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| **Procalcitonin** |
| **Purpose** | This procedure provides instructions for performing ARCHITECT B∙R∙A∙H∙M∙S PROCLCITONIN (PCT) on the Minneapolis Abbott Architect i1000SR and St. Paul DiaSorin LIAISON® XL. |
| **Policy Statements** | This procedure applies to all personnel responsible for performing testing on the Minneapolis’ Abbott Architect i1000SR and St. Paul’s DiaSorin LIAISON® XL. |
| **Principle** | **Minneapolis ABBOTT 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 ARCHITECT iSystem optics.For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.**St. Paul LIAISON® BRAHMS PCT® II GEN** assay uses chemiluminescence immunoassay (CLIA) technology for the in vitro quantitative determination of procalcitonin in human serum and lithium heparin plasma specimens. Used in conjunction with other laboratory findings and clinical assessments, LIAISON® BRAHMS PCT® II GEN intended for use as follows:• To aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock• To aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with severe sepsis or septicshock in the ICU or when obtained in the emergency department or other medical wards prior to ICU admission, using a change in PCT level over time• To aid in decision making on antibiotic therapy for patients with suspected or confirmed lower respiratory tract infections (LRTI) defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD) – in an inpatient setting or an emergency department• To aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsisThe method for the quantitative determination of PCT is a sandwich chemiluminescence immunoassay. A specific monoclonal antibody is coated on the magnetic particles (solid phase); another monoclonal antibody (specific for a different epitope of the procalcitonin molecule) is linked to an isoluminol derivative (isoluminol-antibody conjugate).During the first incubation, PCT present in calibrators, samples or controls binds to the antibody conjugate. Then the solid Phase is added to the reaction. A sandwich is formed only in the presence of PCT molecules that bridge both antibodies. After the second incubation, the unbound material is removed with a wash cycle.Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of PCT concentration present in calibrators, samples or controls. |
| **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, induces an 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** | **Minneapolis: Abbott Architect i1000SR****St. Paul: DiaSorin LIAISON® XL**Backup Method:Mayo Medical Laboratories |
| **Test Code** | **Minneapolis/St. Paul: PROCA** Backup Method:PROCL (Mayo Medical Laboratories) |
| **Reagent** |

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| ***Product Description*** | ***Product Code*** | ***Stability*** |
| Abbott Architect Procalcitonin Reagent kit | 06P2227 | **Store at:** 2 – 8 °C**Unopened/Opened:** Manufacturer expiration date.**On-board:** 25 Days |
| Abbott Architect 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. |
| Abbott Architect Pre-Trigger Solution | 06E23-65 | Refer to Supply Status on Analyzer |
| Abbott Architect Trigger Solution | 06C55-60 | Refer to Supply Status on Analyzer |
| Abbott Architect Wash Buffer | 06C54-58 | Refer to Supply Status on Analyzer |
| Abbott Architect Reaction Vessels  | 07C15 (-02 or -03) | N/A |
| Bio-Rad 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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| **LIAISON® BRAHMS PCT® II GEN** | **REF 318090** | **Store at:** 2 – 8 °C**Unopened/Opened:** Manufacturer expiration date.**On-board:** 12 weeks |
| **See CH 5.551 DiaSorin Liaison XL Operating Procedure for other consumables** |

