Hormone

ichroma™ Total βhCG

INTENDED USE

ichroma™ Total βhCG is a fluorescence immunoassay (FIA) for the quantitative detection of Total βhCG in human whole blood/serum/plasma. It is useful as an aid in management and monitoring of total beta human chorionic gonadotropin (total β-hCG) level in human.

For *in vitro* diagnostic use only.

INTRODUCTION

Human chorionic gonadotropin (hCG) is a glycoprotein hormone secreted by the developing placenta shortly after implantation. hCG can be detected in the urine and serum of pregnant women as early as 6 to 15 days after conception. The concentration of hCG increases to 50 mIU/mL one week post implantation and reaches to about 100 mIU/mL at the time of the first missed menstrual period and the peak at 100,000-200,000 mIU/mL at the first trimester.

PRINCIPLE

This 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-antibodies 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 Total βhCG concentration in the sample.

COMPONENTS

ichroma™ Total βhCG consists of 'cartridges', 'detector tubes', 'detector diluent' and 'sample diluents'.

- The cartridge contains the membrane called a test strip which has anti-human chorionic gonadotropin and mouse IgG-hCG peptide conjugator at the test line, and streptavidin at the control line. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant, and they are further packaged in a box.
- The detector tube has a granule containing biotin-BSA fluorescence conjugate, anti-human chorionic gonado tropin-fluorescence conjugate, bovine serum albumin (BSA) as a stabilizer and sodium azide as a preservative in phosphate buffered saline (PBS). All detector tubes are packed in a pouch.
- The detector diluent contains bovine serum albumin (BSA) as a stabilizer, Tween20 as a detergent and sodium azide as a preservative in phosphate buffered saline (PBS), and it is pre-dispensed in a vial. The detector diluent is packed in a box.
- The sample diluent contains sodium azide as a preservative in phosphate buffer saline (PBS). All sample diluents are packed in a zipper back.

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, detector tube, detector diluent, sample diluent 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 test result(s).
- Do not reuse cartridges, detector tubes or sample diluent. A cartridge should be used for testing one sample only. A detector tube or sample diluent 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 the 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, detector tube, detector diluent, sample diluent 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, detector tubes, detector diluent, sample diluent and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The detector tube, the detector diluent and sample diluent tube contain sodium azide (NaN_3), 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.
- No Biotin interference was observed in ichroma™ Total βhCG when biotin concentration in the sample was below 500 ng/mL. If a patient has been taking biotin at dosage of more than 0.03 mg a day, it is recommended to test again 24 hours after discontinuation of biotin intake.
- **ichroma™ Total βhCG** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ Total βhCG** should be used only in conjunction with the instrument for ichroma™ tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
K_2 EDTA, K_3 EDTA, Lithium heparin

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.

STORAGE AND STABILITY

Storage condition			
Component	Storage Temperature	Shelf life	Note
Cartridge	2 - 30 °C	20 months	Disposable
Detector tube	2 - 30 °C	20 months	Disposable
Detector diluent	2 - 30 °C	20 months	Unopened
	2 - 30 °C	6 months	Opened
Sample diluent	2 - 30 °C	20 months	Disposable

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

MATERIALS SUPPLIED

REF CFPC-41

Components of **ichroma™ Total βhCG**

- Cartridge box:
  - Cartridge 25
  - Detector tube 25
  - Detector diluent 1
  - Sample diluent 25
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ Total βhCG.**

Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ Reader** REF FR203
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™-50** REF FPRR022
  - **ichroma™ 50 Plus** REF FPRR036
  - **ichroma™ M3** REF FPRR035
- **Boditech hCG Control** REF CFPO-232
- **Boditech Hormone Control** REF CFPO-95

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ Total βhCG** is whole blood /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 (whole blood, serum, plasma) may be stored for 24 hours at 15 - 28 °C prior to being tested.
- The samples (whole blood, 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 2 months showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.

TEST SETUP

- Check the contents of **ichroma™ Total βhCG**: Sealed cartridges, detector tubes, a detector diluent, Sample diluents, an ID chip and an instructions for use.
- Ensure that the lot number of the cartridge matches that of the detector tube, the detector diluent, the sample diluent as well as an ID chip.
- If the sealed cartridge, the detector tube, the detector diluent and the sample diluent 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.

