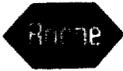


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**Roche Diagnostic Systems**

A Member of the Roche Group

Roche Diagnostic Systems, Inc.  
Branchburg Township  
1080 U.S. Highway 202  
Somerville, New Jersey 08876-3771

Direct Dial  
Fax

## **510(k) Summary**

### **Roche COBAS® INTEGRA Reagent Cassettes**

In accordance with the Safe Medical Devices Act of 1990, a 510(k) summary as outlined in 21 CFR 807.92 is provided herewith.

#### **L Identification of 510(k) Sponsor:**

**Roche Diagnostic Systems, Inc.**  
**a subsidiary of Hoffmann-La Roche, Inc.**  
**Branchburg Township**  
**1080 US Highway 202**  
**Somerville, NJ 08876-3771**

510(k) Submission dated November 5, 1996

**II. Device Name**

The device name, including both the trade/proprietary name and the classification name are provided in the table below.

Proprietary Name	Classification Name	Product Code	CFR Reference Number
<b>COBAS INTEGRA...</b>			
Gamma-Glutamyltransferase - IFCC	Gamma-glutamyl transpeptidase Isoenzymes, Kinetic Method	JQB	862.1360
Lactate Dehydrogenase - IFCC	Lactate Dehydrogenase, NAD Reduction / NADH Oxidation	CFJ	862.1440
Total Protein - urine and CSF	Total Protein, Biuret (Colorimetric)	CEK	862.1635
Lactate	Lactic Acid, Enzymatic Method	KHP	862.1450
Tobramycin	Tobramycin, Fluorescence Polarization Immunoassay	LFW	862.3900
Immunoglobulin A	Immunoglobulins (G, A, M), Nephelometric Method	CFN	862.1330
Immunoglobulin G	Immunoglobulins (G, A, M), Nephelometric Method	CFN	862.1330
Immunoglobulin M	Immunoglobulins (G, A, M), Nephelometric Method	CFN	862.1330

**III. Identification of the legally marketed device to which the 510(k) sponsor claims equivalence:**

The following table identifies the legally marketed devices to which Roche Diagnostic Systems, Inc. claims equivalence.

Product Name	Predicate Product Name	K number	date of substantial equivalence
<b>COBAS INTEGRA...</b>			
Gamma-Glutamyltransferase - IFCC	Roche COBAS INTEGRA, GGT (TRIS)	K951595	9/8/95
Lactate Dehydrogenase - IFCC	Roche COBAS INTEGRA, LD (Lactate - Pyruvate)	K954992	1/25/96
Total Protein - urine and CSF	SIGMA Diagnostics, Microprotein-PR	K853681	10/28/95
Lactate	Boehringer Mannheim, Lactate	K780563	4/18/78
Tobramycin	Abbott Diagnostics, TDX / TDX Flex Tobramycin	K802668	11/24/80
Immunoglobulin A	Behring Diagnostics, N and NA Reagents	K860894	4/15/86
Immunoglobulin G	Behring Diagnostics, N and NA Reagents	K860894	4/15/86
Immunoglobulin M	Behring Diagnostics, N and NA Reagents	K860894	4/15/86

#### **IV. Description of the Device/Statement of Intended Use:**

Through this submission it is the intention of Roche to gain clearance of an additional 5 new COBAS INTEGRA Reagent Cassettes and a modified version of 3 previously cleared reagent cassettes. All of the COBAS INTEGRA Reagent Cassettes contained in this submission are intended for use with the COBAS INTEGRA Analyzer.

The new Reagent Cassettes are:

- **COBAS INTEGRA Gamma- Glutamyltransferase - IFCC:**  
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the catalytic activity of GGT, (EC 2.3.2.2;  $\gamma$ -glutamyl peptide: amino acid  $\gamma$ -glutamyltransferase) in serum and plasma (test GGTI, 0-562).
- **COBAS INTEGRA Lactate Dehydrogenase - IFCC:**  
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the catalytic activity of LDH (EC 1.1.1.27; L-lactate: NAD<sup>+</sup> oxidoreductase ) in serum and plasma (test LDHI, 0-181).
- **COBAS INTEGRA Total Protein - urine and CSF:**  
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the total protein concentration in urine and cerebrospinal fluid (tests TPU, 0-123 and TPC, 0-223).
- **COBAS INTEGRA Lactate:**  
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the lactate concentration in plasma and cerebrospinal fluid (tests LACT, 0-22 and LACTC, 0-122).
- **COBAS INTEGRA Tobramycin:**  
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of tobramycin in serum or heparinized plasma (test TOBR, 0-92).

