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Agilent RoHS Compliant Ion Injector for LC/MS Single Quadrupole and Triple Quadrupole Instruments

Samuel P. Haddad, Jennifer Sanderson, and Paul Tripp

Agilent Technologies, Inc.

Introduction

The ion injector on an Agilent LC/MS system is used as an entry point into the portion of the instrument under vacuum and to accelerate ions into the ion focusing optics. The entrance of the ion injector is charged with the opposite electrical charge of the ionization mode. The opposite polarity pulls ions through the nitrogen drying gas and into the sample entry point of the ion injector. The opposite end of the ion injector is also charged differentially (fragmentor) to accelerate the ion into the focusing optics (Figure 1).

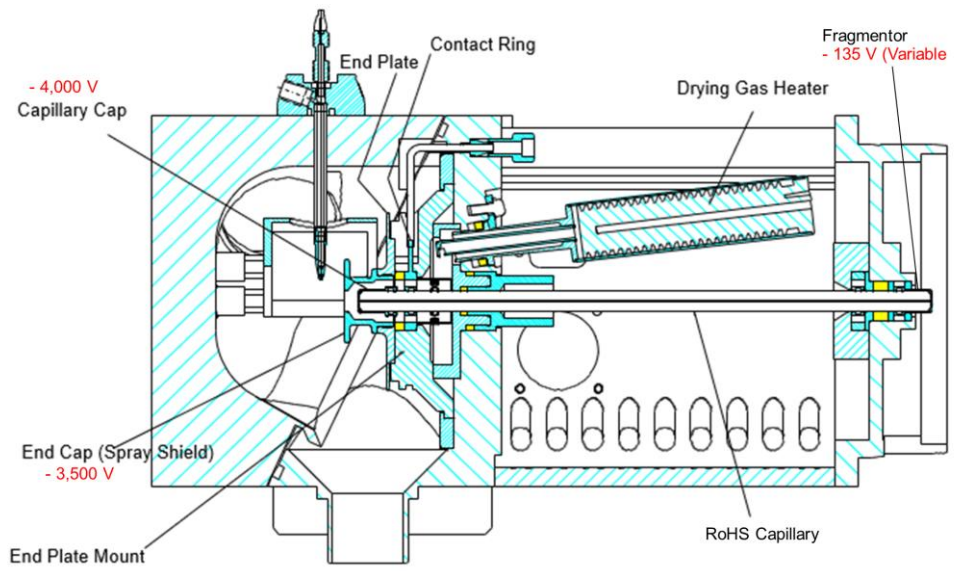

Figure 1. Diagram of the desolvation chamber showing where the RoHS ion injector is located inside the MS source and the applied voltages in positive mode.

Recently, governments globally have begun to reduce the use of hazardous materials in electronic components. Specifically, the Restriction of Hazardous Substances in Electrical and Electronic Equipment (RoHS) Directive in the European Union has been driving this effort. Legacy ion injectors (capillary) were allowed in Agilent instruments under an exception. However, the new model of ion injector (Figure 2) now meets full RoHS compliance without sacrificing previous performance. The current studies demonstrate equivalent functionality between the previous and new ion injector models (Table 1).

Table 1. Description and part numbers for the RoHS and Legacy ion injectors

Description	RoHS part number	Legacy part number
FS Ion Injector, 0.6 mm ID, 180 mm	G3911-30000	G1960-80060
Ultivo and MSD iQ Ion Injector	G3911-30001	G6301-80004

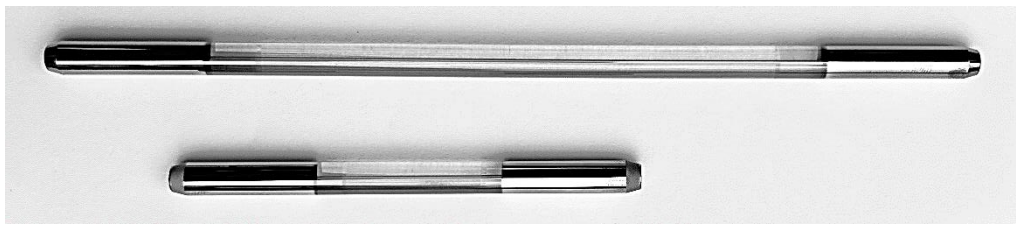

Figure 2. RoHS ion injector, part number G3911-30000 (top) and part number G3911-30001 (bottom).

