RESPONSE BIOMEDICAL

INSTRUCTIONS FOR USE

C1112-Rev. 1.2

# RAMP® Procalcitonin

**WARNING!**

**For *in vitro* diagnostic use only**

Failure to follow RAMP® test procedures may result in invalid and/or erroneous results. Read the entire Instructions For Use prior to performing test.

## INTENDED USE

The RAMP® Procalcitonin assay is a quantitative immunochromatographic test indicated for use as an *in vitro* diagnostic product used with a RAMP® instrument to measure levels of the prohormone procalcitonin (PCT) in human EDTA anti-coagulated whole blood. The RAMP® Procalcitonin assay is intended to be used in conjunction with other laboratory findings and clinical assessments as an aid in the risk assessment of progression to severe sepsis and septic shock.

IVD


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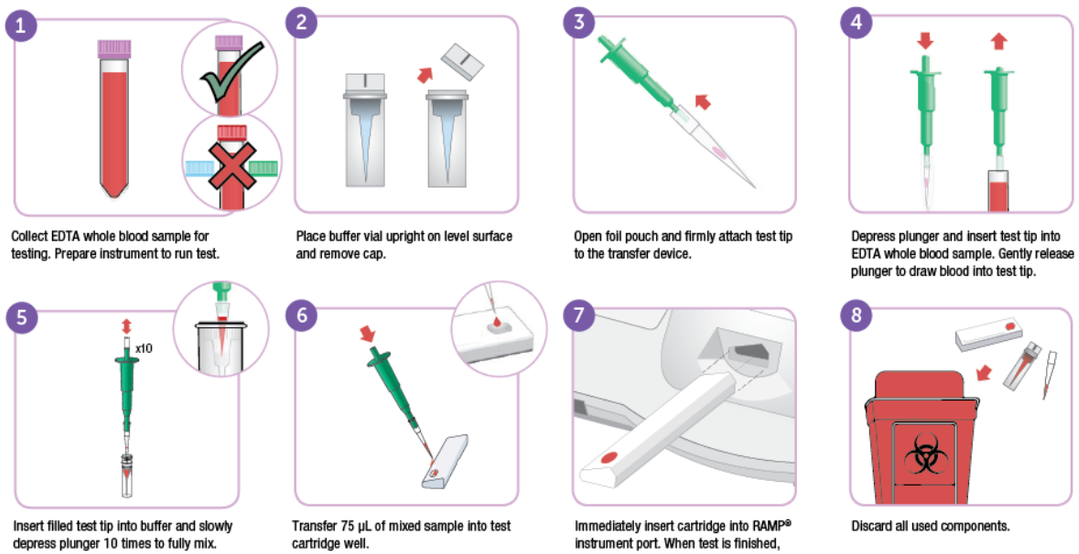
# Running a test




## SUMMARY AND EXPLANATION

In the absence of infection, the prohormone procalcitonin (PCT) is expressed in thyroid C-cells and subsequently undergoes post-translational cleavages to yield mature calcitonin [1]. The circulating plasma concentration of PCT in healthy individuals is very low [2,3]. Conversely, microbial infection triggers a substantial increase in the expression of PCT in non-neuroendocrine cells throughout the body which are unable to perform the necessary post-translational cleavages resulting in increased serum PCT concentrations [1].

Serum concentrations of PCT increase proportionally to the severity of infection, ranging from slightly elevated in infections with minor systemic inflammatory response to very high values in cases of severe sepsis and septic shock [2-4]. Sepsis is a common and frequently fatal condition that is the result of the body's excessive inflammatory response to an infection. Despite advances in critical care medicine, sepsis and septic shock are leading causes of death in intensive care units [4-6].

The speed at which appropriate therapy is provided in sepsis cases impacts patient outcomes [6,7]. The traditional method of sepsis diagnosis however, relies on culturing blood, urine or cerebrospinal fluid which takes upwards of 24 hours, lacks sensitivity and specificity and frequently does not correlate to the manifestation of clinical symptoms [2,3]. Alternatively over 20 years of research suggests PCT is an excellent biochemical marker for sepsis as it is highly specific for bacterial infections and correlates strongly with their extent and severity [4,8-12].

