Infection

# ichroma™ PCT

## INTENDED USE

**ichroma™ PCT** is a fluorescence immunoassay (FIA) for the quantitative determination of PCT (procalcitonin) in human whole blood/serum/plasma. It is useful as an aid in diagnosis, management and monitoring of bacterial infection and sepsis.

For *in vitro* diagnostic use only.

## INTRODUCTION

Identifying sepsis is a daily challenge in intensive care unit of every hospital. Early assessment of sepsis is vital for determination of the appropriate treatment since various therapeutic strategies are known to improve survival of patients with sepsis.

Procalcitonin (PCT) is a precursor of calcitonin with a molecular weight of 12.6-kDa. And in normal conditions, it produces and secretes activated calcitonin in C-cells of the thyroid gland, and it is involved in calcium metabolism. However, in case of systemic infection occurs, procalcitonin is produced in all parenchymal cells.

In healthy people, the concentration of plasma PCT is below 0.1 ng/mL. The level of PCT rises rapidly after a bacterial infection with systemic consequences. It can also be elevated by other situation such as major surgery, severe burns, or in neonates. However, it returns to baseline rapidly. Viral infections, bacterial colonization, localized infections, allergic disorders, autoimmune diseases, and transplant rejection do not usually induce a significant PCT response (values <0.5 ng/mL). Therefore, by evaluating PCT concentrations, the physicians are able to engage in the risk assessment for progression to severe sepsis and septic shock.

## 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 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 PCT concentration in the sample.

## COMPONENTS

**ichroma™ PCT** consists of 'cartridges', 'detector tubes', 'detector diluent'.

- The cartridge contains the membrane called a test strip which has anti-PCT at the test line, and chicken IgY 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 anti-PCT-fluorescence conjugate, anti-chicken IgY-fluorescence conjugate and sodium azide as a preservative in phosphate buffered saline (PBS). All detector tubes are packed in a pouch.
- The detector diluent contains Tween 20 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.

## WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow 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 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 or detector tubes. A cartridge should be used for testing one sample only. A detector tube 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, detector tube, detector 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 and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The detector tube and the detector diluent contain sodium azide ($NaN_3$), and it may cause certain health issues like convulsions, low blood pressure, low 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™ PCT** when biotin concentration in the sample was up to 3,500 ng/mL. If a patient has been taking biotin at dosage of more than 300 mg a day, it is recommended to collect blood again 24 hours after discontinuation of biotin intake.
- **ichroma™ PCT** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ PCT** should be used only in conjunction with instrument for ichroma™ tests.

- Have to use recommended anticoagulant.

| Recommended anticoagulant |
|---|
| $K_2$ EDTA, $K_3$ EDTA, Sodium citrate, Sodium heparin, 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 antigens 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 antigens with time and/or temperature may also cause false negative result as it makes the antigens 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℃ | 20 months | Disposable |
| Detector tube | 2~30℃ | 20 months | Disposable |
| Detector diluent | 2~30℃ | 20 months | Unopened |
| | 2~30℃ | 20 months | Opened |

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

## MATERIALS SUPPLIED

REF CFPC-23-1
Component of **ichroma™ PCT**

- Cartridge box:
  - Cartridge 10
  - Detector tube 10
  - Detector diluent 1
  - ID chip 1
  - Instructions for use 1

## MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately with **ichroma™ PCT**.
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™ M3** REF FPRR035
  - **ichroma™-50** REF FPRR022
  - **ichroma™-50 PLUS** REF FPRR036
- **Printer** REF FPRR007
- **Boditech PCT Control** REF CFPO-97

## SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ PCT** is human whole blood/serum/plasma.

- Take precautions on the collected sample because it's reported the concentration is rapidly changed when the sample for PCT test is kept at room temperature or refrigerated.
- It is recommended to test the sample within 6 hours after collection when collected sample is stored at room temperature.
- 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 (1 day) at 2-8°C prior to being tested. If testing will be delayed more than 24 hours, 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.
- 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™ PCT**: Sealed cartridges, detector tubes, a detector diluent, an ID chip and instructions for use.
- Ensure that the lot number of the cartridge matches that of the detector tube, the detector diluent as well as an ID chip.
- If the sealed cartridge, the detector tube and the detector 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.
- 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™ Reader / ichroma™ II / ichroma™ M3**
Multi test mode

1) Take 150 µL of the 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 within 30 seconds.)
2) Take 150 µL of sample (human whole blood/serum/plasma/control) 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 within 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 12 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 will start the test 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 the 'Multi test mode 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 will start the test automatically after inserting.)
4) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 12 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'.

