08057877500V7.0

HDLC4
HDL-Cholesterol Gen.4

Order information

REF	📖	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08057877190	08057877500	HDL-Cholesterol Gen.4 (700 tests)	System-ID 2071 002	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

12172623122	Calibrator f.a.s. Lipids (3 x 1 mL)	Code 20424
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 20391
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 20391
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 20392
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 20392
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001

English

System information
HDLC4: ACN 20710

Intended use
In vitro diagnostic test for the quantitative determination of the HDL-cholesterol concentration in human serum and plasma on **cobas c** systems.

Summary
Measurements of HDL-cholesterol, performed with this assay in human serum or plasma, are used for screening, aid in diagnosis and monitoring of dyslipidaemias as well as for assessment of cardiovascular risk such as in ASCVD and CHD.

High density lipoproteins (HDL) are responsible for the reverse transport of cholesterol from the peripheral cells to the liver. In the liver, cholesterol is transformed to bile acids which are then excreted into the intestine via the biliary tract.
Monitoring of HDL-cholesterol in serum or plasma is of clinical relevance as the HDL-cholesterol concentration is important in the assessment of atherosclerotic cardiovascular risk (ASCVD).[1] Elevated HDL-cholesterol concentrations protect against coronary heart disease (CHD), whereas reduced HDL-cholesterol concentrations, particularly in conjunction with elevated triglycerides, increase cardiovascular risk.[1]

Two cholesterol related variables that are predictive of cardiovascular disease (CVD) have emerged. These are non-HDL-cholesterol[2,3,4] (= total cholesterol - HDL-cholesterol) and the rate of cholesterol transfer from the macrophages to HDL, also described as cholesterol efflux capacity.[5] Whereas both cholesterol and HDL-cholesterol can be readily determined with high accuracy, currently, non-HDL-cholesterol appears to be best suited for patient management.[2,3,4]

A variety of methods are available to determine HDL-cholesterol, including ultracentrifugation (reference method in combination with cholesterol measurement by the Abell-Kendall method), electrophoresis, high performance liquid chromatography (HPLC), precipitation, and direct methods.[6,7] Of these, the direct methods are used routinely. Roche HDLC4 is also a direct method. The automated HDLC4 assay uses detergents, cholesterol esterase (CHER), cholesterol oxidase (CHOD) and peroxidase to form a colored pigment that is measured optically.[8,9]

The HDLC4 assay meets the 1998 National Institutes of Health (NIH) / National Cholesterol Education Program (NCEP) goals for precision and accuracy.[10,11]

Test principle[8,9]
Homogeneous enzymatic colorimetric test.

Non-HDL lipoproteins such as LDL, VLDL and chylomicrons are combined with polyanions and a detergent forming a water-soluble complex. In this complex the enzymatic reaction of CHER and CHOD towards non-HDL lipoproteins is blocked.
Finally only HDL-particles can react with CHER and CHOD. The concentration of HDL-cholesterol is determined enzymatically by CHER and CHOD.
Cholesterol esters are broken down quantitatively into free cholesterol and fatty acids by CHER.

$$\text{HDL-cholesterol esters} + H_2O \xrightarrow{\text{CHER}} \text{HDL-cholesterol} + RCOOH$$

In the presence of oxygen, cholesterol is oxidized by cholesterol oxidase to Δ^4-cholestenone and hydrogen peroxide.

$$\text{HDL-cholesterol} + O_2 \xrightarrow{\text{CHOD}} \Delta^4\text{-cholestenone} + H_2O_2$$

In the presence of peroxidase, the hydrogen peroxide generated reacts with 4-amino-antipyrine and EMSE[a] to form a dye. The color intensity of this dye is directly proportional to the cholesterol concentration and is measured photometrically.

$$2 H_2O_2 + \text{4-amino-antipyrine} + \text{EMSE} + H^+ + H_2O \xrightarrow{\text{Peroxidase}} \text{colored pigment} + 5 H_2O$$

a) N-ethyl-N-(3-methylphenyl)-N'-succinylethylenediamine

Reagents - working solutions

R1 TAPSO[b] buffer: 62.1 mmol/L, pH 7.77; polyanion: 1.25 g/L; EMSE: 1.08 mmol/L; ascorbate oxidase (cucurbita): ≥ 50 µkat/L; peroxidase (horseradish): ≥ 166.7 µkat/L; detergent; BSA: 2.0 g/L; preservative

R3 Bis-Tris[c] buffer: 20.1 mmol/L, pH 6.70; cholesterol esterase (microorganism): ≥ 7.5 µkat/L; cholesterol oxidase (recombinant E. coli): ≥ 7.17 µkat/L; cholesterol oxidase (microorganism): ≥ 76.7 µkat/L; peroxidase (horseradish): ≥ 333 µkat/L; 4-amino-antipyrine: 1.48 mmol/L; BSA: 3.0 g/L; detergents; preservative

b) 2-Hydroxy-N-tris(hydroxymethyl)methyl-3-aminopropanesulfonic acid

c) Bis(2-hydroxyethyl)iminotris(hydroxymethyl)methane

R1 is in position B and R3 is in position C.