Research suggests that a PCT concentration <0.5 ng/mL can be considered normal while concentrations greater than 2 ng/mL are highly suggestive of severe sepsis [3,13,14]. Other diagnostic and prognostic uses for PCT have been proposed, however there is currently no clearly established role for PCT in the management of conditions such as non-specific complaints, dementia, malaria, tuberculosis, syncope, urinary tract infections and post-cardiac transplant graft failure [2,15].

## TEST PRINCIPLE

The RAMP® Procalcitonin assay is a quantitative immunochromatographic test for the determination of procalcitonin levels in EDTA whole blood. Mixed EDTA whole blood is applied into the sample well of the test cartridge. The red blood cells are retained in the sample pad, and the separated plasma migrates along the strip. Fluorescent-dyed particles coated with anti-procalcitonin antibodies bind to procalcitonin, if present in the sample. As the sample migrates along the strip, procalcitonin-bound particles are captured at the detection zone and excess fluorescent-dyed particles are captured at the control zone.

The RAMP® instrument then measures the amount of fluorescence emitted by the complexes bound at the detection zone and at the control zone. Using a ratio between the two fluorescence values, a quantitative reading is calculated. For further information on the use of the instrument refer to the RAMP® User Manual.

## REAGENTS

- The RAMP® test kit contains all the reagents necessary for the quantification of procalcitonin in EDTA whole blood.
- The sample buffer contains phosphate buffer, animal protein, surfactant, and ProClin®300/ProClin®950 as preservatives.

## STORAGE AND STABILITY

Store at 2 to 8°C (35 to 46°F) up to stated expiry. Do not freeze.

## MATERIALS PROVIDED

Each RAMP® Procalcitonin kit contains enough materials to run 25 tests, including:

- 25 pouches, each containing 1 RAMP® test cartridge and 1 test tip
- 25 RAMP® sample buffer vials
- 1 transfer device for 75 µL
- 1 lot card
- 1 instructions for use (IFU)

## MATERIALS REQUIRED (BUT NOT PROVIDED)

- REF: C1100 RAMP® Reader instrument; or
- REF: C2100 RAMP®200 instrument control module, and
- REF: C3100 RAMP® 200 instrument test module
- Optional Liquid Quality Controls
  - Randox Acusera® Immunoassay Specialty II Quality Control Level 2- Cat No. IAS3118
  - Randox Acusera® Immunoassay Specialty II Quality Control Level 3- Cat No. IAS3119
- Optional accessories such as RAMP® printer and/or barcode scanner
- Specimen collection tubes: EDTA (Venous Whole Blood)

## LOT CARD CALIBRATION

Each RAMP® test kit includes a lot card that is individually packaged in an anti-static pouch. The lot card provides information specific to the kit test cartridge lot, including lot number, expiration date, and standard curve information. For further details on loading lot-specific information, see the RAMP® instrument User Manual. No additional calibration beyond insertion of the lot card is necessary. This operation is required only once per test kit lot.

For each new lot, remove the lot card from its pouch and insert it into the lot card slot on the instrument. Once the lot card has been uploaded, return to its pouch and do not discard. Avoid touching the contacts at the end of the lot card.

## WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use.
- For laboratory use only.
- For use by qualified personnel per local, state, or Federal regulations or accrediting agency requirements.
- Read the entire Instructions for Use (IFU) prior to use. Directions should be read and followed carefully, or invalid or erroneous results may occur.
- Diagnostic and prognostic uses of the RAMP® Procalcitonin assay in non-septic diseases (e.g. non-specific complaints, dementia, malaria, tuberculosis, syncope, urinary tract infections and post-cardiac transplant graft failure) or non-infectious conditions (e.g. burn trauma, extensive surgery, heatstroke and pancreatitis) have not been tested.
- Do not interchange or mix components of different RAMP® tests, lots or components from other manufacturers.
- Do not use the kit or any kit component beyond the stated expiry date.
- Do not use any visibly damaged components.
- Do not insert a cartridge on which blood or any other fluid is spilled, into the instrument.
- Disposal of all waste materials should be in accordance with local guidelines.
- Exercise standard precautions required for handling all laboratory reagents and patient samples.
- The device contains material of animal origin and should be handled as a potential biohazard.
- The sample buffer provided contains ProClin®, a potential skin sensitizer. Avoid spilling or splashing reagents containing ProClin® on skin or clothing. In case of contact, thoroughly flush with water.

