing in Clinical Chemistry-EP07-A2

CLSI-Method Comparison and Bias estimation Using Patients Samples-EP09-A2

CLSI-Protocols for Determination of Limits of Detection and Limits of Quantitation-EP17-A

L. Test Principle:

BUN-Urea is converted to ammonia and CO_2 by the enzyme urease. The ammonia produced is utilized by glutamate dehydrogenase (GLDH) to convert alpha-ketoglutarate (α-KG) to glutamic acid, with the concomitant conversion of NADH to NAD which is measured bichromatically at 340/380 nm, and is proportional to the amount of BUN present.

ISE-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):

The BS-480, BS-490 and CLC720i Chemistry analyzers are identical except for the model names. The sponsor conducted all the performance testing on the BS-480 model only.

1. Analytical performance:

a. Precision/Reproducibility:

Repeatability and total precision of serum BUN, serum ISE and urine ISE were demonstrated by analyzing three aliquots of serum based control material and two aliquots of urine based control material on the BS-480 Chemistry Analyzer. The control pools were analyzed in duplicate, two runs per day over twenty days, as described in CLSI document EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods.

Analyte	Unit	Sample	n	Mean	Repeatability		Total (Within Device) Precision	
					SD	CV%	SD	CV%
Serum BUN	mg/dL	Control pool 1	80	16	0.12	0.7%	0.28	1.7%
		Control pool 2	80	41	0.18	0.4%	0.70	1.7%
		Control pool 3	80	66	0.30	0.5%	1.18	1.8%
Serum Na+	mmol/L	Control pool 1	80	142	0.51	0.4%	1.15	0.8%
		Control pool 2	80	160	0.35	0.2%	1.02	0.6%
		Control pool 3	80	119	0.25	0.2%	0.81	0.7%
Serum K+	mmol/L	Control pool 1	80	3.7	0.01	0.4%	0.03	0.9%
		Control pool 2	80	5.6	0.02	0.3%	0.04	0.7%
		Control pool 3	80	3	0.01	0.4%	0.02	0.8%
Serum CL-	mmol/L	Control pool 1	80	103	0.53	0.5%	0.93	0.9%
		Control pool 2	80	125	0.43	0.3%	0.86	0.7%
		Control pool 3	80	82	0.40	0.5%	0.67	0.8%
Urine Na+	mmol/L	Control pool 1	80	75	1.29	1.7%	2.21	2.9%
		Control pool 2	80	165	1.75	1.1%	2.93	1.8%

Urine K+	mmol/L	Control pool 1	80	34	0.16	0.5%	0.49	1.5%
		Control pool 2	80	97	0.34	0.3%	0.77	0.8%
Urine CL-	mmol/L	Control pool 1	80	76	0.89	1.2%	2.02	2.7%
		Control pool 2	80	202	1.20	0.6%	2.32	1.1%

b. Linearity/assay reportable range:

Linearity claims are validated using CLSI document EP6-A. For the linearity of BUN the low concentration serum pool containing 5.1 mg/dL BUN was collected from hospitals, a concentrated solution of BUN is used to supplement the high concentration serum pool. For serum ISE, the low concentration serum pool was obtained by diluting with 5% BSA, the high concentration serum pool is obtained by spiking with a concentrated solution of NaCl or KCl. For Urine ISE, the low concentration urine pool was obtained by diluting with urine diluent; the high concentration urine pool was obtained by spiking with a concentrated solution of NaCl or KCl. Next, 11 equally spaced samples across the linear range are prepared by using the high and low sample pool. These samples were assayed on the BS-480 chemistry analyzer randomly, and each analyzer was assayed in 4 replicates. The summary of the results are presented in the table below.

Analyte	Unit	Slope	Intercept	Correlation Coefficient	Sample Range Tested	Claimed Measuring Range
Serum BUN	mg/dL	1.0000	-0.0109	0.9992	5 – 165	6 – 152
Serum Na+	mmol/L	1.0001	0.9999	0.9999	69 – 250	100 – 200
Serum K+	mmol/L	1.0001	0.9998	0.9998	0.85 – 9.76	1 – 8
Serum Cl-	mmol/L	0.9999	0.9999	0.9999	44.7 – 186	50 – 150
Urine Na+	mmol/L	1.0001	1.0000	1.0000	10.0 – 614.0	10 – 500
Urine K+	mmol/L	1.0005	0.9997	0.9997	4.0 – 230	5 – 200
Urine Cl-	mmol/L	1.0000	0.9996	0.9996	6.8 – 452.0	15 - 400

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

The BUN calibrators were previously cleared in k070207 and are traceable to NIST; no modification was made.