Precautions and warnings
For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

Reagent handling
Ready for use
The intrinsic color of the reagent does not interfere with the test.

08057877500V7.0

HDLC4

HDL-Cholesterol Gen.4

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Storage and stability

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum.
Plasma: Li-heparin, K_2- and K_3-EDTA plasma.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Collect blood by using an evacuated tube or syringe. Specimens should preferably be analyzed on the day of collection.

Fasting and non-fasting samples can be used.[12,13]

Stability in serum:	72 hours at 15-25 °C[13]
	7 days at 2-8 °C[13]
	12 months at -20 °C (± 5 °C)[14]
	24 months at -70 °C (± 5 °C)[15]

Freeze only once.

Stability in Li-heparin, K_2- and K_3-EDTA plasma:	72 hours at 15-25 °C[13]
	7 days at 2-8 °C[13]
	3 months at -20 °C (± 5 °C) °C[13]
	18 months at -70 °C (± 5 °C)[13]
	18 months at -80 °C (± 5 °C)[16]

Freeze only once.

It is reported that EDTA stabilizes lipoproteins.[17]

See the limitations and interferences section for details about possible sample interferences.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

See "Order information" section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

Test definition

Reporting time	10 min
Wavelength (sub/main)	700/600 nm

Reagent pipetting		Diluent (H$_2$O)
R1	80 µL	–
R3	27 µL	–

Sample volumes	Sample	Sample dilution

	Sample		Diluent (NaCl)
Normal	1.6 µL	–	–
Decreased	8.0 µL	10 µL	90 µL
Increased	1.6 µL	–	–

For further information about the assay test definitions refer to the application parameters setting screen of the corresponding analyzer and assay.

Calibration

Calibrators	S1: H$_2$O
	S2: C.f.a.s. Lipids
Calibration mode	Linear
Calibration frequency	Automatic full calibration
	- after reagent lot change
	Full calibration
	- as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against the designated CDC reference method (ultracentrifugation method).[10] The standardization meets the requirements of the "HDL Cholesterol Method Evaluation Protocol for Manufacturers" of the US National Reference System for Cholesterol, CRMLN (Cholesterol Reference Method Laboratory Network), November 1994.

Quality control

For quality control, use control materials as listed in the "Order information" section. In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 12 weeks.

Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

cobas c systems automatically calculate the analyte concentration of each sample in the unit mmol/L (mg/dL, g/L).

Conversion factors:	mmol/L x 38.66 = mg/dL
	mmol/L x 0.3866 = g/L

Limitations - interference[18]

Criterion: Recovery within ±0.1 mmol/L of initial values of samples ≤ 1 mmol/L (38.7 mg/dL) and within ±10 % for samples > 1 mmol/L.

Icterus:[19] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[19] No significant interference up to an H index of 1200 (approximate hemoglobin concentration: 745 µmol/L or 1200 mg/dL).

Lipemia (Intralipid):[19] No significant interference up to an L index of 2000. No significant interference from native triglycerides up to 13.7 mmol/L or 1200 mg/dL. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Other: Elevated concentrations of free fatty acids and denatured proteins may cause falsely elevated HDL-cholesterol results.

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 2.84 mmol/L (50 mg/dL).

Abnormal liver function affects lipid metabolism; consequently, HDL and LDL results are of limited diagnostic value. In some patients with abnormal liver function, the HDL-cholesterol result may significantly differ from the DCM (designated comparison method) result due to the presence of lipoproteins with abnormal lipid distribution.[20]

2024-07, V 7.0 English

HDLC4

HDL-Cholesterol Gen.4

Drugs: No interference was found at therapeutic concentrations using common drug panels.[21,22]

Statins (Simvastatin) and fibrates (Bezafibrate) tested at therapeutic concentration ranges did not interfere.

N-acetylcysteine: No significant interference from N-acetylcysteine up to a concentration of 2.76 mmol/L (450 mg/L).

Acetaminophen intoxications are frequently treated with N-acetylcysteine. N-acetylcysteine at the therapeutic concentration when used as an antidote and the acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low HDL-cholesterol results.

Metamizole: Venipuncture should be performed prior to the administration of metamizole. Venipuncture immediately after or during the administration of metamizole may lead to falsely low results.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[23]

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED
Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions, refer to the operator's manual.

