Clinical Chemistry

2025/12/08
A93A01468AEN

REF 1300148018
REAGENT 1 38 mL
REAGENT 2 14 mL

IVD CE 2797

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FRANCE

Yumizen C LDL

- Yumizen C230
- Yumizen C240

Diagnostic reagent for quantitative *in vitro* determination of Low Density Lipoprotein Cholesterol (LDL-C) in serum or plasma by colorimetry.

Intended Use

Yumizen C LDL reagent is intended for the quantitative *in vitro* diagnostic determination of Low Density Lipoprotein Cholesterol (LDL-C) in human serum and plasma based on an enzymatic colorimetric assay with accelerator selective detergent methodology.
Clinical laboratories use.
Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders, atherosclerosis, and various liver and renal diseases.
Assessing physiologic and pathologic variations of Low Density Lipoprotein Cholesterol (LDL-C) concentration in human serum and plasma is useful for screening or follow-up of these diseases.

Clinical Interest

Plasma lipoproteins are spherical particles containing varying amounts of cholesterol, triglycerides, phospholipids and proteins. The phospholipid, free cholesterol and protein constitute the outer surface of the lipoprotein particle, while the inner core contains mostly esterified cholesterol and triglyceride. These particles serve to solubilize and transport cholesterol and triglyceride in the bloodstream.
The relative proportions of protein and lipid determine the density of these lipoproteins and provide a basis on which to begin their classification (1). These classes are: chylomicrons, very-low-density lipoprotein (VLDL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Numerous clinical studies have shown that the different lipoprotein classes have very distinct and various effects on coronary heart disease risk (2, 3, 4). The studies all point to LDL cholesterol as the key factor in the pathogenesis of atherosclerosis and coronary artery disease (CAD) (2, 3, 4, 5, 6, 7, 8), while HDL cholesterol has been observed to have a protective effect. Even within the normal range of total cholesterol concentrations, an increase in LDL cholesterol can occur with an associated increased risk for CAD (4).

Method

Yumizen C LDL assay is an homogeneous method for directly measuring LDL-C levels in serum or plasma, without the need for any off-line pretreatment or centrifugation steps.
The method is in a two reagent format and depends on the properties of a unique detergent. This detergent (Reagent 1) solubilizes only the non LDL lipoprotein particles. The cholesterol released is consumed by cholesterol esterase and cholesterol oxidase in a non color forming reaction. A second detergent (Reagent 2) solubilizes the remaining LDL particles and a chromogenic coupler allows for color formation. The enzyme reaction with LDL-C in the presence of the coupler produces color that is proportional to the amount of LDL cholesterol present in the sample.

Reagents

Yumizen C LDL is ready-to-use.

Reagent 1 (R1):	
Buffer	
Detergent 1	< 1.0%
Cholesterol esterase	< 1500 U/L
Cholesterol oxidase	< 1500 U/L
Peroxidase	< 1300 ppg U/L
4-aminoantipyrine (4-AAP)	< 0.1%
Ascorbic acid oxidase	< 3000 U/L
Preservative	

Yumizen C LDL

Reagent 2 (R2):	
Buffer pH 6.3	
Detergent 2	< 1.0%
N,N-bis(4-sulfobutyl)-toluidine, disodium (DsBmT)	< 1.0 mmol/L
Preservative	

Yumizen C LDL should be used according to this notice. The manufacturer cannot guarantee its performance if used otherwise.

Handling

1. Remove the caps of the cassettes.
2. If present, remove foam by using a plastic pipette.
3. Place the cassettes into the refrigerated reagent compartment.

Calibrator

For calibration, use:
ABX Pentra LDL Cal (A11A01678) (not included)
2 x 1 mL (lyophilisate)

Control

For internal quality control, use:

- **ABX Pentra N MultiControl** (1300054414) (not included)
  10 x 5 mL (lyophilisate)
- **ABX Pentra P MultiControl** (1300054415) (not included)
  10 x 5 mL (lyophilisate)

Each control should be assayed daily and/or after a calibration.
The frequency of controls and the confidence intervals should correspond to laboratory guidelines and country-specific directives. You should follow federal, state and local guidelines for testing quality control materials. The results must be within the range of the defined confidence limits. Each laboratory should establish a procedure to follow if the results exceed these confidence limits.