The modified Reagent Cassettes are:

- **COBAS INTEGRA Immunoglobulin A:**  
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the immunological determination of human immunoglobulin A in serum. In addition to the standard application (test IGA, 0-075), the sensitive application (test IGAP, 0-175) is designed for the quantitative determination of low IgA concentrations in e.g. pediatric samples.

- **COBAS INTEGRA Immunoglobulin G:**  
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the immunological determination of human immunoglobulin G in serum. In addition to the standard application (test IGG, 0-076), the sensitive application (test IGGP, 0-176) is designed for the quantitative determination of low IgG concentrations in e.g. pediatric samples.
- **COBAS INTEGRA Immunoglobulin M:**  
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the immunological determination of human immunoglobulin M in serum. In addition to the standard application (test IGM, 0-077), the sensitive application (test IGMP, 0-177) is designed for the quantitative determination of low IgM concentrations in e.g. pediatric samples.

The Analyzer provides quantitative measurement of these analytes via three measuring principles, i.e., absorbance, fluorescence polarization and ion-selective electrodes. The COBAS INTEGRA Reagent Cassettes are compact and preparation-free. Sixty-eight COBAS INTEGRA Reagent Cassettes can be stored on board, 24 hours a day at 2-8°C. Each cassette is barcoded. This barcode label provides the analyzer with specific reagent information such as the lot number, the expiration date and the number of tests.

**V. Summary of the technological characteristics of the new device in comparison to those of the predicate.**

Tables 1 through 8 in the following section of this summary outline the technological characteristics (methodologies) of the COBAS INTEGRA Reagent Cassettes in comparison to those of legally marketed products.

**V. Brief discussion of the clinical and nonclinical tests relied on for a determination of substantial equivalence:**

The following tables 1 through 8 demonstrate the results of clinical and nonclinical studies performed using the COBAS INTEGRA Reagent Cassettes. The significant performance characteristics relied upon for a determination of substantial equivalence are summarized in this chart. This information concludes that the performance of these devices are essentially equivalent to other legally marketed devices of a similar kind.

**Table 1 - Gamma-Glutamyltransferase IFCC**

	<b>COBAS INTEGRA GGT - IFCC</b>	<b>COBAS INTEGRA GGT - (TRIS)</b>
Intended Use	quantitative determination of the catalytic activity of GGT	quantitative determination of the catalytic activity of GGT
Sample type	serum and plasma	serum and plasma
Methodology	kinetic method - International Federation of Clinical Chemistry (IFCC)	kinetic method - Szasz-Persjun
Reagents	R1: Buffer granulate R2: L-γ-glutamyl-3-carboxy-4-nitroanilide granulate with preservative	R1: Buffer granulate R2: L-γ-glutamyl-3-carboxy-4-nitroanilide granulate with preservative
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
<b>Performance Characteristics:</b>		
Assay Range	0 - 1,200 U/L 0 - 12,000 U/L with post dilution	0 - 700 U/L 0 - 2,800 U/L with postdilution
Precision:	Level 1    Level 2	Level 1    Level 2
Mean (U/L)	28            546	37.9        345
%CV (within run)	1.0           1.1	0.67        0.46
%CV (total)	2.7           2.5	1.2           1.4
Accuracy	$y = 1.27x - 0.9$ U/L $r = 0.999$ $n = 202$ vs. COBAS INTEGRA GGT (TRIS)	$y = 1.02x + 0$ U/L $r = 0.998$ $n = 238$

**Table 2 - Lactate Dehydrogenase - IFCC**

	<b>COBAS INTEGRA LDH - IFCC</b>	<b>COBAS INTEGRA LDH - (L - P)</b>
Intended Use	quantitative determination of the catalytic activity of LDH	quantitative determination of the catalytic activity of LDH
Sample type	serum and plasma	serum
Methodology	kinetic method - lactate to pyruvate International Federation of Clinical Chemistry (IFCC)	kinetic method - lactate to pyruvate Gay, McComb, and Bowers
Reagents	R1: Substrate R2: Coenzyme - NADH in TRIS buffer with preservatives and stabilizer	R1: Substrate R2: Coenzyme - NAD
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
<b>Performance Characteristics:</b>		
Assay Range	0 - 1,200 U/L 0 - 12,000 U/L with post dilution	0 - 1,000 U/L 0 - 10,000 U/L with postdilution
Precision:	Level 1    Level 2	Level 1    Level 2
Mean (U/L)	214        339	141        439
%CV (within run)	0.65       0.65	1.3        0.99
%CV (total)	2.6        1.9	2.8        1.5
Accuracy	$y = 1.07x + 0.4$ U/L $r = 0.999$ $n = 106$ vs. COBAS INTEGRA LD (L - P)	$y = 0.95x - 14.3$ U/L $r = 0.999$ $n = 190$ vs. Boehringer Mannheim

