**TITLE: Chemistry Quality Control**

**PRINCIPLE:**

The Chemistry department requires a comprehensive Quality Control program to ensure quality test results as well as meet guidelines and requirements assigned by various regulatory agencies. Quality Control serves to verify the accuracy and precision of reported test values by checking instrument performance, reagent performance and human performance. Quality control issues are detected by embedding select Westgard rules into quality control software such as Unity Bio-Rad Real-Time QC program. The Bio-Rad software creates Levy-Jennings charts that help the technologist visualize the quality control performance. The results of controls are verified for acceptability before reporting patient results and require appropriate action if results are unacceptable.

**Westgard rule definitions:**

**1-2S Rule:** One control value exceeds either +2 Standard Deviations (SD). This is considered a warning rule and requires additional inspection of the control data and monitoring. Approximately one in twenty control values will fall outside the +2 SD rules.

**1-3S Rule:** Control value exceeds + 3SDs. This should occur less than 3 times in 1000 determinations. This is a rejection error indicating the QC run has failed; this could be due to a random and/or systemic error.

**2-2S Rule:** Two consecutivecontrol values either exceed+2 SDs or both controls on the same day exceed either +2 SDs. This is a rejection error indicating the QC run has failed. Errors of this type are generally systematic in nature and they may be due to problems with standards, calibration, reagents or diluents.

**R-4S Rule:** This type of error occurs when the difference between two control values within the run exceeds 4SDs of each other in the opposite direction.

**12X Rule:** This rule looks for the presence of 12 consecutive control values on the same side of the mean, either as 12 values from a single level of control or 12 values over a five-day period from both levels. This error is warning and may be an indication of systematic error.

**2/3-2s:** This is a variation of the 2-2s rule and detects systematic errors. It is triggered when any 2 of 3 levels of QC exceed 2SD on the same side of the mean. This is a rejection error indicating the QC run has failed.

**Reagent and Supply Requirements**

1. All reagents and quality control material must be labeled properly and contain the following information as applicable.
   1. Identity of reagent or quality control product
   2. Lot number
   3. Date when the control is thawed if applicable
   4. Date when the control is opened
   5. Preparation date and technologist initials (if prepared by the laboratory)
   6. Expiration date (update if dates changes when diluted, thawed or opened)
   7. Note: date must include Month/Date/Year
2. Reagents used for Quality Control procedures should be the same reagents used for patient testing
3. Quality Control testing is to be performed by the same personnel who performs testing on patient samples, using the same testing methods as used to report patient results.
4. Equipment used for quality control procedures must be maintained, cleaned and calibrated according to manufacturer’s specifications.
5. The control material which most closely resembles the patient sample being tested is to be run for the indicated test.
6. Specific individual assay calibrators can also be used as a back-up to the existing Quality Control Program. A single calibrator or the set of calibrators for all ranges can be used as needed.
7. Manufacturer’s assayed controls can also be used as a back-up to QC for troubleshooting.
8. Previously run Proficiency survey specimens may be thawed and used as an alternative for QC troubleshooting as well. Expected results can be found in the completed PT binders.