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

TEST PROCEDURE

※ **Sample dilution procedure (>50,000 mIU/mL results)**
If sample value exceeds 50,000 mIU/mL, take 30 µL of the sample (whole blood/serum/plasma) using a pipette to a sample diluent tube and shake it about 10 times.

▶ **ichroma™ Reader, ichroma™ II, ichroma™ M3**

Multi test mode

1) Take 150 µL of detector diluent using a pipette and dispense it to the detector tube containing a granule. When the granule form is completely dissolved in the tube, it becomes detection buffer.
   (The detection buffer must be used immediately. Do not exceed 30 seconds.)
2) Take 50 µL of sample (whole blood) or 30 µL of sample (serum/plasma/control/diluted sample) using a pipette and dispense it to the detector tube.
3) Close the lid of the detector tube and mix the sample thoroughly by shaking it about 10 times.
   (The sample mixture must be used immediately. Do not exceed 30 seconds.)
4) Take 75 µL of the sample mixture and dispense it into the sample well of the cartridge.
5) Leave the cartridge at room temperature for 15 minutes.
   ⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause*

inaccurate test result.

6) 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.
7) Press the 'Select' or tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process.
(ichroma™ M3 is tested automatically after inserting.)
8) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
9) Read the test result on the display screen of the instrument for ichroma™ tests.

Single test mode

1) The test procedure is same with 'Multi test 1) – 4)'.
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) Press the 'Select' or 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 15 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 'Single test mode'.

▶ **ichroma™-50, ichroma™-50 Plus**

1) Insert the tip array in the tip station.
2) Insert the detector tube in the reagent station and cover the reagent station to hold the detector tubes in place.
3) Open the lid of the detector diluent and insert the detector diluent in the diluent station.
4) Insert the cartridge magazine with the cartridges into the magazine station.
5) Insert the sample tube into the blood collection tube rack and load the blood collection tube rack into the sampling station (loading part).
(For diluted samples, load diluted sample tubes into a separate tube rack.)
6) Tap the button located in the upper side of the No. of test cartridge region to select the ID chip that you want to use.
7) When the selected cartridge slot is activated, set the number of the detector tube by tapping.
8) Set the number of pipette tips by tapping.
9) Tap the 'Start' button on the left upper of the main screen to start test.

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays Total βhCG concentration of the test sample in terms of mIU/mL.
- In case of using the sample dilution procedure, multiply result by ten.
(The result of the sample dilution procedure = display result x 10)
- Working range: 5 - 50,000 mIU/mL
- Reference range

Pregnant women (week since LMP*)	Total βhCG level [mIU/mL]
3	5–50
4	5-426
5	18-7,340
6	1,080-56,500
7 – 8	7,650-229,000
9 - 12	25,700-288,000
13 – 16	13,300-254,000
17 – 24	4,060-165,400
25 -40	3,640-117,000

* LMP is the last menstrual periods date from the first day of your last period.

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™ Total βhCG**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
(Please refer to the instructions for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**

Limit of Blank (LOB)	0.780 mIU/mL
Limit of Detection (LOD)	1.760 mIU/mL
Limit of Quantitation (LOQ)	5 mIU/mL

- **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™ Total βhCG** test results did not show any significant cross-reactivity with these biomolecules.

No.	Cross reactivity materials	Conc.
1	FSH	1000 mIU/mL
2	PRL	1000 mIU/mL
3	TSH	1000 mIU/mL
4	LH	1000 mIU/mL

- **Interference**

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

Interference materials	Conc.
D-glucose	600 mM
L-Ascorbic acid	2 mM
Bilirubin [unconjugated]	4 mM
Hemoglobin [human]	20 g/L
Cholesterol	130 mM
Triglyceride	100 mg/mL

- **Precision**

- Repeatability (within-run precision)
- Total precision (within-laboratory precision)
- Lot to lot precision
  3 Lots of **ichroma™ Total βhCG** were tested for 21days. Each standard material was tested 2 times per day. For each test, each material was duplicated.
- Between persons
  Three different persons tested three lots of **ichroma™ Total βhCG,** ten times at each concentration of the control standard.
- Between sites
  One lot of **ichroma™ Total βhCG** tested at three different sites, ten times at each concentration of the control standard.
- Between readers
  One lot of **ichroma™ Total βhCG** tested with three different readers, ten times at each concentration of the control standard.

