GAS CHROMATOGRAPHY (GC) AND HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

Inspector Instructions:

READ	• Sampling of GC/HPLC policies and procedures • Sampling of control, calibration/standards records • Sampling of column verification records • Sampling of records of sample order • Records of signal intensity monitoring
ASK	• How does your laboratory evaluate the effectiveness of hydrolysis? • How does your laboratory evaluate potential carryover? • How have you determined the limit of detection and the AMR?

CHM.16550 Calibration and Calibration Verification — Phase II

Appropriate calibration or calibration verification is performed on each day of patient testing or following the manufacturer's instructions.

NOTE: For qualitative assays, an appropriate calibrator should be run at normal and abnormal levels. For quantitative assays, a multipoint calibration may be required if the measurement has a non-linear response. For some assays, a level near the assay's limit of detection (LOD) or at critical decision point(s) is needed. For measurement systems that have a linear response verified by periodic multipoint calibration verification and AMR verification protocols, a calibration procedure that uses a single calibrator at an appropriate concentration is acceptable. Analyses based on a single point calibration must be controlled by appropriate quality control samples. In addition, inclusion of a negative control (reagent blank) is good laboratory practice.

Evidence of Compliance:

✓ Records of calibration/calibration 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) Clinical and Laboratory Standards Institute. *Gas Chromatography/Mass Spectrometry Confirmation of Drugs; Approved Guideline.* 2nd ed. CLSI Document C43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2010.

CHM.16650 Daily QC - GC and HPLC — Phase II

Appropriate controls are extracted and run through the entire procedure on each day of patient testing.

NOTE: Controls used in chromatographic procedures must evaluate as much of the complete testing process as is technically feasible. The control process includes any pre-treatment, pre-purification or extraction steps, unless non-pretreated control material is appropriate. For qualitative assays, the negative and positive controls should be at concentrations that meaningfully confirm performance below and above the decision threshold for the analyte. For quantitative assays, appropriate controls must include at least one normal sample, and at least one sample reflecting a disease range. For some assays, an additional control concentration may be useful to confirm performance near the assay's LOD, LOQ** or cut-off, if appropriate, or at a concentration consistent with highly abnormal levels that test the AMR.*

**LOD - limit of detection*

***LOQ - limit of quantitation*

If a hydrolysis step is required in the assay, the laboratory includes a control (when available) with each batch to evaluate the effectiveness of hydrolysis.

Evidence of Compliance:

✓ QC records at defined frequency

REFERENCES

1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register.* 2003(Jan 24):5232 [42CFR493.1256(d)(3)(ii)].
2) Clinical and Laboratory Standards Institute. *Gas Chromatography/Mass Spectrometry Confirmation of Drugs; Approved Guideline.* 2nd ed. CLSI Document C43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2010.

CHM.16750 Sample Run Order — Phase II

A record of sample run order is maintained for review.

NOTE: The run list must include blanks, standards, controls, and patients included in each run and be stored with the results of each batch run.

CHM.16770 Chromatographic Characteristics/Column Performance — Phase II

Chromatographic characteristics and column performance are reviewed and approved for each run before results are released.

NOTE: Checks should record testing variables such as flow rate of carrier gas and amount of sample injected and indications of error, including split peaks, doublets, and tailing.

Evidence of Compliance:

✓ Records of review and approval

CHM.16800 Carryover Detection — Phase II

The laboratory has a process to detect and evaluate potential carryover.

NOTE: No matter what type of injection is used, the process must address criteria for the evaluation of potential carryover from a preceding elevated (high concentration) sample to the following sample in each analytical batch analysis.

Evidence of Compliance:

✓ Records of reassessment of samples with potential carryover

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Preliminary Evaluation of Quantitative Medical Laboratory Measurement Procedures.* 4th ed. CLSI guideline EP10. Clinical and Laboratory Standards Institute, Wayne, PA; 2024.
2) Society of Forensic Toxicologists/American Academy of Forensic Sciences. *Forensic Toxicology Laboratory Guidelines.* 2002; 8.2.8:13
3) Clinical and Laboratory Standards Institute. *Gas Chromatography/Mass Spectrometry Confirmation of Drugs; Approved Guideline.* 2nd ed. CLSI Document C43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2010.

CHM.16850 Column Verification — Phase II

New columns are verified for performance before use.

Evidence of Compliance:

✓ Records of column verification

CHM.16950 Column/Detector Monitoring — Phase II

The performance of the column and detector is monitored each day of use.

NOTE: Unextracted standards and extracted calibrators or controls typically containing the target compound(s), may be analyzed each day to monitor critical aspects of column performance. Appropriate criteria for evaluating such parameters as retention time, relative retention time, separation of closely eluting compounds of interest, chromatography quality, and detector response should be established and monitored.

Evidence of Compliance:
- ✓ Records for column and detector monitoring

CHM.17050 Gas Leakage - GC **Phase I**

Gas lines and connections are checked for leaks every time tubing or a connection has been manipulated.

Evidence of Compliance:
- ✓ Records of gas line checks

CHM.17100 Reagent Grade **Phase II**

Reagents, solvents and gases are of appropriate grade.

CHM.17150 Limit of Detection/AMR **Phase II**

The limit of detection (sensitivity) and the AMR for quantitative methods have been determined for each procedure.

Evidence of Compliance:
- ✓ Records of limit of detection and AMR determination

REFERENCES

1) Clinical and Laboratory Standards Institute. *Gas Chromatography/Mass Spectrometry Confirmation of Drugs; Approved Guideline.* 2nd ed. CLSI Document C43-A2. Clinical and Laboratory Standards Institute, Wayne, PA; 2010.

MASS SPECTROMETRY (MS)

Inspector Instructions:

READ	• Sampling of MS policies and procedures • Sampling of calibration and tuning records • Identification criteria compliance
ASK	• How does your laboratory identify possible ion-suppression or enhancement?

CHM.18400 Instrument Calibration **Phase II**

The laboratory calibrates the mass spectrometer and reviews calibration records for acceptability.

REFERENCES