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Area	Laboratory-Chemistry
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Laboratory Performance Guidelines For Analytical Methods

Document Type: Procedure

I. PURPOSE AND OBJECTIVE:

To provide the Chemistry laboratory staff with guidelines for the performance of all analytical methods.

II. STANDARDS PREPARATION:

A. All chemicals used as primary standards must be of high quality and tested for purity before use unless accompanied by appropriate documentation. Appropriate matrix defined by each assay should be used to prepare in-house standards (calibrators) and controls. Only clinical laboratory reagent water (CLRW) should be used for standards and controls requiring water. Wet chemicals should be weighed in a container that minimizes evaporation. All additions should be made with Class A volumetric pipettes or calibrated pipettes. Proper analytical technique requires measures to ensure quantitative transfer of standard materials.

B. In-house standards and controls must be segregated by lot and each lot verified for accuracy before placed into service. Each lot should be identified by date of preparation, date placed in service and expiration date. Expiration dates of in-house standards and controls may be re-assigned by Chemistry faculty only after appropriate evaluation studies are reviewed and signed to verify continuing assay performance.

III. CALIBRATION:

Calibration should be performed according to a manufacturer or laboratory's stated requirements for

frequency and accuracy. All calibration data should be reviewed by a Medical Technologist (MT) for acceptability and retained for future reference according to laboratory retention policy. After calibration, Quality Control (QC) material should be tested and reviewed for acceptability by a medical technologist, Lead, supervisor, or manager, as appropriate for the assay. QC shifts observed with new lots of calibrator should be noted with Leads, supervisors, or managers and may be discussed with a clinical chemist or pathologist, if needed. On automated platforms, calibrations are checked against manufacturer-defined criteria for precision and accuracy where applicable. When calibration fails to meet these criteria, patient testing is not permitted by the automated systems. For lab-developed tests, assigned values for new lots of calibration material should be determined according to the approved procedure for each test.

IV. RECALIBRATION:

A. Each method must be recalibrated as needed to ensure consistent performance.
    1. Recalibration is required:
        a. At manufacturer stated intervals
        b. When indicated by quality control
        c. After a reagent lot change
        d. After failed calibration verification
        e. At least every six months

V. CALIBRATION VERIFICATION:

A. Calibration verification is the process of confirming the validity of a current calibration. It assumes that verification is a satisfactory substitute for recalibration when a calibration relationship is assumed over an extended period of time. In the absence of recalibration, calibration verification must be performed:
    1. At complete changes of reagent
    2. When indicated by quality control
    3. As recommended by the manufacturer
    4. 6 months after the last calibration

B. Calibration verification cannot be satisfied by the use of unassayed control materials. Verification materials must be of an appropriate matrix and have assayed values with manufacturer or laboratory assigned tolerance limits. Recovered results must fall within these limits. In the absence of assayed materials, verification materials may be:
    1. Linearity material of an appropriate matrix supplied by a professional or commercial source
    2. Proficiency testing material, if no other material is available
    3. Previously tested patient samples
    4. Previously tested patient samples altered by addition or dilution of the analyte

5. Primary or secondary reference materials
6. Calibrators at less than the number required for calibration

VI. QUALITY CONTROL:

All sites: Refer to site-specific QC Procedures and Policies.

VII. REAGENT LABELING:

A. Reagents (including calibrators and controls) purchased from manufacturers or prepared in-house must be labeled as appropriate with the following information:
    1. Name of reagent
    2. Quantity/concentration and matrix
    3. Storage requirements
    4. Date opened / prepared
    5. Initials of individual who opened / prepared the reagent
    6. Expiration date
    7. Open expiration date, if opening a container changes the original expiration date
    8. Hazard designation, if known

B. Automated systems help control inventory and may maintain reagent information in electronic form. Additional labeling (e.g., date received) should meet department or workstation requirements.

C. Liquid chemical reagents that do not have a manufacturer-provided expiration date will be assigned ten (10) year expiration; dry/solid chemical reagents without a provided expiration date will be labeled with twenty-five (25) year expiration.

VIII. REAGENT USE:

A. Reagents must be verified for acceptability when first put into use according to site-specific Reagent Lot-to-Lot Comparisons. Components from different lot numbers should not be mixed unless specifically permitted. External controls must be run with each new lot number/ shipment of reagent/cartridges. Controls included with a test kit are external controls.

B. Reagents must be stored according to manufacturer recommendations, or for laboratory-developed tests, according to requirements outlined in method evaluation and laboratory procedures. The laboratory must not use reagents, including calibrators and controls, after manufacturer-assigned expiration dates. In exceptional circumstances where interruption or delay in testing would affect patient safety, laboratory directors must evaluate assay performance and provide written approval for use of expired reagents.

IX. PIPETTE ACCURACY AND PRECISION:

Pipettes used for quantitative dispensing are checked at least annually for accuracy and precision. Fixed and adjustable volume pipettes are checked by a photometric or gravimetric method. The accuracy of

pipettes integrated into automated analyzers is checked each day of patient testing using quality controls, with approved QC ranges determining acceptability. Precision of integrated pipettor systems is checked when QC statistics are evaluated at least monthly. Manufacturer instructions should be followed for monitoring and maintaining pipettor accuracy and precision. Within-run and between-run precision studies may be performed as needed for troubleshooting purposes.

