

K912250



AUG 12 1997

Diagnostic

510(k) Summary

Roche COBAS® INTEGRA Reagent Cassettes

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

I. Identification of 510(k) Sponsor:

Roche Diagnostic Systems, Inc.
a subsidiary of Hoffmann-La Roche, Inc.
Branchburg Township
1080 U.S. Highway 202
Somerville, New Jersey 08876-3771

510(k) Submission dated June 13, 1997

Contact: Maria Feijoo
Regulatory Affairs Associate
Phone: (908) 253-7310
Fax: (908) 253-7547

II. Device Name:

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

Table 1

Proprietary Name	Classification Name	Product Code	Regulation Number
COBAS INTEGRA...			
Ammonia	Ammonia test system, Enzymatic method	JIF	862.1065
αAmylase EPS	Amylase test system, Catalytic method	JFJ	862.1070
Cholesterol	Cholesterol test system, Enzymatic esterase - oxidase method	CHH	862.1175
HDL-Cholesterol	Lipoprotein test system, Phosphotungstic acid method	N/A	862.1475
Creatinine	Creatinine test system, Enzymatic method	JFY	862.1225
Digitoxin	Digitoxin test system, Kinetic interaction of microparticles in solution method	DKQ	862.3300
Gamma-Glutamyltransferase (GGT)	Gamma-glutamyl transpeptidase and isoenzymes test system, Kinetic method	JQB	862.1360
Glucose HK	Glucose test system, Enzymatic method	CFR	862.1345
Lipase	Lipase test system, Turbidimetric method	CET	862.1465
Lysergic acid diethylamide (LSD)	Lysergic acid diethylamide (LSD) test system, Kinetic interaction of microparticles in solution method	N/A	862.3580
Urea	Urea nitrogen test system, Kinetic urease method	CDQ	862.1770
Roche TDM OnLine ...			
Digitoxin Calibrators	Clinical toxicology calibrator, Drug specific	DLJ	862.3200
Digitoxin Controls	Clinical toxicology control material, Drug specific	LAS	862.3280

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.

Table 2

Product Name	Predicate Product Name	K number	Date of substantial equivalence
COBAS INTEGRA...			
Ammonia	Roche Reagent for Ammonia	K913124	8/12/91
αAmylase EPS (Liquid)	COBAS INTEGRA αAmylase (Granulate, CL-PNP-G, method)	K951595	9/8/95
Cholesterol (Liquid)	COBAS INTEGRA Cholesterol (Granulate)	K951595	9/8/95
HDL - Cholesterol (Liquid)	COBAS INTEGRA HDL - Cholesterol (Granulate)	K951595	9/8/95
Creatinine (Enzymatic)	COBAS INTEGRA Creatinine (Kinetic Jaffe)	K951595	9/8/95
Digitoxin	Abbott Diagnostics, TDX / TDX Flex Digitoxin Reagent	K842280	8/16/84
Gamma-Glutamyltransferase (GGT)	COBAS INTEGRA Lipase (Granulate)	K951595	9/8/95
Glucose HK	COBAS INTEGRA Glucose HK (Granulate)	K951595	9/8/95
Lipase	COBAS INTEGRA Lipase (Granulate)	K951595	9/8/95
Lysergic acid diethylamide (LSD)			
Urea	COBAS INTEGRA Urea (Granulate)	K951595	9/8/95
Roche TDM OnLine ...			
Digitoxin Calibrators	Abbott Diagnostics, TDX / TDX Flex Digitoxin Calibrators	K842280	8/16/84
Digitoxin Controls	Abbott Diagnostics, TDX / TDX Flex Digitoxin Controls	K842280	8/16/84

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

The COBAS INTEGRA test applications contained in this submission are intended for use with the COBAS INTEGRA Analyzer. The COBAS INTEGRA Analyzer and COBAS INTEGRA Reagent cassettes together provide an integrated system for *in vitro* diagnostic testing. The COBAS INTEGRA Analyzer along with 96 other Roche COBAS INTEGRA Reagent Cassettes were previously cleared on September 8, 1995 (K951595); January 25, 1996 (K954992); July 23, 1996 (K961824); October 31, 1996 (K963292); and January 21, 1997 (K964457).