Limits and ranges
Measuring range
0.08-3.88 mmol/L (3.09-150 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 0.08 mmol/L (3.09 mg/dL)
Limit of Detection	= 0.08 mmol/L (3.09 mg/dL)
Limit of Quantitation	= 0.08 mmol/L (3.09 mg/dL)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a precision of ≤ 30 % CV. It has been determined using low concentration HDL-cholesterol samples.

Expected values
mmol/L

	No risk	Moderate risk	High risk
Females[7,24,25]	> 1.68 mmol/L	1.15-1.68 mmol/L	< 1.15 mmol/L
Males[7,24,25]	> 1.45 mmol/L	0.90-1.45 mmol/L	< 0.90 mmol/L

mg/dL

	No risk	Moderate risk	High risk
Females[7,24,25]	> 65 mg/dL	45-65 mg/dL	< 45 mg/dL
Males[7,24,25]	> 55 mg/dL	35-55 mg/dL	< 35 mg/dL

National Cholesterol Education Program (NCEP) guidelines:[26]

< 40 mg/dL: Low HDL-cholesterol (major risk factor for CHD)

≥ 60 mg/dL: High HDL-cholesterol ("negative" risk factor for CHD)

HDL-cholesterol is affected by a number of factors, e.g. smoking, exercise, hormones, sex and age.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

National Cholesterol Education Program (NCEP) guidelines are based on serum values. When classifying patients, serum or serum equivalent values should be used. Therefore the NCEP recommends using a factor of 1.03 to convert EDTA plasma values to serum values. A later study found EDTA plasma concentrations to be 4.7 % lower than those in serum.[27] To comply with the 1998 NCEP goal of a bias < 5 % it is recommended that each laboratory validates this conversion factor and enters it into the test parameters for HDL-cholesterol.[28]

Treatment goals for non-HDL-cholesterol have been proposed:[2]

	NCEP ATP III	ADA/AHA Guidelines for patients with increased cardiometabolic risk
Optional goal for very-high/highest risk patients (known CVD, diabetes with elevated risk)	< 3.37 mmol/L (< 130 mg/dL)	< 2.59 mmol/L (< 100 mg/dL)
Optional goal for those with established cardiovascular disease and multiple major risk factors	< 2.59 mmol/L (< 100 mg/dL)	
Optional goal for high-risk patients, CHD-risk-equivalent (Framingham 10-year risk score > 20 %/10 years, diabetes without other major risk factors)	< 3.37 mmol/L (< 130 mg/dL)	< 3.37 mmol/L (< 130 mg/dL)
Optional goal for moderately-high/intermediate risk patients (≥ 2 major CVD risk factors, Framingham 10-year risk score from 10-20 %)	< 4.14 mmol/L (< 160 mg/dL)	< 3.37 mmol/L (< 130 mg/dL)
Optional goal for high-risk patients, CHD-risk-equivalent (Framingham 10-year risk score > 20 %/10 years, diabetes without other major risk factors)	< 3.37 mmol/L (< 130 mg/dL)	

Specific performance data
Representative performance data on the analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision
Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Repeatability	Mean	SD	CV
	mmol/L	mmol/L	%
PCCC1[d]	0.764	0.00290	0.4
PCCC2[e]	1.45	0.00690	0.5

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Human serum 1	0.148	0.00177	1.2
Human serum 2	1.07	0.00512	0.5
Human serum 3	1.49	0.00673	0.5
Human serum 4	1.92	0.00715	0.4
Human serum 5	3.53	0.0152	0.4

Intermediate precision	Mean	SD	CV
	mmol/L	mmol/L	%
PCCC1[d]	0.760	0.00630	0.8
PCCC2[e]	1.44	0.00974	0.7
Human serum 1	0.148	0.00229	1.5
Human serum 2	1.07	0.00708	0.7
Human serum 3	1.49	0.0105	0.7
Human serum 4	1.92	0.0145	0.8
Human serum 5	3.54	0.0249	0.7

d) PreciControl ClinChem Multi 1

e) PreciControl ClinChem Multi 2

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Method comparison

HDL-cholesterol values for human serum and plasma samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 70

Passing/Bablok[29]	Linear regression
y = 1.001x - 0.0175 mmol/L	y = 1.012x - 0.0274 mmol/L
τ = 0.976	r = 1.000

The sample concentrations were between 0.110 and 3.57 mmol/L.

HDL-cholesterol values for human serum and plasma samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 70

Passing/Bablok[29]	Linear regression
y = 1.011x - 0.0242 mmol/L	y = 1.028x - 0.0389 mmol/L
τ = 0.977	r = 1.000

The sample concentrations were between 0.110 and 3.57 mmol/L.

