510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k071211

B. Purpose for Submission:

To extend the indications for use claim to include use at point of care sites

C. Measurand:

Aspartate aminotransferase (AST)

Glucose

C-reactive protein (CRP)

Chloride

Potassium

Sodium

D. Type of Test:

Photometric, turbidimetric or ion selective quantitative assays

E. Applicant:

Roche Diagnostics Corp.

F. Proprietary and Established Names:

Cobas c 111 analyzer
Aspartate aminotransferase (ASTL/ASTPL)
C-Reactive Protein Latex (CRPLX)
Glucose HK (GLUC2)
ISE Chloride Electrode
ISE Potassium Electrode
ISE Sodium Electrode

G. Regulatory Information:

Product Code	Classification		Regulation Section	Panel
CIT	II	Aspartate amino transferase (AST/SGOT) test system	21 CFR 862.1100	75 Clinical Chemistry
CFR	II	Glucose test system	21 CFR 862.1345	75 Clinical Chemistry
DCN	II	C-reactive protein immunological test system	21 CFR 866.5270	81 Immunology
CEM	II	Potassium test system	21 CFR 862.1600	75 Clinical Chemistry
CGZ	II	Chloride test system	21 CFR 862.1170	75 Clinical Chemistry
JGS	II	Sodium test system	21 CFR 862.1665	75 Clinical Chemistry
JJE	Class I	Discrete photometric chemistry analyzer	21 CFR 862.2160	75 Clinical Chemistry

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   cobas c 111 analyzer:

   The Roche **cobas c** 111 analyzer is an *in-vitro* diagnostic analyzer capable of performing clinical chemistry, specific protein and electrolyte tests for professional settings and small laboratories, specialized testing and CLIA-licensed doctor's offices.
   Analytes are measured photometrically or turbidimetrically; the analyzer also has an optional ISE module for measuring sodium, potassium and chloride.

   Reagents:
   Aspartate aminotransferase (ASTL/ASTPL)
   In vitro test for the quantitative determination of AST in human serum and plasma

on the cobas c111 system. Aspartate amino transferase measurements are used in the diagnosis and treatment of certain types of liver and heart disease.

C-Reactive Protein Latex (CRPLX)
In vitro test for the quantitative immunological determination of human C-reactive protein in human serum and plasma on the cobas c111 system. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues.

Glucose HK (GLUC2)
In vitro test for the quantitative determination of glucose concentration in human serum and plasma on the cobas c111 system. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus and idiopathic hypoglycemia.

ISE Chloride Electrode
The chloride electrode for the cobas c111 system is intended for the quantitative determination of chloride in diluted serum, plasma, and urine. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

ISE Potassium Electrode
The potassium electrode for the cobas c111 system is intended for the quantitative determination of potassium in diluted serum, plasma, and urine. Measurements of potassium are used to monitor electrolyte balance in the diagnosis and treatment of diseases conditions characterized by low or high blood potassium levels.

ISE Sodium Electrode
The sodium electrode for the cobas c111 system is intended for the quantitative determination of sodium in diluted serum, plasma, and urine. Measurements of sodium are used in the diagnosis and treatment of aldosteronism (excessive secretion of the hormone aldosterone), diabetes insipidus (chronic excretion of large amounts of dilute urine, accompanied by extreme thirst), adrenal hypertension, Addison's disease (caused by destruction of the adrenal glands), dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   Roche Diagnostics cobas c 111

I. Device Description:

The Roche **cobas c** 111 analyzer is an *in-vitro* diagnostic analyzer capable of performing clinical chemistry, specific protein and electrolyte tests for professional settings and small laboratories, specialized testing and CLIA-licensed doctor's offices. Analytes are measured photometrically or turbidimetrically; the analyzer also has an optional ISE module for measuring sodium, potassium and chloride.

Aspartate aminotransferase (ASTL/ASTPL) reagent consists of a primary reagent containing l-aspartate, malate dehydrogenase (MDH) from porcine heart, albumin (bovine), TRIS buffer and preservative. The reagent also contains pyridoxal phosphate (PYP) and NADH, 2-oxoglutarate, preservatives and additives.