The COBAS INTEGRA Analyzer utilizes three measuring principles, i.e., absorbance, fluorescence polarization and ion-selective electrodes. The analyzer has a throughput of up to 600 tests per hour with STAT samples prioritized and tested immediately. Random sample access, robotics and a user interface optimize time management and streamline workflow. The COBAS INTEGRA can store up to 68 COBAS INTEGRA Reagent Cassettes on board, 24 hours a day at 2-8°C. The COBAS INTEGRA Reagent Cassettes are compact and preparation-free with the added convenience of long term on-board stability. Barcode readers are used to identify newly loaded reagent cassettes, samples for patient identification, and rack inserts and to read calibration and control data from the cassette label. COBAS INTEGRA tests include chemistry, drugs of abuse, immunology, ion selective electrodes, therapeutic drug monitoring, and hematology reagents. For additional information on the COBAS INTEGRA Analyzer and its constituent modules, please refer to the Operator's Manual in Volumes 1 through 2, pages 92-703, of the original 510(k) submission (K951595).

Through this submission, it is the intention of Roche Diagnostic Systems to gain clearance for an additional 4 COBAS INTEGRA Reagent Cassettes and 2 ancillary reagents as well as modifications to 7 previously cleared COBAS INTEGRA Reagent Cassettes. These reagents have been modified from granulate to liquid form.

The new Reagent Cassettes and ancillary reagents are:

COBAS INTEGRA Ammonia (NH₃):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the ammonia concentration in plasma (test NH₃, 0-045).

COBAS INTEGRA Creatinine Enzymatic (CREAE):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the creatinine concentration in serum (test CREAE, 0-014), and urine (test CREEU, 0-114).

COBAS INTEGRA Digitoxin (DIGIT):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of digitoxin in serum or heparinized plasma (test DIGIT 0-259).

Roche TDM OnLine Digitoxin Calibrators:

are intended for use with the Roche reagents for Digitoxin and the COBAS Chemistry systems for the quantitative determination of digitoxin in serum and plasma.

Roche TDM OnLine Digitoxin Controls:

are quality control samples intended for use on COBAS chemistry systems with Roche reagents and calibrators for the quantitative determination of digitoxin assays.

COBAS INTEGRA Lysergic acid diethylamide (LSD):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the qualitative determination of lysergic acid diethylamide (LSD) in urine (test LSD, 0-001)

The modified Reagent Cassettes are:

COBAS INTEGRA α Amylase EPS (AMYLL):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the catalytic activity of amylase in serum, plasma (test AMY-L, 0998) and urine (test AMY-UL 0-999).

COBAS INTEGRA Cholesterol (CHOLL):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of total cholesterol (test CHOLL, 0-001) and HDL - cholesterol concentration in serum and plasma in clinical laboratories.

COBAS INTEGRA HDL - Cholesterol Application (HDLL):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of total cholesterol and HDL - cholesterol (test HDLL, 0-002) concentration in serum and plasma in clinical laboratories.

COBAS INTEGRA Gamma - Glutamyltransferase (GGTL):

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; γ -glutamyl peptide: amino acid γ -glutamyltransferase) in serum and plasma (test GGTL, 0-599).

COBAS INTEGRA Glucose HK Liquid (GLUCL):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the glucose concentration in serum, plasma (test GLUL, 0-991), urine (test GLULU, 0-992), and cerebrospinal fluid (test GLULC, 0-993).

COBAS INTEGRA Lipase (LIPL):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the catalytic activity of lipase in serum and plasma (test LIPL, 0-200).

COBAS INTEGRA Urea/BUN (UREAL):

contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the urea/BUN (blood urea nitrogen), in serum, plasma (test UREL, 0-003) and urine (test URELU, 0-004).

The clinical utility and methodology of each reagent cassette are further described in the test specific COBAS INTEGRA Method Manual sheets, contained in the test specific sections of this submission.

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

Tables 3-13 outline the technological characteristics (methodologies) of the COBAS INTEGRA Reagents in comparison to those of legally marketed predicate products.

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

Tables 3-13 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 this device is essentially equivalent to other legally marketed devices of a similar kind.

Table 3 - Ammonia (NH₃)

	COBAS INTEGRA Ammonia	Roche Reagent for Ammonia
Intended Use	quantitative determination of the ammonia concentration	quantitative determination of the ammonia concentration
Sample type	plasma	plasma
Methodology	enzymatic, with glutamate dehydrogenase	enzymatic, with glutamate dehydrogenase
Reagents	R1: Enzyme (liquid) R2: Coenzyme (liquid)	R1: Enzyme (liquid) R2: Coenzyme (liquid)
Calibrator	Roche Ammonia/Ethanol/CO ₂ Calibrator	Roche Ammonia/Ethanol/CO ₂ Calibrator
Controls	Roche Ammonia/Ethanol Controls	Roche Ammonia/Ethanol Controls
Performance Characteristics:		
Assay Range	0 - 700 µmol/L (0 - 1190 µg/dL)	0 - 700 U/L 0 - 2,800 U/L with postdilution
Precision:	Level 1	Level 2
Mean (µmol/L)	48.8 (83.0 µg/dL)	226 (384 µg/dL)
%CV (within run)	3.1	2.0
%CV (total)	5.2	2.5
Sensitivity	0.76 ΔA per µmol/L	0.0009 ΔA per µmol/L
Accuracy:		
Sample size (n)	164	95
Corr. Coefficient (r)	0.997	0.992
Lin. Regression	1.03x - 2.8 µmol/L vs. Roche Reagent for Ammonia	1.02x + 3.2 µmol/L

