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| **Procalcitonin** |
| **Purpose** | This procedure provides instructions for performing ARCHITECT B∙R∙A∙H∙M∙S PROCLCITONIN (PCT) on the Abbott Architect i1000SR |
| **Policy Statements** | This procedure applies to all personnel responsible for performing testing on the Abbott Architect i1000SR |
| **Principle** | The ARCHITECT B∙R∙A∙H∙M∙S PCT assay is a Chemiluminescent Microparticle immunoassay (CMIA) for the quantitative determination of Procalcitonin (PCT) in human serum and plasma. The ARCHITECT B∙R∙A∙H∙M∙S PCT assay is indicated to be used in conjunction with clinical evaluation and other laboratory findings to aid in:The ARCHITECT B∙R∙A∙H∙M∙S PCT assay is a two-step immunoassay for the quantitative determination of PCT in human serum and plasma (lithium heparin and K2EDTA) using CMIA technology with flexible assay protocols, referred to as Chemiflex.1. Sample and anti-PCT coated paramagnetic microparticles are combined. The PCT present in the sample binds to the anti-PCT coated microparticles.2. After washing, anti-PCT acridinium-labeled conjugate is added to create a reaction mixture.3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of PCT in the sample and the RLUs detected by the ARCHITECTiSystem optics.For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3. |
| **Clinical Significance** | Sepsis is a daily challenge in the hospital setting. Today various therapeutic strategies are known to improve survival in patients with sepsis. Early assessment is important for determination of the appropriate treatment.PCT is a 116 amino acid protein prohormone of calcitonin (CT). Under normal metabolic conditions, hormonally active CT is produced and secreted in the C-cells of the thyroid gland after specific intracellular proteolytic activity. In healthy individuals, the intact PCT is not secreted from the thyroid and levels in the blood are very low.Response to inflammatory stimuli, including bacterial infections, inducesan increased expression of the CALC-I gene with production and secretion of intact PCT from all parenchymal tissues and differentiated cell types throughout the body.In healthy people, plasma PCT concentrations are found to be below 0.1 ng/mL.7 Depending on the clinical background, a PCT concentration above 0.1 ng/mL can indicate clinically relevant bacterial infection, requiring antibiotic treatment.8 PCT levels rise rapidly (within 6–12 hours) after an infectious bacterial insult with systemic consequences. The magnitude of the increase in PCT concentration correlates with the severity of the bacterial infection. At a PCT concentration > 0.5 ng/mL, a patient should be considered at risk of developing severe sepsis or septic shock.9, 10 On the other hand, the relief of the septic infection is accompanied by a decrease in the PCT concentration, which returns to normal with a half-life of 24 hours11, 12 (i.e., the continuous decline of PCT is indicative of effective source control measures and has been implicated in the safe de-escalation of antibiotic therapy). By evaluating PCT concentrations, the physician may use the findings to aid in the risk assessment of critically ill patients for progression to severe sepsis and septic shock. In addition, the change of PCT levels over time offers information about the risk of mortality after diagnosis of severe sepsis or septic shock. |
| **Instrument** | **PRIMARY METHOD: Abbott Architect i1000SR**Backup Method:Mayo Medical Laboratories |
| **Test Code** | **PRIMARY METHOD: PROCA** Backup Method:PROCL (Mayo Medical Laboratories) |
| **Reagent** |

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| ***Product Description*** | ***Product Code*** | ***Stability*** |
| Procalcitonin Reagent kit | 06P2227 | **Store at:** 2 – 8 °C**Unopened/Opened:** Manufacturer expiration date.**On-board:** 25 Days |
| Procalcitonin Calibrator | 06P2201 | **Store at:**  -10°C. Thaw only three times, then discard.**To Use**: See calibration section. **Unopened**: Manufacturer expiration date.**Opened**: Store at -10 °C and store until Manufacturer expiration date. |
| Pre-Trigger Solution | 06E23-65 | Refer to Supply Status on Analyzer |
| Trigger Solution | 06C55-60 | Refer to Supply Status on Analyzer |
| Wash Buffer | 06C54-58 | Refer to Supply Status on Analyzer |
| Reaction Vessels  | 07C15 (-02 or -03) | N/A |
| Liquichek Specialty Immunoassay Controls (LQSI) | Level 1 - 364Level 2 - 365Level 3 - 366 | **Unopened storage:** ≤-20°C**To Use:** Thaw at Room Temperature, not more than 1 hour.Do not allow to stand at room temperature longer than 20 minutes.**Once Opened, Store:** 2-8°C**Stability:** 30 Days |

