

NOTE: The matrix of the sample (ie, the environment in which the sample is suspended or dissolved) may influence the measurement of the analyte. In many cases, the method manufacturer will recommend suitable materials. Other suitable materials for AMR verification include the following:

1. Linearity material of appropriate matrix, eg, CAP CVL Survey-based or other suitable linearity verification material
2. Previously tested patient/client specimens, that may be altered by admixture with other specimens, dilution, spiking in known amounts of an analyte, or other technique
3. Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method
4. Patient samples that have reference method assigned target values
5. Control materials, if they adequately span the AMR and have method-specific target values

Factors to consider in verifying the AMR are the expected analytic imprecision near the limits, the clinical impact of errors near the limits, and the availability of test specimens near the limits. 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 and activities to the upper and lower limits of the AMR are defined at the laboratory director's discretion.

Evidence of Compliance:

- ✓ Records of AMR verification

REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1255]
- 2) Shah VP, Midha KK, G, Dighe S, et al. Bioanalytical Method Validation - *Pharm Res*. 1992;9(4):588-92.
- 3) Hartmann C, Smeyers-Verbeke J, Massart DL, McDowall RD. Validation of bioanalytical chromatographic methods. *J Pharm Biomed Anal*. 1998;17(2):193-218.
- 4) Findlay JW et al. Analytical Methods Validation - Bioavailability, Bioequivalence and Pharmacokinetic Studies. *Pharm Res*. 2000;17(12):1551-7.
- 5) Killeen AA, Long T, Souers R, Styler P, Ventura CB, Klee GG. Verifying Performance Characteristics of Quantitative Analytical Systems: Calibration Verification, Linearity, and Analytical Measurement Range. *Arch Pathol Lab Med*. 2014;138(9): 1773-81.

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CHM.13600 AMR Verification

Phase II



Verification of the analytical measurement range (AMR) is performed at least every six months and following defined criteria. Records are retained.

NOTE: The AMR must be verified at least every six months after a method is initially placed in service and if any of the following occur:

1. At changes of reagent lots unless the laboratory can demonstrate that the use of different lots does not affect the accuracy of patient/client results, and the range used to report patient/client test data
2. If QC shows an unusual trend or shift or is outside acceptable limits, and the system cannot be corrected to bring control values into the acceptable range
3. After major preventive maintenance or change of a critical instrument component
4. When recommended by the manufacturer

It is not necessary to independently verify the AMR if the calibration of an assay includes calibrators that span the full range of the AMR, with low, midpoint and high values represented (ie, three points) and if the system is calibrated at least every six months. A one-point or two-point calibration does not include all of the necessary points to verify the AMR.

AMR verification is not required for calculated test results as long as the individual results contributing to the calculation have AMR verification.

AMR verification is not required for methods that measure an analyte quantitatively or semi-quantitatively yet report a qualitative value based on concentration threshold. For such methods, eg, drugs of abuse, refer to checklist requirement CHM.13750.

Evidence of Compliance:

- ✓ Records of AMR verification, as required, at least every six months

REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24): [42CFR493.1255]

CHM.13710 Diluted or Concentrated Samples**Phase II**

If a result is greater than or less than the AMR, a numeric result is not reported unless the sample is processed by dilution, a mixing procedure or concentration so that the result falls within the AMR.

NOTE:

1. A measured value that is outside the AMR may be unreliable and should not be reported in routine practice. Dilution, a mixing procedure* or concentration of a sample may be required to achieve a measured analyte activity or concentration that falls within the AMR. The result must be within the AMR before it is mathematically corrected by the concentration or dilution factor to obtain a reportable numeric result.
2. For each analyte, the composition of the diluent solution and the appropriate volumes of sample and diluent must be specified in the procedure manual. Specifying acceptable volumes is intended to ensure that the volumes pipetted are large enough to be accurate without introducing errors in the dilution ratio.
3. All dilutions, whether automatic or manual, should be performed in a way that ensures that the diluted specimen reacts similarly to the original specimen in the assay system. For some analytes, demonstrating that more than one dilution ratio similarly recovers the elevated concentration may be helpful.
4. This checklist requirement does not apply if the concentration or activity of the analyte that is outside the AMR is reported as "greater than" or "less than" the limits of the AMR.

*This procedure is termed the "method of standard additions." In this procedure, a known quantity (such as a control) is mixed with the unknown, and the concentration of the mixture is measured. If equal volumes of the two samples are used, then the result is multiplied by two, the concentration of the known subtracted, and the concentration of the unknown is the difference.

Evidence of Compliance:

- ✓ Patient reports or worksheets

REFERENCES

- 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Oct 1):[42CFR493.1282(b)(1)(ii)]

CHM.13720 Maximum Dilution**Phase II**

For analytes that may have results falling outside the limits of the AMR, the laboratory defines the maximum dilution that may be performed to obtain a reportable numeric result.

NOTE:

1. For each analyte, the laboratory procedure defines the maximum dilution that falls within the AMR and that can be subsequently corrected by the dilution factor to obtain a reportable numeric result. Note that for some analytes, an acceptable dilution procedure may not exist because dilution would alter the analyte or the matrix causing erroneous results, eg, free drugs or free hormones. Also note that, for some analytes, there may be no clinical relevance to reporting a numeric result greater than a stated value.
2. Analytes for which a dilution procedure is unable to bring the activity or concentration into the AMR should be reported as "greater than" the highest estimated values.
3. Establishment of allowable dilutions is performed when a method is first placed into service. The laboratory director is responsible for establishing the maximum allowable dilution of samples that will yield a credible laboratory result for clinical use.