Poster Reprint

ASMS 2025
Poster number MP 565

Evaluation of System Robustness for a High Performance Small Form Factor LC/MS Single Quadrupole System

Olivier Chevalier, Patrick Batoon, Lee Bertram, Xiaoli Dong, Russell Burge

Agilent Technologies Inc, Santa Clara, CA

Introduction

Single quadrupole LC/MS systems are basic expressions of quadrupole mass filter technology, allowing users to detect ions with sufficient confidence for identification and detection. Because of their simplicity, they are often considered the immediate advancement from UV-Vis and UV-DAD for chromatographic applications, providing information rich data about the analyte such as molecular weight, charge state, elemental composition, without consuming large amounts of sample. However, quadrupole mass spectrometers are still highly complex systems, involving collection and transmission of analytes and matrix contaminants, which can render the instrument to system soiling, ion optics contamination, degradation of detector performance over time, and other issues not typically seen with light-based detectors.

This poster is a demonstration of system robustness & ruggedness against these factors over a series of 800 consecutive injections.

The *New* Pro iQ and Pro iQ Plus Mass Detectors

The Pro iQ and Pro iQ plus sytems are the next generation of Agilent's LC/MS Single Quadrupole instruments --- these systems features a breakthrough, compact small-form factor design, while providing the sensitivity, speed, and m/z transmission range of larger systems.

	Pro iQ	Pro iQ Plus
Mass Range	m/z 2-1600	m/z 2-3000
Sensitivity (IDL)	IDL <100 fg	IDL <25 fg
Detection	Routine	Routine, Trace Analysis, and Extended Mass Range
Applications	Purification, Detection, Quantitation, Biomolecule Deconvolution	

Experimental

Small Molecules in Crashed Plasma Matrix

- LC/MS 7-analyte system suitability standard (5191-4544)
- CD-1 (ICR) Mouse Plasma (MSE00PL32NC-0105086)

To a commercial mouse plasma aliquot (2mL) was added 8mL of cold Methanol. Resulting mixture was vortexed and kept on ice before being centrifuged at 15,000 RPM for 15 minutes at 4 °C. Supernatant was collected and spiked with Disco7 mix.

LC Method Parameters

- 1290 Infinity III LC System

LC Parameter	Value
Column	Poroshell 120 EC-C18, 50 x 2.1 mm, 1.9 µm
Mobile Phase A	H2O + 0.1% FA
Mobile Phase B	ACN + 0.1% FA
Flow Rate	1 mL/min
Injection Volume	1.0µL
Column Temp.	40°C
Gradient Program	Time (min) %B 0.0 3 1.50 97 1.90 97 2.00 3 2.25 3 3.00 End Run

Mass Spectrometer Parameters

- Pro iQ Plus with Agilent Jet Stream source

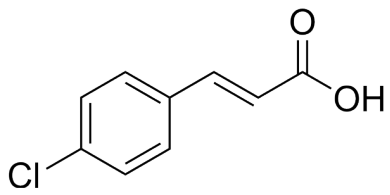
Parameter	Positive	Negative
Ion Source	Agilent Jet Stream (AJS)	
Drying Gas Temp	300 °C	300 °C
Drying Gas Flow	13 L/min	13 L/min
Nebulizer	35 PSI	35 PSI
Capillary Voltage	3000 V	3000 V
Sheath Gas Temp	250 °C	250 °C
Sheath Gas Flow	12 L/min	12 L/min
Nozzle Voltage	1500 V	1500 V

Results and Discussion

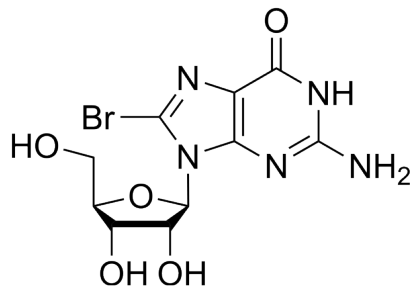
LC/MS 7-analyte System Suitability Standard

The LC/MS 7-analyte System Suitability Standard (LCMS-7) was designed to test chromatography and ionization conditions. It is comprised of 3 pharmaceutical analytes and 4 phthalates (representative of Extractables & Leachables)