The Glucose HK (GLUC2) reagent is a dual reagent system. Reagent 1 consists of TRIS buffer, NADP and preservatives. Reagent 2 consists of HEPES buffer, hexokinase (yeast) and glucose-6-phosphate dehydrogenase.

The C-reactive Protein latex (CRPLX) is a dual reagent system. Reagent 1 consists of TRIS buffer with bovine serum albumin and immunoglobulins (mouse) and preservatives. Reagent 2 is latex particles coated with anti-CRP (mouse) in glycine buffer and preservatives.

The Sodium, Potassium and Chloride ISE Electrode are comprised of the ISE solution 1 or 2 (volume dependant), indirect calibrator, ISE reference solution, activator, ISE deproteinizer and ISE etcher.

J. Substantial Equivalence Information:

1. Predicate device name(s) and k numbers:

Cobas c 111 analyzer	-k051595
Aspartate Aminotransferase (AST)	-k951595
Glucose Gen. 2 (GLUC2)	-k980996
CRP Latex (CRPLX)	-k981897
Chloride electrode (ISE-Cl)	-k963627
Potassium electrode (ISE-K)	-k963627
Sodium electrode (ISE-Na)	-k963627

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

   See 1 above.

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use for the reagents	AST: In vitro test for the quantitative determination of aspartate aminotransferase (AST) in human serum and plasma on the **cobas c** 111 system. Glucose: In vitro test for the quantitative determination of glucose in human serum and plasma on the **cobas c** 111 system. CRP: In vitro test for the quantitative determination of C-reactive protein in human serum and plasma on the cobas c 111 system. ISE-Cl: The chloride electrode for the **cobas c** 111 system is intended for the quantitative determination of chloride in diluted serum, plasma and urine. ISE-K: The potassium electrode for the **cobas c** 111 system is intended for the quantitative determination of chloride in diluted serum, plasma and urine. ISE-Na: The sodium electrode for the **cobas c** 111 system is intended for the quantitative determination of chloride in diluted serum, plasma and urine.	Same
Instrument	Cobas c 111	Same
Sample Type	AST: serum and plasma Glucose: serum and plasma CRP: serum and plasma	Same

Similarities		
Item	Device	Predicate
	ISE-Cl: serum, plasma and urine ISE-K: serum, plasma and urine ISE-Na: serum, plasma and urine	
Traceability/ Standardization	AST: standardized against the original IFCC formulation using calibrated pipettes together with manual photometer providing absolute values and the substrate-specific absorptivity, Glucose: standardized against ID/MS CRP: standardized against the reference preparation of the IRMM – BCR470/CRM470 (RPPHS – Reference Preparation for Proteins in Human Serum) ISE-Cl/K/Na: standardized against primary calibrators prepared gravimetrically from purified salts	Same
Measuring range	AST: 2-700 U/L Glucose: 0.11-40 mmol/L CRP: 1-200 mg/L ISE-Cl: 20-250 mmol/L ISE-K: 1-100 mmol/L ISE-Na: 20-250 mmol/L	Same

Differences		
Item	Device	Predicate
Intended use modified	The Roche cobas c111 analyzer is an in-vitro diagnostic analyzer capable of performing clinical chemistry, specific protein and electrolyte tests.	The Roche cobas c111 analyzer is an in-vitro diagnostic analyzer capable of performing clinical chemistry, specific protein and electrolyte tests *in the professional setting and small laboratories, specialized testing and CLIA-licensed doctor's office.*
Operators	Professional setting	Point-of-care setting

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

CLSI EP5-A – Evaluation of Precision Performance of Quantitative Measurement Methods

L. Test Principle:

The aspartate aminotransferase (ASTL) assay uses enzymatic activation. AST in a sample catalyzed the transfer of an amino group between L-aspartate and 2-oxoglutarate to form oxaloazcetate and L-glutamate. The oxaloacetate then reacts with NADH, in the presence of malate dehydrogenase (MDH), to form NAD+. Pyridoxal phosphate serves as a coenzyme in the amino transfer reaction. The rate of the NADH oxidation is directly proportional to the catalytic AST activity. It is determined by measuring the decrease in absorbance.