**Table 3 Total Protein - Urine and CSF**

	<b>COBAS INTEGRA Total Protein - Urine / CSF</b>	<b>Sigma Diagnostics Microprotein - PR</b>
<b>Intended Use</b>	quantitative determination of total protein	quantitative determination of total protein
<b>Sample type</b>	urine and cerebrospinal fluid	urine and cerebrospinal fluid
<b>Methodology</b>	colorimetric method using pyrogallol-red molybdate complex	colorimetric method using pyrogallol-red molybdate complex
<b>Reagents</b>	R1: Pyrogallol red and sodium molybdate in buffer with detergents and stabilizer	1. Pyrogallol red and sodium molybdate in buffer with chelating agent, stabilizer, surfactant and preservative
<b>Calibrator</b>	Roche Calibrator (human)	Sigma Protein Standard Solution
<b>Controls</b>	recommended : Biorad Lyphocheck Urine Controls	Sigma urine and CSF Controls
<b>Performance Characteristics:</b>		
<b>Assay Range</b>	1 - 250 mg/dL 1 - 250 mg/dL with post dilution	1 - 200 mg/dL
<b>Precision ( Urine):</b>	Level 1    Level 2    Level 3	Level 1    Level 2    Level 3
Mean (mg/dL)	17.4        57.4        107.6	7.69        26.96        135.49
%CV (total)	8.2         2.9         2.4	9.37        6.42        2.57
<b>Precision ( CSF):</b>	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mg/dL)	28.9        951	37.87        69.86        121.25
%CV (total)	1.3         0.80	3.47        2.65        2.29
<b>Accuracy (Urine)</b>	$y = 0.89x + 0$ mg/L $r = 0.992$ n = 274 vs. Sigma	$y = 1.005x + 0.458$ $r = 0.997$ n = 95 vs. similar commercially available method

**Table 4 - Lactate**

	<b>COBAS INTEGRA Lactate</b>	<b>Boehringer Mannheim Lactate - on Hitachi 911 Analyzer</b>
<b>Intended Use</b>	quantitative determination of lactate	quantitative determination of lactate
<b>Sample type</b>	plasma and cerebrospinal fluid	plasma and cerebrospinal fluid
<b>Methodology</b>	colorimetric (LOX/PAP) with lactate oxidase and 4-aminoantipyrine	colorimetric - lactate to pyruvate (NAD Reduction/NADH Oxidation)
<b>Reagents</b>	R1: Lactate oxidase (microbial) in TRIS buffer with stabilizer and preservative	R1: NAD in carbonate buffer with preservatives R2: LD (porcine muscle) and ALT (porcine heart)
<b>Calibrator</b>	Roche Calibrator (human)	BM Standard 1
<b>Controls</b>	Roche Control Serum N and P (human)	Precitrol - N and A Control Serum
<b>Performance Characteristics:</b>		
<b>Assay Range</b>	0 - 180 mmol/L 0 - 1,800 mmol/L with post dilution	Up to 100 mg/dL Up to 199 mg/dL with postdilution
<b>Precision (Control Sera):</b>	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mg/dL)	12.6      47.7	7.7      23.5      55.1
%CV (within run)	0.92      0.62	2.7      1.1      0.7
%CV (total)	1.2      1.1	3.8      1.3      0.9
<b>Precision (CSF):</b>	Level 1    Level 2	
Mean (mg/dL)	20.7      74.7	
%CV (within run)	0.90      0.89	
<b>Accuracy</b>	$y = 1.00x - 0.1$ mmol/L $r = 0.999$ n = 224 vs. <b>Boehringer Mannheim 911</b>	$y = 0.985x - 0.09$ $r = 0.999$ n = 57 vs. <b>Boehringer Mannheim 717</b>

