| **Creatinine on Abbott** | | | | |
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| **Purpose** | This procedure provides instructions for ENZYMATIC CREATININE ON ABBOTT INSTRUMENTATION. The enzymatic creatinine method is an *in vitro* diagnostic test for the quantitative measurement of creatinine in human serum and plasma on the Abbott Architect c4000 or Abbott Alinity c automated chemistry analyzers. | | | |
| **Policy Statements** | This procedure applies to all personnel responsible for operating the Abbott Architect c4000 or Abbott Alinity c at Children’s Minnesota Laboratory. This assay is also referred to as CrEnz. | | | |
| **Principle** | Creatinine in the sample is hydrolyzed by creatininase to creatine. Creatine is in turn hydrolyzed by creatinase to sarcosine and urea. Sarcosine from this reaction is oxidized by sarcosine oxidase to glycine and formaldehyde, with the concomitant production of hydrogen peroxide. The hydrogen peroxide reacts with 4-aminoantipyrine and ESPMT (N-ethyl-N-sulfopropyl-m-toluidine) in the presence of peroxidase to yield a quinoneimine dye. The resulting change in absorbance at 548 nm is proportional to the creatinine concentration in the sample. This enzymatic method is sensitive and specific for creatinine and is not affected by endogenous substances, such as ketoacids,  cephalosporins, and bilirubin that interfere with the Jaffe method. | | | |
| **Clinical Significance** | Creatine is involved in energy storage in skeletal muscle and other tissues and is synthesized in the liver from amino acids and transported in the blood to muscle. There the enzyme CPK catalyzes the reaction of creatine with ATP to form phosphocreatine. Creatinine is a catabolic end product. Creatinine is excreted from the body via the urine by glomerular filtration and is formed at a nearly constant rate proportional to the body muscle mass. Reduced renal function results in an increased serum creatinine concentration. Measurement of serum creatinine is used to diagnose and monitor acute and chronic renal disease, estimate glomerular filtration rate (GFR), or assess the status of renal dialysis patients. | | | |
| **Analyzer** | **Minneapolis: Abbott Alinity c (Sunquest method code: MALIC)**  **St. Paul: Abbott Architect c4000 (Sunquest method code: ARCH4)** | | | |
| **Sunquest Test Codes** | CREA: Creatinine in serum and plasma | | | |
| **Specimen** | Sample:  Plasma (lithium heparin with or without gel) preferred. Sodium heparin plasma or serum (with or without gel) also acceptable. Refer to specimen collection procedures.  **Minimum sample volume:** 200 µL preferred, 150 µL minimum  **Stability when separated from cells/gel:** RT / 7 days, 2-8 °C / 7 days, < -20°C / 90 days  **Rejection criteria:** Unlabeled tube, sample type other than serum or heparinized plasma. See Interferences section for how to handle lipemic samples.  **Preparation:**   1. Whole blood specimens should be centrifuged following complete clot formation, according to Specimen Processing procedures prior to analysis. 2. Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of two hours from the time of collection. 3. Specimens should be free of particulate matter. 4. Transfer serum or plasma to a properly labeled pilot tube or aliquot cup. Architect and Alinity systems utilize a specimen level detect mechanism, so special racks specific to tube-type are not required. 5. Minimum labeling includes sample accession ID, and/ or patient name, medical record number, collection date and time. | | | |
| **Reagents** | **Alinity c and Architect c4000:**  **Reagent Handling**  Upon receipt, place reagent cartridges in an upright position for 8 hours before use to allow bubbles that may have formed to dissipate.  If a reagent cartridge is dropped, place in an upright position for 8 hours before use to allow bubbles that may have formed to dissipate.  Reagents are susceptible to the formation of foam and bubbles. Bubbles may interfere with the detection of the reagent level in the cartridge and cause insufficient reagent aspiration that may adversely affect results. Use a pipette to remove all bubbles prior to loading on the Alinity or Architect system.   * Do not use reagents beyond the expiration date. * Do not pool reagents within a kit or between kits. * Do not use components from one lot with components from another lot.   **Alinity c:**  Reagents may be stored on or off the system. If removed from the system, store reagents with new replacement caps in an upright position at 15 - 30 °C. For reagents stored off the system, it is recommended that they be stored in their original trays or boxes to ensure they remain upright.  **Alinity c:**   |  |  |  | | --- | --- | --- | | ***Product Description*** | ***Product Code*** | ***Stability*** | | Abbott Alinity c Creatinine Reagent  CHC# 32625 | 08P01-20 | **Store at:** 2 – 8°C  **Unopened:** Manufacturer’s printed expiration date  **On-board: 30 days**  **Opened, off the analyzer (with clean caps):** Manufacturer’s printed expiration date. (Reagents may be stored on or off the system. The system tracks time onboard.) | | Abbott Alinity c Clinical Chemistry Calibrator  CHC# 32633 | 08P65-03 | **Store at:** 2 – 8 °C  **Unopened:** Manufacturer’s printed expiration date  Reconstitute with exactly 3.0 mL of DI water. Swirl gently. Let stand at room temp for 30 minutes. Invert gently prior to sampling. Use small portion for calibration, then label 5 aliquots, each with 0.5 mL of calibrator, with the lot number, expiration date, and date reconstituted.  Store at **<-20°C for up to 14 days**. Use thawed aliquots one time only. Discard all frozen aliquots after 14 days. | | | | |
|  | **Architect c4000:**   |  |  |  | | --- | --- | --- | | ***Product Description*** | ***Product Code*** | ***Stability*** | | Abbott Architect Creatinine Reagent  CHC# 32546 | 08L24-31 | **Store at:** 2 – 8°C  **Unopened:** Manufacturer’s printed expiration date.  **On-board:** 60 Days | | Abbott Architect Clinical Chemistry Calibrator  CHC# 32566 | 06K30-10 | **Store at:** 2 – 8 °C  **Unopened:** Manufacturer’s printed expiration date  Reconstitute with exactly 3.0 mL of DI water. Swirl gently. Let stand at room temp for 30 minutes. Invert gently prior to sampling. Use small portion for calibration, then label 5 aliquots, each with 0.5 mL of calibrator, with the lot number, expiration date, and date reconstituted.  Store at **<-20°C for up to 14 days**. Use thawed aliquots one time only. Discard all frozen aliquots after 14 days. | | | | |
| **Risk and Safety** | |  | | --- | | **CAUTION:** For in vitro diagnostic use. This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens. Appropriate Personal Protective Equipment (PPE) must be worn according to Children’s Minnesota Laboratory policies. Current SDSs are kept on the [Children’s StarNet](https://msdsmanagement.msdsonline.com/a07dc954-23d8-42a9-b591-ef5763cdfd33/ebinder/?nas=True) page  R1 Reagent: Contains methylisothiazolone. Causes skin irritation. May cause an allergic skin reaction. Causes serious eye irritation.  Dispose of used reagent in normal trash. Unused (expired) reagents and Multiconstituent Calibrator should be disposed of in Regulated Medical Waste (red trash). | | | | |
| **Calibration** | **Alinity c** and **Architect c4000:**   |  |  | | --- | --- | | Assay Range: | 0.10 – 40.00 mg/dL | | Reference Material: | Abbott Alinity Clinical Chemistry Calibrator  Abbott Architect Clinical Chemistry Calibrator | | Suggested Calibration Levels: | See lot-specific assay set point documentation | | Calibration Scheme: | 1 level, Linear data reduction method | | Calibration Frequency: | Alinity c: 7 days  Architect c4000: 60 days | | AMR | AMR is verified twice annually using the Maine Standards GC1 Product # 1100ab by running all applicable levels in triplicate. Assay results are submitted to Maine Standards for compilation and comparison to peers. Results are reviewed and approved by the Technical Specialist. Any questionable results are investigated and corrective actions documented. | | | | |
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| **Quality Control** | **Alinity c and Architect c4000:**  Bio-Rad Liquichek™ Unassayed Chemistry Control (Human) Levels 1 & 2  **Frequency:** Two levels each day of use  **Stability:** Once thawed, opened, and stored tightly capped at 2 to 8°C, this product will be labeled with an expiration date equal to the shortest stability of the included analytes, which is **6 days.**  **Preparation**:  This product should be treated the same as patient specimens and run in accordance with the instructions accompanying the instrument, kit, or reagent being used.   * To thaw the product, allow it to stand at room temperature (18° to 25°C) until completely thawed but no longer than one (1) hour. * After thawing, the product **MUST** be gently swirled and inverted several times to ensure homogeneity. * For optimal analyte stability in the thawed state, promptly return to 2 to 8°C storage after each use and minimize the time at room temperature to no more than 20 minutes daily. * **Before each use**, gently swirl the contents until homogeneous with no visible signs of precipitate.   **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 (insert hyperlink) 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. | | | |