▶ **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).
6) Tap the button located in the upper side of the No. of test cartridge region to select 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 PCT concentration of the test sample in terms of ng/mL.
- Working range : 0.1-100 ng/mL
- Cut-off: 0.5 ng/mL
  - **ichroma™ PCT** test should be considered as a screening tool only. In case of a positive result (above 0.5 ng/mL), consult a physician to discuss the test result. The physician may decide further course of action.
  - Test result of > 2 ng/mL may reflect severe sepsis.
  - The table below is cited for reference to the status according to the PCT concentration.

| PCT [ng/mL] | state |
|---|---|
| PCT < 0.05 | Healthy adult |
| 0.05 ≤ PCT < 0.5 | Systemic infection is unlikely although localized infection is possible |
| 0.5 ≤ PCT < 2.0 | Systemic infection is possible but other conditions (e.g. major trauma, recent surgery, severe cardiogenic shock) may also induce significant PCT rises. |
| 2.0 ≤ PCT < 10.0 | sepsis is likely, unless other cause are known |
| PCT ≥ 10.0 | High likelihood of severe bacterial sepsis or septic shock |

## 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™ PCT**. For more information regarding 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) | 0.042 ng/mL |
| Limit of Detection | (LoD) | 0.060 ng/mL |
| Limit of Quantitation | (LoQ) | 0.100 ng/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™ PCT** test results did not show any significant cross-reactivity with these biomolecules.

| Cross-reactants | Concentration |
|---|---|
| CEA | 500 µg/mL |
| AFP | 300 µg/mL |

| | |
|---|---|
| ALT | 500 µg/mL |
| Troponin I | 500 µg/mL |
| Pro-BNP | 100 ng/mL |
| Pro-GRP | 100 ng/mL |
| Pro-ANP | 100 ng/mL |

- Interference

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

| Interferents | Concentration |
|---|---|
| Bilirubin (unconjugated) | 0.3 mmol/L |
| Cholesterol | 6 mmol/L |
| Glucose | 60 mmol/L |
| Ascorbic acid | 300 µmol/L |
| Triglyceride, total | 20 mmol/L |
| $K_2$ EDTA | 4.0 µmol/L |
| $K_3$ EDTA | 4.0 µmol/L |
| Li-Heparin | 400 µmol/L |
| Sodium-Heparin | 400 µmol/L |
| Sodium Citrate | 4.0 mol/L |
| Biotin | 3,500 ng/mL |

## ■ Precision

- Single-site study

Repeatability (within-run precision)
within-laboratory precision (Total precision)
Lot to lot precision

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

| PCT [ng/mL] | Single-site study | | | | | |
|---|---|---|---|---|---|---|
| | Repeatability | | Within-laboratory precision | | Lot to lot precision | |
| | AVG [ng/mL] | CV (%) | AVG [ng/mL] | CV (%) | AVG [ng/mL] | CV (%) |
| 0.5 | 0.50 | 3.8 | 0.50 | 4.1 | 0.50 | 4.0 |
| 12.5 | 12.54 | 4.5 | 12.57 | 4.4 | 12.51 | 4.1 |
| 50.0 | 49.96 | 4.0 | 49.87 | 3.8 | 49.84 | 4.0 |

- Multi-site study

Reproducibility

1 Lot of **ichroma™ PCT** 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.

| PCT [ng/mL] | Multi-site study | |
|---|---|---|
| | Reproducibility | |
| | AVG [ng/mL] | CV (%) |
| 0.5 | 0.50 | 5.4 |
| 12.5 | 12.62 | 5.6 |
| 50.0 | 50.51 | 5.6 |

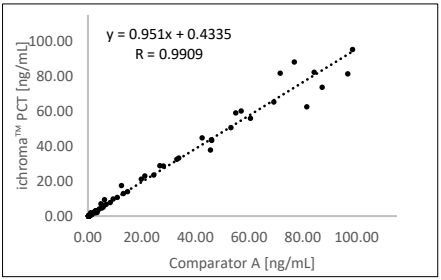
## ■ Accuracy

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

| PCT [ng/mL] | Lot 1 | Lot 2 | Lot 3 | AVG [ng/mL] | Recovery (%) |
|---|---|---|---|---|---|
| 50.00 | 50.67 | 49.23 | 49.87 | 49.92 | 99.84 |
| 20.00 | 20.09 | 20.11 | 19.92 | 20.04 | 100.19 |
| 10.00 | 9.98 | 10.27 | 10.13 | 10.12 | 101.24 |
| 5.00 | 4.97 | 4.97 | 4.98 | 4.98 | 99.53 |
| 2.00 | 2.02 | 1.97 | 1.98 | 1.99 | 99.45 |
| 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 100.07 |

## ■ Comparability

PCT concentration of 100 clinical samples were quantified independently with **ichroma™ PCT (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.



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

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

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