Table 4 - Creatinine (CREAE)

	COBAS INTEGRA Creatinine (Enzymatic, PAP)		COBAS INTEGRA Creatinine (Kinetic, Jaffé)	
Intended Use	quantitative determination of the catalytic activity of α amylase		quantitative determination of the catalytic activity of α amylase	
Sample type	serum, plasma and urine		serum, plasma and urine	
Methodology	enzymatic colorimetric method (PAP)		Jaffé, buffered, kinetic method	
Reagents	R1: Enzyme (liquid) R2: Substrate (liquid)		R1: Alkaline buffer (liquid) R2: Picric acid (liquid)	
Calibrator	Roche Calibrator (human)		Roche Calibrator (human)	
Controls	Roche Control Serum N and P (human)		Roche Control Serum N and P (human)	
Performance Characteristics for serum and plasma:				
Assay Range	0 - 2000 μ mol/L (0-22.6 mg/dL) 0 - 20000 μ mol/L (0-226 mg/dL) with post dilution		0 - 1300 μ mol/L (0-15 mg/dL) 0 - 13000 μ mol/L (0-1470 mg/dL) with post dilution	
Precision: Mean (μ mol/L)	Level 1 99.4 (1.1mg/dL)	Level 2 535 (6.0 mg/dL)	Level 1 85.5 (0.97mg/dL)	Level 2 624 (7.1 mg/dL)
%CV (within run)	1.6	0.88	1.5	1.1
%CV (total)	2.2	1.5	1.9	1.5
Sensitivity	2.2 X 10 ⁻⁴ Δ A per μ mol/L (1.9 X 10 ⁻⁴ Δ A per mg/dL)		8.0 X 10 ⁻⁵ Δ A/min per μ mol/L (1.7 X 10 ⁻³ Δ A/min per mg/dL)	
Accuracy: Sample size (n) Corr. Coefficient (r) Lin. Regression	238 0.999 1.08x - 30.6 μ mol/L vs. COBAS INTEGRA Creatinine (Jaffé)		256 0.999 0.87x - 2 μ mol/L	
Performance Characteristics for urine:				
Assay Range	0 - 40 mmol/L (0-450 mg/dL) 0 - 200 mmol/L (0-2260 mg/dL) with post dilution		0 - 32.5 mmol/L (0-367 mg/dL) 0 - 130 mmol/L (0-1470 mg/dL) with post dilution	
Precision: Mean (mmol/L)	Level 1 4.1 (46.7 mg/dL)	Level 2 14.0 (159 mg/dL)	Level 1 5.3 (60 mg/dL)	Level 2 19 (216 mg/dL)
%CV (within run)	0.88	0.87	1.5	1.0
%CV (total)	1.1	0.93		
Sensitivity	5.7 X 10 ⁻³ Δ A per mmol/L (5.1 X 10 ⁻² Δ A per mg/dL)		Not specified in labeling	
Accuracy: Sample size (n) Corr. Coefficient (r) Lin. Regression	116 0.999 0.99x - 0.28 mmol/L vs. COBAS INTEGRA Creatinine (Jaffé)		Not specified in labeling	

Table 5 - Digitoxin Reagent, Calibrators, and Controls (DIGIT)