| **Interferences** | **Alinity c and Architect c4000:**  Interference studies were conducted by Abbott Diagnostics Division and effects were assessed by Dose Response and Paired Difference methods at the medical decision levels of the analyte. Interference is less than 10% at creatinine concentration levels of 0.5 mg/dL and 1.0 mg/dL for:   * Hemoglobin: up to 2000 mg/dL * Total Bilirubin: up to 60 mg/dL   Interferences from medication or endogenous substances may affect results.  Alpha-methyldopa concentrations of 71 µmol/L at creatinine concentrations of 1.20 mg/dL cause decreases of greater than 20% in creatinine concentration.  Direct bilirubin concentrations greater than 26 mg/dL cause greater than 15% decrease in creatinine.  Lipemia causes interference. Clarify samples that are moderately lipemic by ultracentrifugation. Attach appropriate comment (-LINT) to the result.  For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation. | | | |
|  | **Alinity c and Architect c4000:** | | | |
| **Reference Intervals** | |  |  | | --- | --- | | Age | Creatinine | | 0 – 14 days | 0.32 -0 .92 mg/dL | | 15 days – 2 years | 0.10 – 0.36 mg/dL | | 2 – 4 years | 0.20 – 0.43 mg/dL | | 5 – 11 years | 0.31 – 0.61 mg/dL | | 12 – 14 years | 0.45 – 0.81 mg/dL | | 15 – 18 years female | 0.49 – 0.84 mg/dL | | 15 – 18 years male | 0.62 – 1.08 mg/dL | | Adult female | 0.72 – 1.25 mg/dL | | Adult male | 0.57 – 1.11 mg/dL | |  | | | | | | |
| **Critical Values** | None. | | | |
| **Limitations** | The instrument reporting system contains flags and comments to provide the user with information regarding instrument processing errors, instrument status information and potential errors in creatinine results. Refer to the [Abbott Architect](https://starnet.childrenshc.org/References/labsop/chem/operator/abbott-architect-operations-manual.pdf) or [Alinity](https://starnet.childrenshc.org/References/labsop/chem/operator/alinity-ci-series-operations-manual.pdf) Operator’s Guides for the meaning of report flags and comments, and instructions for addressing them. Do not report results until a report containing flags and/or comments is resolved.  For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.  • Very rarely, unreliable results (i.e. pseudohypercreatininemia) secondary to occurrence of monoclonal protein have been described in patients affected by Waldenstrom’s macroglobulinemia (only IgM type) or by monoclonal gammopathy of unknown significance (IgG or IgM).  • N-acetyl-L-cysteine at therapeutically achieved concentrations may lead to falsely low results in serum/plasma samples.  • Alpha-methyldopa may cause falsely low results in serum/plasma samples. | | | |
| **Dilutions** | |  |  | | --- | --- | | **Alinity c and Architect c4000:** | | | Auto Dilution: | None | | Maximum Manual Dilution: | 1:2 | | Diluent: | Saline | | Manual Dilution: | Follow Abbott [Architect Operator’s Manual](https://starnet.childrenshc.org/References/labsop/chem/operator/abbott-architect-operations-manual.pdf) or [Alinity Operator’s Manual](https://starnet.childrenshc.org/References/labsop/chem/operator/alinity-ci-series-operations-manual.pdf) instructions for programming manual dilutions. The operator must enter the dilution factor when ordering the manual dilution. The system will use this dilution factor to automatically calculate the concentration of the sample and report the result.  If a diluted sample result is less than the lower value of the measuring interval of 0.10 mg/dL, do not report the result. Rerun and/or investigate for other possible causes of error. | | | | |
| **Result Reporting** | **Alinity c and Architect c4000:**   * Results between 0.10 – 40.00 mg/dL without error messages are released * Results below 0.10 mg/dL: report as < 0.10 mg/dL instead of the numerical value. * Results > 40.00 mg/dL without error messages should be manually diluted with a maximum dilution of 1:2 as noted above. * Results > 80.00 mg/dL after manual dilution are reported as > 80.00 mg/dL rather than the numerical value. | | | |
| **Specimen Storage** | Promptly stopper tested specimen and store upright in a specimen rack. Every 8 hours remove specimens to refrigerator/freezer storage. Samples are retained 7 days in specimen storage freezer. | | | |
| **References** | 1. Jacobs & DeMott Laboratory Test Handbook, Lexi-Comp, Inc., Hudson, OH, 5th Edition, 2001 2. Architect Creatinine Enzymatic Package Insert, Abbott Laboratories Diagnostics Division, Abbott Park, IL 60064, July 2013. 3. Alinity Creatinine Enzymatic Package Insert, Abbott Laboratories Diagnostics Division, Abbott Park, IL 60064, April 2018. 4. CALIPER pediatric reference range database. (2019). Retrieved October 3, 2019, from https://caliper.research.sickkids.ca/#/ 5. Alinity c Clinical Chemistry Calibrator Package Insert, Abbott Laboratories Diagnostics Division, Abbott Park, IL 60064, December 2018. 6. Architect Clinical Chemistry Calibrator Package Insert, Abbott Laboratories Diagnostics Division, Abbott Park, IL 60064, December 2017. 7. Bio-Rad Liquichek Unassayed Chemistry Control Product Insert, Bio-Rad Laboratories, Irvine, CA 92618 | | | |
| **Historical Record** | **Version** | **Written/Revised by:** | **Effective Date:** | **Summary of Revisions** |
| 1 | Erin Bartos | 10/15/2019 | New Procedure for Abbott analyzers |
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