The glucose hexokinase (GLUC2) assay is a UV test with enzymatic reference method that utilizes hexokinase. The hexokinase catalyzes the phosphorylation of glucose to glucose-6-phosphate by ATP. Glucose-6-phosphate dehydrogenase oxidizes glucose-6-phosphate in the presence of NAHP to gluconate-6-phosphate. The rate of NADPH formation during the reaction is directly proportional to the glucose concentration and is measured photometrically.

The C-reactive protein (latex) (CRPLX) is a particle enhanced turbidimetric assay. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The precipitate is determined turbidimetrically.

The sodium, potassium and chloride ion-selective electrode (ISE) have a selective membrane in contact with both the test solution and an internal filling solution. The internal filling solution contains the test ion at a fixed concentration. The membrane EMF is determined by difference in concentration of the test ion in the test solution and the internal filling solution. The EMF develops according to the Nerst equation for a specific ion in solution. The complete measurement system for a particular ion includes the ISE, a reference electrode and electronic circuits to measure and process the EMF to give the test ion concentration. The sodium and potassium electrodes are based on neutral carriers and the chloride electrode is based on an ion exchanger.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   Within-run precision studies were conducted in three physician office laboratories (POL) using trained medical technicians to test for potential systematic and random error. Two controls materials and two sample pools (prepared daily) were run in triplicates for 9 to 15 days (site-dependant) at two

US sites and one European site.

The sponsor also conducted an imprecision study according to modified CLSI EP5-A. Two controls and two human serum pools (normal and evaluated) were run in triplicate for twenty-one days in one US and one foreign site. The second US site conducted the study with the two controls and two human serum pools in triplicate twice a day for ten days.

The combined results from all three POL sites and materials are shown in the combined tables below:

Within-Run Controls

Assay	POL sites concentration (mean)		POL sites (range % CV or SD (unit))		Hospital Sites concentration (mean)		Hospital Sites (average % CV or SD (unit))	
	PNU	PPU	PNU	PPU	PNU	PPU	PNU	PPU
AST (U/L)	41.1	137.9	1.1–3.6%	0.4-0.9%	41.4	138.9	2.19	0.93
GLUC (mg/dL)	96.1	255.5	0.3-1.0%	0.5-1.2%	94.0	250.4	0.50	0.33
CRP (mg/dL)	0.8	4.8	0.3-0.9%	0.3-0.5%	0.8	4.7	0.86	0.37
Sodium (mmol/L)	126.7	149.9	0.2-1.0%	0.2-0.5%	128.0	152.4	0.42	0.36
Potassium (mmol/L)	3.5	6.6	0.2-1.2%	0.012-0.109 SD	3.5	6.7	0.41	SD 0.03
Chloride (mmol/L)	86.2	118.5	0.23-0.64 SD	0.24-0.99%	87.8	120.8	SD 0.43	0.37

PNU= PreciNorm Universal Control, PPU=PreciPath Universal Control

Within-Run Human Samples

	POL sites concentration (mean)		POL sites (range % CV or SD (unit))		Hospital Sites concentration (mean)		Hospital Sites (ge % CV or SD(unit))	
	HS 1	HS2	HS 1	HS2	HS 1	HS2	HS 1	HS2
AST (U/L)	19.0	46.9	0.46-1.48 SD	0.8-5.2%	19.5	188.5	SD 0.85	0.69
GLUC (mg/dL)	89.1	168.3	0.2-1.1%	0.4-0.9%	86.2	216.8	0.39	0.48
CRP (mg/dL)	0.6	2.4	1.1-2.3%	0.6-2.1%	0.7	7.1	SD 0.007	0.57
Sodium (mmol/L)	144.0	134.2	0.2-0.5%	0.2-0.4%	137.2	146.4	0.46	0.49
Potassium (mmol/L)	4.5	4.5	0.3-0.7%	0.3-0.5%	4.2	5.3	0.42	0.49
Chloride (mmol/L)	104.5	97.9	0.2-0.5%	0.2-0.6%	102.9	113.4	0.43	0.48

HSP1=Human Serum Pool 1 (normal), HSP2= Human Serum Pool 2 (elevated).