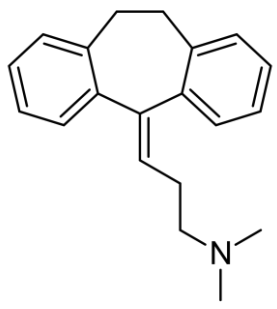
4-Chlorocinnamic Acid (4-CC)



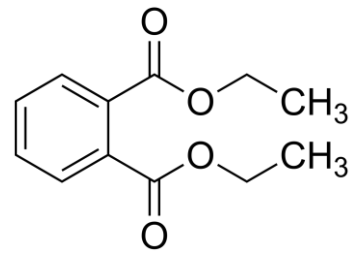
8-Bromoguanosine (8-BG)



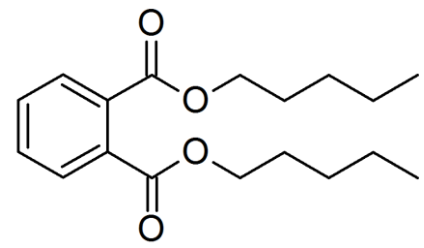
Amitriptyline (AMI)



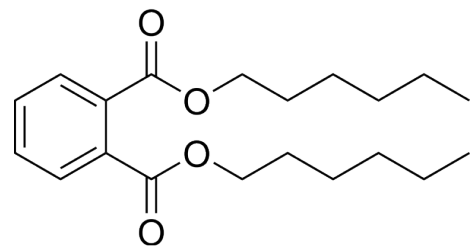
Diethyl Phthalate (DEP)



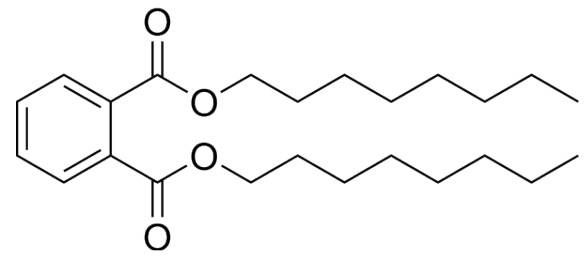
Diamyl Phthalate (DAP)



Dihexyl Phthalate (DHP)



Dioctyl Phthalate (DOP)



Mass Spectrometer Detection Parameters

Start mass	End mass	Scan time	Fragmentor	Polarity	Compound name	Mass	Quad Res	Dwell
m/z 50	m/z 850	127 ms	100 V	Positive		MS Full Scan Parameters		
m/z 50	m/z 850	127 ms	100 V	Negative				
Targeted Compound Detection MS SIM Parameters			100 V	Negative	8-BG	m/z 360	Unit	30 ms
			100 V	Negative	4-CC	m/z 181	Unit	30 ms
			100 V	Positive	DOP	m/z 390.7	Unit	30 ms
			100 V	Positive	DHP	m/z 335	Unit	30 ms
			100 V	Positive	DAP	m/z 307	Unit	30 ms
			100 V	Positive	AMI	m/z 278	Unit	30 ms
			100 V	Positive	DEP	m/z 223	Unit	30 ms

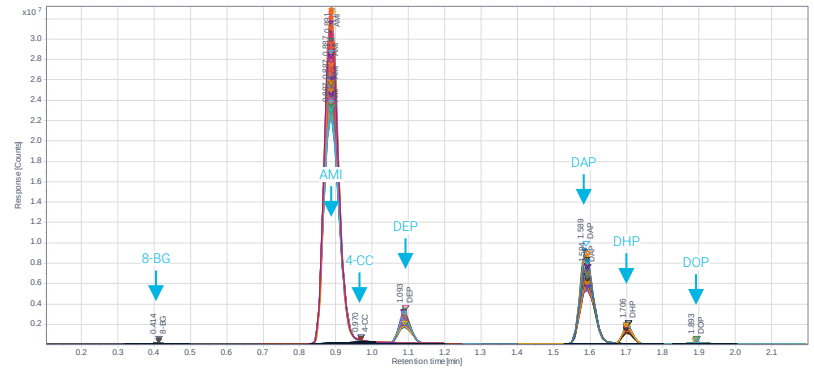
System Robustness across 800 Consecutive Injections

