cobas Lipid Panel

CHOL-TRIGL-HDL-LDL

REF 06380115119

Σ 10

SYSTEM **cobas b** 101

English

Intended use

The cobas b 101 is an in vitro diagnostic test system designed to quantitatively determine total cholesterol (TC), high-density lipoprotein cholesterol (HDL), and triglycerides (TG) in human capillary and venous whole blood or plasma by photometric transmission measurement. A calculated value for low-density lipoprotein (LDL), non-HDL and a TC/HDL ratio is provided by the cobas b 101 system. The system is intended for professional use in a clinical laboratory setting, or point of care (PoC) locations

Cholesterol determinations are used in characterizing an individual's risk of developing atherosclerotic disease and aid in the diagnosis and treatment of disorders involving elevated cholesterol levels as well as lipid and lipoprotein metabolic disorders. The determination of triglycerides is utilized in the diagnosis and treatment of patients having diabetes mellitus, metabolic syndrome, lipid metabolism disorders, liver obstruction, and numerous other endocrine diseases.

Note : Please note that the catalogue number appearing on the package insert retains only the first 8 digits of the licensed 11-digit catalogue number: 06380115190 for the cobas Lipid Panel. The last 3 digits -190 have been replaced by -119 for logistic purposes.

Summary

Cholesterol determinations are used in characterizing an individual's risk of developing atherosclerotic disease and aid in the diagnosis and treatment of disorders involving elevated cholesterol levels as well as lipid and lipoprotein metabolic disorders.[1] Determination of HDL-cholesterol is of clinical importance since an inverse correlation exists between HDL-cholesterol concentrations and the risk of atherosclerotic disease. Elevated HDL-cholesterol concentrations reduce the risk for coronary heart disease, while reduced HDL-cholesterol concentrations, particularly in conjunction with elevated triglycerides, increase the cardiovascular risk. Strategies have emerged to increase the level of HDL-cholesterol to treat cardiovascular disease.[3, 4] The determination of triglycerides is utilized in the diagnosis and treatment of patients having diabetes mellitus, metabolic syndrome, lipid metabolism disorders, liver obstruction, and numerous other endocrine diseases.[5] The determination of a full lipid panel and the calculation of the LDL-cholesterol concentration according to Friedewald's formula is commonly practiced.[6] Low Density Lipoproteins (LDL) play a key role in causing and influencing the progression of atherosclerosis, and in particular, coronary artery disease. The majority of cholesterol stored in atherosclerotic plaques originates from LDL. The LDL-cholesterol value is the most powerful clinical predictor among all of the single parameters with respect to coronary atherosclerosis. Therefore, therapies focusing on lipid reduction primarily target the reduction of LDL-cholesterol.[7]

Test principle

The erythrocytes of the capillary or venous blood sample are separated from the plasma by centrifugation. In the next step, the plasma sample is diluted with phosphate buffer. The HDL test uses a precipitation method with Mg^{2+} and phosphotungstic acid as a precipitant reagent. The components except for HDL-cholesterol are precipitated and removed. The **cobas b** 101 system determines total cholesterol and HDL-cholesterol by an enzymatic method. Cholesterol esters in the sample are hydrolyzed to cholesterol and fatty acids. Cholesterol and NAD+ generate cholestenone and NADH in the prescence of cholesterol dehydrogenase. WST8 is reduced to formazan dye by diaphorase and NADH through oxidation-reduction reaction. The color intensity of formazan is measured at a specific wave length of 460 nm and is directly proportional to the concentration of HDL-cholesterol and total cholesterol in the sample.

$$\text{Cholesterol esters} \xrightarrow{\text{Cholesterol esterase}} \text{Cholesterol + Fatty acids}$$

$$\text{Cholesterol + NAD}^{+} \xrightarrow{\text{Cholesterol dehydrogenase}} \text{Cholestenone + NADH}$$

$$\text{NADH + WST8} \xrightarrow{\text{Diaphorase}} \text{NAD}^{+} \text{ + Formazan dye}$$

