

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

A. 510(k) Number:

k080468

B. Purpose for Submission:

New submission for LIASYS test system.

C. Measurand:

Glucose, Urea Nitrogen, Creatinine, Aspartate Amino Transferase, Potassium, Chloride and Sodium

D. Type of Test:

Quantitative photometric and ion selective electrodes

E. Applicant:

AMS S.R.L. Analyzer Medical System

F. Proprietary and Established Names:

LIASYS

G. Regulatory Information:

1. Regulation section:

21CFR Sec.-862.1345 - Glucose Test System.

21CFR Sec.-862.1770 - Urea Nitrogen Test System.

21CFR Sec.-862.1225 - Creatinine Test System.

21CFR Sec.-862.1100 - Aspartate Amino Transferase (AST/SGOT) Test System.

21CFR Sec.-862.1600 - Potassium Test System.

21CFR Sec.-862.1170 - Chloride Test System.

21CFR Sec.-862.1665 - Sodium Test System.

21CFR Sec.-862.2160 - Discrete Photometric Chemistry Analyzer For Clinical Use.

2. Classification:

Class II

3. Product code:

CFR - Hexokinase, Glucose

CDN - Urease, Photometric, Urea Nitrogen

CGX - Alkaline Picrate, Colorimetry, Creatinine

CIT - NADH Oxidation/NAD Reduction, AST/SGOT

CEM - Electrode, Ion Specific, Potassium

CGZ - Electrode, Ion-Specific, Chloride

JGS - Electrode, Ion Specific, Sodium

JJE - Analyzer, Chemistry (Photometric, Discrete), For Clinical Use

4. Panel:
Chemistry (75)

H. Intended Use:

1. Intended use(s):
See Indication(s) for use below
2. Indication(s) for use:

The “Liasys” is a random access, computer controlled, counter top, clinical analyzer for clinical chemistry. The instrument provides the *In Vitro* diagnostic quantitative measurements for glucose, urea nitrogen, creatinine and AST in serum, and for sodium, potassium and chloride in serum. Other various chemistry assays may be adaptable to this instrument.

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. Urea Nitrogen measurements are use in the diagnosis and treatment of certain renal and metabolic diseases. Measurements of Creatinine are used in the diagnosis and treatment of muscle diseases and endocrine disorders. Aspartate amino transferase (AST) quantitative measurements are used in the diagnosis and treatment of certain types of liver and heart disease. Sodium measurements are used in the diagnosis and treatment of aldosteronism, diabetes insipidus and other diseases involving electrolyte imbalance. Measurements of Potassium are used to monitor electrolyte balance 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 such as cystic fibrosis and diabetic acidosis.

3. Special conditions for use statement(s):
For prescription use
4. Special instrument requirements:
LIASYS Analyzer

I. Device Description:

The LIASYS is a random access, computer controlled, counter top, clinical analyzer for clinical chemistry. The system can perform 200 tests per hour and has a machine cycle of 18 seconds. Its execution time ranges from a minimum of 48 seconds to a maximum of 756, depending on the analysis method chosen. The “Lyasis” is an open system that allows configuration with different reagents selected by the customer in order to fit their needs. The daily routine analysis can be carried out according to patient sample arrival in a sequential and continuous manner. The work list is organized using a loading rack holding up to 16 patient samples plus a STAT rack for 14 patient samples.

The applicant recommends International Laboratory electrodes, which were used to establish performance for Sodium, Potassium and Chloride.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Roche Cobas Mira, Medica Easystat ISE, Roche Urea Nitrogen, Roche Glucose, Roche Creatinine, Roche AST.
2. Predicate 510(k) number(s):
k920402, k063376, k954000, k953847, k941837 and k896238, respectively
3. Comparison with predicate:

Description	LIASYS	Roche Cobas Mira
System Principle	Automatic, random access, computer controlled, counter top, non-stop loading clinical chemistry and immunoturbidimetric analysis instrument	Random Access, sample selective analysis
Throughput	200 tests per hour	120 test per hour
Configuration	Analytical Unit & CPU	Analytical Unit, Control Unit
Optical Measurement		
Measurement Modes	Absorbance	Absorbance
Detector	Photometer: double ray	Photodiode
Optical System	Wavelength 340 to 620 nm	Wavelength 340 to 600 nm
Filters	Interferential filters	Five filters: 340, 405, 500, 600 nm
Linear Absorbance Range	0.001/2.500 Abs	At 340 nm 0-2.4A
Light Source	6V/10W halogen bulb	Xenon Flash Tube
Data Processing		
Calibration Curve	End point, Fixed Time, Kinetic, Bi-chromatic, Differential	Endpoint, logit/log4, logit/log5, exponential 5, polynomial 5, linear interpolation, linear regression and linear search for enzymes
Cuvettes	Reaction Cuvettes	Disposable Cuvette Segments
Number of cuvettes	60 Individually replaceable cuvettes	12 cuvettes per segment, Six segment, total 72 cuvettes

Cuvette Washing	Consists of 5 probes, which empty, wash and dry the reaction cuvette	No cuvette washing
Path Length	10 mm	6 mm
Cuvette volume	300-670 uL	150-600 uL
Diluent Volume	3-99 uL	2-95 uL
Reagent volume	3-500 uL	100-600 uL
Sample/Reagent Delivery		
Pipetting System	Single probe equipped with: Volume level sensor, pre-heating (37°C) and automatic probe washing	XYZ pipetting system
Sample Dispense	2-99 uL	2-95uL

ISE		
Description	Liasys	Medica Module
System Principle	Ion selective electrode technology	Ion selective electrode technology
Throughput	Serum 120 tests/hr Urine 60 tests/hr	Serum 120 tests/hr Urine 60 tests/hr
Fluids Measured	Serum	Serum, Urine, Plasma or whole blood
Clinical measurements	Chloride, Potassium & Sodium	Chloride, Potassium & Sodium
Electrode Maintenance	Maintenance free electrodes 6 months or 10000 samples	Maintenance free electrodes 6 months or 10000 samples
ISE Detector		
Modes of Analysis		
Reagents/Calibrators	Calibrator A, Calibrator B, Cleaning Solution, Urine diluent and reference solution	Calibrator A, Calibrator B, Cleaning Solution, Urine diluent and reference solution
Cleaning	After 8 hours or 50 samples per day	After 8 hours or 50 samples per day
Calibration Frequency	Every 8 hours	Every 8 hours
Sample Volume	Serum, 70 uL	Serum, plasma & whole blood: 70 uL Urine: 160 uL
Pipetting System	Single probe pipetting	Single probe pipetting
Fluid Verification		
Sample Dispensing	70 uL	70 uL
Reagent Dispense	181-499	100-600uL

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

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

L. Test Principle:

Glucose

The AMS Diagnostics glucose hexokinase method is based on a modification of Slein, using hexokinase and glucose-6-phosphate-dehydrogenase to catalyze the reaction. 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 340 nm. The increase is directly proportional to the amount of glucose in the sample.

Blood Urea Nitrogen (BUN)

Urea has been determined by the direct method where urea condenses with diacetyl to form a chromagen and an indirect method where ammonia is measured as a product of Urease action on urea. The liberated ammonia has been measured using Nessler's reagent and by the Berthelot reaction. Talke and Schubert introduced a totally enzymatic procedure in 1965 utilizing Urease and Glutamate Dehydrogenase. The AMS procedure is based on a modification of their method. Urea is hydrolyzed by urease in the presence of water to produce ammonia and carbon dioxide. The liberated ammonia reacts with α -Ketoglutarate in the presence of NADH to yield glutamate. An equimolar quantity of NADH undergoes oxidation during the reaction resulting in a decrease in absorbance that is directly proportional to the urea nitrogen concentration in the sample.

Creatinine

Jaffe described a method in 1886 for the determination of creatinine involving a protein free filtrate and a reaction with picric acid in alkaline solution. The AMS method is based on a modification of this procedure, incorporating a surfactant and other ingredients to minimize protein and carbohydrate interferences. Creatinine reacts with picric acid in alkaline conditions to form a color complex which absorbs at 510 nm. The rate of formation of color is proportional to the creatinine in the sample.