**Procedure**

1. Quality Control must be included in all aspects of chemistry testing and is to be tested in the same manner as patient samples.
2. All control material should be treated as a bio-hazardous material and discarded properly.
3. The Architect control material is preprogrammed into the Abbott Architect analyzers. To run QC select the correct barcoded tube, place a clean sample cup into the tube, add the stated amount of QC (located on the bar code label) into the cup and load on the analyzer. Once all the tests are completed, review the results to make sure there were not any aspiration errors or outliers. If the run is acceptable, press Select All and Release. This will transmit the results to the Unity Bio-Rad Real Time Unity QC program.
4. Follow manufacturer’s recommendations for control frequency; Chemistry QC must be run as follows:
   1. Once every 24 hours when patient testing is ordered
   2. After each calibration
   3. After major maintenance or part replacement
   4. When a new lot of reagent is put into use
   5. Every 8 hours for Na+, K+ and Chloride on both Abbott Architects
   6. Every 30 days for ROM Plus external QC for existing lots. New lots must have external QC performed before being put in use for patient testing.
   7. Ketone QC is required when opening a new bottle of Ketone reagent tablets and every 24 hours when patient testing is performed.
   8. Body Fluid pH QC is to be run once every 24 hours when patient testing is performed.
5. For tests that report qualitative results based on a quantitative measurement using a threshold (cut-off) to discriminate between a positive and negative clinical interpretation, the pos and neg controls must have values appropriately near the cut-off value.
6. Test all new incoming lots of **QC** prior to putting them into use- See attached instructions for setting up lot correlations.
   1. During the QC lot change period for assayed controls, test the new lot of QC along with current lot. Compare the mean and SD to the manufacturer’s ranges and the Laboratory Comparison Evaluation in the Bio-Rad evaluation report.
   2. For Unassayed controls, obtain 20 data points to initially establish the mean and SD for the new lot.
   3. Enter the new lot of QC into the Unity Bio-Rad Real-Time QC program by duplicating the new lot of QC under the lot tab. Select the new lot from the drop-down box when prompted.
7. Test all new incoming lots of reagents before use for patient testing, comparing quality control results as well as random patient samples to those obtained with prior reagent lots –see SOP CH330 “Reagent Handling and Validation”.
8. Review and save all control data in the Bio-Rad Unity QC program (manual tests should be entered into TQC program- see SOP CH 320- TQC for Manual Chemistry Testing).
9. Osmolality testing is to be entered manually into the Unity QC program.

**Quality Control Products and Instructions for use**

1. Bio-Rad Multiqual Level 1 and Level 3 Unassayed Controls:
2. Store the controls at -20 degrees C until they are ready to be thawed.
3. Allow the control to stand at room temperature (18-25ºC) for 1 hour or until completely thawed. A precipitate may be present that dissolves upon mixing.
4. Invert the vials 10-15 times before use.
5. Remove the cap/stopper and dispense the volume required for testing.
6. Replace the cap/stopper. Store at 2-8ºC.
7. Controls thawed and unopened are stable for 30 days at 2 to 8º C. Controls that are thawed and opened are stable for 7 days at 2 to 8º C and controls stored at -20º C are stable until the expiration date on the box.
8. Bio-Rad Liquichek Cardiac Markers Plus Control LT levels 1 and 3:
9. Store the controls at -20ºC until they are ready to be thawed.
10. Thaw the controls at room temperature prior to use.
11. Invert the vials 10-15 times then swirl contents until homogeneous before use.
12. Remove the cap/stopper and dispense the sample volume required for testing.
13. Replace the cap/stopper.
14. Frozen control is stable until the expiration date on the box and the individual vials.
15. Controls thawed and opened are stable for 5 days at 2 to 8º C.
16. Bio-Rad Liquichek Urine Control Levels 1 and 2:
17. No preparation required.
18. Unopened bottles are stable until the expiration date on the bottle when stored at 2 to 8º C.
19. Opened bottles of control are stable for 30 days when stored at 2 to 8º C.
20. If evidence of gross contamination, discard immediately.
21. Bio-Rad Liquichek Immunoassay Plus Control Levels 1, 2, and 3:
22. Store the controls at -20º C until they are ready to be thawed.
23. Allow the control to stand at room temperature for 1 hour or until completely thawed.
24. Invert the vials 10-15 times before use.
25. Once thawed stored unopened at 2 to 8º C, the control is stable for 30 days- Note the date that the control was thawed on the label.
26. Once the control is thawed and opened, the control is stable for 14 days when stored at 2-8º C. Folate is stable for 4 days.
27. Bio-Rad Spinal Fluid Control Levels 1 and 2
28. No preparation is required.
29. Controls that are stored unopened at 2 to 8º C are stable until the expiration date on the box and the individual bottle labels.
30. Once opened, the control set is stable for 30 days or until the printed expiration date, whatever comes first.

