

Diabetes

ichroma™ Cystatin C

INTENDED USE

ichroma™ Cystatin C is a fluorescence Immunoassay (FIA) for the quantitative determination of cystatin C in human serum/plasma. It is useful as an aid in management and monitoring of renal disease.

For *in vitro* diagnostic use only.

INTRODUCTION

The level of serum cystatin C has been proposed as a simple, accurate, and rapid endogenous marker of glomerular filtration rate (GFR) in research and clinical practice. The measurement of serum cystatin C may detect mild to moderate decrease in GFR that are not evident with the serum creatinine measurement.

In kidney transplant patients, cystatin C was reported to be more sensitive than serum creatinine for detecting decreases in GFR and delayed graft function, offering an opportunity for timely intervention.

PRINCIPLE

The test uses a sandwich immunodetection method; the detector recombinant protein in buffer binds to antibody in sample, forming recombinant protein-antibody complexes, and migrates onto nitrocellulose matrix to be captured by the other immobilized-antigen on test strip.

The more antibody in sample forms the more recombinant protein-antibody complex and leads to stronger intensity of fluorescence signal on detector recombinant protein, which is processed by Instrument for ichroma™ tests to show cystatin C concentration in sample.

COMPONENTS

ichroma™ Cystatin C consists of 'Cartridges', 'Detection Buffer Tubes' and an 'ID chip'.

- The cartridge contains a test strip, the membrane which has anti human cystatin C at the test line, while chicken IgY at the control line.
- Each cartridge is individually sealed in an aluminum foil pouch containing a desiccant. 25 sealed cartridges are packed in a box which also contains an ID chip.
- The detection buffer contains anti human cystatin C-fluorescence conjugate, anti chicken IgY-fluorescence conjugate, bovine serum albumin (BSA) as a stabilizer and sodium azide in phosphate buffered saline (PBS) as a preservative.
- The detection buffer is pre-dispensed in a tube. 25 detection buffer tubes are packaged in a box and further packed in a Styrofoam box with ice-pack for the shipment.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Carefully follow the instructions and procedures described in this 'Instruction for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (test cartridge, ID chip and detection buffer) 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 misleading of test result(s).
- Do not reuse. A detection buffer tube should be used for processing one sample only. So should a test cartridge.
- The test cartridge should remain sealed in its original pouch

before use. Do not use the test cartridge, if is damaged or already opened.

- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with the regulations. Sample with severe hemolytic and hyperlipidemia cannot be used and should be recollected.
- Just before use, allow the test cartridge, detection buffer and sample to be at room temperature for approximately 30 minutes.
- **ichroma™ Cystatin C** as well as the instrument for ichroma™ tests should be used away from vibration and/or magnetic field. During normal usage, it can be noted that instrument for ichroma™ tests may produce minor vibration.
- Used detection buffer tubes, pipette tips and test cartridges should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- An exposure to larger quantities of sodium azide may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.
- **ichroma™ Cystatin C** will provide accurate and reliable results subject to the following conditions.
 - Use **ichroma™ Cystatin C** should be used only in conjunction with instrument for ichroma™ tests.
 - Any anticoagulants other than EDTA, sodium citrate should be avoided.

STORAGE AND STABILITY

- The cartridge is stable for 20 months (while sealed in an aluminum foil pouch) if stored at 4-30 °C.
- The detection buffer pre-dispensed in a tube is stable for 20 months if stored at 2-8 °C.
- 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. The non-responsiveness of the antigen to the antibodies is most common where the epitope is masked by some unknown components, so as not to be detected or captured by the antibodies. The instability or degradation of the antigen with time and/or temperature may cause the false negative as it makes 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 including clinical symptoms and other relevant test results.

MATERIALS SUPPLIED





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Components of **ichroma™ Cystatin C**

- Cartridge Box:
 - Cartridges 25
 - ID Chip 1
 - Instruction For Use 1
- Box containing Detection Buffer Tubes
 - Detection Buffer Tubes 25

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ Cystatin C**.

- Please contact our sales division for more information.
- Instrument for ichroma™ tests
 - **ichroma™ Reader**  FR203
 - **ichroma™ II**  FPRR021
 - **ichroma™ D**  13303
- ichroma™ Printer**  FPRR007

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ Cystatin C** is human serum/plasma.

- It is recommended to test the sample within 24 hours after collection.
- The serum or plasma should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- Samples may be stored for up to two weeks at 2-8 °C prior to being tested. If testing will be delayed more than two weeks, samples should be frozen at -20 °C.
- Samples stored frozen at -20 °C for 3 months showed no performance difference.
- Once the sample was frozen, it should be used one time only for test, because repeated freezing and thawing can result in the change test values.

TEST SETUP

- Check the contents of **ichroma™ Cystatin C**: Sealed Cartridge, Detection Buffer Tubes and ID Chip.
- Ensure that the lot number of the cartridge matches that of the ID chip, diluent as well as the detection buffer.
- Keep the sealed cartridge (if stored in refrigerator) and the detection buffer tube at room temperature for at least 30 minutes just prior to the test. Place the cartridge on a clean, dust-free and flat surface.
- Turn on the instrument for ichroma™ tests.
- Insert the ID Chip into the ID chip port of the instrument for ichroma™ tests.
- Press the 'Select' button on the instrument for ichroma™ tests. (Please refer to the 'Instrument for ichroma™ tests Operation Manual' for complete information and operating instructions.)