X. CARRYOVER:

A. Carryover is evaluated initially at the time of validation of a test system, as defined in site-specific New Test Methods. For these studies, the laboratory should use the EP Evaluator Carryover module or Microsoft Excel, which requires statistical comparisons of several low samples run separately and after high samples in a defined sequence.

B. Additionally, carryover must be evaluated after major maintenance or repair of a pipette/auto-sampler assembly to evaluate any change in extent of carryover defined at validation. For this purpose, or for routine troubleshooting, carryover may be evaluated by testing a low concentration sample (1), followed by a high concentration sample, followed by the same low concentration sample (2) to determine a % Interaction:

$$\% \text{ Interaction} = \frac{[\text{Low Result (2)} - \text{Low Result (1)}] \times 100}{\text{High Result}}$$

This calculates the percent of a leading sample that is transferred into the sample following it (carryover). Acceptable values may vary according to the imprecision of the method and range of possible values for the analyte and should be judged by a Lead, supervisor, manager, clinical chemist, or pathologist.

C. It may also be evaluated by testing a blank sample after a positive sample such as a standard. Using this approach, it is calculated as follows:

$$\% \text{ Interaction} = (\text{Blank Result} / \text{Standard Result}) \times 100$$

XI. ANALYTICAL MEASUREMENT RANGE:

A. The analytical measurement range (AMR) is established by the range of linearity of the method. It is the range of values that a method can directly measure on a specimen without dilution or concentration. The AMR is established at the time of assay validation and verified at least every six months to be within established tolerances for each assay.

B. AMR verification requires the use of assayed or acceptable materials at the mid-range, and at or reasonably near the lower and upper limits of the AMR. As long as they satisfy these requirements, materials specified for calibration or calibration verification meet the criteria for AMR verification.

C. AMR verification studies are reviewed for acceptability by a Lead, supervisor, or manager in Automated Chemistry. If established acceptability criteria are not met (e.g., EP Evaluator criteria based on established total allowable error), further review by a technical director is required. See Laboratory Chemistry Total Error Allowable.

D. Linearity materials for Analytical Measurement Range (AMR) verification are used according to

instructions from the manufacturers. For some analytes, these materials do not cover the entire range of values reported. For example, ammonia's (NH3) lower limit of the AMR is approximately 40% of the lowest level of the linearity materials. Medical and technical directors have approved the indicated AMR to allow monitoring of ammonia levels at the lower concentrations. These benefits outweigh the relatively small risk of not formally verifying the full reportable range. This approach is consistent with CAP instructions indicating: "*It may be difficult to obtain specimens with values near the limits for some analytes. In such cases, reasonable procedures should be adopted based on available specimen materials. The closeness of sample concentrations or activities to the instructions for verifying the AMR must be followed, when available. The laboratory director must define limits for accepting or rejecting verification tests of the AMR.*"

XII. MAXIMUM DILUTION:

During method validation, maximum dilution for each analyte is defined by the laboratory based on what is clinically relevant and analytically valid. The appropriate diluent(s) for each analyte, as well as volumes of sample and diluent are validated at that time. Both automated and manual dilutions must be performed according to these parameters.

XIII. RESULT VERIFICATION:

All patient results must be verified for acceptability prior to reporting, whether they are entered manually into the computer or uploaded automatically from an interfaced analyzer. If auto-verification is in effect, results that satisfy established rules may be released without review by the operator. In the absence of auto-verification, results must by reviewed by the person performing the test. Results which are entered manually into the computer must be reviewed by another individual.

XIV. REFERENCES:

CAP Inspection and Accreditation checklists

Approval Signatures

Step Description	Approver	Date
Medical Directors	Ann Marie Blenc: System Med Dir, Hematopath	2/15/2024
Medical Directors	Muhammad Arshad: Chief, Pathology	2/6/2024
Medical Directors	Jeremy Powers: Chief, Pathology	1/17/2024

Medical Directors	Vaishali Pansare: Chief, Pathology	1/12/2024
Medical Directors	Ryan Johnson: OUWB Clinical Faculty	1/11/2024
Medical Directors	John Pui: Chief, Pathology	1/11/2024
Policy and Forms Steering Committee Approval (if needed)	Leah Korodan: Mgr, Division Laboratory	1/11/2024
	Caitlin Schein: Staff Physician	1/11/2024
	Nga Yeung Tang: Tech Dir, Clin Chemistry, Path	1/2/2024
	Qian Sun: Tech Dir, Clin Chemistry, Path	12/28/2023
	Michelle Alexander: Medical Technologist Lead	12/28/2023
	Jennifer Yaker: Mgr, Laboratory	11/29/2023
	Kristen DiCicco: Mgr, Laboratory	11/13/2023
	Katherine Persinger: Mgr, Laboratory	11/13/2023
	Christopher Ferguson: Mgr, Laboratory	11/8/2023
	Kristin Russell: Supv, Laboratory	11/8/2023
	Ashley Beesley: Mgr, Laboratory [KG]	11/8/2023
	Leah Korodan: Mgr, Division Laboratory	11/8/2023

Applicability

Dearborn, Farmington Hills, Grosse Pointe, Royal Oak, Taylor, Trenton, Troy, Wayne