1. Bio-Rad Liquichek Ammonia Control Levels 1 and 3
2. No preparation is required.
3. Controls that are stored unopened at 2 to 8º C are stable until the expiration date on the box and the individual bottle labels.
4. Once opened, the control set is stable for 20 days or until the printed expiration date, whatever comes first.
5. Lyphochek Diabetes Control Level 1 and 2
6. The controls will remain stable until the expiration date on the vial when stored unopened at -10 to -70º C
7. Thawed and unopened controls are stable for 6 months when stored unopened at 2-8º C
8. The thawed and opened control is stable for 14 days when stored tightly capped at 2-8ºC
9. Liquichek Urine Toxicology Control- Level S1E and S2E
10. The control is stable until the expiration date when stored unopened at 2-8ºC .
11. Once opened, the control is stable for 30 days when stored tightly capped at

2-8ºC

1. Liquichek Immunology Control – Levels 1 and 3
2. Product is stable unopened until the exp. date when stored at -20 to -70ºC.
3. Thaw controls at room temperature prior to use. Thawed and unopened this control is stable for 45 days.
4. Once opened the control is stable for 30 days when stored tightly capped at 2 to 8º C.

J. Alta Diagnostics, Inc. Urine Control - Positive

1. No preparation is required.
2. Store at 2 to 8º C.
3. Stable until the expiration on the bottle.

K. Osmometer Clinitrol 290 Standard:

1. No preparation is required.
2. Store at 20 to 25º degrees C (room temperature).
3. Stable until the expiration date on the bottle.
4. Osmometer 50 and 850 Calibration Standards:
5. No preparation is required.
6. Store at 20 to 25º degrees C (room temperature)
7. Stable until the expiration date on the box.
8. pH 4.0, 7.0 and 10.0 Buffer Solutions:
9. No preparation is required.
10. Store at 20 to 25º degrees C (room temperature).
11. Stable until the expiration date on the box.
12. Lyphochek Specialty Immunoassy Control Level 1 and 3
13. This QC is stable unopened until the expiration date when stored at 2 to 8º C
14. Reconstitute with 2 ml distilled or deionized water. Replace the stopper and allow to stand for 15 minutes swirling occasionally.
15. Reconstituted and refrigerated this control is stable for 30 days except PTH is stable for 4 days and PCT is stable for 3 days when stored tightly capped at 2 to 8º C
16. Frozen aliquots stored at -20 to -70 º C are stable for 30 days.
17. Viroclear, Virotrol I, Virotrol III and Virotrol HIV 2, Virotrol HIV-1 Ag and Syphilis
18. No preparation is required.
19. Store at 2-8ºC
20. Unopened control is stable until expiration date on container when stored at 2 to 8ºC
21. Opened control is stable for 60 days when stored tightly capped at 2 to 8ºC.
22. Liquichek Tumor Marker Control Level 1 and 3
23. Product is stable unopened until the expiration date when stored at -20 to -70ºC.
24. Thaw controls at room temperature prior to use. Thawed and unopened this control is stable for 14 days
25. Once opened this QC is stable for 10 days when stored tightly capped at 2-8º C

1. Liquichek Therapeutic Drug Monitoring (TDM) Level 1 and 3

1. Product is stable unopened until the expiration date when stored at -20 to -70ºC.

2. Thaw controls at room temperature prior to use. Thawed and unopened this control is stable for 180 days at 2-8º C .

3. Once opened the control is stable for 30 days when stored tightly capped at 2-8º C

R. Rupture of Membrane (ROM) External Negative and Positive QC

1. Product is stable unopened until the expiration date on the box when stored at 20- 25 ºC.

2. Gently bend or squeeze the control vial breaking the glass ampule inside. Mix the controls 4-5 times before use.

3. Use immediately and discard remaining control materials.

S. pH Body Fluid Buffered Solutions 4.0, 7.0 and 10.0

1. Store at room temperature 20-25ºC.

2. Product is stable until the expiration date listed on the bottle.

**Results**

1. If QC is flagged as out of control:
   * 1. **Do not run or report any patient tests until the issue is resolved.**
     2. Use available information to aide in troubleshooting such as reagent and calibration history, QC expiration, instrument maintenance records, review of CAP surveys and review of Levy-Jennings charts to look for QC shifts or trends.