The triglycerides test is an enzymatic method. Triglycerides in the sample are hydrolyzed to glycerol and fatty acids by lipoprotein lipase. Glycerol and NAD^{+} generate dihydroxyacetone and NADH in the prescence of glycerol dehydrogenase. WST8 is reduced to formazan dye by diaphorase and NADH through oxidation-reduction reaction. The color intensity of the formazan is proportional to triglyceride concentration and calculated by measuring at a wavelength of 460 nm.

$$\text{Triglycerides} \xrightarrow{\text{Lipoprotein Lipase}} \text{Glycerol + Fatty acids}$$

$$\text{Glycerol+ NAD}^{+} \xrightarrow{\text{Glycerol dehydrogenase}} \text{Dihydroxyacetone + NADH}$$

$$\text{NADH + WST8} \xrightarrow{\text{Diaphorase}} \text{NAD}^{+} \text{ + Formazan dye}$$

Low density lipoprotein (calculated)

Where the concentration of triglycerides is < 400 mg/dL (4.52 mmol/L), the LDL cholesterol is calculated using the Friedewald formula.
LDL = TC – HDL – TG/5 (measured in mg/dL).[8] Where the concentration of triglycerides is ≥ 400 mg/dL (4.52 mmol/L), the calculated LDL-cholesterol is not reported. The formula is also not valid for non-fasting patients and patients with Type III hyperlipoproteinemia (dysbetalipoproteinemia).

Total Cholesterol/HDL ratio and Non-high density lipoprotein

The **cobas b** 101 instrument calculates the TC/HDL ratio as well as the non-HDL cholesterol (TC – HDL) from the measured values. Where the measured values data are not available, the TC/HDL ratio or non-HDL-cholesterol values are not reported.

Reagents

One test contains:

Dilution buffer: potassium dihydrogenphosphate 57 µg, dipotassium hydrogenphosphate 0.3 mg, potassium chloride 2.2 mg, sodium azide 42 µg (≤ 0.02 %)

Precipitant: magnesium sulfate heptahydrate 48 µg, sodium phosphotungstate n-hydrate 24 µg

Lipoprotein-lipase 0.096 U, cholesterol esterase 0.5 U, diaphorase 0.77 U, nicotinamide adenine dinucleotide 51 µg, tetrazolium salt 38 µg, glycerol dehydrogenase 0.75 U, cholesterol dehydrogenase 0.84 U

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

Reagent handling

Carefully tear open the foil pouch at the tear notch until one side is open.

Discard the disc if the foil pouch is found open or damaged, or if the disc is damaged, or the desiccant is missing, or loose desiccant particles or any other dirt or particles especially at the blood application zone are found.

Use **cobas** Lipid Control in the same way as a blood sample.

Storage and stability

Store at 2-30 °C until the expiration date printed on the pouch. Do not freeze. If stored in a refrigerator, allow the test to warm up in the closed pouch for at least 20 minutes before use. Once the pouch is opened, use the test within 20 minutes. Protect the disc from direct sunlight. Do not store opened pouches in a refrigerator.

Note: Open the pouch just before use when using control materials.

Specimen collection and preparation

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

Use fresh capillary blood, K_2- or K_3-EDTA venous whole blood or plasma. Do not use other anticoagulants or other additives. Do not freeze samples.

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We recommend to use EDTA samples within 2 hours to comply with the NCEP goal of bias < 3 % for total cholesterol and bias < 5 % for high density lipoprotein cholesterol. Assure that the lanced site is clean and dry, and free from fatty substances. The marking on the disc clearly shows where to apply the sample. If samples are used from a venipuncture or control material, use a standard pipette or dropper to form a drop. The disc is self-filling. Do not push the sample into the disc. Do not use syringes. Assure that the disc is free from blood outside the sample application zone and the hinge cover.

Sample volume:19 µL

Sample stability on disc

After applying blood to the disc, insert it into the instrument within 8 minutes. Please follow instructions in the operator's manual.