LCMS-7 in crashed mouse plasma was injected nonstop over the 800 injections period. The injection-to-injection time was ~5 minutes/run, resulting in 2.5 days of nonstop detection. Raw RT and Signal statistics are below:

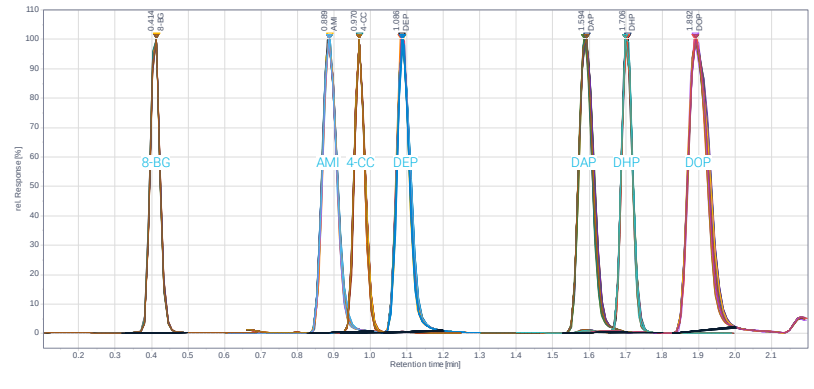
	DEP	AMI	DAP	DHP	DOP	4-CC	8-BG
Raw Abundance Statistics							
Area mean	5906853	76993643	19124964	2965189	532561	538071	243576
Area RSD	**13.108%**	**9.008%**	**11.404%**	**11.178%**	**5.526%**	**5.87%**	**6.812%**

	DEP	AMI	DAP	DHP	DOP	4-CC	8-BG
Retention Time Statistics							
RT mean	1.09 min	0.888 min	1.593 min	1.701 min	1.893 min	0.971 min	0.414 min
RT RSD	**0.176%**	**0.144%**	**0.1%**	**0.102%**	**0.066%**	**0.026%**	**0.23%**

Raw Abundance (every 25 inj)



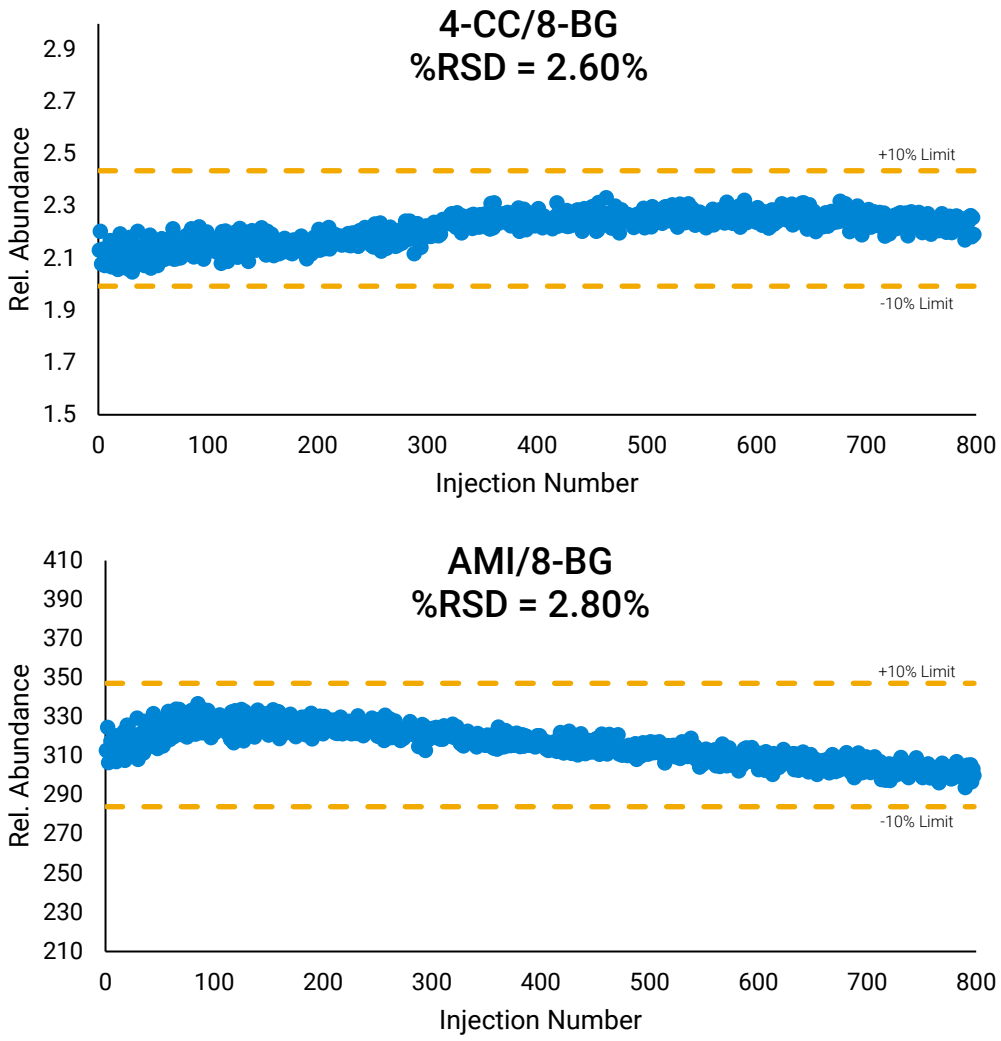
Normalized Abundance (every 25 inj)

