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:
### Table

<table>
<thead>
<tr>
<th>Product Code</th>
<th>Classification</th>
<th>Regulation Section</th>
<th>Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIT</td>
<td>II</td>
<td>Aspartate amino transferase (AST/SGOT) test system</td>
<td>21 CFR 862.1100</td>
</tr>
<tr>
<td>CFR</td>
<td>II</td>
<td>Glucose test system</td>
<td>21 CFR 862.1345</td>
</tr>
<tr>
<td>DCN</td>
<td>II</td>
<td>C-reactive protein immunological test system</td>
<td>21 CFR 866.5270</td>
</tr>
<tr>
<td>CEM</td>
<td>II</td>
<td>Potassium test system</td>
<td>21 CFR 862.1600</td>
</tr>
<tr>
<td>CGZ</td>
<td>II</td>
<td>Chloride test system</td>
<td>21 CFR 862.1170</td>
</tr>
<tr>
<td>JGS</td>
<td>II</td>
<td>Sodium test system</td>
<td>21 CFR 862.1665</td>
</tr>
<tr>
<td>JJE</td>
<td>Class I</td>
<td>Discrete photometric chemistry analyzer</td>
<td>21 CFR 862.2160</td>
</tr>
</tbody>
</table>

### 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),
derhydration, 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:**

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

<table>
<thead>
<tr>
<th>Item</th>
<th>Device</th>
<th>Predicate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ISE-Cl: serum, plasma and urine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISE-K: serum, plasma and urine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISE-Na: serum, plasma and urine</td>
<td></td>
</tr>
<tr>
<td>Traceability/</td>
<td>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</td>
<td>Same</td>
</tr>
<tr>
<td>Standardization</td>
<td>CRP: standardized against the reference preparation of the IRMM – BCR470/CRM470 (RPPHS – Reference Preparation for Proteins in Human Serum)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISE-Cl/K/Na: standardized against primary calibrators prepared gravimetrically from purified salts</td>
<td></td>
</tr>
<tr>
<td>Measuring range</td>
<td>AST: 2-700 U/L</td>
<td>Same</td>
</tr>
<tr>
<td></td>
<td>Glucose: 0.11-40 mmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CRP: 1-200 mg/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISE-Cl: 20-250 mmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISE-K: 1-100 mmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISE-Na: 20-250 mmol/L</td>
<td></td>
</tr>
</tbody>
</table>

### Differences

<table>
<thead>
<tr>
<th>Item</th>
<th>Device</th>
<th>Predicate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intended use modified</td>
<td>The Roche cobas c111 analyzer is an in-vitro diagnostic analyzer capable of performing clinical chemistry, specific protein and electrolyte tests.</td>
<td>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.</td>
</tr>
<tr>
<td>Operators</td>
<td>Professional setting</td>
<td>Point-of-care setting</td>
</tr>
</tbody>
</table>
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 oxaloacetic acid 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. Analytical performance:
   
   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

<table>
<thead>
<tr>
<th>Assay</th>
<th>POL sites concentration (mean)</th>
<th>POL sites concentration (range % CV or SD (unit))</th>
<th>Hospital Sites concentration (mean)</th>
<th>Hospital Sites concentration (range % CV or SD (unit))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PNU</td>
<td>PPU</td>
<td>PNU</td>
<td>PPU</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>41.1</td>
<td>137.9</td>
<td>1.1–3.6%</td>
<td>0.4–0.9%</td>
</tr>
<tr>
<td>GLUC (mg/dL)</td>
<td>96.1</td>
<td>255.5</td>
<td>0.3–1.0%</td>
<td>0.5–1.2%</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>0.8</td>
<td>4.8</td>
<td>0.3–0.9%</td>
<td>0.3–0.5%</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>126.7</td>
<td>149.9</td>
<td>0.2–1.0%</td>
<td>0.2–0.5%</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>3.5</td>
<td>6.6</td>
<td>0.2–1.2%</td>
<td>0.012–0.109 SD</td>
</tr>
<tr>
<td>Chloride (mmol/L)</td>
<td>86.2</td>
<td>118.5</td>
<td>0.23–0.64 SD</td>
<td>0.24–0.99%</td>
</tr>
</tbody>
</table>

PNU= PreciNorm Universal Control, PPU=PreciPath Universal Control

### Within-Run Human Samples

<table>
<thead>
<tr>
<th>Assay</th>
<th>POL sites concentration (mean)</th>
<th>POL sites concentration (range % CV or SD (unit))</th>
<th>Hospital Sites concentration (mean)</th>
<th>Hospital Sites concentration (range % CV or SD (unit))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HS 1</td>
<td>HS 2</td>
<td>HS 1</td>
<td>HS 2</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>19.0</td>
<td>46.9</td>
<td>0.46–1.48 SD</td>
<td>0.8–5.2%</td>
</tr>
<tr>
<td>GLUC (mg/dL)</td>
<td>89.1</td>
<td>168.3</td>
<td>0.2–1.1%</td>
<td>0.4–0.9%</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>0.6</td>
<td>2.4</td>
<td>1.1–2.3%</td>
<td>0.6–2.1%</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>144.0</td>
<td>134.2</td>
<td>0.2–0.5%</td>
<td>0.2–0.4%</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.5</td>
<td>4.5</td>
<td>0.3–0.7%</td>
<td>0.3–0.5%</td>
</tr>
<tr>
<td>Chloride (mmol/L)</td>
<td>104.5</td>
<td>97.9</td>
<td>0.2–0.5%</td>
<td>0.2–0.6%</td>
</tr>
</tbody>
</table>

HSPT=Human Serum Pool 1 (normal), HSP2= Human Serum Pool 2 (elevated).
### Total Controls

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

PNU= PreciNorm Universal Control, PPU=PreciPath Universal Control

### Total Human Samples

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

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:
\[ y = 0.989x + 1.276 \text{ U/L} \]
\[ \tau = 0.8316 \]
\[ r = 0.9906 \]
range = 93-286.48 U/L
n = 333

Glucose:
\[ y = 0.997x + 2.069 \text{ mg/dL} \]
\[ \tau = 0.9217 \]
\[ r = 0.9954 \]
range= 42.4-404.80 mg/dL
n = 333

CRP:
\[ y = 1.058x + 0.022 \text{ mg/L} \]
\[ \tau = 0.9789 \]
\[ r = 0.9988 \]
range= 0.010-75/990 mg/L
n = 326
ISE-Cl:
y = 1.011x – 0.51 \text{ mmol/L}
\tau = 0.7532
r = 0.9243
\text{range} = 65.20-111.90 \text{ mmol/L}
n = 280

ISE-K:
y = 0.943x + 0.189 \text{ mmol/L}
\tau = 0.8835
r = 0.9824
\text{range} = 2.950-8.290 \text{ mmol/L}
n = 280

ISE-Na:
y = 1.064x – 9.818 \text{ mmol/L}
\tau = 0.6920
r = 0.9366
\text{range} = 87.9-146.4 \text{ 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.