| **Carbamazepine** |
| --- |
| **Purpose** | This procedure provides instructions for performing CARBAMAZEPINE ON ABBOTT INSTRUMENTATION. Carbamazepine assay is used for the *in vitro* quantitative measurement of carbamazepine in human serum or plasma on the Alinity c analyzer.The measurements obtained are used in monitoring levels of carbamazepine to help ensure appropriate therapy. |
| **Policy Statements** | This procedure applies to all personnel responsible for operating the Alinity c at Children’s Minnesota Laboratory, St. Paul. |
| **Principle** | The Alinity c Carbamazepine assay is a homogeneous particle enhanced turbidimetric inhibition immunoassay (PETINIA) used for the analysis of carbamazepine in serum or plasma. The assay is based on competition between drug in the sample and drug coated onto a microparticle for antibody binding sites of the carbamazepine antibody reagent. The carbamazepine-coated microparticle reagent is rapidly agglutinated in the presence of the anti-carbamazepine antibody reagent and in the absence of any competing drug in the sample. The rate of absorbance change is measured photometrically, and is directly proportional to the rate of agglutination of the particles. When a sample containing carbamazepine is added, the agglutination reaction is partially inhibited, slowing down the rate of absorbance change. A concentration-dependent classic agglutination inhibition curve can be obtained, with maximum rate of agglutination at the lowest carbamazepine concentration and the lowest agglutination rate at the highest carbamazepine concentration.**Methodology**: Particle-enhanced turbidimetric inhibition immunoassay (PETINIA)For additional information on system and assay technology, refer to the Alinity ci-series Operations Manual, Section 3. |
| **Clinical Significance** | Monitoring of blood levels can increase efficacy and safety of anticonvulsants for the following reasons:* Carbamazepine concentrations correlate better with pharmacologic activity than does dosage.
* Changes in carbamazepine half-life with prolonged treatment and individual differences in carbamazepine metabolism make it difficult to predict serum concentrations from the administered dosage, particularly during concomitant therapy with other anticonvulsants. Monitoring helps physicians individualize dosage regimens.
* Carbamazepine is safe and effective only in a narrow range of concentrations

Factors that can influence the relationship between carbamazepine serum or plasma concentrations and clinical response include the type and severity of seizures, age, general state of health, and use of other drugs. See drug package insert for further information. The concentration of carbamazepine in serum or plasma depends on the time of the last drug dose; mode of administration; concomitant drug therapy; sample condition; time of sample collection; and individual variations in absorption, distribution, biotransformation, and excretion. These parameters must be considered when interpreting results. |
| **Analyzer** | **St. Paul: Abbott Alinity c (Sunquest method code: SALIC)****Backup:** MedTox Laboratory; send STAT courier if necessary. |
| **Sunquest Test Codes** | **CARB** |
| **Specimen** | Sample: Plasma or Serum**Preferred:** Lithium heparin (with or without gel)**Alternative**: Serum tubes (with or without gel), Lithium heparin, EDTA plasma**Minimum sample volume:** 0.6 whole blood0.0 plasma/ serum **Stability when separated from cells/gel:** 20 to 25°C: 2 days2 to 8°C: 7 days-20°C: 1 month**Rejection criteria:** Unlabeled tube, sample type other than serum or acceptable plasma**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 directly to a properly labeled pilot tube.
5. Architect and Alinity systems utilize a specimen level detect mechanism, so special racks specific to tube-type are not required.
6. Minimum labeling includes sample accession ID, and/ or patient name, medical record number, collection date and time.
 |
| **Reagents** | **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.**Carbamazepine reagent will be stored off the system until Patient or Proficiency testing is required. Follow the steps below to prepare the reagent for use:** * Take the open reagent from the fridge and gently MIX 5 times. If there is not an open reagent use an unopened reagent and document the open date on the reagent and gently MIX 5 times.
* Remove any bubbles formed due to mixing.
* Uncap reagent and put on any lane of the Alinity c.
* Calibrate as needed.
* Perform QC- do not perform patient testing until QC is acceptable.
* Perform Patient testing, Result normally.
* Removed reagent from the Alinity c, store reagent with new replacement caps in an upright position at 2 to 8°C. Reagent are stable until the Expiration Date when stored off the instrument. Store reagent in the original box to ensure it remains upright.