Aspartate Aminotransferase (AST/SGOT)

In 1955 Karmen developed a kinetic assay procedure for AST which was based upon the use of malate dehydrogenase and NADH. Henry in 1960 and Amador and Wacker in 1962 later presented optimized procedures. These modifications increased accuracy

and lowered the effect of interfering substances. The IFCC5 published a recommended method that Included P-5-P in 1986. The AMS method is based on IFCC recommendations but does not contain P-5-P. Aspartate aminotransferase (AST) catalyzes the transfer of the amino group from L-aspartate to 2-oxoglutarate to yield oxalacetate and L-glutamate. The oxaloacetate undergoes reduction with simultaneous oxidation of NADH to NAD in the malate dehydrogenase (MDH) catalyzed indicator reaction. The resulting rate of decrease in absorbance at 340nm is directly proportional to the AST activity. Lactate dehydrogenase (LDH) is added to prevent interference from endogenous pyruvate which is normally present in serum.

Sodium, Potassium, and Chloride

The AMS measurement is based on ion selective electrode technology. The flow-through sodium electrode uses selective membrane tubing, specially formulated to be sensitive to sodium ions. The potassium and chloride electrodes employ similar designs with appropriate selective membrane materials. The potential of each electrode is measured relative to a fixed, stable voltage established by the double-junction silver/silver chloride reference electrode. An ion selective electrode develops a voltage that varies with the concentration of the ion to which it responds. The relationship between the voltage developed and the concentration of the sensed ion is logarithmic, as expressed by the Nernst equation.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Three levels of samples were evaluated; the value of one level of which is in the normal range, the other two levels above or below the normal range. Each run included normal, and abnormal control material to evaluate validity of the assay.

Within Run Precision was performed by running each precision sample twenty times in a single run. Total Run Precision was performed with 2 runs consisting of 2 measurements per run over a 10 day period.

Glucose			
Within Run	Level 1	Level 2	Level 3
Mean (mg/dL)	63.4	99.2	305.6
S.D. (mg/dL)	0.8	0.7	1.6
C.V. (%)	1.3	0.7	0.5
Total			
Mean (mg/dL)	63.5	100.9	305.0
S.D. (mg/dL)	1.0	2.3	3.4
C.V. (%)	1.5	2.2	1.1

BUN				
Within Run	Level 1	Level 2	Level 3	
Mean (mg/dL)	12.8	47.8	73.9	
S.D. (mg/dL)	0.2	0.6	0.9	
C.V. (%)	1.3	1.3	1.2	
Total				
Mean (mg/dL)	12.0	48.0	73.3	
S.D. (mg/dL)	0.2	0.9	1.3	
C.V. (%)	1.3	1.9	1.7	

Creatinine				
Within Run	Level 1	Level 2	Level 3	
Mean (mg/dL)	1.33	7.21	11.41	
S.D.(mg/dL)	0.05	0.19	0.22	
C.V. (%)	3.6	2.6	1.9	
Total				
Mean (mg/dL)	1.45	7.51	11.39	
S.D.(mg/dL)	0.06	0.22	0.31	
C.V. (%)	3.8	3.0	2.8	

AST				
Within Run	Level 1	Level 2	Level 3	
Mean (U/L)	29.5	126.7	199.0	
S.D. (U/L)	0.7	0.9	2.1	
C.V. (%)	2.2	0.7	1.0	
Total				
Mean (U/L)	29.6	128.1	201.5	
S.D. (U/L)	0.7	1.2	2.4	
C.V. (%)	2.2	0.9	1.2	

Sodium				
Within Run	Level 1	Level 2	Level 3	
Mean (mmol/L)	109.2	134.4	149.9	
S.D.(mmol/L)	0.7	0.3	0.8	
C.V. (%)	0.7	0.2	0.5	
Total				
Mean(mmol/L)	109.0	137.5	149.2	
S.D.(mmol/L)	1.2	1.87	1.2	
C.V. (%)	1.1	1.4	0.8	

Potassium				
Within Run	Level 1	Level 2	Level 3	
Mean (mmol/L)	2.62	4.10	6.20	
S.D.(mmol/L)	0.04	0.04	0.05	
C.V. (%)	1.5	1.1	0.9	