	COBAS INTEGRA Digitoxin & Roche - TDM OnLine Digitoxin Calibrators & Controls			Abbott TDx/TDxFLx Digitoxin Reagent, Calibrators & Controls		
Intended Use	quantitative determination of digitoxin			quantitative determination of digitoxin		
Sample type	serum and heparinized plasma			serum and plasma		
Methodology	kinetic interaction of microparticles in solution (KIMS)			fluorescence polarization (FPIA)		
Reagents	R1: Anti-digitoxin monoclonal antibody (mouse) in buffer (liquid) R2: Conjugated digitoxin derivative microparticles in buffer (liquid)			R1: Digitoxin Antiserum (Rabbit) in buffer R2: Digitoxin Fluorescein tracer in buffer		
Calibrator Levels (in human serum)	0, 7.5, 15, 30, 45, 65 ng/mL			0, 5.0, 10.0, 20.0, 40.0, 80.0 ng/mL		
Controls Levels (ng/mL) (in human serum)	Level 1 12.0 - 18.0	Level 2 24.0 - 36.0	Level 3 36.0 - 54.0	Level 1 5.4- 9.6	Level 2 12.0- 18.0	Level 3 26.5 - 43.5
Performance Characteristics:						
Assay Range	2.0 - 65 ng/mL			2.0 - 80 ng/mL		
Precision:	Level 1	Level 2	Level 3	Level 1	Level 2	Level 3
Mean (ng/mL)	10.4	19.5	37.1	7.5	15.0	35.0
% CV (within run)	6.0	3.9	3.6	7.05	4.87	4.72
%CV (total)	7.4	4.5	3.7	10.61	7.19	8.46
Sensitivity	2.0 ng/mL			2.0 ng/mL		
Accuracy:						
Sample size (n)	232			178		
Corr. Coefficient (r)	0.973			0.967		
Lin. Regression	0.945x + 1.19 ng/mL vs. Abbott TDx/TDxFLx Digitoxin			1.060 + 0.729 ng/mL		

Table 6 - Lysergic acid diethylamide (LSD)

	COBAS INTEGRA LSD			Roche Abuscreen RIA for LSD			
Intended Use	qualitative detection of LSD and its metabolites			detection of LSD and its metabolites			
Sample type	urine			urine			
Methodology	kinetic interaction of microparticles in solution (KIMS)			competitive binding to antibody of ¹²⁵ I-radiolabeled antigen and unlabeled antigen			
Cutoff	0.5 ng/mL			0.5 ng/mL			
Reagents	R1: Buffer R2: conjugated LSD derivative microparticles in buffer R3: LSD polyclonal antibody (goat) in buffer			R1: LSD polyclonal (rabbit) antibody in buffer R2: ¹²⁵ I-LSD in buffer R3: Anti-rabbit immunoglobulin serum (goat) in buffer			
Calibrator	Roche Abuscreen Calibration Standard			Roche Abuscreen Calibration Standard			
Controls	Roche Abuscreen Reference Controls and Calibrator			Roche Abuscreen Reference Controls and Calibrator			
Performance Characteristics:							
Assay Range	0 - 1 ng/mL			0 - 1 ng/mL			
Precision:	Level 1	Level 2	Level 3	L1	L2	L3	L4
Mean	O.D.	O.D.	O.D.	ng/mL	ng/mL	ng/mL	ng/mL
%CV (within run)	0.978	0.913	0.870	0.0	0.25	0.5	1.0
	1.3	0.7	1.3	0.6	1.3	1.6	1.8
Sensitivity	0.10 ng/mL of LSD at > 95% confidence			0.25 ng/mL of LSD at > 99% confidence			
Accuracy:							
Positive Samples		INTEGRA	GC/MS	RIA		GC/MS	RIA
	+	39	39	39	+	21	21
	-	0	0	0	-	0	0

Table 7 - α -Amylase (AMYLL)

	COBAS INTEGRA α-Amylase EPS (Liquid)	COBAS INTEGRA α-Amylase (Granulate)
Intended Use	quantitative determination of the catalytic activity of α amylase	quantitative determination of the catalytic activity of α amylase
Sample type	serum, plasma and urine	serum, plasma and urine
Methodology	enzymatic colorimetric method using the substrate 4,6-ethylidene-p-nitrophenyl- α ,D-maltoheptaoside	enzymatic colorimetric method with 2-chloro-4-nitrophenyl- β -D-maltoheptaoside
Reagents	R1: Enzyme (liquid) R2: Substrate (liquid)	R1: Enzyme (granulate) R2: Substrate (granulate)
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
Performance Characteristics for serum and plasma:		
Assay Range	0 - 2000 U/L 0 - 10000 U/L with post dilution	0 - 2000 U/L 0 - 20000 U/L with post dilution
Precision:	Level 1	Level 2
Mean (U/L)	76	498
%CV (within run)	1.6	1.3
%CV (total)	2.3	2.6
Sensitivity	1.9×10^{-4} Δ A/min per U/L	1.5×10^{-4} Δ A/min per U/L
Accuracy:		
Sample size (n)	114	212
Corr. Coefficient (r)	0.996	0.992
Lin. Regression	$0.43x + 4$ U/L vs. COBAS INTEGRA α -Amylase (granulate)	$0.98x - 19$ U/L
Performance Characteristics for urine:		
Assay Range	0 - 2000 U/L 0 - 10000 U/L with post dilution	0 - 2000 U/L 0 - 20000 U/L with post dilution
Precision:	Level 1	Level 2
Mean (U/L)	183	603
%CV (within run)	1.3	1.6
%CV (total)	1.7	1.6
Sensitivity	1.9×10^{-4} Δ A/min per U/L	Not specified in labeling
Accuracy:		
Sample size (n)	150	Not specified in labeling
Corr. Coefficient (r)	0.988	
Lin. Regression	$0.44x + 0$ U/L vs. COBAS INTEGRA α -Amylase (granulate)	

