Best Practices for Maintaining Data Quality in LC-MS

William Clarke, PhD, MBA, DABCC
Associate Professor of Pathology
Johns Hopkins University School of Medicine
Disclosures

- Research & Consulting: Thermo Fisher Scientific
- Disclosed through JHU Office of Policy Coordination
- I will not be discussing specific technology in this presentation
Objectives

• Discuss Common Problems with LC and MS Data Quality

• Review General Approach to LC-MS Troubleshooting

• Discuss Practical Examples & Responses
LC-MS
LC-MS
HPLC/UPLC System Components

MS System Components

http://www.premierbiosoft.com/tech_notes/mass-spectrometry.html
CHROMATOGRAPHY
Common Problems in LC

• Peak Shape
• Variance in retention time
• Carryover
• Unexpected pressure changes
• Leaks
Peak Shape Issues

• Fronting

• Tailing

• Broadening

• Split Peaks
Peak Fronting
Peak Tailing

http://blog.restek.com/?p=7404
Peak Broadening

Split Peaks

http://chromservis.cz/group/hints-and-tips
Shifts in Retention Time
Carryover

Pressure Problems

Good Pressure Trace  Bad Pressure Trace
Leaks

http://www.technobuffalo.com/2013/07/15/controlled-smartphone-leaks-an-old-but-important-strategy/
Common Problems in MS

• Lack of Signal

• Increased Signal Variability

• Increased Background
Disappearing Signal

http://www.platformbedsonline.com/blog/interior-design/what-is-disappearing-design/
Causes for Loss of Signal

- Clogging of probe capillary
- Electronics failure
- Ion flight path interruption
  - Source charging
  - Ion guide deposition (pre-quadrupole)
- Loss of mass calibration integrity
  - Temperature fluctuation
Signal Instability
Causes for Signal Instability

• Nebulizer gas supply
  – Low/interrupted
• Ion source problems
  – Clog
  – Heater malfunction
Increased Background
What Increases the Baseline?

• Deposition in source
• Ion guide deposition
• Electronic ‘noise’
  – Electron multiplier voltage too high
• Nebulizer/collision gas supply quality
PRACTICAL EXAMPLES
Problem:
2/18/2013

Loss of signal observed for analytes in pain management run.
Loss of signal observed for analytes in pain management run.

Resolution:

2/18/2013

Upon investigation, we discovered that mobile phase A and B had been switched. Reversed the bottles and signal was restored.
Problem: 7/5/2013

Signal for pain management is very low, peak shape is degraded and signal to noise ratio is higher than usual.
Problem: 7/5/2013

Signal for pain management is very low, peak shape is degraded and signal to noise ratio is higher than usual.

Resolution: 7/5/2013

The discharge current is very unstable: ranging from 0.5-13, where the value should be 4. APCI needle and source housing were replaced, but still observed the same variability in the discharge current. Observed that the ion sweep cone had a good bit of white deposition on it and I replaced it with a clean one. Discharge current stabilized and I was able to achieve acceptable signal. Discharge current is the setting which applies charge to the ions and if it is unstable, will see low and variable signal.
6/28/2013

Loss of signal observed for analytes in ARV run. Screen shot of internal standard XIC.
Problem: 6/28/2013
Loss of signal observed for analytes in ARV run. Screen shot of internal standard XIC.

Resolution: 6/28/2013
HESI probe needle replaced; signal restored.
Problem:
08/26/2013
Loss of signal observed for analytes in voriconazole run. Screen shot of internal standard and analyte mass chromatograms.
Problem:
08/26/2013

Loss of signal observed for analytes in voriconazole run. Screen shot of internal standard and analyte mass chromatograms.

Resolution:
08/26/2013

Upon autosampler observation, injection syringe was not picking up sample. Transferred sample to vial insert; signal restored.
General Approach to Troubleshooting and Maintaining Data Quality

• Keep good records
• Regular preventative maintenance (don’t miss!)
• Track QC and system suitability to find problems early
• Troubleshooting
  – Look for the easy answer first
  – Systematic investigation of components
  – Change one thing at a time
  – If a change doesn’t fix it → put it back
QUESTIONS??

IF THERE ARE NO QUESTIONS, WE'LL MOVE ON TO THE NEXT CHAPTER.
I HAVE A QUESTION.

CERTAINLY, CALVIN. WHAT IS IT?
WHAT'S THE POINT OF HUMAN EXISTENCE?

I MEANT ANY QUESTIONS ABOUT THE SUBJECT AT HAND.
OH.

FRANKLY, I'D LIKE TO HAVE THE ISSUE RESOLVED BEFORE I EXPEND ANY MORE ENERGY ON THIS.

wclarke@jhmi.edu