The ISE modules, including the calibrators, were previously cleared in k072018; no modification was made.

d. Detection limit:

The limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) evaluations followed CLSI t EP17-A2. For the determination of LoB, two reagent lots and five blank samples were prepared. All samples were assayed in four

replicates per reagent lot per day for three days on the BS-480 chemistry analyzer for each analyte. A total of 60 measurements were obtained per reagent lot.

For the determination of LoD, five samples with low analyte concentrations were measured. In total 60 measurements were obtained per reagent lot.

For the determination of LoQ, five low level samples of known measurand concentration were prepared. The BUN concentrations were obtained from dilution calculation with a serum sample whose measurand concentration was determined by a reference method. The ISE concentrations were obtained from dilution calculation with salt solution whose measurand concentration was determined by theoretical spike. All samples were assayed in four replicates per reagent lot per day for three days. Results from the detection limit studies are summarized in the table below.

Analyte	Unit	LoB	LoD	LoQ
Serum BUN	mg/dL	0.2	0.3	4.8
Serum Na+	mmol/L	3.7	5.1	48.0
Serum K+	mmol/L	0.21	0.24	0.69
Serum Cl-	mmol/L	1.2	3.7	36.6
Urine Na+	mmol/L	3	4.5	10
Urine K+	mmol/L	1	1.2	3.3
Urine Cl-	mmol/L	1	2.6	6.3

e. Analytical specificity:

The effects of potentially interfering substances were determined by using 2 sample pools (normal and abnormal) according to CLSI document EP7-A2. Bilirubin, hemoglobin, lipemia (Intralipid, 20% emulsion, used to emulate extremely turbid samples), and ascorbic acid were tested as potential interfering substances. For each tested substance, a series of five samples with increasing interferent concentrations were prepared. Each series of pools were assayed 3 times. The bias between the control pool and test pool were calculated. The sponsor defines non-significant interference as ≤ +/-10% bias) when the concentrations of interference materials is below the ones in the following table.

Item	Highest Concentration Tested that showed no significant interference			
	Total Bilirubin (mg/dL)	Hemoglobin (mg/dL)	Lipemia (mg/dL)	Ascorbic Acid (mg/dL)
Serum BUN	40	500	1000	30
Serum Na^+	40	500	1000	30
Serum K^+	40	*	1000	30
Serum Cl^-	40	500	1000	30
Urine Na^+	40	500	1000	30
Urine K^+	40	125	1000	30
Urine Cl^-	40	250	1000	30

* Hemolysis can lead to falsely elevated K+ values; the sponsor has put the following limitation in the labeling: “Hemolyzed samples should not be tested for potassium. “

The sponsor also tested the effects of potentially interfering exogenous substances. Testing for each analyte was performed at two concentration levels (low and high). For each potential exogenous interfering substance, a series of five samples with increasing interferent concentrations were prepared. Each series of pools were assayed 3 times. The bias between the control pool and test pool were calculated. There was non- significant interference with Na^+, K^+, and Cl^- by the following drugs at the concentration ranges indicated below: (Sponsor defines non-significant interference as $\leq \pm$ 10%)

Drug interferents	Drug level tested (mg/dL)
Imipramine	0.15
Procainamide	15
Nortriptylne	0.23
Hydroxytyramine	50.4
Valproic acid	75.5
Chlorpromazine	6
Salicylic acid	70.5
Acetylsalicylic acid	1201
Erythromycin	7.1
Ethosximide	30.5
Acetaminophen	242
Ampicillin	6

There was significant interference for Ibuprofen, Benzalkonium Chloride, and Potassium Thiocynate, when these analytes and interferents were tested in the concentration ranges indicated below: (Sponsor defines significant interference as $\geq \pm$ 10%).