Table 8 - Cholesterol (CHOLL)

	COBAS INTEGRA Cholesterol (Liquid)	COBAS INTEGRA Cholesterol (Granulate)
Intended Use	quantitative determination of total cholesterol & HDL cholesterol	quantitative determination of total cholesterol & HDL cholesterol
Sample type	serum and plasma	serum and plasma
Methodology	enzymatic, colorimetric method using cholesterol esterase, cholesterol oxidase and 4-aminoantipyrine	enzymatic, colorimetric method using cholesterol esterase, cholesterol oxidase and 4-aminoantipyrine
Reagents	R: Cholesterol esterase, cholesterol oxidase and 4-aminoantipyrine (liquid)	R: Cholesterol esterase, cholesterol oxidase and 4-aminoantipyrine (granulate)
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
Performance Characteristics:		
Assay Range	0 - 18.1 mmol/L (0 - 700 mg/dL) 0 - 181 mmol/L (0 - 7000 mg/dL) with post dilution	0 - 20.7 mmol/L (0 - 800 mg/dL) 0 - 207 mmol/L (0 - 8000 mg/dL) with post dilution
Precision:	Level 1	Level 2
Mean (mmol/L)	5.3 (205 mg/dL)	6.7 (259 mg/dL)
%CV (within run)	1.3	1.1
%CV (total)	2.2	2.5
Sensitivity	$8.8 \times 10^{-2} \Delta A$ per mmol/L ($2.3 \times 10^{-3} \Delta A$ per mg/dL)	$6.4 \times 10^{-2} \Delta A$ per mmol/L ($1.7 \times 10^{-3} \Delta A$ per mg/dL)
Accuracy:		
Sample size (n)	214	240
Corr. Coefficient (r)	0.998	0.995
Lin. Regression	$0.99x + 0.0$ mmol/L vs. COBAS INTEGRA Cholesterol (granulate)	$1.04x + 0.1$ mmol/L

Table 9 - HDL - Cholesterol Application (HDLL)

	COBAS INTEGRA HDL - Cholesterol Application (for use with COBAS INTEGRA Cholesterol Liquid Reagent)	COBAS INTEGRA HDL - Cholesterol Application (for use with COBAS INTEGRA Cholesterol Granulate Reagent)
Intended Use	quantitative determination HDL cholesterol	quantitative determination HDL cholesterol
Sample type	serum and plasma	serum and plasma
Methodology	Phosphotungstic acid pretreatment	Phosphotungstic acid pretreatment
Reagents	Roche Separating Reagent for HDL - Cholesterol used with COBAS INTEGRA Cholesterol <i>liquid</i> reagent	Roche Separating Reagent for HDL - Cholesterol used with COBAS INTEGRA Cholesterol <i>granulate</i> reagent
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
Performance Characteristics:		
Assay Range	0 - 5.0 mmol/L (0 - 193 mg/dL)	
Precision:	Level 1	Level 2
Mean (mmol/L)	0.20 (7.7 mg/dL)	1.91 (73.8mg/dL)
%CV (within run)	1.51.3	0.26
%CV (total)	3.0	1.6
Sensitivity	8.8 X 10 ⁻² ΔA per mmol/L (2.3 X 10 ⁻³ ΔA per mg/dL)	
Accuracy:	6.4 X 10 ⁻² ΔA per mmol/L (1.7 X 10 ⁻³ ΔA per mg/dL)	
Sample size (n)	240	232
Corr. Coefficient (r)	0.999	0.998
Lin. Regression	0.99x + 0.03 mmol/L vs. COBAS INTEGRA HDL - Cholesterol Application (granulate)	0.99x - 0.05 mmol/L

Table 10 - Gamma-Glutamyltransferase (GGTL)