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| **Sample** | **Minneapolis Abbott Architect i1000SR****Preferred Container:** SST (gold, marble)Also Acceptable:Lithium Heparin (green top), Red no gel***(The same sample matrix/tube type and campus/analyzer should be used for patients testing throughout admission due to variations in measurement between sample tube types and instrumentation.)*****Draw Volume:** 0.5 mL -1.0 mL blood.**Processed Volume:**  Preferred: 0.3 mL plasma, serum  Minimum: 0.15 mL plasma, serum  Note: Minimum volume does not permit repeat analysis**Stability:**24 hour in 2-8° refrigerator. Freeze if not tested within 24 hours.15 days in -20° freezer or 5 freeze thaw cycles\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**St. Paul DiaSorin LIAISON® XL** **Preferred Container:** SST (gold, marble)Also Acceptable:Lithium Heparin (green top), Red no gel***(The same sample matrix/tube type and campus/analyzer should be used for patients testing throughout admission due to variations in measurement between sample tube types and instrumentation.)*****Preferred Draw Volume:** 1.8 mL**Minimum Draw Volume:** 0.9 mL**Minimum Processed Volume:** 0.3 mL**Stability:** 24 hour in 2-8° refrigerator. Freeze if not tested within 24 hours.15 days in -20° freezer or 5 freeze thaw cycles**Processing**:Centrifuge specimen within one hour of collection. **Minneapolis** Remove serum/plasma within 2 hours into a screw-capped round bottom plastic vial (send outs tube). For minimum volume, use the ARCHITECT Sample Cups on top of a sendouts tube and label the ARCHITECT Sample cup with a foot label. **St. Paul** Remove serum/plasma within 2 hours into a screw-capped micro container for Liaison XL if minimum volume. If adequate volume, the primary tube may be used. See Operator’s manual for details.**Rejection:*** Specimens not removed from red cells within 2 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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|  | **Minneapolis Abbott Architect i1000SR** | **St. Paul DiaSorin LIAISON® XL** |
| Analytical Measuring Range: | 0.02 – 100.00 ng/mL | 0.02 – 100.00 ng/mL |
| Reference Material: | ARCHITECT B.R.A.H.M.S PCT Calibrators | LIAISON® BRAHMS PCT® II GEN 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 | A= Lot specific B= Lot specific |
| Verification Scheme: | n=6 | N/A |
| 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
 | * A new lot of Reagent/Integral is used.
* A new lot of Starter Kit is used.
* The previous calibration was performed more than 8 weeks before.
* The analyzer has been serviced.
* Quality controls lie outside the expected ranges.
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**Minneapolis Abbott Architect i1000SR****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 manufacturer 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.**St. Paul DiaSorin LIAISON® XL**LIAISON® BRAHMS PCT® II GEN calibrators are supplied lyophilized. They are included in the integral kit. Calibrators are kit lot specific and must not be interchanged with a reagent integral from a different lot.* Reconstitute the vial contents with 1.3 mL deionized or distilled water.
* Allow the vials to stand for 15 minutes at 18°-25°C to achieve complete dissolution.
* Mix vials thoroughly by gentle inversion; avoid foaming and bubbles.

Recalibration is mandatory whenever at least one of the following conditions occurs:Refer to the relevant analyzer [operator's manual](https://starnet.childrenshc.org/References/labsop/chem/operator/diasorin-liaison-xl-operation-manual.pdf) or [LIAISON® Quick Guide](https://starnet.childrenshc.org/References/labsop/chem/operator/diasorin-xl-quickguide.pdf) for calibration instructions.LIAISON® XL Analyzer: Calibrator values are stored in the Radio Frequency IDentification transponder (RFID Tag) and are lot specific.**Stability:****Lyophilized:** Stable at 2°-8°C until the expiry date. Upon receipt, the calibrators must be stored at 2°-8°C in an upright position to prevent adherence of the lyophilized pellet to the vial cap.**Reconstituted**: after each use, calibrators must be stored deep-frozen (–20°C or below). Mix thawed calibrators well before testing. The results show no significant differences when calibrators go through 3 freeze-thaw cycles.**Warning: Do not leave the reconstituted calibrators at room temperature longer than the time required to process them on the analyzer. After use, stop the vials promptly and store them at –20°C or below, in an upright position**LIAISON® XL calibrator values are stored in the Radio Frequency IDentification transponder (RFID Tag). |
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| **AMR** | **Minneapolis Abbott Architect i1000SR****AMR:** 0.02 – 100.00 ng/mLVerification of AMR is accomplished with each calibration at an interval no longer than every 6 months. **St. Paul DiaSorin LIAISON® XL**AMR 0.02-100 ng/Ml**LIAISON® BRAHMS PCT® II GEN Verifiers PN** **318092 at intervals no longer than 6 months, per CAP regulations.**Reconstitute the vial contents with 1.1 mL of the Diluent provided in the package.– Allow the vials to stand for 10-15 minutes at 18°-25°C to achieve complete dissolution.– Mix vials thoroughly by gentle inversion; avoid foaming.– Each calibration verifier solution allows at least 8 tests to be performed.– The minimum volume required is 250 μL (100 μL control + 150 μL dead volume).Each verifier must be run a minimum of 3 replicates. Values should be entered into EP Evaluator and will be reviewed by the Technical Specialist of chemistry for acceptability. |
| **Quality Control** | **Minneapolis Abbott Architect i1000SR*** Bio-Rad Lyphochek Specialty Immunoassay Levels 1, 2 and 3
* **Frequency:** Three levels each day of use.
* **Stability:** 3 days at 2°-8°C
* **Preparation**: Reconstitute with exactly 2.0 mL of DI water. Let vials sit for 15 minutes and gently swirl to ensure homogeneity.

