COLA Mass Spec Criteria
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DESCRIPTION:
Kathy Nucifora, COLA Accreditation Division Director, will present the COLA requirements for laboratories performing LC/MS/MS by discussing each of the COLA MSPEC criteria.

About the Speaker:
Kathy received her Bachelor’s degree in Medical Technology from Ball State University, and her Master of Public Health (MPH) Degree from Wichita State University.

Kathy has a wide range of experience managing clinical laboratories, including large and small POLs, and large and small hospital laboratories. She has also taught Clinical Chemistry and Urinalysis in the MLT program at the Community College of Baltimore County, and has lectured on many relevant laboratory topics to a variety of audiences.

Kathy served on the CLSI workgroup that developed companion products for Evaluation Protocol 23 (EP23), and currently serves on the Editorial Review Board for Lab Tests Online. Kathy has been the Accreditation Division Manager at COLA since 2009, and she has since been promoted to Director of Accreditation.
COLA requirements for LC/MS/MS

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MSPEC 1

Check tuning

Does the laboratory have a written procedure, approved by the Laboratory Director, for check tuning each mass spectrometer which includes acceptance parameters and frequency requirements?

At a minimum, the lab must perform electronic tuning at the frequency recommended by the manufacturer. The procedure should include the indicators that would constitute the need for a check tune beyond the established frequency. Tuning must be documented and maintained.
MSPEC 2

Mass calibration

Does the laboratory have a written procedure, approved by the Laboratory Director, for the performance of mass calibration, which includes acceptance parameters and frequency requirements?

Mass calibration should be performed minimally at the frequency specified by the manufacturer, if applicable, or for troubleshooting purposes when QC or other routine quality checks do not fall within established parameters. The procedure should include the indicators that would constitute the need for a mass calibration beyond the established frequency.

Mass calibration must be documented and maintained.

MSPEC 3

Ion suppression

For each reportable analyte, has the laboratory evaluated the specimen matrix for ion suppression?

As part of the method validation for each analyte, interference caused by ion suppression should be evaluated using spiked standards comparisons. The Laboratory Director must review the ion suppression studies to evaluate standards recovery of and decide if further studies are necessary. Adjustments to procedures for identification and quantification of the target analyte must be documented.

Ion suppression studies must be repeated if there is a change in specimen type for any given analyte.
Internal Standard

Are target specific isotopically labeled internal standards used? Or if selected surrogates are used as internal standards are these surrogates similar to the target analyte in physicochemical properties?

The internal standard is critical to the mass spectrometry technique. It is the basis for correcting various sample specific variables such as recovery and matrix effects. To be so used, the internal standards must respond as the target during the total testing process, from sample prep through chromatography and spectrometry. The optimal internal standard is an isotope of the target analyte, identical in all chemical and analytical aspects but with a different mass clearly distinguished by mass spectroscopy. Therefore, isotopes of the target analytes are strongly encouraged to be used as internal standards.

Internal Standard

The internal standard for each analyte is commonly a stable isotope-labeled analog of the measured analyte. A co-eluting isotopically labeled internal standard would correct for sample specific anomalies in chromatography and mass spectrometry. For example, isotopically labeled internal standards correct for target specific variables and matrix effects such as ion suppression or enhancement.

To fully correct for chromatographic variables and matrix effects, ion suppression/enhancement the internal standard must elute from the LC column at the same or nearly the same retention time as the target analyte. Special care must be taken if the internal standard used is not an isotope of the target analyte.
**MSPEC 4**

**Identification criteria**

Does the laboratory procedure for each analyte reported using mass spectrometry include specific peak identification criteria approved by the Laboratory Director?

The procedure must include the laboratory’s criteria for evaluating the mass spec chromatogram, based upon credible reference materials and the laboratory’s own validation studies. Identification criteria may include elution time, qualifier/quantifier ion ratios limits, abundance, calibration, S/N ratio, quality control or other laboratory specific parameters. Identification criteria specific to a particular reported analyte must be defined.