	COBAS INTEGRA GGTL (Liquid)	COBAS INTEGRA GGT (Granulate)
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 - Szasz-Persjun	kinetic method - Szasz-Persjun
Reagents	R1: Buffer (liquid) R2: L-γ-glutamyl-3-carboxy-4-nitroanilide (liquid)	R1: Buffer (granulate) R2: L-γ-glutamyl-3-carboxy-4-nitroanilide (granulate)
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
Performance Characteristics:		
Assay Range	0 - 600 U/L 0 - 6000 U/L with post dilution	0 - 700 U/L 0 - 7000 U/L with post dilution
Precision:	Level 1	Level 2
Mean (U/L)	21	428
%CV (within run)	0.83	0.54
%CV (total)	2.8	1.5
Sensitivity	$6.8 \times 10^{-4} \Delta A/\text{min per U/L}$	$5.0 \times 10^{-4} \Delta A/\text{min per U/L}$
Accuracy:		
Sample size (n)	196	238
Corr. Coefficient (r)	0.999	0.998
Lin. Regression	$1.00x - 1.2 \text{ U/L vs. COBAS INTEGRA GGT (granulate)}$	$1.00x + 0 \text{ U/L}$

Table 11 - Glucose (GLUCL)

	COBAS INTEGRA Glucose (Liquid)	COBAS INTEGRA Glucose (Granulate)
Intended Use	quantitative determination of glucose	quantitative determination of glucose
Sample type	serum, plasma, urine and Cerebrospinal fluid (CSF)	serum, plasma, urine and Cerebrospinal fluid (CSF)
Methodology	enzymatic reference method with hexokinase	enzymatic reference method with hexokinase
Reagents	R: Enzyme (liquid)	R1: Buffer (granulate) R2: Enzyme (granulate)
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
Performance Characteristics for serum and plasma:		
Assay Range	0 - 40 mmol/L (0-720 mg/dL) 0 - 400 mmol/L (0-7200 mg/dL) with post dilution	0 - 40 mmol/L (0-720 mg/dL) 0 - 400 mmol/L (0-7200 mg/dL) with post dilution
Precision:	Level 1	Level 2
Mean (mmol/L)	5.3 (96 mg/dL)	33.2 (598 mg/dL)
%CV (within run)	1.7	0.72
%CV (total)	2.6	1.5
Sensitivity	5.4×10^{-2} ΔA per mmol/L (3.0×10^{-3} ΔA per mg/dL)	9.3×10^{-2} ΔA per mmol/L (5.2×10^{-3} ΔA per mg/dL)
Accuracy:		
Sample size (n)	220	254
Corr. Coefficient (r)	0.999	0.997
Lin. Regression	1.05x - 0.2 mmol/L vs. COBAS INTEGRA Glucose (granulate)	0.98x + 0.1 mmol/L

Table 11 - Glucose - Continued

Performance Characteristics for urine:				
Assay Range	0 - 40 mmol/L (0-720 mg/dL) 0 - 400 mmol/L (0-7200 mg/dL) with post dilution		0 - 16 mmol/L (0-288 mg/dL) 0 - 160 mmol/L (0-2880 mg/dL) with post dilution	
Precision:	Level 1	Level 2	Level 1	Level 2
Mean (mmo/L)	1.7 (31 mg/dL)	37.1 (668 mg/dL)	0.27 (4.9 mg/dL)	0.48 (8.6 mg/dL)
%CV (within run)	1.7	1.8	2.0	0.99
%CV (total)	4.3	2.9		
Sensitivity	5.4 X 10 ⁻² ΔA per mmol/L (3.0 x 10 ⁻³ ΔA per mg/dL)		2.2 X 10 ⁻¹ ΔA per mmol/L (1.3 X 10 ⁻² ΔA per mg/dL)	
Accuracy:			Not specified in labeling	
Sample size (n)	120			
Corr. Coefficient (r)	0.999			
Lin. Regression	1.01x -0.02 mmol/L vs. COBAS INTEGRA Glucose (granulate)			
Performance Characteristics for CSF:				
Assay Range	0 - 40 mmol/L (0-720 mg/dL) 0 - 400 mmol/L (0-7200 mg/dL) with post dilution		0 - 20 mmol/L (0-360 mg/dL) 0 - 360 mmol/L (0-3600 mg/dL) with post dilution	
Precision:	Level 1	Level 2	Level 1	Level 2
Mean (mmo/L)	1.7 (31 mg/dL)	3.3 (59 mg/dL)	4.7 (85 mg/dL)	10.3 (186 mg/dL)
%CV (within run)	1.6	1.8	0.57	0.23
%CV (total)	2.3	1.9		
Sensitivity	5.4 X 10 ⁻² ΔA per mmol/L (3.0 x 10 ⁻³ ΔA per mg/dL)		1.8 X 10 ⁻¹ ΔA per mmol/L (1.0 x 10 ⁻² ΔA per mg/dL)	
Accuracy:			Not specified in labeling	
Sample size (n)	212			
Corr. Coefficient (r)	0.999			
Lin. Regression	1.02x -0.17 mmol/L vs. COBAS INTEGRA Glucose (granulate)			