**St. Paul DiaSorin LIAISON® XL*** **LIAISON® Control BRAHMS PCT® II GEN**
* **Frequency:** two levels each day of use.
* **PREPARATION OF REAGENTS**
* Reconstitute the vial contents with 1.1 mL of the Diluent provided in the package.
* Allow the vials to stand for 10-15 minutes at 18°-25°C to achieve complete dissolution.
* Mix vials thoroughly by gentle inversion; avoid foaming.
* Each control vial allows at least 8 tests to be performed.
* The minimum volume required is 250 μL (100 μL control + 150 μL dead volume).
* **Lyophilized**: Stable at 2°-8°C until the expiry date. Upon receipt, the controls must be stored at 2°-8°C in an upright position to prevent adherence of the lyophilized pellet to the vial cap.
* **Reconstituted**: After reconstitution, controls are stable for 8 weeks at –20°C. Mix thawed controls well before testing. After each use, controls have to be stored deep-frozen (–20°C or below). The results show no significant differences when controls go through seven freeze-thaw cycles

**Acceptable ranges:** * Non-Bio-Rad controls will utilize manufacturer ranges and 2 SD Westgard rules.
* New lots of Bio-Rad controls should be run for 20 days in parallel with the current lot whenever possible prior to switching to the new lot.
* Refer to the [Westgard Rules in Chemistry procedure](https://starnet.childrenshc.org/References/labsop/chem/quality/ch-2.18-westgard-rules-in-chemistry.pdf) for current Westgard rules in place for each analyte.
* **Acceptable ranges are current in Unity Real Time only.** Quality Control results must be rejected in Sunquest when the results cross the interface.
* In the event of a QC failure, refer to the [Unity Real Time QC Review, General User](https://starnet.childrenshc.org/References/labsop/chem/quality/ch-2.17-unity-real-time-qc-review-general-user.pdf) and navigate to the QC Troubleshooting section.

Do not load or release patients until QC is acceptable in Unity Real Time.  |
| **Dilutions** | **Minneapolis Abbott Architect i1000SR*** 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. **Technical range** 0.02 – 1000.00 ng/mL**St. Paul DiaSorin LIAISON® XL*** The highest reportable value without dilution is 100 ng/mL.
* Samples with PCT levels above the assay range may be manually diluted with the Diluent included in LIAISON® Control BRAHMS PCT® II GEN kit ([REF] 318091) and programmed on the analyzer.
* Maximum dilution is 1:2.
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| **Limitations** | The same sample matrix/tube type and instrumentation should be used for patients testing throughout admission due to variations in measurement. Per manufacturers: 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** | **Minneapolis/St. Paul**

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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** | **Minneapolis Abbott Architect i1000SR Method Code: AI1*** 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

**St. Paul DiaSorin LIAISON® XL Method Code: XL*** 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 200.00 ng/mL report as >200.00
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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/R01LIAISON® BRAHMS PCT® II GEN ([REF] 318090) Directions for Use, DiaSorin, Inc, Stillwater, MN 55082, March 2018LIAISON® Control BRAHMS PCT® II GEN ([REF] 318091) Directions for Use, DiaSorin, Inc, Stillwater, MN 55082, March 2018LIAISON® BRAHMS PCT® II GEN Verifiers ([REF] 318092)Directions for Use, DiaSorin, Inc, Stillwater, MN 55082, March 2018 |
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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 |
|  | 2 | Stephen Gripentrog, Erin Bartos | August 13, 2019 | Added DiaSorin LIAISON® XL for St. Paul. Updated storage conditions to match.  |