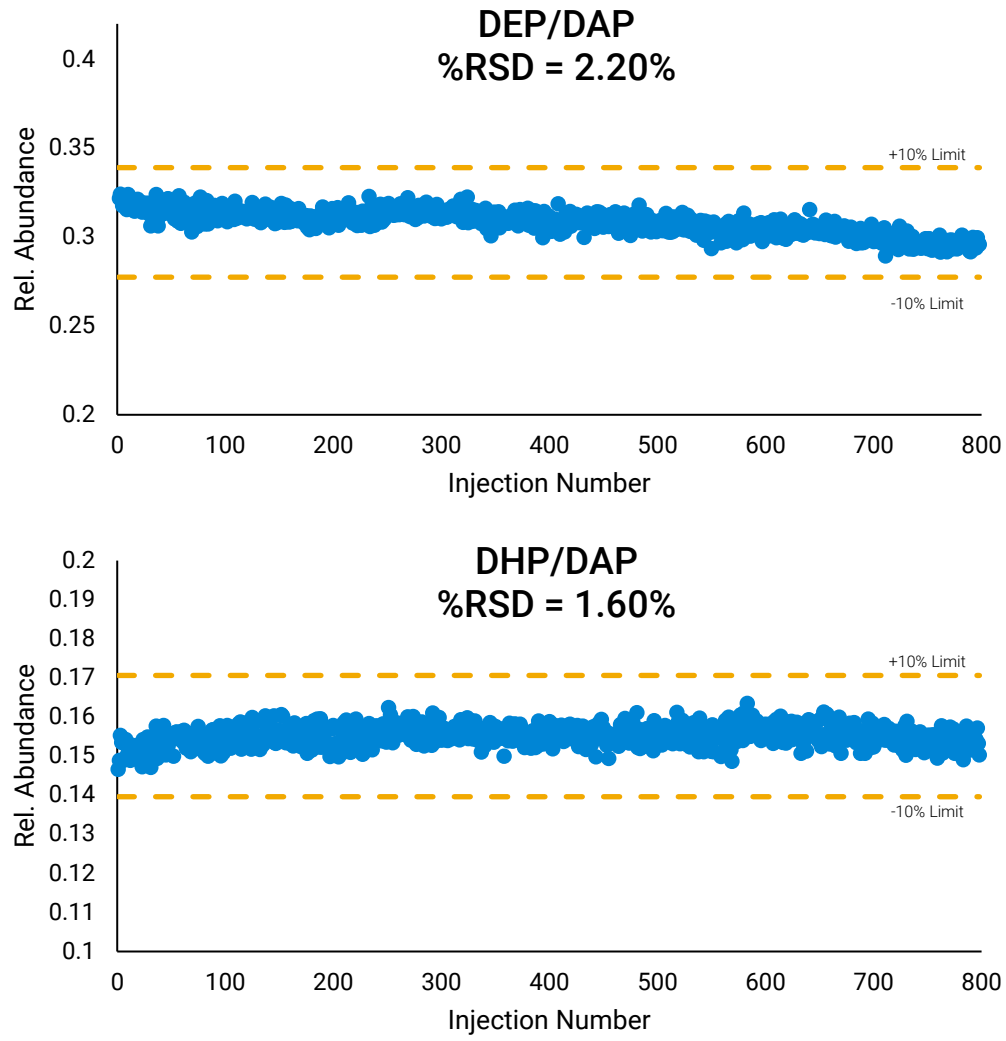


Results and Discussion

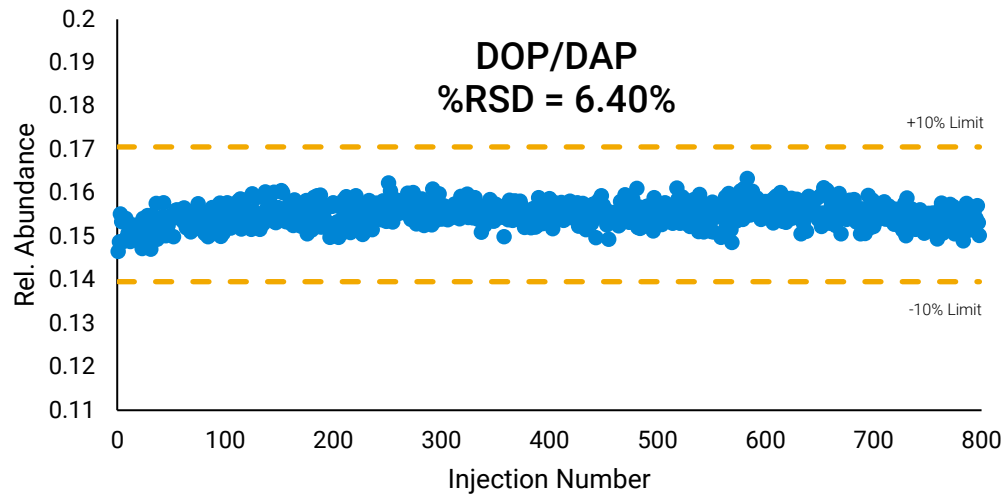
System Robustness across 800 Consecutive Injections (cont.)

The plots below are the relative abundances, corrected according to the chemical classes. The active pharmaceutical components are corrected with 8-Bromoguanosine (8-BG), while the phthalates were correct with Diamyl Phthalate (DAP). Although raw abundances over time resulted in RSD<15%, when corrected with an Internal-standard, relative abundances resulted in RSD<7% - demonstrating excellent detection stability over the course of this experiment.





	4-CC/8-BG	AMI/8-BG	DEP/DAP	DHP/DAP	DOP/DAP
Relative Abundance Statistics					
Rel. Area mean	2.215	315.641	0.308	0.155	0.028
StDev	0.057	8.789	0.0067	0.0025	0.0018
%RSD	**2.60%**	**2.80%**	**2.20%**	**1.60%**	**6.40%**
-10% Limit	1.993	284.077	0.277	0.140	0.025
+10% Limit	2.436	347.205	0.339	0.171	0.031



Conclusions

- 800 injections of crashed rat plasma injected into the Infinity III 1290 HPLC and Pro iQ plus system
- Data was acquired in Mixed Mode (Scan+SIM) with rapid polarity switching for the full duration of the experiment
- Raw Abundance resulted in %RSD <15%, which includes factors like system soiling, column and detector aging, accumulation of material over time.
- When normalized against an internal standard Rel. Abundance %RSD<3%, except for DOP/DAP (Rel. Abundance %RSD<7%)

https://www.agilent.com/en/promotions/asms

This information is subject to change without notice.

DE-006690

© Agilent Technologies, Inc. 2025
Published in USA, May 15, 2025

Agilent
Trusted Answers