TEST PROCEDURE

- 1) Transfer 10 µL of sample (human serum/plasma/control) using a transfer pipette to a tube containing the detection buffer.
- 2) Close the lid of the detection buffer tube and mix the sample thoroughly by shaking it about 10 times. (The sample mixture must be used immediately.)
- 3) Pipette out 75 µL of the sample mixture and load it into a sample well in the Test Cartridge.
- 4) Leave the sample-loaded cartridge at room temperature for 10 minutes.
 - ▲ Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inexact 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 has been marked on the cartridge especially for this purpose.
- 6) Press 'Select' button on the instrument for ichroma™ tests to start the scanning process.
- 7) 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.

INTERPRETATION OF TEST RESULT

- Instrument for ichroma™ tests calculates the test result automatically and displays cystatin C concentration of the test sample in terms of mg/L.
- The cut-off (reference range)

Concentration of cystatin C in healthy individuals

Age range	Reference Range
18 - 50 years old	0.56 - 0.90 mg/L
51 - 70 years old	0.58 - 1.09 mg/L

- Concentration of cystatin C vs. GFR

Stage	cystatin C (mg/L)	GFR (ml/min/1.73m ²)	State
Normal	0.52-0.91	≥ 90	Normal GFR
1	0.91-1.1	≥ 90	Kidney damage with normal
2	1.1-1.7	60-89	Mild Decrease
3	1.7-2.5	30-59	Moderate Decrease
4	2.5-4.0	15-29	Severe Decrease
5	> 4.0	< 15	ESRD (Kidney failure)

- Prognosis of CKD by GFR and albumin categories

		Albuminuria categories		
		A1	A2	A3
Stage	GFR	< 30 mg/L	30-300 mg/L	> 300 mg/L
1	≥90	Low risk	Medium risk	High risk
2	60-89			
3	45-59	Medium risk	High risk	
4	30-44	High risk		
5	15-29	Very high risk.		
6	<15			

- Working range: 0.1-7.5 mg/L.

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.
- The control tests should be performed immediately after opening a new test lot to ensure the test performance is not altered.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are not provided with **ichroma™ Cystatin C**. 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

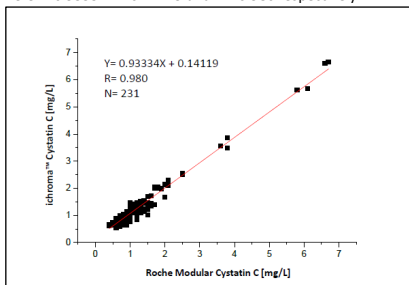
- Specificity:** There, in test samples, are biomolecules such as EDTA, urea, sodium citrate, D-glucose, heparin in higher concentration than their normal physiological levels. But this doesn't interfere with the **ichroma™ Cystatin C** test measurements, nor occurs any significant cross-reactivity.

Interference	Concentration
EDTA	100 mg/ml
Urea	2 mg/ml
Sodium Citrate	22 mg/ml
D-Glucose	10 mg/ml
Heparin	10 KU/ml

- **Prozone/Hook Effect:** No prozone/hook effect was observed with **ichroma™ Cystatin C** at cystatin C concentrations less to 8 mg/L.
- **Precision:** The intra-assay precision was calculated by one evaluator, who tested different concentration of control standard ten times each with three different lots of **ichroma™ Cystatin C**. The inter-assay precision was confirmed by 3 different evaluators with 3 different lots, testing ten times each different concentration.

Cystatin C [mg/L]	Intra-assay		Inter-assay	
	Mean	CV (%)	Mean	CV (%)
0.5	0.48	3.11	0.48	2.66
1	0.99	1.38	0.98	3.18
2.5	2.35	1.84	2.32	3.04

- **Comparability:** Cystatin C concentrations of 231 plasma samples were quantified independently with **ichroma™ Cystatin C** and Roche Modular as per prescribed test procedures. Test results were compared and their comparability was investigated with linear regression and coefficient of correlation (R). Linear regression and coefficient of correlation between the two tests were $Y=0.93334X + 0.14119$ and $R = 0.980$ respectively.



REFERENCES

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2. Shemesh O, Golbetz H, Kriss JP, Myers BD. Limitations of Creatinine as a filtration marker in glomerulopathic patients. Kidney Int 1985;28: 830-8.
3. Abrahamson M, Olafsson I, Palsdottir A, Ulvsback M, Lundwall A, Jenson O, et al. Structure and expression of the human cystatin C gene. Biochem J 1990; 268: 287-94.
4. Newman DJ: Cystatin C. Ann Clin Biochem 2002; 39: 89-104.
5. Kazama JJ, Kutsuwada K, Ataka K, Maruyama H, Gejyo F. Serumcystatin C reliably detects renal dysfunction in patients with various renal diseases. Nephron 2002; 91: 13-20.
6. Jung K and Jung M. Cystatin C: a promising marker of

Glomerular filtration rate to replace creatinine. Nephron 1995; 70: 370-1.

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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