Experimental

Chemicals and reagents

Pharmaceutical standards were obtained from Cerrilliant (Round Rock, TX). LC/MS grade water (part number: 5191–5121), acetonitrile (part number: 5191–5101), and formic acid (part number: G2453-85060) were obtained from Agilent Technologies, Inc. (Santa Clara, CA)

Pharmaceuticals on the MSD iQ (G6160A)

Typically, the LC/MSD is used to look at product, purity, or process chemistry in pharmaceutical manufacturing. A selective ion monitoring (SIM) method was developed to look at pharmaceutical compounds in neat solvent. An Agilent Infinity II LC, consisting of a binary pump, multisampler, and column compartment, was used with an MSD iQ single quadrupole. A gradient elution methodology consisting of solvent A as 0.1% formic acid in water and solvent B as acetonitrile, was used. SIM MS ions and retention times are shown in Table 2. For all SIM transitions the fragmentor voltage was 100.

Table 2. Instrument parameters for the SIM method on the G6160A

Analyte Name	SIM Ion (m/z)	RT (mins)
Amitriptyline (AMI)	278.1	4.824
Carbamazepine (CAR)	236.9	4.706
Diltiazem (DIL)	415.1	4.449
Diphenhydramine (DIP)	256.6	4.232
Fluoxetine (FLU)	310.1	4.942
Haloperidol (HAL)	376.1	4.441
Lorazepam (LOR)	320.8	5.001
Methylphenidate (MET)	234.3	3.298
Sertraline (SER)	306.0	4.997

Pharmaceuticals in human urine on the Ultivo TQ (G6465B)

A multiple reaction monitoring (MRM) method was developed to detect pharmaceuticals in human urine diluted 10:1 with 0.1% formic acid in water. An Agilent Infinity II LC, consisting of a binary pump, multisampler, and column compartment was used with the Ultivo. A gradient elution methodology consisting of solvent A as 0.1% formic acid in water and solvent B as acetonitrile, was used. MRM MS parameters are listed in Table 3.

Table 3. Instrument parameters for the MRM method on the G6465B.

Analyte Name	Precursor Ion (m/z)	Product Ions (m/z)	Frag (V)	CE (V)	RT (mins)
Amitriptyline (AMI)	278.2	233.1, 90.9	110.0	16,32	4.780
Carbamazepine (CAR)	237.1	194, 193	110.0	20,44	4.689
Diltiazem (DIL)	415.2	177.9, 108.9	110.0	28,70	4.397
Diphenhydramine (DIP)	256.2	167, 164.9	80.0	12,56	4.184
Fluoxetine (FLU)	310.1	148, 44.1	80.0	4,16	4.896
Haloperidol (HAL)	376.2	164.9, 122.9	140.0	28,48	4.400
Lorazepam (LOR)	321.0	274.9, 229	110.0	32,32	4.984
Methylphenidate (MET)	234.1	84, 56	110.0	24,60	3.261
Sertraline (SER)	306.1	274.9, 158.8	80.0	8,32	4.955