HDL-cholesterol values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 75

Passing/Bablok[29]	Linear regression
y = 1.000x - 0.0200 mmol/L	y = 1.000x - 0.0159 mmol/L
τ = 0.994	r = 1.000

The sample concentrations were between 0.115 and 3.67 mmol/L.

References

1   Mach F, Baigent C, Catapano AL, et al. ESC Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J 2020 Jan 1;41(1):111-188.

2   Blaha MJ, Blumenthal RS, Brinton EA, et al. The importance of non-HDL cholesterol reporting in lipid management. J Clin Lipidol 2008 Aug;2(4):267-73.

3   Boekholdt SM, Arsenault BJ, Mora S, et al. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins: a meta-analysis. JAMA 2012 Mar 28;307(12):1302-9.

4   Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2889-2934.

5   Rohatgi A, Khera A, Berry JD, et al. HDL cholesterol efflux capacity and incident cardiovascular events. N Engl J Med 2014 Dec 18;371(25):2383-93.

6   Langlois MR, Blaton VH. Historical milestones in measurement of HDL-cholesterol: Impact on clinical and laboratory practice. Clin Chimica Acta 2006;369:168-178.

7   Assmann G, Schriewer H, Schmitz G, et al. Quantification of high-density-lipoprotein cholesterol by precipitation with phosphotungstic acid/MgCl2. Clin Chem 1983;29(12):2026-2030.

8   Miida T, Nishimura K, Okamura T, et al. Validation of homogeneous assays for HDL-cholesterol using fresh samples from healthy and diseased subjects. Atherosclerosis 2014;233(1):253-9.

9   Katayama Y, Soya H, Fujinaka M, et al. Evaluation of New Homogeneous Assay Kit to Determine HDL-C with a High Reactivity with Cholesterol in Various Types of HDL. AACC Meeting 2009, Poster Abstract B-103.

10 Kimberly M, Leary E, Cole T, et al. Selection, Validation, Standardization and Performance of a Designated Comparison Method for HDL-Cholesterol for Use in the Cholesterol Reference Method Laboratory Network. Clin Chem 1999;45:1803-1812.

11 Saraf S, Ray KK. Guidelines in the USA, a viewpoint contrary to those guidelines in Europe, Canada, Britain and the International Atherosclerosis Society. Curr Opin Lipidol 2014 Dec;25(6):413-7.

12 Sidhu D, Naugler C. Fasting time and lipid levels in a community-based population: A cross sectional study. Arch. Intern. Med. Dec 10, 2012; 172(22):1707-10.

13 Ontario Community Laboratory Guideline for Adult Lipid Testing (CLP017) 2013.

14 Jansen EHLM, Beekhof PK, Schenk E. Long Term Stability of Lipid Metabolism in Frozen Human Serum: Triglycerides, Free Fatty Acids, Total-, HDL- and LDL-cholesterol, Apolipoprotein-A1 and B. J Mol Biomark Diagn 2014;5:4.

15 Shih WJ, Bachorik PS, Haga JA, et al. Estimating the Long-Term Effects of Storage at -70°C on Cholesterol, Triglyceride, and HDL-Cholesterol Measurements in Stored Sera. Clin Chem 2000 Mar;46(3):351-64.

16 Kronenberg F, Lobentanz EM, König P, et al. Effect of sample storage on the measurement of lipoprotein[a], apolipoproteins B and A-IV, total and high density lipoprotein cholesterol and triglycerides. J Lipid Res. 1994 Jul;35(7):1318-28.

17 Cooper GR, Myers GL, Smith SJ, et al. Standardization of Lipid, Lipoprotein, and Apolipoprotein Measurements. Clin Chem 1988;34(8B):B95-B105.

18 Kadri N, Douville P, Lachance P. Letter to editor. Clin Chem 2002;48:964.

19 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

20 Dati F, Metzmann E. Proteins Laboratory Testing and Clinical Use, Verlag: DiaSys; 1. Auflage (September 2005), page 242-243; ISBN-10: 3000171665.

21 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

22 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.

23 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

24 Thomas L, ed. Labor und Diagnose, 4th ed. Marburg: Die Medizinische Verlagsgesellschaft 1992;208.

25 Assmann G. At what levels of total low- or high-density lipoprotein cholesterol should diet/drug therapy be initiated? European guidelines. Amer J Cardiol 1990;65:11F.

26 Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). NIH Publication No 01-3670; May 2001.

27 Cloey T, Bachorik PS, Becker D, et al. Reevaluation of Serum-Plasma Differences in Total Cholesterol Concentration. JAMA 1990 May 23-30;263(20):2788-9.

28 National Cholesterol Education Program Recommendations for Measurement of High-Density Lipoprotein Cholesterol: Executive Summary. Clin Chem 1995;41:1427-1433.

29 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
⟶	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606

Roche