

Cardiac

ichroma™ LDL cholesterol Direct

INTENDED USE

ichroma™ LDL cholesterol Direct is a fluorescence immunoassay for the quantitative determination of LDL cholesterol in human serum/plasma. It is useful as an aid in management and monitoring of heart disease and stroke.
For *in vitro* diagnostic use only.

INTRODUCTION

Cholesterol is a component of cell membranes and a precursor for steroid hormones and bile acids synthesized by body cells and absorbed with food. Cholesterol is transported in plasma via lipoproteins, namely complexes between lipids and apolipoproteins. There are four classes of lipoproteins: high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL) and chylomicrons. While LDL is involved in the cholesterol transport to the peripheral cells, HDL is responsible for the cholesterol uptake from the cells. The four different lipoprotein classes show distinct relationship to coronary atherosclerosis.³ LDL cholesterol contributes to atherosclerotic plaque formation within the arterial intima and is strongly associated with coronary heart disease (CHD) and related mortality. Even with total cholesterol within the normal range an increased concentration of LDL cholesterol indicates high risk^{4,5,6,7}.

PRINCIPLE

The test uses a sandwich immunodetection method.

The detector antibodies in buffer bind to antigens in the sample, forming antigen-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized-CDC (Cholesterol Dependent Cytolysin) protein on a test strip.

More antigens in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by the instrument for ichroma™ tests to show LDL cholesterol concentration in the sample.

COMPONENTS

ichroma™ LDL Cholesterol Direct consists of 'cartridges', and 'detection buffers'

- The cartridge contains the membrane called a test strip which has cholesterol dependent cytolysin (CDC) at the test line, and Rabbit IgG at the control line. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant in a box.
- The detection buffer contains anti-human LDL-fluorescence conjugate, anti-rabbit IgG fluorescence conjugate, bovine serum albumin (BSA) as a stabilizer and

sodium azide as a preservative in phosphate buffered saline (PBS). It is pre-dispensed in tubes. The detection buffer tubes are packaged in a detection buffer box and further packed in a Styrofoam box with ice-pack for the shipment.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, detection buffer and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect of test result(s).
- Do not reuse cartridges or detection buffers. A cartridge should be used for testing one sample only. A detection buffer should be used for processing of one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use cartridge, if pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- If test components and/or sample are stored in refrigerator, then allow cartridge, detection buffer and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for ichroma™ tests may generate slight vibration during use.
- Used cartridges, detection buffer and pipette tips and should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The detection buffer contains sodium azide (NaN₃), and they may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- **ichroma™ LDL cholesterol Direct** will provide accurate and reliable results subject to the below conditions.
 - Use **ichroma™ LDL cholesterol Direct** should be used only in conjunction with instrument for ichroma™ tests.
 - Have to use recommended anticoagulant.

Recommended anticoagulant

EDTA, heparin, Sodium citrate

STORAGE AND STABILITY

Storage condition		
Component	Storage Temperature	Shelf life
Cartridge	2 - 30 °C	20 months
Detection buffer	2 - 8 °C	20 months

- After the cartridge pouch is opened, the test should be performed immediately.

LIMITATION OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the antigen to the antibodies which is the most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the antigen with time and/or temperature may also cause false negative result as it makes the antigen unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician in conjunction with clinical symptoms and other relevant test results.

MATERIALS SUPPLIED

REF CFPC-128

Components of **ichroma™ LDL cholesterol Direct**

- | | |
|-------------------------|----|
| ■ Cartridge Box: | |
| - Cartridge | 25 |
| - Sample collector | 25 |
| - ID chip | 1 |
| - Instructions for use | 1 |
| ■ Detection buffer box | |
| - Detection buffer tube | 25 |

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ LDL cholesterol Direct**.
Please contact our sales division for more information.

- | | |
|---------------------------------|--------------|
| ■ Instrument for ichroma™ tests | |
| - ichroma™ II | REF FPRR021 |
| - ichroma™ III | REF FPRR037 |
| - ichroma™ M3 | REF FPRR035 |
| ■ Boditech Cholesterol Control | REF CFPO-312 |

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ LDL cholesterol Direct** is human serum/plasma.

- It is recommended to test the sample within 24 hours after collection.
- The samples (serum, plasma) should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- The samples (serum, plasma) may be stored for a week at 2-8 °C prior to being tested. If testing will be delayed more than a week, samples (serum, plasma) should be frozen at -20 °C.
- The samples (serum, plasma) stored frozen at -20 °C for 3 months showed no performance difference.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.

TEST SETUP

- Check the contents of ichroma™ LDL Cholesterol Direct: Sealed cartridges, detection buffer tubes, an ID chip and an instructions for use.
- Ensure that the lot number of the cartridges matches that of the detection buffer tube as well as an ID chip.
- If the sealed cartridge and the detection buffer have been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.
- Turn on the instrument for ichroma™ tests.
- Insert the ID chip into the 'ID chip port'.

※ Please refer to the instrument for ichroma™ tests operation manual for complete information and operating instructions.

TEST PROCEDURE

► ichroma™ II, ichroma™ M3

※ Make a puncture on the top of the detection buffer tube by inserting an empty sample collector.

Multi test mode

- 1) Take 5 µL of sample (serum/plasma/control) using a sample collector.
- 2) Assemble sample collector onto the detection buffer tube and mix the sample thoroughly by shaking it about 10 times
(The sample mixture must be used immediately. Do not exceed 30 seconds.)
- 3) Discard 2 drops of sample mixture and dispense 2 drops of the sample mixture into the sample well of the cartridge.
- 4) Leave the cartridge at room temperature for 10 minutes.
- ⚠ Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.

