Evaluation of LCMSMS Deuterium Scrambling in Clinically Significant Small Molecules

Introduction and Objective:
LCMSMS is a powerful tool that brings numerous benefits to the clinical sample-analysis arena. However, due to the complexity of the identification process and some unique challenges that still accompany these benefits, even following sample extraction and cleanup, mass effects from the samples can cause interference in the mass spectra.

Materials and Methods


Investigation of Testosterone Scrambling

Conclusions

- Scrambling was observed for several of the analytes at select transitions. In all cases, scrambling was mitigated or eliminated by optimizing instrument conditions and transition selection.
- Awareness of potential scrambling is important for proper internal standard selection.
- Scrambling was observed on both the Agilent 6410 triple quadrupole and the Waters Xevo G2 Q-ToF at approximately the same degree. For a specific transition, scrambling ratios were consistent between solvent and serum. No matrix effects on scrambling.
- Direct infusion can provide rapid and accurate determination of scrambling ratios. Infusion and chromatographic injection results were consistent.
- Scrambling may be mitigated or eliminated by altering instrument conditions and transition selection. However, there is a need to consider potential impact of scrambling on transitions chosen for optimal sensitivity.
- Deuterium labeled internal standards are a viable option for LC/MS/MS analysis with selection of the appropriate transition. Deuterated standards can be more cost effective than 13C labeled internal standards, more readily available and with lower cost per test. 13C labeled internal standards are more effective when deuterium scrambling issues can be resolved.

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