If a reagent cartridge is dropped, place in an upright position for 1 hour 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 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.
 |
|  |

|  |  |  |
| --- | --- | --- |
| ***Product Description*** | ***Product Code*** | ***Stability*** |
| Abbott Alinity c Carbamazepine Reagent Kit | 08P5820 | **Store at:** 2 to 8°C**Unopened:** until manufacturer’s printed expiration date**On-board**: 45 days**Opened expiration:** until manufacturer’s printed expiration date when stored tightly capped in the refrigerator |
| Abbott Alinity c TDM Multiconstituent Calibrator Kit | 08P7404 | **Store at:** 2 to 8°C**Unopened:** until manufacturer’s printed expiration date**Opened expiration:** 60 days when stored tightly capped in the refrigerator |

 |
| **Risk and Safety** | This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens.The following warnings and precautions apply to: R1 Contains bis tris propane and sodium azide.Special disposal not indicated.

|  |
| --- |
| Safety data sheets (MSDS/SDS) available on [Children’s Intranet](https://starnet.childrenshc.org/emergency-and-safety/)  |

 |
| **Calibration** |

|  |  |
| --- | --- |
| Assay Range: | 0.04 to 20.00 μg/mL |
| Reference Material: | Alinity c TDM Multiconstituent Calibrator Kit |
| Suggested Calibration Levels: | Approximate values:CAL 1: 0 CAL 2: 2CAL 3: 4CAL 4: 8CAL 5: 12CAL 6: 20 |
| Calibration Scheme: | 5 Levels, Spline data reduction method |
| Calibration Frequency: | 7 Days, and with every new lot. Calibration may be required after maintenance to critical parts or after field service procedures have been performed. |
| AMR | AMR is verified with each calibration.  |

 |
| **Quality Control** | **QC Material:** Bio-Rad Immunoassay Plus Control Levels 1 and 3.**Frequency:** 2 levels every 24 hours**Stability:** 2 Year shelf life when stored at -20 to -70°C. When thawed and opened, minimizing exposure to room temperatures, the control is stable for 14 days when stored consistently at 2-8°C **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 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** | **Hemolysis, Icterus & Lipemia (HIL) Index Values:**

|  |  |  |
| --- | --- | --- |
| **H** | **I** | **L** |
| **-** | **-** | **-** |

At HIL levels at or above the specified cutoff value, append the appropriate comment AFTER visually confirming presence of interferent: -HP for “Hemolysis present, may affect results.” -BIN for “Bilirubin Interference”-LINT for “Lipid Interference” * Endogenous substances were tested and did not result in any clinically significant interference.
 |
|  |  |
| **Reference Intervals** | Therapeutic Concentration: 4.00 - 8.00 µg/mL |
| **Critical Values** | >20.00 µg/mLCritical results must be called according to Critical Values Policy |
| **Limitations** | There is some cross-reactivity with metabolites of carbamazepine. Refer to the Instructions for Use for more information.**For diagnostic purposes**:Interfering heterophile antibodies occur at low frequency in the general population. These antibodies can cause auto-agglutination of the microparticle reagent leading to erroneous results that may be unexpectedly low or unexpectedly high. An erroneous result could lead to incorrect patient management; incorrect patient management could potentially cause serious injury or death. Test results should not be used in isolation to make patient management decisions. Results should always be assessed in conjunction with the patient’s medical history, clinical examinations, and other clinicopathological findings. An alternative test method should be used to confirm results when results are inconsistent with clinical expectations. |
| **Dilutions** |

|  |  |
| --- | --- |
| Max Auto Dilution: | 1:2.01 |
| Maximum Manual Dilution: | None specified |
| Diluent: | Onboard diluent  |
| Manual Dilution: | Follow Abbott [Alinity Operator’s Manual](https://starnet.childrenshc.org/References/labsop/chem/operator/alinity-ci-series-operations-manual.pdf) instructions for programming automated dilutions. The system will 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 0.04, do not report the result. Rerun and/or investigate for other possible causes of error. |

 |
| **Result Reporting** | * Results between 0.04 and 20.00 µg/mL without error messages are released
* Results below 0.04 without error messages are reported as < 0.04 µg/mL
* Results > 20.00 should be diluted using the onboard automated 1:2.01. Release results without error messages following this dilution.
* Results > 40.20 following automated dilution are reported as > 40.20 µg/mL
 |
| **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. Abbott Alinity c Carbamazepine Reagent Kit Instructions for Use, Abbott Diagnostics Division, Abbott Park, IL USA. Revised September 2019
2. Abbott Alinity c TDM Multiconstituent Calibrator Package Insert, Abbott Diagnostics Division, Abbott Park, IL USA. Revised July 2018
3. Bio-Rad Liquichek Immunoassay Plus Package Insert, Bio-Rad Laboratories, Irvine CA USA.
 |
| **Historical Record** | **Version** | **Written/Revised by:** | **Effective Date:** | **Summary of Revisions** |
|  | Elauteria Earnhardt |  | New Procedure for Abbott analyzers |
| 1 | Erin Bartos | October 28, 2020 | Added dilution, reporting, critical values, reference ranges, calibrator, AMR, QC material, etc for new procedure. |
|  | 2 | Matt Johnson | 5/18/2022 | Edited reagent handling section. Will keep in fridge when no patient testing done.  |