

IMM.33900 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

IMM.33905 Cut-Off Values for Qualitative Tests Phase II

For qualitative tests that use a quantitative cut-off value to distinguish positive from negative results, the analytic performance around the cut-off value is verified or established initially, and reverified at least every six months thereafter.

NOTE: This requirement applies to tests that report qualitative results based on a quantitative measurement using a threshold (cut-off value) to discriminate between positive and negative results for clinical interpretation. It does not apply to methods where the laboratory is not able to access the actual numerical value from the instrument.

Appropriate materials for establishment and verification of the cut-off are identical to those recommended for calibration verification. The requirement can be satisfied by the process of calibration or calibration verification using calibrators or calibration verification materials with values near the cut-off. It may also be satisfied by the use of QC materials that are near the cut-off value if those materials are claimed by the method manufacturer to be suitable for verification of the method's calibration process.

Verification of the cut-off should also be performed at changes of lots of analytically critical reagents (unless the laboratory director has determined that such changes do not affect the cut-off); after replacement of major instrument components; after major service to the instrument; and when QC materials reflect an unusual trend or shift, or are outside of the laboratory's acceptable limits, and other means of accessing and correcting unacceptable control values fail to identify and correct the problem.

For FDA-cleared or approved tests, the clinical appropriateness of the cut-off value is evaluated as part of the clinical validation performed by the manufacturer. For laboratory-developed tests and modified FDA-cleared or approved tests refer to COM.40640 for validation of clinical claims.

Evidence of Compliance:

- ✓ Records of initial establishment and verification of cut-off value at defined frequency

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) 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): [42CFR493.1253].

IMM.33910**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. 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.

Evidence of Compliance:

- ✓ Patient results or worksheets

CONTROLS

Controls are samples that act as surrogates for patient specimens. They are processed like a patient sample to monitor the ongoing performance of the entire analytic process.

CONTROLS - WAIVED TESTS**Inspector Instructions:**

 ASK	<ul style="list-style-type: none"> • How do you determine when QC is unacceptable and when corrective actions are needed?