**Table 5 - Tobramycin**

	<b>COBAS INTEGRA Tobramycin</b>	<b>Abbott TDX/TDX Flex Tobramycin</b>
<b>Intended Use</b>	quantitative determination of tobramycin	quantitative determination of tobramycin
<b>Sample type</b>	serum and heparinized plasma	serum and plasma
<b>Methodology</b>	fluorescence polarization	fluorescence polarization
<b>Calibrators</b>	0, 1, 2, 4, 7, 10 µg/mL	0, 0.5, 1.5, 3.0, 6.0, 10.0 µg/mL
<b>Reagents:</b>	R1: Anti-tobramycin monoclonal antibody (mouse) in buffer R2: Fluorescein labeled tobramycin derivative in buffer	R1: Tobramycin Antiserum (sheep) in buffer R2: Fluorescein tracer in buffer
<b>Performance Characteristics:</b>		
<b>Assay Range</b>	0.04 - 10 µg/mL	0.18 - 10.0 µg/mL
<b>Precision:</b>	Level 1    Level 2    Level 3	Level 1    Level 2    Level 3
<b>Mean (mg/dL)</b>	1.4        3.5        7.5	0.98       4.02       8.15
<b>%CV (total)</b>	6.0        4.5        4.0	5.18       4.45       4.62
<b>Accuracy</b>	y = 0.854 +0.015 r = 0.996 n = 196 vs. Abbott TDX	y = 0.934 +0.248 µg/mL r = 0.951 n = 170 vs. enzyme immunoassay
<b>Sensitivity</b>	0.04 µg/mL	0.18 µg/mL

**Table 6 - Immunoglobulin A**

	<b>COBAS INTEGRA IgA (modified)</b>	<b>COBAS INTEGRA IgA (currently marketed)</b>	<b>Behringer N and NA Reagents</b>
<b>Intended Use</b>	quantitative determination of human IgA, and a sensitive application for quantitative determination of low IgA concentrations (pediatric)	quantitative determination of human IgA	quantitative determination of human serumproteins
<b>Sample type</b>	serum	serum	serum, umbilical cord serum or cerebrospinal fluid
<b>Methodology</b>	Immunoturbidimetric	Immunoturbidimetric	Immunoturbidimetric
<b>Reagents</b>	R1: Anti-IgA T antiserum (rabbit) specific for human IgM in phosphate buffer R2: IgA in diluted serum (human) with stabilizer	R1: Anti-IgA T antiserum (rabbit) specific for human IgM in phosphate buffer R2: IgA in diluted serum (human) with stabilizer	1. Antiserum to human IgA 2. Phosphate-buffered saline
<b>Calibrator</b>	Roche Serumproteins T Standard	Roche Serumproteins T Standard	Behringer N Protein Standard
<b>Controls</b>	Roche Serumproteins T Control	Roche Serumproteins T Control	Behringer N/T Protein Control Serum (human)
<b>Performance Characteristics:</b>			
<b>Assay Range</b>	0.11 - 3.54 g/L 0.04 - 10.6 g/L with rerun	0.95 - 15.2 g/L 0.32 - 36.5 g/L with rerun	not specified in labeling
<b>Precision (standard application):</b> Mean (g/mL) %CV (within run) %CV (total)	Level 1    Level 2 2.3        3.5 1.4        0.81 2.8        1.8	Level 1    Level 2 2.3        3.5 1.4        0.81 2.8        1.8	not specified in labeling
<b>Precision (Pediatric application):</b> Mean (mg/dL) %CV (within run) %CV (total)	Level 1    Level 2 1.17       3.28 1.1        0.96 3.0        1.0	not applicable	not specified in labeling
<b>Accuracy (standard application)</b>	$y = 0.97x - 0.05$ g/L $r = 0.989$ $n = 400$ vs. Behringer	$y = 0.97x - 0.05$ g/L $r = 0.989$ $n = 400$ vs. Behringer	not specified in labeling
<b>Accuracy (pediatric application)</b>	$y = 1.01x + 0.01$ g/L $r = 0.996$ $n = 204$ vs. Behringer	not applicable	not specified in labeling