Drug interferents	ISE application	Drug level tested (mg/dL)	Effect
Ibuprofen	Serum K^+	506	Decrease Potassium by 0.5 mmol/L at the concentration of 3.25 mmol/L and by 0.59 mmol/L at the concentration of 5.39 mmol/L.
	Serum CL^-	380	Increases Chloride by 15.4 mmol/L at the concentration of 99 mmol/L and by 14.6 mmol/l at the concentration of 119.3 mmol/L
Benzalkonium Chloride	Serum Na^+	7.7	Increases Sodium by 21.5 mmol/L at the concentration of 130.5 mmol/L and by 17.4 mmol/L at the concentration of 146.1 mmol/L
	Serum K^+	5.2	Increases Potassium by 0.38

			mmol/L at the concentration of 2.97 mmol/L.
Potassium Thiocynate	Serum K^+	6.1	Increases Potassium by 0.71 mmol/L at the concentration of 2.97 mmol/L and by 0.65 mmol/L at the concentration of 5.08 mmol/L
	Serum CL^-	12.2	Increases Chloride by 13.4 mmol/L at the concentration of 90.1 mmol/L and by 14.4 mmol/L at the concentration of 111.2 mmol/L.

The sponsor cites the following reference for exogenous interference of BUN in the labeling.

Young DS. *Effects of Drugs on Clinical Laboratory Tests*, 5th ed. AACC Press, 2000

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison was performed according to CLSI document EP9-A2, 120- 132 samples for each analyte were assayed in duplicate on the BS-480 Chemistry Analyzer and the BS-400 Chemistry Analyzer (predicate device). The first of the duplicate results from the BS-480 chemistry analyzer were compared against the predicate's results. The slope, intercept, and correlation coefficient were obtained using Passing-Bablok analysis. The total numbers of altered (spiked and diluted) samples were no more than 19% of the total samples tested. Statistical results are shown in the table below.

Analyte	Unit	Sample Range Tested	n	Slope	Intercept	Correlation Coefficient
Serum BUN	mg/dL	6.0– 147	120	0.9912	0.0494	1.000
Serum Na+	mmol/L	100–200	132	0.9613	3.243	0.998
Serum K+	mmol/L	1.4 – 7.3	120	0.9570	0.0914	1.000
Serum Cl-	mmol/L	55 – 147.0	125	0.9537	4.216	0.998
Urine Na+	mmol/L	12 – 473	120	0.9925	-0.9291	1.000

Urine K+	mmol/L	5 – 192	120	0.9677	0.6774	1.000
Urine Cl-	mmol/L	16 - 396	120	1.006	2.704	1.000

b. Matrix comparison :

A Matrix comparison study was conducted following CLSI document EP-9-A2. Samples were tested on the The BS-480 analyzer. The study was conducted using 67 paired serum and lithium heparin plasma samples drawn from the same individuals. Statistical results using Passing-Bablok analysis are shown in the table below.

Analyte	Unit	N	Sample range	Slope	Intercept	Correlation Coefficient
Na+	mmol/L	67	103. – 186	0.971	2.9	0.995
K+	mmol/L	67	1.2 – 6.9	0974	-0.17	0.992
Cl-	mmol/L	67	70 – 143	1.005	-0.1	0.995

The sponsor concluded that Lithium heparin plasma is acceptable to be used with their ISE (Na+, K+ and Cl-) assay.

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:
BUN – serum: 7-18 mg/dL
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

References:
Tietz, N.W., Fundamentals of clinical chemistry, 6th Edition, W.B. Saunders Co., Philadelphia, PA, 2008

N. Instrument Name:

BS-480 Chemistry Analyzer, BS-490 Chemistry Analyzer, and CLC720i Chemistry Analyzer

O. System Descriptions:

1. Modes of Operation:

   Random access instrument with optional 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:

   Manual or sample barcode option

4. Specimen Sampling and Handling:

   Random access and stat mode operation. Samples are loaded on a sample wheel.

5. Calibration:

   The sponsor recommends BUN calibration every 14 days. The recommended calibrators are provided in the labeling.
   The sponsor recommends that the user perform an ISE two-point calibration every 8 hours. If the user is running more than 50 serum samples a day; both cleaning and two-point calibration must be performed after every 50 samples to ensure reliable operation of the ISE Module.

6. Quality Control:
   In the labeling, the sponsor recommends the controls should be run at least with every working shift in which BUN assays are performed. It is recommended that each laboratory establish its own frequency of control determination. The recommended control materials are provided in the labeling. The sponsor recommends the QC materials should be run after each calibration of the ISE module.

P. Proposed Labeling:

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

Q. Conclusion:

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