Total			
Mean (mmol/L)	2.55	3.93	6.11
S.D. (mmol/L)	0.07	0.08	0.09
C.V. (%)	2.6	2.0	1.5
Chloride			
Within Run	Level 1	Level 2	Level 3
Mean (mmol/L)	80.8	99.0	111.6
S.D.(mmol/L)	0.6	0.3	0.7
C.V. (%)	0.7	0.3	0.6
Total			
Mean (mmol/L)	80.7	98.7	111.8
S.D.(mmol/L)	0.8	1.75	0.8
C.V. (%)	1.0	1.8	0.7

b. *Linearity/assay reportable range:*

The claimed measuring range for Glucose is 15 to 500 mg/dL, BUN is 2.0 - 115 mg/dL for Creatinine is 0.3 - 20.0 mg/dL, and for ALT is 4 - 600 U/L are supported by the below linearity data and limit of quantitation. The claimed measuring range for sodium is 27 – 200 mmol/L, potassium is 0.4 – 20.0 mmol/L, Chloride is 27 – 200 mmol/L are supported on the below linearity data.

Analyte	Slope	Intercept	R ²	Range tested
Glucose	0.9968	0.4	0.9999	0.0 to 528 mg/dL
BUN	0.9650	0.0	0.9967	0.0 to 133 mg/dL
Creatinine	0.9983	0.27	0.9982	0.2 to 24.2 mg/dL
ALT	1.0120	1.89	0.9995	0.2 to 713.5 U/L
Sodium	1.006	-0.7	0.9998	27 to 200 mmol/L
Potassium	1.003	0.05	0.9981	0.4 to 19.9 mmol/L
Chloride	0.99536	-0.97	0.9991	27 to 200 mmol/L

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

No information on traceability was provided. The labeling recommends the use of a generic calibrator for all analytes except AST which is based upon the millimolar absorptivity of NADH.

d. *Detection limit:*

Limit of detection (LOD) and Limit of Quantitation (LOQ) were evaluated following NCCLS EP17-A guidelines for AST, BUN, Creatinine and Glucose. A known concentration of analyte and a blank sample were tested over a period of 3 days, 30 replicates each day. Statistical Analysis was performed based on NCCLS EP17-A recommendations.

Glucose LOD: 1.9 mg/dL.
BUN LOD: 0.4 mg/dL.
Creatinine LOD: 0.1 mg/dL.
AST LOD: 3 U/L.

Glucose LOQ: 14.27 mg/dL.
BUN LOQ: 1.98 mg/dL.
Creatinine LOQ: 0.3 mg/dL.
AST LOQ: 3.59 U/L.

e. *Analytical specificity:*

Studies were performed to support the interference claims presented in the labeling as follows:

Glucose

Hemoglobin:

Use fresh un-hemolyzed serum removed from the clot as soon as possible.

Bilirubin: No significant interference ($\pm 10\%$) from bilirubin up to 23.2 mg/dL.

Lipemia: No significant interference ($\pm 10\%$) from lipemia up to 248 mg/dL measured as triglycerides.

A number of drugs and substances may affect the accuracy of this test. See Young, D.S., et al, Clin. Chem., 21:1D, (1975).

BUN

Hemoglobin:

No significant interference ($\pm 10\%$) from hemoglobin up to 1000 mg/dL.

Bilirubin:

No significant interference ($\pm 10\%$) from bilirubin up to 23.2 mg/dL.

Lipemia:

No significant interference from lipemia ($\pm 10\%$) up to 877 mg/dL measured as triglycerides.

For a comprehensive review of drug interference see Young, et al. See Young, D.S., et al, Clin. Chem., 21:1D, (1975).

Creatinine

Hemoglobin:

No significant interference ($\pm 10\%$) from hemoglobin up to 1000 mg/dL.

Bilirubin:

No significant interference ($\pm 10\%$) from bilirubin up to 23.2 mg/dL.

Lipemia:

No significant interference ($\pm 10\%$) from lipemia up to 560 mg/dL measured as triglycerides.

A number of drugs and substances may affect the accuracy of creatinine. See Young, D.S., et al, Clin. Chem., 21:1D, (1975).