## QUALITY CONTROL

Refer to the RAMP® User Manual for full details on quality control operation and troubleshooting.

**SYSTEM QUALITY CONTROL**

The RAMP® instrument has error checking and self-diagnostic functions (Internal Quality Control (IQC)) that assure system integrity. These include algorithms and measurements used to confirm acceptable operator technique, sample handling, and test performance. Frequency of IQC may be programmed at desired intervals.

Valid results are displayed only after all performance requirements have been met.

**PROCEDURAL CONTROLS**

- Each RAMP® assay has built-in controls. Test cartridges have a control zone that is scanned as part of the test protocol to ensure proper sample flow.
- Control limits for each lot of test cartridges are established during the manufacturing process and are incorporated in the test-specific lot parameters. If a control result does not meet specifications, the sample result is not reported and a message is displayed.

**LIQUID QUALITY CONTROL (LQC)**

- It is recommended that quality control materials be run with the RAMP® test in conformance with Federal, state and local requirements for quality control testing.
- While the running of commercial control materials are recommended, it is not a requirement to use, or assure, performance of the RAMP® test unless specified by local regulations or institutional requirements.
- To run a LQC sample, follow the instructions under the "Procedure" section in this IFU. Treat the control as a whole blood sample.

## TEST RUN MESSAGES

When the RAMP® instrument is unable to continue a specific task it will emit an audio alarm and display a message. Refer to the RAMP® User Manual 'Troubleshooting Guide' section for a full description of all messages. If repeated tests give unexpected or inconsistent results, contact Response Biomedical Technical Support for assistance.

## SAMPLE COLLECTION & PREPARATION

- Use ONLY EDTA Whole Blood (Plastic $K_2$EDTA tubes are recommended). Other sample types and anticoagulants have not been evaluated. Do not use samples that have been frozen.

- Avoid short draws and blood samples that show gross hemolysis as these may interfere with the test and cause erroneous results. If this occurs, another blood sample should be obtained and tested.
- Testing must be completed within 2 hours of phlebotomy. However, if this is not possible, the EDTA whole blood can be stored for up to 2 days at 2 to 8°C. If stored, allow blood samples to equilibrate to 18 to 25°C for at least 15 minutes prior to use.

## PROCEDURE

Prior to sample preparation allow all components to come to room temperature (18 to 25°C) for at least 15 minutes.

- Keep the test cartridge and test tip in the sealed foil pouch until ready for use. Once opened, test cartridges and test tips must be used or discarded within 60 minutes.
- The test cartridge, test tip, and buffer vial should be discarded after a single-use. Do not reuse.

1. Prepare RAMP® instrument for test cartridge. Refer to the appropriate RAMP® User Manual for detailed instructions on Starting a Test.
2. Ensure that the EDTA whole blood or sample is well mixed by gentle inversion.
3. Uncap the buffer vial and place upright on a clean, dry level surface, or in a holder.
4. Open a test pouch and remove the test cartridge and tip. Place the test cartridge on a clean, level surface. Firmly attach the test tip to the supplied transfer device.
5. Before inserting the test tip into the sample, fully depress the transfer device plunger.
6. Insert the tip into sample and fully release plunger. The test tip should fill with 75 µL of blood
7. Immediately transfer the filled test tip into the buffer vial close to, but not touching, the bottom.
8. Mix sample slowly by fully pressing and releasing the plunger 10 times; while keeping the tip submerged in the buffer for optimal mixing and to minimize air bubbles.
9. Once mixing is complete, draw 75 µL of sample into the test tip by releasing the plunger one final time and immediately dispense liquid into the sample well of the test cartridge. Small droplets may remain in the tip; this is expected.
10. Immediately insert the test cartridge fully into the instrument and press until firm resistance is felt.
11. The instrument will draw the cartridge in and test development will begin.
12. The instrument will analyze the cartridge and report the result in approximately 15 minutes.
13. Record the result, if required. For additional information on printing and/or uploading results, please refer to the User Manual.
14. Remove the used test cartridge and discard all used test components according to local biohazard procedures. DO NOT reuse.

