interaction with other programs must be clearly stated. The level of detail should be adequate to support troubleshooting, system modifications, or additional programming.

Evidence of Compliance:

- ✓ Records of validation and revalidation after modifications **AND**
- ✓ Records of monitoring for changes to software update tools and other change impacting performance

REFERENCES

1) Vincente FB, Lin DC, Haymond S. Automation of chromatographic peak review and order to result data transfer in a clinical mass spectrometry laboratory. *Clin Chim Acta.* 2019;498(11):84-9.

*****REVISED** 08/24/2023***

FDT.25130 Identification Criteria - Mass Spectrometry Phase II

The identification criteria for analytes detected by mass spectrometry methods (eg, GC/MS, LC-MS/MS) are defined.

NOTE: For single-stage mass spectrometry, one acceptable criterion for compound identification using ion ratios is that the unknown result must have ion ratios within a prescribed acceptance or tolerance limit of calibrator ratios. This limit should be supported by either literature references or through experimental means. Such ion ratio tolerance limits may differ based on the technique applied (eg, GC/MS versus LC/MS) as well as the analyte(s) being determined (eg, compounds with mainly ions of low abundance); thus, a defined limit to cover all methods and analytes cannot be given.

In tandem mass spectrometry using multiple reaction monitoring (MRM), there is at least one transition monitored for the internal standard and another for the analyte.

Evidence of Compliance:

- ✓ QC and test records

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Gas Chromatography/Mass Spectrometry Confirmation of Drugs; Approved Guideline - Second Edition.* CLSI Document C43-A2. (ISBN 1-56238-720-0). Clinical and Laboratory Standards Institute, 940 West Valley Road, Wayne, PA 19087-1898, USA, 2010.
2) Official Journal of the European Communities. Commission Decision implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results (17.8.2002)
3) Clinical and Laboratory Standards Institute (CLSI). *Liquid Chromatography-Mass Spectrometry Methods;* 2nd ed. CLSI document C62. Clinical and Laboratory Standards Institute, Wayne, PA; 2022.

*****NEW** 08/24/2023***

FDT.25150 Matrix Effect Assessment of Mass Spectrometry Assays - Validation Phase II

There is a record of assessment of matrix effects in development and validation of mass spectrometry assays.

NOTE: Matrix effects can affect analyte ionization and performance in both directions: suppression, or less frequently, enhancement. Evaluation of matrix effects must be performed during assay development and validation.

Examples of evaluation protocols may include:

1 *Post Column Infusion - Constant infusion of analyte followed by injection of blank matrix specimen extracts to measure ionization response.*
2 *Mobile Phase/Post Extractions Spiking - Compare response of analyte spiked into mobile phase to that of analyte spiked into blank matrix specimen extracts.*
3 *Internal standard monitoring - Evaluate trends in internal standard abundance and signal to noise ratios during an analytical run that includes blank and spiked matrix specimen extracts.*

The minimum number of different matrix sources may vary based on the matrix, analytical targets, and assay design. Associated data should be used to evaluate the impact of matrix effect on results and define appropriate acceptance criteria for each reportable analyte during routine testing of donor samples.

REFERENCES
1) Annesley TM. Ion Suppression in Mass Spectrometry. *Clin. Chem.* 49, pp. 1041-1044 (2003).
2) Krull I, and Swartz M. Quantitation on Method Validation. *LC-GC,* 16. pp. 1084-1090 (1998).

*****REVISED** 08/24/2023***

FDT.25210 Matrix Effect Assessment of Mass Spectrometry Assays - Routine Monitoring **Phase II**

The laboratory evaluates mass spectrometry assays for possible ion-suppression or enhancement in donor samples during routine testing.

NOTE: Ion suppression (or less frequently, ion enhancement) is a recognized analytical anomaly in mass spectrometry assays. Such suppression can lead to false negative results or poor quantitative analyses (especially near assay limit of quantitation). While difficult to predict and observe from specimen to specimen, certain precautions should be used to try to detect ion suppression or enhancement.

Routine monitoring of the signal intensity of internal standard(s) is an effective way to recognize signal suppression/enhancement in a single patient sample, due to unexpected interfering components of the matrix. Internal standards to be used are those that cover the areas of the elution profile where matrix effects are most pronounced, and that the suitability of these internal standards has been determined (ie, with acceptance limits) during assay development and validation. Internal standard abundance acceptance criteria may be based on signal to noise ratio or may be compared to internal standard abundance in QC samples. As an example, for isotopically-labeled internal standards, if there is poor recovery of the internal standard, a signal to noise ratio greater than 3:1 should still suffice for acceptance of the specimen in question. If recovery of the isotopically-labeled internal standard is considered poor, then an alternate analysis should be considered, eg, the method of standard addition. For analogue-type internal standards, internal standard recovery may be used as a guide for identification of ion suppression/enhancement, although another option, such as the method of standard addition, would be a reasonable alternative. It should be noted that even isotopically-labeled internal standards do not always readily identify ion suppression or enhancement.

Evidence of Compliance:

✓ Records of monitoring using internal standards **OR** records for alternative methods used

REFERENCES
1) Clinical and Laboratory Standards Institute (CLSI). *Liquid Chromatography-Mass Spectrometry Methods;* 2nd ed. CLSI document C62. Clinical and Laboratory Standards Institute, Wayne, PA; 2022.

FDT.25280 Reinjection/Reanalysis **Phase II**

The laboratory defines situations when reinjection or reanalysis is required.

PERSONNEL

The laboratory must be staffed by appropriately qualified and trained personnel under the guidance of the laboratory director. Records of the qualifications and training must be kept and be available for review. Minimum personnel qualifications for analytical testing in the FDT laboratory must be equivalent to those defined in the Personnel section of the Laboratory General Checklist (GEN.54750).

The laboratory must have an organizational chart, personnel policies, and job descriptions that define qualifications and duties for all positions. Personnel files must contain qualifications and continuing education records for each employee.