Materials Required but not Provided

- Automated clinical chemistry analyzer: Yumizen C230/C240
- Calibrator: **ABX Pentra LDL Cal** (A11A01678)
- Controls:
  ABX Pentra N MultiControl (1300054414)
  ABX Pentra P MultiControl (1300054415)
- Standard laboratory equipment.

Specimen

This device intended testing population is general population.

Specimen types

- Serum.
- Plasma in lithium heparin.

Anticoagulants other than those listed have not been tested by HORIBA and are therefore not recommended for use with this assay.
These specimens should be drawn from the patient after 12 - 14h fast.

Stability (9)

- Serum: Collect whole blood by venipuncture and allow to clot. Centrifuge and remove the serum as soon as possible after collection (within 3 hours).
- Plasma: Centrifuge and remove the plasma as soon as possible after collection (within 3 hours).

- At 20-25°C: 1 day
- At 4-8°C: 7 days
- At -20°C: 3 months

Reference Range (10)

Each laboratory should establish its own reference ranges. The values given here are used as guidelines only.

The following NCEP cutpoints for patient classification are used for the prevention and management of coronary heart disease.

LDL Cholesterol	Classification
< 130 mg/dL (< 3.36 mmol/L)	Desirable
130 - 159 mg/dL (3.36 - 4.11 mmol/L)	Borderline high risk
160 mg/dL (4.14 mmol/L)	High risk

Clinical sensitivity and specificity, positive predictive value and negative predictive value are not commonly reported for this analyte. This is largely attributed to the fact that this analyte is not sole indicator for the intended purpose and patient treatment decision making. To arrive at a

Yumizen C LDL

diagnosis and a course of treatment, results from others routine clinical chemistry tests should be used in conjunction with other diagnostic information and the attending health-care professional's evaluation of the patient's condition.

Storage and Stability

Stability before opening:

Stable up to the expiry date on the label if stored at 2-8°C. Store protected from light.

Stability after opening:

Refer to the paragraph "Performance on Yumizen C230/C240".

Do not freeze.

Waste Management

Please refer to local legal requirements.

General Precautions

- This reagent is for professional *in vitro* diagnostic use only.
  For laboratory use.
- For prescription use only.
- This reagent is classified as non-hazardous in compliance with regulation (EC) N°.1272/2008.
- **Reagent 1 (R1):**
  Warning: This reagent is obtained from substances of animal origin. Consequently, it should be treated as potentially infectious and handled with the appropriate cautions in accordance with good laboratory practices (11).
- Do not pipette by mouth.
- Do not replenish the reagents.
- Do not swallow. Avoid contact with skin and mucous membranes.
- Observe the standard laboratory precautions for use.
- The reagent cassettes are disposable and should be disposed of in accordance with the local legal requirements.
- Please refer to the SDS associated with the reagent.
- Do not use the product if there is visible evidence of biological, chemical or physical deterioration.
- Do not use the product if the recommended storage conditions, including temperature, are not followed.
- User must be trained by a HORIBA representative before attempting to operate the device.
- It is the user's responsibility to verify that this document is applicable to the reagent used.
- For technical assistance, you can call +33 (0)4 67 14 15 16.
- Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the country in which the user and/or the patient is established.

Performance on Yumizen C230/C240

Lot to Lot Variability

The recovery of samples (serum and plasma) done during QC release of three consecutive lots of reagent shows that the lot to lot variability is within specification: < 10%.

Serum, plasma

The performance data listed below have been obtained on the Yumizen C230/C240 analyzer.
The assay has not been tested or certified to meet CRMLN laboratory criteria.

Number of tests: approximately 192 tests

On Board Reagent Stability

Once opened, the reagent cassette placed in the refrigerated Yumizen C230/C240 compartment is stable for 28 days.