- 5) To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
- 6) Tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process.
(ichroma™ M3 is tested automatically after inserting.)
- 7) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
- 8) Read the test result on the display screen of the instrument for ichroma™ tests.

Single test mode

- 1) The test procedure is same with the 'Multi test mode 1) - 3)'.
- 2) Insert the sample-loaded cartridge into the holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked

on the cartridge especially for this purpose.

- 3) Tap the 'Start' button on the instrument for ichroma™ tests.
(ichroma™ M3 is tested automatically after inserting.)
- 4) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 10 minutes.
- 5) Read the test result on the display screen of the instrument for ichroma™ tests.

► ichroma™ III

- 1) The test procedure is same with the 'Single test mode'.

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays LDL cholesterol concentration of the test sample in terms of mg/dL.
- The cut-off (reference value)

Status	Conc.
Optimal	<100 mg/dL
Near optimal	100-129 mg/dL
Borderline high	130-159 mg/dL
High	160-189 mg/dL
Very high	>190 mg/L

- Working range : 10-300 mg/dL

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with ichroma™ LDL Cholesterol Direct. For more information regarding obtaining the control materials, contact [Boditech Med Inc.'s Sales Division for assistance](#).
(Please refer to the instruction for use of control material.)

PERFORMANCE CHARACTERISTICS

■ Analytical sensitivity

- Limit of Blank (LoB) 2.9 mg/dL
- Limit of Detection (LoD) 6.8 mg/dL
- Limit of Quantitation (LoQ) 10.0 mg/dL

■ Analytical Specificity

- Cross-reactivity

Biomolecules listed in the following table were added to the test sample(s) at concentrations much higher than their normal physiological levels in the blood. **ichroma™ LDL cholesterol Direct** test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactivity material	Conc.
Ascorbic acid	30 mg/dL
Bilirubin	20 mg/dL
Intralipid	500 mg/dL
Hemoglobin	5,000 mg/dL

- Interference

Interferents listed in the following table were added to the test samples at the concentration mentioned below. **ichroma™ LDL Cholesterol Direct** test results did not show any significant interference with these materials.

Interference material	Conc.
Apolipoprotein A1	500 µg/mL
Cholesterol	2 µg/mL
HDL	4 µg/mL

■ Precision

- Single-site study

Repeatability (within-run precision)

Total precision (within-laboratory precision)

Lot to lot precision

3 Lots of **ichroma™ LDL Cholesterol Direct** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.

- Multi-site study

Reproducibility

1 Lot of **ichroma™ LDL Cholesterol Direct** was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per and 5 replicates per day.

Conc [mg/dL]	Repeatability		Total precision		Lot to lot precision	
	AVG	CV (%)	AVG	CV (%)	AVG	CV (%)
25	25.11	11.61	24.98	10.92	25.01	10.90
50	49.93	11.95	50.31	12.21	50.06	11.47
100	102.75	11.38	102.85	11.39	100.60	12.28

Conc [mg/dL]	Reproducibility	
	AVG	CV (%)
25	24.98	11.48
50	49.73	12.50
100	99.85	11.61

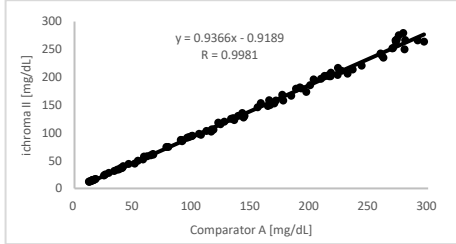
■ Accuracy

The accuracy was confirmed by testing with 3 different lots of **ichroma™ LDL cholesterol Direct**. The tests were repeated 10 times at each concentration of the control standard

conc. [mg/dL]	Lot 1	Lot 2	Lot 3	AVG	Recovery (%)
6.00	5.82	6.27	5.89	6.00	100%
10.00	10.21	10.30	10.29	10.27	103%
30.00	29.43	29.65	29.29	29.46	98%
60.00	58.63	62.84	59.09	60.19	100%
75.00	72.93	75.78	75.77	74.83	100%
100.00	103.44	100.66	98.64	100.91	101%
150.00	149.39	148.62	146.82	148.27	99%

■ Comparability

LDL Cholesterol concentrations of 100 serum samples were quantified independently with ichroma™ LDL Cholesterol Direct (**ichroma™ II**) and **Comparator A** as per prescribed test procedures. Test results were compared and their comparability was investigated with linear regression and correlation coefficient (R). The regression equation and correlation coefficient are as follows.



REFERENCES

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3. Kenneth R and Feingold, MD. Introduction to Lipids and Lipoproteins. Endotext [Internet]. 2021.
4. Brian A. Ference et al., Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J.* 2017. 38(32): 2459–2472.
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6. Hao W and Friedman A. The LDL-HDL profile determines the risk of atherosclerosis: a mathematical model. *PLoS One.* 2014. 12;9(3):e90497.
7. Frank M Sacks et al., Coronary heart disease in patients with low LDL-cholesterol: benefit of pravastatin in diabetics and enhanced role for HDL-cholesterol and triglycerides as risk factors. *Circulation.* 2002. 26;105(12):1424-8.

Note: Please refer to the table below to identify various symbols

	Sufficient for <n> tests
	Read instruction for use
	Use by Date
	Batch code
	Catalog number
	Caution
	Manufacturer
	Authorized representative of the European Community
	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

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