For additional information on the general operation and troubleshooting of the instrument, please refer to the RAMP® User Manual.

## LIMITATIONS

- Factors such as technical or procedural errors or the presence of substances in blood specimens other than those that have been evaluated (see Interference section of this IFU), may interfere with the RAMP® test and cause erroneous results.
- As with any immunoassay, patient specimens may contain heterophilic antibodies that may result in either falsely elevated or depressed results. Presence of these antibodies may be due to elevated levels of rheumatoid factor, treatment with mouse monoclonal antibodies for diagnostic or therapeutic purposes, or other undetermined factors. The RAMP® test has been formulated to reduce the effects of heterophilic antibodies, but complete elimination of heterophilic interference from all samples cannot be guaranteed.

## EXPECTED VALUES

The RAMP® Procalcitonin Expected Values (reference range) study was conducted at one clinical site and included 125 apparently healthy individuals (59 women, 66 men). The normal range for the RAMP® Procalcitonin assay (determined as the 95th percentile of these results) includes values ≤0.36 ng/mL. No statistically significant bias due to gender, age or ethnicity was observed in this study. Each laboratory should investigate the transferability of the expected values to its own patient population and, if necessary, determine its own reference range.

## PERFORMANCE CHARACTERISTICS

**MEASUREMENT RANGE**

0.20 to 200.0 ng/mL.

PCT levels in excess of 200 ng/mL are reported as greater than (>) 200.0 ng/mL, values below 0.20 ng/mL are reported as less than (<) 0.20 ng/mL.

**DETECTION LIMIT**

To determine the Limit of Blank (LoB), 60 replicates of a blank material were tested. The LoB, estimated as the non-parametric determination of the 95th percentile of all 60 replicates, was determined to be < 0.20 ng/mL.

To determine the Limit of Detection (LoD), 15 replicates each of 4 low level EDTA whole blood samples were tested over 4 runs. The LoD was calculated to be 0.36 ng/mL.

**PRECISION**

Repeatability and precision estimates were obtained using three levels of frozen control materials (spiked pooled plasma samples) and three lots of RAMP® Procalcitonin assays, tested in duplicate over 20 days, two runs per day for a total of 80 replicates per level. The precision of the RAMP® Procalcitonin test is shown in the following table.

| Mean Value (ng/mL) | Repeatability | Within-Laboratory Precision |
|---|---|---|
| | %CV | %CV |
| 0.58 | 16.0 – 18.7 | 15.8 – 19.3 |
| 2.72 | 8.0 – 9.0 | 7.7 – 9.3 |
| 92.7 | 6.6 – 8.5 | 7.2 – 9.4 |

Precision estimates for whole blood samples were obtained using spiked EDTA whole blood and one lot of RAMP® Procalcitonin assays. Whole blood samples were evaluated at three levels across the reportable range of the RAMP® Procalcitonin assay and were each tested in replicates of 10 in a single run. The precision performance of the RAMP® Procalcitonin assay was found to be 14.1, 6.8 and 8.2 %CV at 0.75, 3.00 and 103.2 ng/mL respectively.

**ANALYTICAL SPECIFICITY**

No cross-reactivity was observed for calcitonin (up to 5 ng/mL), katacalcin (up to 10 ng/mL) or α-CGRP and β-CGRP (up to 30 ng/mL).