Sample volume: 2 µL/test

Lowest Detectable Level

The lowest detectable level represents the lowest measurable level of analyte that can be distinguished from zero. It is calculated as the absolute mean plus three standard deviations of 20 replicates of an analyte free sample. The lowest detectable level is estimated at 0.006 mmol/L (0.232 mg/dL).

Limit of Quantitation

The limit of quantitation is determined according to CLSI (NCCLS), EP17-A2 protocol (12) and equals 0.04 mmol/L (1.55 mg/dL).

Yumizen C LDL

Accuracy and Precision

Repeatability (within-run precision)

Repeatability according to the recommendations found in the CLSI (NCCLS), EP05-A3 protocol (13) with samples tested 20 times:

- 2 controls
- 3 specimens (low / medium / high levels)

	Mean value mmol/L	Mean value mg/dL	CV %
Control specimen 1	1.39	53.87	1.9
Control specimen 2	2.40	93.03	1.0
Specimen 1	2.13	82.58	2.7
Specimen 2	3.63	140.57	1.3
Specimen 3	5.86	226.63	2.7

Reproducibility (total precision)

Reproducibility according to the recommendations found in the CLSI (NCCLS), EP05-A3 protocol (13) with samples tested in duplicate for 20 days (2 series per day):

- 2 controls
- 3 specimens (low / medium / high levels)

	Mean value mmol/L	Mean value mg/dL	CV %
Control specimen 1	1.36	52.63	2.6
Control specimen 2	2.38	92.11	3.5
Specimen 1	2.06	79.72	3.7
Specimen 2	4.13	159.83	3.1
Specimen 3	5.31	205.50	3.4

Measuring Range

The assay confirmed a measuring range from 0.04 mmol/L (1.55 mg/dL) to 10.0 mmol/L (387.0 mg/dL).
The measuring range is extended up to 40 mmol/L (1548 mg/dL) with the automatic post-dilution.
The reagent linearity has been assessed up to 10.0 mmol/L (387.0 mg/dL) according to the recommendations found in the CLSI (NCCLS), EP06-Ed2 protocol (14).

Correlation

Patient samples: Serum
Number of patient samples: 105

Specimens are correlated with a commercial reagent taken as reference according to the recommendations found in the CLSI (NCCLS), EP09c protocol (15).
Values ranged from 0.25 mmol/L (9.68 mg/dL) to 7.63 mmol/L (295.28 mg/dL).
The equation for the allometric line obtained using Passing-Bablok regression procedure (16) is:
Y = 0.9344 X + 0.077 (mmol/L)
Y = 0.9344 X + 2.980 (mg/dL)
with a correlation coefficient r^2 = 0.984.

Interferences

Haemoglobin: No significant influence is observed up to 579 µmol/L (1000 mg/dL).
Triglycerides: No significant influence is observed up to a triglyceride concentration of 4.65 mmol/L (406.44 mg/dL).
Total Bilirubin: No significant influence is observed up to 1107.23 µmol/L (64.77 mg/dL).
Direct Bilirubin: No significant influence is observed up to 515.55 µmol/L (30.16 mg/dL).

Other limitations are given by Young as a list of drugs and preanalytical variables known to affect this methodology (17, 18).

Calibration Stability

The reagent is calibrated on Day 0. The calibration stability is checked by testing 2 control specimens.
The calibration stability is 14 days.
Note: A recalibration is recommended when reagent lots change, and when quality control results fall outside the range established.

Conversion Factor

mmol/L x 0.387 = g/L
mmol/L x 38.7 = mg/dL

Reference

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2. National Comittee for Clinical Laboratory Standards, Preparation and Testing of Reagent Water in the Clinical Laboratory - Third Edition; Approved Guideline NCCLS Document C3-A3 (1997).

Yumizen C LDL

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14. Evaluation of Linearity of Quantitative Measurement Procedures. 2nd Edition, CLSI (NCCLS) guideline EP06-Ed2 (2020) **40** (16).
15. Measurement Procedure Comparison and Bias Estimation Using Patient Samples. Approved Guideline, 3rd ed., CLSI (NCCLS) document EP09c (2018) **38** (12).
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