Table 12 - Lipase (LIPL)

	COBAS INTEGRA Lipase (Liquid)	COBAS INTEGRA Lipase (Granulate)
Intended Use	quantitative determination of the catalytic activity of lipase	quantitative determination of the catalytic activity of lipase
Sample type	serum and plasma	serum and plasma
Methodology	turbidimetric method with triolein	turbidimetric method with triolein
Reagents	R: triolein and colipase (liquid)	R: triolein and colipase (granulate)
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
Performance Characteristics:		
Assay Range	0 - 600 U/L 0 - 3000 U/L with post dilution	0 - 700 U/L 0 - 3500 U/L with post dilution
Precision:	Level 1	Level 2
Mean (U/L)	126	515
%CV (within run)	1.9	1.3
%CV (total)	3.1	2.9
Sensitivity	$6.4 \times 10^{-5} \Delta A/\text{min}$ per U/L	$5.6 \times 10^{-5} \Delta A/\text{min}$ per U/L
Accuracy:		
Sample size (n)	198	262
Corr. Coefficient (r)	0.976	0.976
Lin. Regression	$0.82x + 16$ U/L vs. COBAS INTEGRA Lipase (granulate)	$1.06x - 7$ U/L

Table 13 - Urea/BUN (UREAL)

	COBAS INTEGRA UREA/BUN (Liquid)	COBAS INTEGRA UREA/BUN (Granulate)
Intended Use	quantitative determination of urea/BUN	quantitative determination of urea/BUN
Sample type	serum, plasma and urine	serum, plasma and urine
Methodology	kinetic test with urease and glutamate dehydrogenase	kinetic test with urease and glutamate dehydrogenase
Reagents	R: urease and glutamate dehydrogenase (liquid)	R: urease and glutamate dehydrogenase (granulate)
Calibrator	Roche Calibrator (human)	Roche Calibrator (human)
Controls	Roche Control Serum N and P (human)	Roche Control Serum N and P (human)
Performance Characteristics for serum and plasma:		
Assay Range	0 - 40 mmol/L (0-12 mg/dL) 0 - 400 mmol/L (0-2400 mg/dL) with post dilution	0 - 55 mmol/L (0-330 mg/dL) 0 - 550 mmol/L (0-3300 mg/dL) with post dilution
Precision: Mean (mmol/L)	Level 1 4.1 (24.6 mg/dL)	Level 2 31.0 (186 mg/dL)
%CV (within run)	2.3	0.89
%CV (total)	3.9	2.8
Sensitivity	$2.2 \times 10^{-2} \Delta A/\text{min}$ per mmol/L ($3.3 \times 10^{-3} \Delta A/\text{min}$ per mg/dL)	$6.8 \times 10^{-3} \Delta A/\text{min}$ per mmol/L ($1.1 \times 10^{-3} \Delta A/\text{min}$ per mg/dL)
Accuracy: Sample size (n) Corr. Coefficient (r) Lin. Regression	236 0.999 1.00x + 0.1 mmol/L vs. COBAS INTEGRA Urea/BUN (granulate)	234 0.999 1.01x + 0.30 mmol/L
Performance Characteristics for urine:		
Assay Range	0 - 2000 mmol/L (0-12 g/dL) 0 - 6000 mmol/L (0-36 g/dL) with post dilution	0 - 2200 mmol/L (0-13.2 g/dL) 0 - 5500 mmol/L (0-33 g/dL) with post dilution
Precision: Mean (mmo/L)	Level 1 421 (2.53 g/dL)	Level 2 679 (4.08 g/dL)
%CV (within run)	1.3	1.2
%CV (total)	1.8	1.8
Sensitivity	$2.0 \times 10^{-2} \Delta A/\text{min}$ per mmol/L ($3.3 \times 10^{-2} \Delta A/\text{min}$ per g/dL)	Not specified in labeling
Accuracy: Sample size (n) Corr. Coefficient (r) Lin. Regression	120 0.999 1.0x + 1.3 mmol/L vs. COBAS INTEGRA Urea/BUN (granulate)	Not specified in labeling



Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG 12 1997

Ms. Maria Feijoo
• Regulatory Affairs Associate
Roche Diagnostic Systems, Inc.
1080 U.S. Highway 202
Somerville, NJ 08876-3771

Re: K972250
Roche COBAS® INTEGRA Reagent Cassettes & Ancillary Reagents
Regulatory Class: II
Product Code: JFJ, CDQ, CDT, CET, CFR, CGX, CHH, LAS, DLJ,
DLB, JIF, JQB, LFM
Dated: June 13, 1997
Received: June 16, 1997

Dear Ms. Feijoo:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Pre-market Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirement, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your pre-market notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal Laws or Regulations.