Assay

Instructions for use

- Wash hands with soap. Warm water helps to stimulate the blood flow. Rinse the fingers extensively. Dry hands.
- Disinfect the fingertip by wiping three times the area to be lanced with a cotton swab or sterile gauze pad impregnated with 70 %-100 % isopropanol emollient free or 70 %-100 % ethanol emollient free; repeat the procedure with a second cotton swab or sterile gauze pad impregnated with 70 %-100 % isopropanol emollient free or 70 %-100 % ethanol emollient free, then dry with a cotton swab or sterile gauze pad.
- Prick the patient's finger by applying a single-use disposable lancing device (e.g. Accu-Chek Safe-T-Pro Plus). Make sure to follow the according lancing device instructions for obtaining a blood sample.
- Wipe off the first drop of blood with a swab.
- With the imprinted side of the disc facing upwards, position the disc's suction point above the drop of blood. The disc is self-filling.
- Apply blood and observe that it has filled the marked area. Check the sample volume: turn the disc on its backside. The area marked in blue has to be filled completely with blood. Do not push the blood into the disc.
- Press hinge cover down firmly to close the disc.
- Assure that the disc is free from blood outside the sample application zone and the hinge cover.
- Insert the disc into the **cobas b** 101 instrument. Close the lid.
- The measurement starts automatically.

For more details, please refer to the **cobas b** 101 Quick Reference Guide or **cobas b** 101 Operator's Manual.

Materials provided

REF 06380115190, **cobas** Lipid Panel, 10 tests

Materials required (but not provided)

- Single use disposable lancing device (e.g. Accu-Chek Safe-T-Pro Plus)
- REF 06380182190, **cobas** Lipid Control
- REF 06378668190, **cobas b** 101 instrument
- Optical check disc
- General laboratory equipment (e.g., sample transfer pipette for venous blood or alcohol wipes for the fingerstick)
- Timer

Calibration

Traceability: Total cholesterol and HDL-cholesterol are traceable to the designated CDC reference methods (Abell/Kendall as reference method for total cholesterol).[9] Triglycerides are traceable to the ID/MS method.[10]

The instrument automatically reads in the lot-specific calibration data from the barcode information printed on the disc, eliminating the need for calibration by the user.

Quality control

For quality control, use **cobas** Lipid Control.

The control intervals and limits should be adapted to each laboratory's individual requirements. 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.

QC info disc

Every **cobas** Lipid Control kit contains a lot-specific QC info disc for quality control. This QC info disc contains the target values and ranges for the **cobas** Lipid Panel.

The instrument display prompts the user to insert the QC info disc. The **cobas b** 101 instrument reads the disc providing the lot specific target ranges.

Display of results

At the end of the automatic determination, the **cobas b** 101 instrument displays the result in approximately 6 minutes. The measured total cholesterol, HDL-cholesterol, triglycerides and calculated LDL-cholesterol result will be displayed in mg/dL or mmol/L depending on the setting. Please refer to the operator's manual.

Limitations - interference

Drugs: No interference was found at therapeutic concentrations using common drug panels.[11,12]

Hematocrit levels between 30 % and 55 % do not affect results.

Total cholesterol

Icterus:[13] No significant interference up to 15 mg/dL for conjugated bilirubin and up to 30 mg/dL for unconjugated bilirubin.

Hemolysis: No significant interference up to a hemoglobin concentration of 200 mg/dL.

Ascorbic acid: no significant interference up to 5 mg/dL.

Lipemia (Intralipid): No significant interference up to 500 mg/dL.

Criterion: Recovery within ± 10 % of initial values at a cholesterol concentration of 200 mg/dL (5.2 mmol/L).

Triglycerides

To test triglycerides or calculate LDL using the **cobas** Lipid Panel test ensure that the subject fasts for 9-12 hours before the sample is collected.

Icterus: No significant interference up to a conjugated/unconjugated bilirubin concentration of 15 mg/dL.

Hemolysis: No significant interference up to a hemoglobin concentration of 200 mg/dL.

Ascorbic acid: no significant interference up to 5 mg/dL.

Criterion: Recovery within ± 10 % of initial values at triglyceride levels of 203 mg/dL (2.3 mmol/L).