Results and Discussion

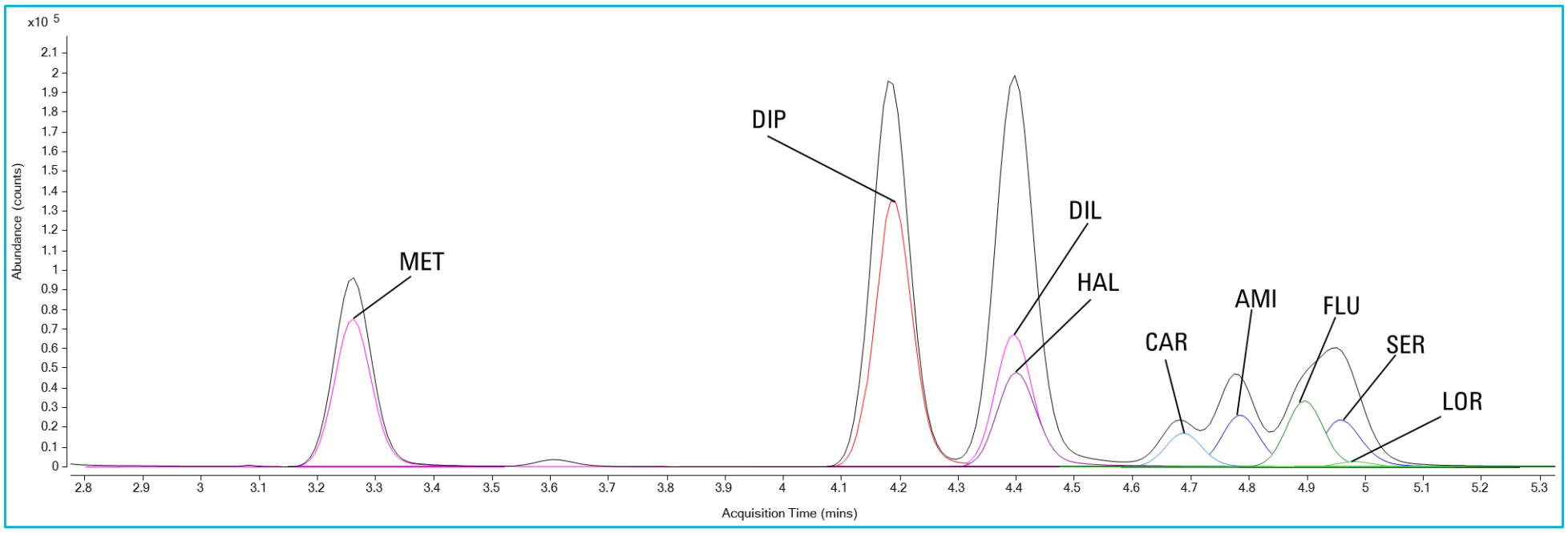

Figure 2. Total Ion Chromatogram (TIC) and Extracted Ion Chromatograms (EICs) of target pharmaceuticals at 1 part per billion.

A — MSD iQ Accuracy (%) at 10 ppb

RoHS	Analyte	Legacy
91.9	AMI	99.6
103.4	CAR	86.5
92.7	DIL	98.9
100.3	DIP	101.3
91.9	FLU	96.2
104.9	HAL	99.4
99.8	LOR	104.3
96.6	MET	100.6
91.4	SER	96.1

B — MSD iQ Precision (%RSD) at 10 ppb

RoHS	Analyte	Legacy
0.97	AMI	0.76
1.43	CAR	2.17
1.36	DIL	0.65
1.67	DIP	0.98
0.30	FLU	1.35
0.44	HAL	1.11
1.24	LOR	0.70
0.54	MET	0.44
0.94	SER	1.59

C — MSD iQ Accuracy (%) at 100 ppb

RoHS	Analyte	Legacy
97.2	AMI	100.6
106.5	CAR	95.2
97.5	DIL	100.7
97.2	DIP	94.3
95.3	FLU	97.6
102.6	HAL	101.5
104.8	LOR	107.0
97.9	MET	100.5
96.4	SER	96.1

D — MSD iQ Precision (%RSD) at 100 ppb

RoHS	Analyte	Legacy
0.30	AMI	1.00
0.13	CAR	1.37
0.29	DIL	0.95
0.46	DIP	1.49
0.51	FLU	1.27
0.25	HAL	0.86
0.70	LOR	0.99
0.28	MET	0.95
0.52	SER	1.54

Figure 3. Comparison of the RoHS and Legacy ion injector method validation parameters on the MSD iQ (G6160A). (A) Percent accuracy at 10 parts per billion. (B) Precision (%RSD) at 10 parts per billion. (C) Percent accuracy at 100 parts per billion. (D) Precision (%RSD) at 100 parts per billion.