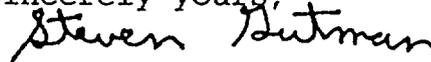
Page 2

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>".

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known) _____

Device Name: Roche COBAS® INTEGRA Reagent Cassettes for:

1. Ammonia
2. αAmylase EPS (liquid reagent)
3. Cholesterol (liquid reagent)
4. HDL - Cholesterol Application
5. Creatinine (enzymatic)
6. Digitoxin
7. Gamma-Glutamyltransferase (liquid reagent)
8. Glucose HK (liquid reagent)
9. Lipase (liquid reagent)
10. Lysergic acid diethylamide (LSD)
11. Urea (liquid reagent)

Ancillary Reagents:

12. Roche TDM OnLine Digitoxin Calibrators
13. Roche TDM OnLine Digitoxin Controls

Indications for Use:

1. COBAS INTEGRA Ammonia (NH3):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the ammonia concentration in plasma (test NH3, 0-045).

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use
(Per 21 CFR 801.109)

OR

Over-The-Counter Use
(Optional Format 1-2-96)

Division Sign-Off
Office of Clinical Laboratory Devices
Device Number 1247250

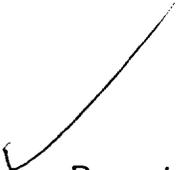
510(k) Number (if known) _____

Indications for Use (continued):

2. COBAS INTEGRA α Amylase EPS (AMYLL):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the catalytic activity of amylase in serum, plasma (test AMY-L, 0998) and urine (test AMY-UL 0-999).
3. COBAS INTEGRA Cholesterol (CHOLL):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of total cholesterol (test CHOLL, 0-001) and HDL - cholesterol concentration in serum and plasma in clinical laboratories.
4. COBAS INTEGRA HDL - Cholesterol Application (HDLL):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of total cholesterol and HDL - cholesterol (test HDLL, 0-002) concentration in serum and plasma in clinical laboratories.
5. COBAS INTEGRA Creatinine Enzymatic (CREAE):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the creatinine concentration in serum (test CREAE, 0-014), and urine (test CREEU, 0-114).

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON
ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

 Prescription Use
(Per 21 CFR 801.109)

OR

____ Over-The-Counter Use
(Optional Format 1-2-96)

510(k) Number (if known) _____

Indications for Use (continued):

6. COBAS INTEGRA Digitoxin (DIGIT):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of digitoxin in serum or heparinized plasma (test DIGIT 0-259).
7. COBAS INTEGRA Gamma - Glutamyltransferase (GGTL):
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; γ -glutamyl peptide: amino acid γ -glutamyltransferase) in serum and plasma (test GGTL, 0-599).
8. COBAS INTEGRA Glucose HK Liquid (GLUCL):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the glucose concentration in serum, plasma (test GLUL, 0-991), urine (test GLULU, 0-992), and cerebrospinal fluid (test GLULC, 0-993).
9. COBAS INTEGRA Lipase (LIPL):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the catalytic activity of lipase in serum and plasma (test LIPL, 0-200).

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON
ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use
(Per 21 CFR 801.109)

OR

Over-The-Counter Use
(Optional Format 1-2-96)

510(k) Number (if known) _____

Indications for Use (continued):

10. COBAS INTEGRA Lysergic acid diethylamide (LSD)
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the qualitative determination of lysergic acid diethylamide (LSD) in urine (test LSD, 0-001)
11. COBAS INTEGRA Urea/BUN (UREAL):
contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of the urea/BUN (blood urea nitrogen), in serum, plasma (test UREL, 0-003) and urine (test URELU, 0-004).
12. Roche TDM OnLine Digitoxin Calibrators:
are intended for use with the Roche reagents for Digitoxin and the COBAS Chemistry systems for the quantitative determination of digitoxin in serum and plasma.
13. Roche TDM OnLine Digitoxin Controls:
are quality control samples intended for use on COBAS chemistry systems with Roche reagents and calibrators for the quantitative determination of digitoxin assays.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON
ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use
(Per 21 CFR 801.109)

OR

Over-The-Counter Use
(Optional Format 1-2-96)