Conc.	Repeatability		Total precision	
[mIU/mL]	AVG	CV (%)	AVG	CV (%)
50	49.26	7.99	48.80	7.73
1600	1623.76	7.43	1619.98	6.85
12000	12240.38	7.25	12230.42	7.01
37000	37218.54	6.86	37007.33	7.07
Conc.	Lot to lot		Between-persons	
[mIU/mL]	AVG	CV (%)	AVG	CV (%)
50	48.90	7.95	50.03	8.64
1600	1604.86	6.58	1587.23	7.60
12000	11936.59	7.12	11838.19	7.05
37000	37207.80	6.93	36617.35	6.58
Conc.	Between-sites		Between-readers	
[mIU/mL]	AVG	CV (%)	AVG	CV (%)
50	50.27	8.59	51.62	8.02
1600	1598.78	7.38	1616.61	6.72
12000	12139.81	5.89	12025.37	6.64
37000	36552.92	7.01	37101.85	8.35

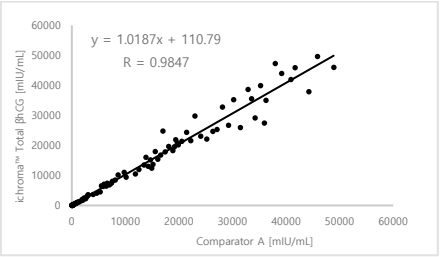
- **Accuracy**

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

Expected value [mIU/mL]	Lot 1	Lot 2	Lot 3	AVG	Recovery (%)
5	5.12	5.14	5.11	5.13	103
20	19.72	20.30	20.62	20.21	101
200	199.5	199.2	208.7	202.46	101
2000	1965.5	1970.1	1923.4	1952.99	98
5000	4896.4	4742.5	4966.2	4868.35	97
10000	9824.2	9920.9	9983.7	9909.59	99
25000	25145.0	25238.0	24717.4	25033.44	100
31250	31168.6	31113.0	30659.5	30980.36	99
50000	50071.3	47918.3	50562.0	49517.17	99

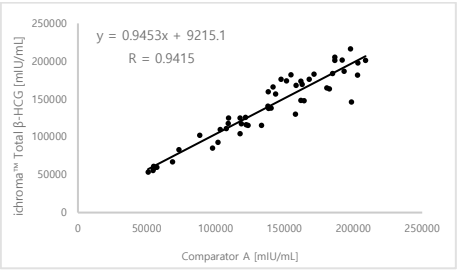
- **Comparability**

Total βhCG concentrations of 100 clinical samples were quantified independently with **ichroma™ Total βhCG (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.



- **Comparability-dilution method**

Total βhCG concentrations of 50 clinical samples were quantified independently with **ichroma™ Total βhCG (ichroma™ II)** and **comparator A** 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 correlation coefficient (R). The regression equation and correlation coefficient are as follows.



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1. Braunstein GD, JL Vaitukaitis, PP Carbone, GT Ross “Ectopic production of human chorionic gonadotropin by neoplasms”, Ann. Intern Med. 1973; 78(1): 39-45.
2. Steier JA, P Bergsjo, OL Myking “Human chorionic gonadotropin in maternal plasma after induced abortion, spontaneous abortion and removed ectopic pregnancy”, Obstet. Gynecol. 1984; 64(3): 391-394.
3. Lenton EA, LM Neal, R Sulaiman “Plasma concentration of human chorionic gonadotropin from the time of implantation until the second week of pregnancy”, Fertil. Steril. 1982; 37(6): 773-778.
4. Batzer FR. “Hormonal evaluation of early pregnancy”, Fertil. Steril. 1980; 34(1): 1-13.

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

For technical assistance, please contact:
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