Total Controls

Assay	POL sites concentrations (mean)		POL sites (range % CV or SD (unit))		Hospital Sites concentrations (mean)		Hospital Sites (average % CV or SD (unit))	
	PNU	PPU	PNU	PPU	PNU	PPU	PNU	PPU
AST (U/L)	40.2	137.0	2.9-3.8%	1.7-2.8%	41.6	139.6	3.2	1.7
Glucose (mg/dL)	93.0	247.1	1.6-4.1%	1.4-4.1%	91.7	244.4	1.0	0.9
CRP (mg/dL)	0.8	4.8	1.6-4.2%	1.2-5.1%	0.8	4.7	1.5	1.3
Sodium (mmol/L)	126.5	151.0	1.6-1.9%	1.5-2.0%	125.3	149.8	0.9	1.0
Potassium (mmol/L)	3.4	6.6	1.7-1.8%	0.1-0.2SD	3.4	6.6	1.1	SD 0.07
Chloride (mmol/L)	87.2	120.0	1.5-2.1 SD	1.6-3.0%	85.6	118.5	SD 0.9	1.0

PNU= PreciNorm Universal Control, PPU=PreciPath Universal Control

Total Human Samples

Assay	POL sites concentrations (mean)		POL sites (range % CV)		Hospital Sites concentrations (mean)		Hospital Sites (average % CV or SD (unit))	
	HS I	HS 2	HS I	HS 2	HS 1	HS 2	HS I	HS 2
AST (U/L)	16.4	48.7	0.9-1.8 SD	2.5-3.8%	SD 1.2	3.7	SD 1.3	2.9
Glucose (mg/dL)	97.5	130.7	1.8-4.3%	1.9-4.6%	2.6	2.8	1.2	2.2
CRP (mg/dL)	4.1	4.7	3.3-3.7%	2.8-3.4%	3.7	3.2	SD 0.01	1.5
Sodium (mmol/L)	139.9	131.6	1.5-1.9%	1.5-1.7%	1.6	1.6	1.2	1.4
Potassium (mmol/L)	4.5	4.5	1.2-1.8%	1.4-1.8%	1.4	1.6	1.0	1.1
Chloride (mmol/L)	104.7	104.6	1.3-1.5%	1.4-1.8%	1.4	1.6	0.9	0.8

HSP1=Human Serum Pool 1 (normal), HSP2= Human Serum Pool 2 (elevated).

b. *Linearity/assay reportable range:*

Previously established for predicate devices.

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

Previously established for predicate devices.

d. *Detection limit:*

Previously established for predicate devices.

e. Analytical specificity:

Previously established for predicate devices.

f. Assay cut-off:

Previously established for predicate devices.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed at three Point-of-Care sites using serum and plasma samples. Each site ran seven fresh human samples each day for 20 days (8 samples in the US for 6 to 10 days) on the cobas c 111 (y) and the cobas integra 400 (x).

The following is the comparison from the three point-of-care sites.

AST:
Passing Bablok:
y = 0.989x + 1.276 U/L
τ = 0.8316
r = 0.9906
range = 93-286.48 U/L
n = 333

Glucose:
y = 0.997x + 2.069 mg/dL
τ = 0.9217
r = 0.9954
range= 42.4-404.80 mg/dL
n = 333

CRP:
y = 1.058x + 0.022 mg/L
τ = 0.9789
r = 0.9988
range= 0.010-75/990 mg/L
n = 326

ISE-Cl:
y = 1.011x – 0.51 mmol/L
τ = 0.7532
r = 0.9243
range= 65.20-111.90 mmol/L
n = 280

ISE-K:
y = 0.943x + 0.189 mmol/L
τ = 0.8835
r = 0.9824
range= 2.950-8.290 mmol/L
n = 280

ISE-Na:
y = 1.064x – 9.818 mmol/L
τ = 0.6920
r = 0.9366
range= 87.9-146.4 mmol/L
n = 280

b. Matrix comparison:

Previously established for predicate devices.

3. Clinical studies:

a. Clinical Sensitivity:

Previously established for predicate devices.

b. Clinical specificity:

Previously established for predicate devices.

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

Previously established for predicate devices.

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Previously established for predicate devices.

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.