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| **Sample** | **Preferred Container:** SST (gold, marble)Also Acceptable:Lithium Heparin (green top), Red no gel, or K2EDTA (purple top)***(The same sample matrix/tube type should be used for patients testing throughout admission due to variations in measurement between sample tube types.)*****Draw Volume:** 0.5 mL -1.0 mL blood.**Processed Volume:**  Preferred: 0.3 mL plasma, serum or EDTA plasma Minimum: 0.15 mL plasma, serum or EDTA plasma  Note: Minimum volume does not permit repeat analysis**Stability:** 24 hours at room temperature 48 hour in 2-8° refrigerator 15 days in -20° freezer**Processing**:Centrifuge specimen within one hour of collection. Remove serum/plasma within 8 hours into a screw-capped round bottom plastic vial (send outs tube). For minimum volume, use the ARCHITECT Sample Cups on top of the sendouts tube and label the ARCHITECT Sample cup with a foot label. For PTHB: Calcium should be performed on a separate aliquot, and placed into a Vista sample cup for analysis on the Vista. **Rejection:*** Specimens not removed from red cells within eight hours of collection.
* Mislabeled or unlabeled specimen
* Grossly hemolyzed specimens
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| **Special Safety Precautions**  | Follow Children’s Laboratory Safety guidelines when handling patient samples and reagents. Safety data sheets (MSDS/SDS) available on [Children’s intranet](http://starnet.childrenshc.org/emergency-and-safety/) |
| **Calibration**  |

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| Analytical Measuring Range: | 0.02 – 100.00 ng/mL |
| Reference Material: | ARCHITECT B.R.A.H.M.S PCT Calibrators |
| Suggested Calibration Levels | A = 0.00 ng/mLB = 0.10 ng/mLC = 0.50 ng/mLD = 12.10 ng/mLE = 20.50 ng/mLF = 100.00 ng/mL |
| Verification Scheme: | n=6 |
| Verification Frequency: | * For each new lot of reagent
* After major maintenance or service, if indicated by quality control results
* As indicated in laboratory quality control procedures
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**Calibrator****To Use:** Thaw calibrators at room temperature until completely thawed (30-60 minutes).Prior to use, mix by gentle inversion (10 times). Avoid more than **3 freeze/thaw cycles**. Discard after thawed for the 3rd time.**Unopened:** Manufacturer expiration date.**Opened**: Store at -10 °C and store until Manufacture expiration date• Calibration Range: 0.02 - 100.00 ng/mLFor detailed information on how to perform an assay calibration, refer to the ARCHITECT System operations Manual, Section 6. |
| **AMR** | **AMR:** 0.02 – 100.00 ng/mLVerification of AMR is accomplished with each calibration at an interval no longer than every 6 months.  |
| **Quality Control** | Bio-Rad Lyphochek Specialty Immunoassay Levels 1, 2 and 3**Frequency:** Three levels each day of use.**Stability:** 30 Day at -20 to -70°C.**Preparation**: Reconstitute with exactly 2.0 mL of DI water. Let vials sit for 15 minutes and gently swirl to ensure homogeneity. Pipette 0.5 mL into 4 sendout aliquot tubes with screw caps. Label the aliquots with LYSI1, LYSI2, or LYSI3, the lot number, date made, initials of person making the controls, and the expiration date. Freeze in the Special Chemistry Freezer in the designated LYSI QC rack. Thaw one aliquot for each level each day of use.**Sunquest Control names:** Level 1 = C-LYSI1, Level 2 = C-LYSI2, Level 3= C-LYSI3**Acceptable ranges:** * Ranges are current in Sunquest and the instrument. Refer to the Quality Control in Chemistry procedure for QC exception codes.
* If a control value is outside the confidence interval, the determination must be repeated. If the repeat determination confirms the deviation, a new reference curve should be established.
* Do not release patient results until the cause of deviation has been identified and corrected
* When a new lot of assayed control is received, validate the manufacturer’s insert range by running the new lot in parallel with the current lot, and confirming that the results obtained are within the stated range
* When a new lot of unassayed control is received, verify new ranges by running the new lot in parallel with the current lot 30 times, and calculate a new range using the method mean ± 3 SD. Ranges are current in Sunquest and the instrument. Refer to the Quality Control Procedure for QC exception codes
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| **Dilutions** | Results flagged > 100.00 ng/mL:The system performs a 1:10 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.  |
| **Limitations****Limitations cont.** | **Technical range** 0.02 – 1000.00 ng/mLThe same sample matrix/tube type should be used for patients testing throughout admission due to variations in measurement.ARCHITECT B∙R∙A∙H∙M∙S PCT results should not be used interchangeably with other methods for PCT determination for monitoring patients. Increased PCT levels may not always be related to systemic bacterial infection. There are a few situations where PCT levels may be elevated by non-bacterial causes. These include, but are not limited to, the following:* Neonates at < 48 hours of life (physiological elevation
* First days after a major trauma, major surgical intervention, severe burns, or treatment with OKT3 (muromonab-CD3) antibodies and other drugs stimulating the release of proinflammatory cytokines
* Patients with invasive fungal infections
* Patients with acute attacks of Plasmodium falciparum malaria
* Patients with prolonged or severe cardiogenic shock, prolonged severe organ perfusion anomalies, small cell lung cancer, severe liver cirrhosis and acute or chronic viral hepatitis23, or medullary C-cell carcinoma of the thyroid

Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as ARCHITECT B∙R∙A∙H∙M∙S PCT that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.Heterothallic antibodies in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed. Additional information may be required for diagnosis. Rheumatoid factor (RF) in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays. |
| **Reference Intervals** |

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| AGE | Range (ng/mL) |
| Newborns |
| 0-6 hours | < or = 2 |
| 6-12 hours | < or = 8 |
| 12-18 hours | < or = 15 |
| 18-30 hours | < or = 21 |
| 30-36 hours | < or = 15 |
| 36-42 hours | < or = 8 |
| 42-48 hours | < or = 2 |
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| Infants > 48 hours – Adult | < or = 1 |

**PCT <0.1 ng/mL** No systemic inflammatory response. **PCT < 0.5 ng/mL** Minor or no significant systemic inflammatory response. Local inflammation and local infection are possible. **PCT ≥ 0.5 to < 2 ng/mL** Moderate risk for progression to severe systemic infection (Severe Sepsis). Patient should be closely monitored clinically, and retested if indicated. Note: Increased PCT levels are not always related to infection. Increases may also be seen in: * First days after major trauma, major surgery, severe burns, treatment with drugs that stimulate release of pro-inflammatory cytokines.
* Patients with invasive fungal infections and acute infection with plasmodium falciparum malaria.
* Prolonged or severe cardiogenic shock, prolonged severe organ perfusion anomalies, small cell lung cancer, and medullary C-cell carcinoma of the thyroid.

**PCT ≥ 2 and < 10 ng/mL** Severe systemic inflammatory response, most likely due to sepsis, unless other causes are known. High risk for progression to severe systemic infection. **PCT ≥ 10 ng/mL** HIGH LIKELIHOOD OF SEVERE SEPSIS OR SEPTIC SHOCK. Procalcitonin levels >10ng/ml are almost exclusively due to severe bacterial sepsis or septic shock.  |
| **Result Reporting** | * Results between 0.02-10.00 ng/mL without error messages are released automatically
* If there is not enough sample to repeat append the code “-UNQ” (Unable to Quantitate Further) to the result
* Result below 0.02 ng/mL report as <0.02
* Results above 1000.00 ng/mL report as >1000.00
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| **References** | Chiesa, C., et al (1998). Reliability of procalcitonin concentration for the diagnosis of sepsis in critically ill neonates. Clinical Infectious Disease, 26, 664-72The Children’s Hospital, Aurora, CO. PCT result comments 10/2009Mayo Medical Laboratories, Test cone 83169: Procalcitonin – Clinical and Interpretive GuildARCHITECT B∙R∙A∙H∙M∙S PCT package insert. Abbott laboratories. Abbott Park, IL June 2017 G1-0601/R01 |
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| **Historical Record** | **Version** | **Written/Revised by:** | **Effective Date:** | **Summary of Revisions** |
| 1 | Stephen Gripentrog/Erin Bartos | 4/24/2018 | Initial Version |