3. To view the Levy-Jennings charts: open Bio-Rad Unity QC program and the QC product you are investigating, select the specific analyte then in the menu bar select LJ to view the graph.

4. Review all levels of QC to determine how the analyte QC has been trending over the entire AMR .

5. Previously graded CAP survey material may be used to assist in troubleshooting unresolved issues.

1. Once the QC issue is resolved, determine if a retrospective review of samples is required.
   * 1. If QC failure is due to quality control material only, no further follow up is required.
     2. If QC failure is solved by changing any system component used for patient testing, a retrospective review is required.
2. Retrospective review of samples involves looking back at results reported back to the last successful control run.
   * 1. Select and rerun up to a 10 random selection of patient specimens from the last time controls were acceptable.
     2. If the comparison of the random patient specimen results fall within the evaluation criteria for comparison of analytes, no corrections are required.
     3. If comparison of the random patient’s results fall outside the evaluation criteria notify Lead Tech or Manager.
     4. The Lead or Manager will consult with the Medical Director to determine if all reported results need to be rerun and corrected.
3. Document the cause for any out of control situations in the Bio-Rad Unity Real-Time QC program.

**QC Review**

**Daily Quality control Review in Bio-Rad Unity Software**

* 1. Daily quality control review is to be performed by the testing personnel.
     1. Log into the Bio-Rad Unity software program.
     2. Under the review tab, select Bench Review. All QC pending review will be highlighted in green font.
     3. Select pending QC by the specific analyzer, then by QC product
     4. Review all data points: pay close attention to the outliers (QC failure will be highlighted in a red/pink color, warnings are highlighted in yellow).
     5. All QC failures must have an action comment attached. To attach a comment, right click in the action box and enter the appropriate action then select apply. Make sure failed QC is rejected and the QC which is acceptable is marked as reviewed.
     6. When QC has been deemed acceptable, select the review check box in the upper left corner of the screen and select save.
  2. Review Levy Jennings charts for shifts or trends.
     1. Levy-Jennings charts can be found in the Bio-Rad Unity software by selecting the QC product then select the specific analyte. Once selected in the menu bar select LJ to view the chart. You can change the date range to see all data entered for the lot number.
  3. Observe the effect of new reagent lots and instrument elements by running new lot validation testing.
  4. Be observant of delta failures, critical values and technical limits when running patients.
  5. An additional Supervisor Review in the Bio-Rad Unity QC program will be performed by the Lead Tech or designee.

**Monthly Quality Control Review**

A. QC data will automatically be submitted to the Bio-Rad QC program on the 5th day of each month. This submission includes all accepted data from the previous month.

B. On Receipt of Peer Group Evaluation Reports

* + 1. Review data reports for outliers due to errors in data entry.
    2. Correct prospective control values; if erroneous data was submitted for evaluation, data can be re-evaluated based on the correct statistics.
    3. Compare means for each analyte to the mean of other laboratories using your method and the selected method. If significant bias is present, study and revise the procedure, or adjust the means to match the peer group.
    4. Compare the Standard Deviations (SD) to the average SD of peer laboratories, using your method and coefficient of variation (CV) compare values to the CV summary data for each analyte.
    5. Follow up on all evaluation reports that show evidence of bias, imprecision or potential instrument malfunctions.
    6. Previously run Proficiency Survey specimens, linearity or another manufacturer’s Quality Control may be used as a reference tool for troubleshooting QC exceptions and outliers.
    7. Sign and date the Bio-Rad Monthly Evaluation reports, addressing any QC issues found and follow up action performed.
    8. File the reports in the QC folder located in the Chemistry Department.

**References**

1. Bio-Rad Control package inserts
2. Reagent kit and product package inserts
3. CLIA 88’ Regulations
4. CAP Checklist
5. Manufacturer’s Procedure Manuals