Fatty substances such as hand creams or soaps may contain glycerol which leads to false high triglyceride results and also false negative results for the calculated LDL.

High density lipoprotein

Icterus: No significant interference up to 15 mg/dL for conjugated bilirubin and up to 30 mg/dL for unconjugated bilirubin.

Hemolysis: No significant interference up to a hemoglobin concentration of 200 mg/dL.

Lipemia (Intralipid): No significant interference up to 500 mg/dL.

Ascorbic acid: no significant interference up to 5 mg/dL.

Criterion: Recovery ≤ 10 % of initial value at a HDL concentration of 50 mg/dL (1.3 mmol/L).

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

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

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

Limits and ranges

Measuring range

Cholesterol: 50-500 mg/dL or 1.28-12.95 mmol/L

Triglycerides: 45-650 mg/dL or 0.50-7.35 mmol/L

HDL-cholesterol: 15-100 mg/dL or 0.38-2.60 mmol/L

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Expected values

The European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) jointly published 2011 ESC/EAS guidelines for the management of dyslipidemia.[14] The new guideline recommends the assessment of total cardiovascular (CV) risk. Those with known Cardiovascular disease (CVD), type 2 diabetes or type 1 diabetes with microalbuminuria, very high levels of individual risk factors, chronic kidney disease (CKD) are at high or very high total CV risk and need active management of all risk factors. For all other patient groups, the use of a risk estimation system such as SCORE[15] is recommended to estimate total CV risk because many people have several risk factors which, in combination, may result in unexpectedly high levels of total CV risk. Recommendations for lipid analyses for characterization of dyslipidemia before treatment: TC and LDL-C are recommended to be used for the primary lipid analysis for risk estimation of total CV risk; TG gives additional information on risk and is indicated for risk estimation; HDL-C contributes substantially to risk estimation.

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

Recommendations for lipid analyses as treatment target in the prevention of CVD

Concluding from the available data, an absolute reduction to an LDL-C level < 70 mg/dL (< 1.8 mmol/L) or at least 50 % relative reduction in LDL-C provides the best benefits in terms of CVD reduction. Clinical judgement is required before a final treatment plan is implemented.

National Cholesterol Education Program (NCEP) guidelines

The Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, or ATP III) presents the National Cholesterol Education Program's (NCEP's) updated recommendations for cholesterol testing and management. The ATP III classifications are as follows:

Analyte	Concentration mg/dL (mmol/L)	Classification
LDL-cholesterol	< 100 (< 2.59)	Optimal
	100-129 (2.59-3.34)	Near optimal/above optimal
	130-159 (3.37-4.12)	Borderline high
	160-189 (4.14-4.90)	High
	≥ 190 (≥ 4.92)	Very high
HDL-cholesterol	< 40 (< 1.04)	Low
	≥ 60 (≥ 1.55)	High
Total cholesterol	< 200 (< 5.18)	Desirable
	200-239 (5.18-6.19)	Borderline high
	≥ 240 (≥ 6.20)	High
Triglycerides	< 150 (< 1.70)	Normal
	150-199 (1.70-2.25)	Borderline high
	200-499 (2.26-5.64)	High
	≥ 500 (≥ 5.65)	Very high

The NCEP guidelines are based on serum values, and when classifying patients, serum or serum equivalent values should be used. Therefore, the NCEP recommends a factor of 1.03 to convert EDTA plasma values to serum values. Roche recommends that each laboratory validates its own conversion factor.

Non-high density lipoprotein

The NCEP ATP III gave the following recommendation: In persons with high triglycerides > 200 mg/dL (> 2.26 mmol/L), VLDL cholesterol should be combined with LDL-cholesterol, yielding non-HDL-cholesterol. The latter constitutes "atherogenic cholesterol" and should be a secondary target of therapy. After LDL goal is reached, secondary goal for non-HDL shall be set at 30 mg/dL (0.78 mmol/L) higher than LDL goal.