**Table 7 - Immunoglobulin G**

	<b>COBAS INTEGRA IgG (modified)</b>	<b>COBAS INTEGRA IgG (currently marketed)</b>	<b>Behringer N and NA Reagents</b>
<b>Intended Use</b>	quantitative determination of human IgG, and a sensitive application for quantitative determination of low IgG concentrations (pediatric)	quantitative determination of human IgG	quantitative determination of human serumproteins
<b>Sample type</b>	serum	serum	serum, umbilical cord serum or cerebrospinal fluid
<b>Methodology</b>	Immunoturbidimetric	Immunoturbidimetric	Immunoturbidimetric
<b>Reagents</b>	R1: Anti-IgG T antiserum (rabbit) specific for human IgM in phosphate buffer R2: IgG in diluted serum (human) with stabilizer	R1: Anti-IgG T antiserum (rabbit) specific for human IgM in phosphate buffer R2: IgG in diluted serum (human) with stabilizer	1. Antiserum to human IgG 2. Phosphate-buffered saline
<b>Calibrator</b>	Roche Serumproteins T Standard	Roche Serumproteins T Standard	Behringer N Protein Standard
<b>Controls</b>	Roche Serumproteins T Control	Roche Serumproteins T Control	Behringer N/T Protein Control Serum (human)
<b>Performance Characteristics:</b>			
<b>Assay Range</b>	4.0 - 63.8 g/L 1.0 - 153 g/L with rerun	4.7 - 75 g/L 1.2 - 180 g/L with rerun	not specified in labeling
<b>Precision (standard application):</b>			not specified in labeling
Mean (g/mL)	Level 1    Level 2 12.9        25.5	Level 1    Level 2 12.9        25.5	
%CV (within run)	2.0        1.4	2.0        1.4	
%CV (total)	2.9        1.9	2.9        1.9	
<b>Precision (Pediatric application):</b>		not applicable	not specified in labeling
Mean (mg/dL)	Level 1    Level 2 7.1        16.9		
%CV (within run)	0.81       0.83		
%CV (total)	3.0        1.3		
<b>Accuracy (standard application)</b>	$y = 1.02x - 0.9$ g/L $r = 0.996$ $n = 244$ vs. Behringer	$y = 1.02x - 0.9$ g/L $r = 0.996$ $n = 244$ vs. Behringer	not specified in labeling
<b>Accuracy (pediatric application)</b>	$y = 0.93x + 0.30$ g/L $r = 0.986$ $n = 212$ vs. Behringer	not applicable	not specified in labeling

**Table 8 - Immunoglobulin M**

	<b>COBAS INTEGRA IgA (modified)</b>	<b>COBAS INTEGRA IgA (currently marketed)</b>	<b>Behringer N and NA Reagents</b>
Intended Use	quantitative determination of human IgM, and a sensitive application for quantitative determination of low IgM concentrations (pediatric)	quantitative determination of human IgM	quantitative determination of human serumproteins
Sample type	serum	serum	serum, umbilical cord serum or cerebrospinal fluid
Methodology	Immunoturbidimetric	Immunoturbidimetric	Immunoturbidimetric
Reagents	R1: Anti-IgM T antiserum (rabbit) specific for human IgM in phosphate buffer R2: IgM in diluted serum (human) with stabilizer	R1: Anti-IgM T antiserum (rabbit) specific for human IgM in phosphate buffer R2: IgM in diluted serum (human) with stabilizer	1. Antiserum to human IgM 2. Phosphate-buffered saline
Calibrator	Roche Serumproteins T Standard	Roche Serumproteins T Standard	Behringer N Protein Standard
Controls	Roche Serumproteins T Control	Roche Serumproteins T Control	Behringer N/T Protein Control Serum (human)
<b>Performance Characteristics:</b>			
Assay Range	0.31 - 5.0 g/L 0.11 - 12.1 g/L with rerun	0.47 - 7.5 g/L 0.16 - 18 g/L with rerun	not specified in labeling
Precision (standard application): Mean (g/mL) %CV (within run) %CV (total)	Level 1    Level 2 0.6        1.9 2.6        2.0 3.1        2.2	Level 1    Level 2 0.6        1.9 2.6        2.0 3.1        2.2	not specified in labeling
Precision (Pediatric application): Mean (mg/dL) %CV (within run) %CV (total)	Level 1    Level 2 0.44       1.08 1.9        1.6 4.9        2.1	not applicable	not specified in labeling
Accuracy (standard application)	$y = 1.12x - 0.06$ g/L $r = 0.994$ n = 400 vs. Behringer	$y = 1.12x - 0.06$ g/L $r = 0.994$ n = 400 vs. Behringer	not specified in labeling
Accuracy (pediatric application)	$y = 1.17x - 0.03$ g/L $r = 0.984$ n = 214 vs. Behringer	not applicable	not specified in labeling