Roche

Diagnostics

K973284
Dec 18, 1997

510(k) Summary

Roche COBAS INTEGRA® HDL-D Reagent Cassette

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 August 28, 1997

Contact: Maria Feijoo
Manager, Regulatory Affairs
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 Table 1.

Table 1

Proprietary Name	Classification Name	Product Code	Regulation Number
COBAS INTEGRA HDL - Cholesterol Direct	Cholesterol test system	CHH	862.1175

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

The COBAS INTEGRA HDL-D Reagent Cassette is substantially equivalent to the currently marketed COBAS INTEGRA HDL reagent system (K951595).

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

The COBAS INTEGRA HDL-D reagent cassette is 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 107 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); January 21, 1997 (K964457) and August 12, 1997 (K972250).

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 the COBAS INTEGRA HDL-D Cassette.

The COBAS INTEGRA HDL-D reagent cassette is an *in vitro* diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of High Density Lipoprotein cholesterol direct (HDL-D) in serum and plasma.

Low HDL levels are recognized as a strong and common risk factor for atherosclerotic Coronary Artery Disease (CAD). Therefore, determination of HDL cholesterol is routinely offered as part of a lipid profile. Usually VLDL and LDL are selectively precipitated from serum or plasma samples followed by determination of cholesterol in the HDL - containing supernatant. These techniques require a centrifugation step to remove the precipitated lipoproteins and thus cannot be fully automated. The COBAS INTEGRA HDL - Cholesterol Direct, however, allows for the

direct specific determination of HDL cholesterol in the presence of LDL, VLDL and chylomicrons without any sample pretreatment. Therefore, lending itself to automated routine analysis.

The principle of the COBAS INTEGRA HDL-D reagent cassette is based on the absorption of synthetic polyanions to the surface of lipoproteins. LDL, VLDL, and chylomicrons are transformed into a detergent-resistant form, whereas HDL is not. Combined action of polyanions and detergent solubilizes cholesterol from HDL, but not from LDL, VLDL, and chylomicrons. Solubilized cholesterol is oxidized by the sequential enzymatic action of cholesterol esterase and cholesterol oxidase. The hydrogen peroxide produced in this reaction is reacted with chromogens to form a colored dye. The increase in absorbance at 552 nm is directly proportional to the HDL cholesterol concentration of the sample.

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

The COBAS INTEGRA HDL-D reagent cassette is similar to the COBAS INTEGRA HDL reagent system in that HDL cholesterol is quantitated using an enzymatic, colorimetric method (CHOD/PAP).

The differences are that the current COBAS INTEGRA HDL application requires pretreatment of the sample with a separating reagent prior to analysis whereas the COBAS INTEGRA HDL-D reagent cassette measures the HDL cholesterol concentration directly in the sample.

The current COBAS INTEGRA HDL reagent application is used in conjunction with the Roche HDL Cholesterol Precipitating Reagent and the COBAS INTEGRA Cholesterol reagent cassette (K951595). The Roche HDL Cholesterol Precipitating Reagent uses phosphotungstic acid and magnesium ions to precipitate the chylomicrons, VLDL, and LDL. After centrifugation, HDL remaining in the supernatant is quantitated by its cholesterol content using an enzymatic, colorimetric method (CHOD/PAP).

A summary of the similarities, differences and performance characteristics between the COBAS INTEGRA HDL-D reagent cassette and the COBAS INTEGRA HDL reagent system are listed in Table 2.

Table 2

	COBAS INTEGRA HDL-D reagent cassette		COBAS INTEGRA HDL reagent system	
Intended Use	quantitative determination of HDL cholesterol		quantitative determination of HDL cholesterol	
Methodology	Selective inhibition colorimetric assay (no pretreatment required)		Phosphotungstic acid pretreatment used with colorimetric method (CHOD/PAP)	
Sample type	Serum and plasma		Serum and plasma	
Calibrator	Roche HDL Calibrator Direct lyophilized human serum Assigned value ~1.58 mmol/L (61 mg/dL)		Roche Calibrator (human) Assigned value ~4.08 mmol/L (158 mg/dL) (undiluted)	
Controls	Roche Control Serum N and P (human)		Roche Control Serum N and P (human)	
Reagent type	Liquid		Granulate	
Reagent (active ingredients)	R1: MOPS Polyanions 4 - Amino-antipyrine Mg Cl R2: N,N-bis-m-toluidine Cholesterol esterase Cholesterol oxidase Horseradish		Pretreatment: Phosphotungstic acid R: HEPES Sodium cholate 4 - Chlorophenol 4 - Amino-antipyrine Cholesterol esterase Cholesterol oxidase Horseradish	
On-board Stability	12 weeks		8 weeks	
Performance Characteristics:				
Assay range	0.01 - 4.0 mmol/L (0.386 - 155 mg/dL)		0 - 5.0 mmol/L (0 - 193 mg/dL)	
Precision: Mean (mmol/L) (mg/dL) % CV (within run) % CV (total)	Level 1 0.60 mmol/L (23.2 mg/dL) 1.4 2.2	Level 2 1.41 mmol/L (54.6 mg/dl) 1.1 2.3	Level 1 0.82 (31.7 mg/dL) 1.2 2.7	Level 2 1.42 (54.9 mg/dL) 0.85 5.5
Sensitivity	8.2 X 10^{-2} ΔA per mmol/L (2.1 X 10^{-3}ΔA per mg/dL)		6.4 X 10^{-2} ΔA per mmol/L (1.7 X 10^{-3}ΔA per mg/dL)	
Accuracy: Sample size (n) Corr. Coefficient Linear regression	 258 0.901 0.77x + 0.33 mmol/L (0.77x + 12.8 mg/dL)		 232 0.998 0.99x - 0.05 mmol/L (0.99x - 1.93 mg/dL)	

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

Table 2 shows the clinical and nonclinical performance characteristics of the COBAS INTEGRA HDL-D Reagent Cassette. This information demonstrates that the performance of this device is substantially equivalent to the currently marketed COBAS INTEGRA HDL reagent system.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 18 1997

Maria Feijoo
Manager, Regulatory Affairs
Roche Diagnostic Systems, Inc.
1080 U.S. Highway 202
Somerville, New Jersey 08876-3771

Re: K973284
COBAS INTEGRA HDL-D
Regulatory Class: I
Product Code: LBR, CHH
Dated: November 25, 1997
Received: November 26, 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 (Premarket 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 requirements, 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 premarket 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.

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 Gutman

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 HDL-D Reagent Cassette

Indications for Use:

The cassette COBAS INTEGRA HDL - Cholesterol Direct (HDL-D) contains an *in vitro* diagnostic reagent system intended for use on COBAS INTEGRA for the quantitative determination of HDL - cholesterol direct concentration in serum and plasma.

V. Michelle Cheatham for A.W. Montgomery

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K973284

(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)