Total cholesterol/High density lipoprotein ratio

Many studies show that the TC/HDL ratio is a powerful predictor of CHD risk.[16,17] The TC/HDL ratio predicts the risk of coronary heart disease regardless of the absolute LDL- and HDL-cholesterol. Even so, ATP III does not consider the total cholesterol/HDL-cholesterol ratio as a specified lipid target of therapy. Instead, LDL-cholesterol is retained as the primary target of lipid-lowering therapy. The total cholesterol/HDL-cholesterol ratio is also not recommended as a secondary target of therapy. Treatment according to ratios will divert priority from specific lipoprotein fractions as targets of therapy.

Specific performance data

Representative performance data are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using controls in a CLSI EP5-A2 protocol. Whole blood samples were measured using a modified CLSI protocol in 5 series of 4 replicates in one day. The following results were obtained:

Sample			Repeatability		Intermediate precision	
		Mean value mg/dL (mmol/L)	SD mg/dL (mmol/L)	CV %	SD mg/dL (mmol/L)	CV %
Control/Level 1 (n[a)] = 84)	TC	145 (3.76)	2.7 (0.069)	1.8	3.0 (0.078)	2.1
	TG	97 (1.10)	1.3 (0.015)	1.3	1.4 (0.016)	1.4
	HDL	42 (1.08)	1.4 (0.037)	3.5	1.4 (0.037)	3.5
Control/Level 2 (n = 84)	TC	269 (6.96)	4.8 (0.123)	1.8	5.1 (0.131)	1.9
	TG	395 (4.46)	4.2 (0.048)	1.1	4.3 (0.049)	1.1
	HDL	69 (1.78)	1.9 (0.048)	2.7	2.1 (0.055)	3.1
Whole blood 1 (n = 20)	TC	166 (4.29)	3.1 (0.080)	1.9	3.7 (0.095)	2.2
	TG	336 (3.80)	4.0 (0.045)	1.2	4.4 (0.050)	1.3
	HDL	38 (0.97)	0.9 (0.023)	2.4	1.4 (0.035)	3.6
Whole blood 2 (n = 20)	TC	228 (5.89)	3.8 (0.099)	1.7	4.5 (0.117)	2.0
	TG	346 (3.91)	7.1 (0.080)	2.0	11.8 (0.133)	3.4
	HDL	46 (1.19)	1.5 (0.038)	3.2	1.7 (0.043)	3.6
Whole blood 3 (n = 20)	TC	184 (4.75)	2.9 (0.076)	1.6	3.0 (0.077)	1.6
	TG	135 (1.52)	1.6 (0.018)	1.2	5.0 (0.057)	3.7
	HDL	48 (1.24)	1.2 (0.031)	2.5	1.3 (0.033)	2.7

a) n = no. of samples

Method comparison

A comparison study with EDTA whole blood samples measured with **cobas** Lipid Panel (y) on the **cobas b** 101 instrument with respective methods on the **cobas** c 501 analyzer (x) gave the following correlations:

Passing/Bablok[18]

Cholesterol:

y = 1.000x – 0.110 mmol/L

r = 0.991, n = 69

Sample range: 2.88-7.72 mmol/L

Mean bias (%) = -2.39 %

Bias at medical decision ranges:

low: 200 mg/dL (5.2 mmol/L): -2.1 %

high: 240 mg/dL (6.2 mmol/L): -1.8 %

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Triglycerides:

y = 1.020x – 0.009 mmol/L

r = 0.996, n = 68

Sample range: 0.52-4.57 mmol/L

Mean bias (%) = 0.45 %

Bias at medical decision ranges:

low: 150 mg/dL (1.7 mmol/L): 1.5 %

high: 200 mg/dL (2.26 mmol/L): 1.6 %

High density lipoprotein:

y = 1.056x – 0.080 mmol/L

r = 0.981, n = 67

Sample range: 0.78-2.42 mmol/L

Mean bias (%) = 0.58 %

Bias at medical decision ranges:

low: 40 mg/dL (1.04 mmol/L): -2.1 %

high: 60 mg/dL (1.55 mmol/L): 0.4 %

References

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For further information, please refer to the appropriate Operator's Manual for the instrument concerned, and the Method Sheets of all necessary components.

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.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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