**MSPEC 4.1 (NEW)**

**Signal to noise ratio**

Do the peak identification criteria for each reported analyte include a review of the Signal to Noise (S/N) ratio with a defined minimum S/N of 10:1 or greater, for both the quantifier and qualifier ions, when used to confirm the presence of an analyte?

The capability of the instrument to detect a signal above background noise is critical to low end sensitivity of the assay method.
MSPEC 5

Chromatogram review

Are all sample chromatograms reviewed for accuracy prior to release of the patient report?

_Chromatograms must be reviewed for accuracy by qualified high complexity testing personnel who have documented training and competency assessment._

MSPEC 6

Qualitative QC

If the laboratory uses a cutoff value for reporting positive or negative, do the quality control materials used for each analyte include one with an expected result that is below the positive cutoff value and one with an expected result that is above the positive cutoff value?

_In order for QC to be relevant, materials that challenge the positive cutoff or decision point, on both sides, should be used. This criterion also applies to other methods that have a positive cutoff value._
MSPEC 6.1 (NEW)

QC

Are a minimum of a blank and two levels of QC included with each analytic run?

To account for changes during the run, it is good laboratory practice to run a blank and two levels at the beginning AND two levels at the end of each analytical run. For large runs (>50 samples), two levels of QC in the middle of the run is useful.

MSPEC 7

Technical Supervisor

Does the person designated as Technical Supervisor for the mass spectrometry have the CLIA-defined qualifications for the position plus at least one year of training and/or experience specifically in mass spectrometry?

The Technical Supervisor is a critical position in the mass spectrometry laboratory. Due to the unique expertise required for accurate results in a mass spec lab, COLA requires that the Technical Supervisor have specific documented training or experience related to the clinical use of mass spectrometry. In order to meet the CLIA-defined responsibility of competency assessment, the Technical Supervisor must be well-versed in the day to day operation and critical review of mass spec data.
**MSPEC 8 (NEW)**

**Run-to run retention time monitoring**

Is retention time difference between the quantitation ion and the internal standard monitored for each analyte from run-to-run?

The laboratory must establish acceptability thresholds for run-to-run retention time variability, and take corrective action when the established acceptability thresholds are exceeded.

For accurate peak identification, retention time variance, relative to the internal standard must be monitored. Factors that affect the retention time include temperature, mobile phase solvents, and chromatography column age.

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**MSPEC 9 (NEW)**

**Carryover**

Does the laboratory have a written procedure for performing a carryover study and for identifying and correcting possible carryover errors?

This is commonly done by requiring that a blank sample be injected and analyzed following a sample with a high concentration of the measured analyte. The laboratory procedure defines limits of acceptability and appropriate action(s) when carryover is suspected and exceeds acceptable limits.
MSPEC 10 (NEW)

Method comparisons
As part of the method validation, has the laboratory evaluated each mass spec analyte using comparison testing with another CLIA certified laboratory performing mass spec analyses?

The laboratory must document comparison studies for specimens using another CLIA certified lab that tests for the same analyte(s). Specimens used in the comparison studies must included, at a minimum, a blank (target analyte absent) and two specimens in which the target analyte is present – one with a quantitative value in the lower half of the reportable range and one with a quantitative value in the upper half of the reportable range.

MSPEC 10 (continued)

Method comparisons

The Lab Director must define acceptable limits for bias, and any discrepant results should be investigated and explained by the LD or TS. There may also be rare instances when another CLIA certified lab may not be available for comparison studies. In these rare instances, labs must document rationale for not completing these studies and the LD must approve these actions. For rarely detected analytes, it is acceptable to use spiked samples for comparison testing.

Relative analytical costs and shipping fees are not appropriate reasons for excluding comparison studies.
**MSPEC 11 (NEW)**

**Specimen integrity**

For each analyte tested using mass spectrometry, has the laboratory established requirements for specimen acceptability, including storage temperature and specimen age requirements, prior to testing?

*Specimen stability studies for both primary specimens and extractions must be included with the lab method validation study. Test procedures must include criteria for specimen rejection, including specimen transport, storage, and age limitation criteria validated by the lab and approved by the Laboratory Director.*

**Contact information**

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