AST

Hemoglobin:

Use non-hemolyzed serum, as red blood cells contain AST. No significant

interference ($\pm 10\%$) from hemoglobin up to 300 mg/dL

Bilirubin:

No significant interference ($\pm 10\%$) from bilirubin up to 23.2 mg/dL.

Lipemia:

No significant interference ($\pm 10\%$) from lipemia up to 167 mg/dL measured as triglycerides.

See Young, et al. for other interfering substances

ISE

Un-hemolyzed serum is recommended.

No significant interference ($\pm 10\%$) or ± 3 units up to:

	Hemolysis	Lipemia	Bilirubin
Na (Sodium)	1000 mg/dL	982.5 mg/dL	30.6 mg/dL
K (Potassium)	800 mg/dL	982.5 mg/dL	30.6 mg/dL
CL (Chloride)	300 mg/dL	982.5 mg/dL	30.6 mg/dL

See Young, et al. for other interfering substances.

- f. *Assay cut-off:*
Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Studies using serum were performed between this procedure and a similar methodology yielded the following results:

Glucose

Number of samples:	73
Range of samples:	18-500 (mg/dL)
Correlation Coefficient:	0.9974
Slope:	1.0999
Intercept:	3.3 (mg/dL)

BUN

Number of samples:	85
Range of samples:	3 – 112 (mg/dL)
Correlation Coefficient:	0.9974
Slope:	1.004
Intercept:	-0.57 (mg/dL)

Creatinine

Number of samples:	76
Range of samples:	0.30 – 20.3 (mg/dL)
Correlation Coefficient:	0.9934
Slope:	1.042
Intercept:	-0.14 (mg/dL)

AST

Number of samples: 84
Range of samples: 6 - 596 (U/L)
Correlation Coefficient: 0.9995
Slope: 0.9658
Intercept: -0.7 (U/L)

Sodium

Number of samples: 64
Range of samples: 98 - 150 (mmol/L)
Correlation Coefficient: 0.9932
Slope: 0.9330
Intercept: 2.2 (mmol/L)

Potassium

Number of samples: 64
Range of samples: 1.6 – 10.30 (mmol/L)
Correlation Coefficient: 0.9986
Slope: 1.007
Intercept: -0.17 (mmol/L)

Chloride

Number of samples: 64
Range of samples: 54 - 190 (mmol/L)
Correlation Coefficient: 0.9998
Slope: 0.9692
Intercept: -2.3 (mmol/L)

- b. *Matrix comparison:*
Not Applicable
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:
The reference ranges are provided in the labeling based upon published values as follows:
Glucose: 70-105 mg/dL
Tietz, N.W., Fundamentals of Clinical Chemistry, 2nd ed., W.B. Saunders Co., Philadelphia, p.243, (1976).

BUN: 7-18 mg/dL

Tietz, N.W., Fundamentals of Clinical Chemistry, 2nd ed., W.B. Saunders Co., Philadelphia,(1976).

Creatinine: 0.60 – 1.40 mg/dl

Henry RJ (Ed), Clin. Chem., Principles and Technics (2nd Ed), Harper and Row, 1974;548-551.

AST: 5-34 U/L (37°C)

Tietz, N.W., Fundamentals of Clinical Chemistry, 2nd ed., W.B. Saunders Co., Philadelphia,(1976).

ISE

Na: 136 – 145 mmol/L

K: 3.5 – 5.1 mmol/L

CL: 98 – 107 mmol/L

Tietz, textbook of Clinical Chemistry 2nd ed, Philadelphia, W.B. Saunders, (1994) pg: 1357, 1360 and 1370.

N. Instrument Name:

LIASYS Analyzer

O. System Descriptions:

1. Modes of Operation:

Random access analyzer

2. Software:

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

Yes or No

3. Specimen Identification:

Bar-code option for positive sample identification

4. Specimen Sampling and Handling:

5 Sample racks hold up to 64

5. Calibration:

End point, Fixed Time, Kinetic, Bi-chromatic, Differential

6. Quality Control:

The analyzer has a built in quality control program. The labeling for each analyte recommends the use of two external quality control materials to be assayed according to government guidelines.

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

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.