**LINEARITY**

A spiked EDTA whole blood sample (250 ng/mL) was serially diluted ten times using normal EDTA blood. The linearity was determined by testing three (3) replicates of each concentration and baseline. Linear regression analysis of actual PCT versus expected PCT concentration resulted in an R > 0.99, a slope with 95% CI of 0.93 to 1.02.

**HOOK EFFECT**

No high dose hook effect was observed for the RAMP® Procalcitonin assay up to the highest level tested (~2,000 ng/mL).

**INTERFERENCE**

None of the following factors has been found to influence the RAMP® Procalcitonin assay

- Hemolysis (hemoglobin to 500 mg/dL)
- Bilirubinemia (conjugate bilirubin to 40 mg/dL; unconjugated bilirubin to 40 mg/dL)
- Hyperlipidemia (triglycerides to 3260 mg/dL)
- Human serum albumin (to 2.4 g/dL)

However it is recommended not to use samples that appear to be clearly hemolyzed, lipemic or icteric and to collect a new sample if possible.

11 commonly used pharmaceutical compounds were evaluated for potential interference in the RAMP® Procalcitonin assay. Compounds were evaluated by spiking different concentrations of each individual potential interferent into EDTA whole blood with procalcitonin added to provide levels of ~0.50 and ~10 ng/mL. The pharmaceutical compounds listed in the following table were tested at the indicated concentration and found to have no interference with the RAMP® Procalcitonin assay.

| Tested Compound | Tested Concentration |
|---|---|
| Acetaminophen | 180 mg/dL |
| Acetylsalicylic Acid | 240 mg/dL |
| Ibuprofen | 144 mg/dL |
| Cefotaxime | 200 mg/dL |
| Dobutamine | 25 µg/mL |
| Dopamine | 30 mg/dL |
| Heparin Sodium Salt | 28.8 U/mL |
| Noradrenalin | 5 µg/mL |
| Vancomycin | 1.8 mg/mL |
| Imipenem | 100 mg/dL |
| Furosemide | 40 mg/dL |

## REFERENCES


**[1].** Muller et al. 2001. *J Clin Endocrinol Metab.* **86**: 396-404
**[2].** Jin et al. 2010. *Lab Med*. **41**(3):173-7
**[3].** McGee et al. 2009. *Clin Lab News*. **35**(7)
**[4].** Muller et al. 2000. *Crit Care Med.* **28(4)**: 977-983
**[5].** Angus et al. 2001. *Crit Care Med*. **29**(7): 1303-10
**[6].** Clec'h et al. 2004. *Crit Care Med.* **32(5) :** 1166-1169
**[7].** Dellinger et al. 2013. *Crit Care Med.* **41(2) :** 580-637
**[8].** Assicot et al. 1993. *Lancet* **341**: 515-518
**[9].** Schuetz et al. 2011. *BMC Medicine*. **9**:107-15
**[10].** Christ-Crain et al. 2004. *Lancet* **363**: 600-607
**[11].** Uzzan et al. 2006. *Crit Care Med.* **34**: 1996-2003
**[12].** Kutz et al. 2015. *Critical Care* **19**: 74
**[13].** Becker et al. 2008. *Crit Care Med.* **36(3):** 941-952
**[14].** Meisner 2014. *Ann Lab Med*. **34(4):** 263-273
**[15].** Schneider et al. 2007. *Pathology* **39**(4): 383-390


## GLOSSARY OF SYMBOLS

| | | |
|---|---|---|
| EC REP<br>**Authorized Representative in European Community** | LOT<br>**Batch Code** | REF<br>**Catalogue Number** |
| **Caution** | CE<br>**CE Mark** | **Consult Instructions for Use** |
| Σ<br>**Contains Sufficient for <n>Tests** | **Do Not Reuse** | IVD<br>**In vitro Diagnostic Medical Device** |
| **Harmful, Irritant** | **Manufacturer** | **Temperature Limit** |
| **Use-by Date** | | |

## PRODUCT SUPPORT / ASSISTANCE

If you have any questions regarding the use of this product please contact Response Biomedical Corp. Technical Support:

- Within US or Canada (+1.866.525.7267)
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- By email at techsupport@responsebio.com

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