Instrument Detection Limit (ppb) at 10 ppb spike level

RoHS	Analyte	Legacy
2.67	AMI	2.27
4.42	CAR	5.61
3.78	DIL	1.91
5.01	DIP	2.98
0.83	FLU	3.87
1.40	HAL	3.31
3.69	LOR	2.18
1.57	MET	1.33
2.58	SER	4.57

Figure 4. Comparison of the RoHS and Legacy ion injector instrument detection limits (IDL) at the 10 parts per billion spiking level.

Chromatographic performance

To effectively compare the RoHS vs Legacy ion injectors a robust and highly repeatable methodology was required. On both the single quadrupole and triple quadrupole instruments, chromatographic separation was as expected (Figure 2). Weak base target analytes were chosen for analysis in positive mode because they perform well in the mobile phase conditions selected and are not subject to transformation or sorptioning under current chromatographic conditions.

Results and Discussion

A — Limit of Detection (LOD) at 10 ppt spike level

RoHS	Analyte	Legacy
1.70	AMI	2.00
2.30	CAR	2.00
0.90	DIL	1.00
1.00	DIP	1.30
1.00	FLU	1.80
1.30	HAL	1.70
2.50	LOR	2.20
1.40	MET	1.70
2.10	SER	1.70

B — Limit of Quantitation (LOQ) at 10 ppt spike level

RoHS	Analyte	Legacy
5.80	AMI	6.60
7.60	CAR	6.70
3.10	DIL	3.20
3.50	DIP	4.20
3.50	FLU	6.00
4.30	HAL	5.80
8.40	LOR	7.30
4.70	MET	5.80
6.90	SER	5.50

C — Ultivo Accuracy (%) at 10 ppt

RoHS	Analyte	Legacy
100.0	AMI	99.0
101.0	CAR	98.0
97.0	DIL	98.0
99.0	DIP	98.0
99.0	FLU	102.0
101.0	HAL	100.0
98.0	LOR	87.0
98.0	MET	97.0
101.0	SER	103.0

D — Ultivo Precision (%RSD) at 10 ppt

RoHS	Analyte	Legacy
5.80	AMI	6.60
7.50	CAR	6.90
3.20	DIL	3.30
3.50	DIP	4.30
3.50	FLU	5.90
4.30	HAL	5.70
8.50	LOR	8.50
4.80	MET	6.00
6.80	SER	5.40

E — Ultivo Accuracy (%) at 100 ppt

RoHS	Analyte	Legacy
101.1	AMI	102.5
105.5	CAR	103.8
107.0	DIL	109.3
104.9	DIP	105.3
98.6	FLU	101.7
103.2	HAL	103.6
103.4	LOR	105.6
106.1	MET	106.2
100.5	SER	104.2

F — Ultivo Precision (%RSD) at 100 ppt

RoHS	Analyte	Legacy
2.00	AMI	2.70
2.20	CAR	2.90
1.30	DIL	1.70
1.50	DIP	1.70
1.50	FLU	2.10
1.30	HAL	1.60
1.60	LOR	3.70
2.10	MET	2.20
1.40	SER	1.90

Figure 5. Comparison of the RoHS and Legacy ion injector method validation parameters on the Ultivo TQ (G6465B). (A) Limit of detection at the 10 part per trillion spiking level. (B) Limit of quantitation at the 10 part per trillion spiking level. (C) Percent accuracy at 10 parts per trillion. (D) Precision (%RSD) at 10 parts per trillion. (E) Percent accuracy at 100 parts per trillion. (F) Precision (%RSD) at 100 parts per trillion.

RoHS and Legacy Ion Injector Comparison on the MSD iQ (G6160A)

Before application work was performed, 10 autotunes were performed on both the RoHS and Legacy capillary. All tunes passed and showed no significant differences in how the tune algorithm applied physical parameters to the instrument. An eight-point calibration curve was made ranging from 5 to 500 ppb and all R^2 values were > 0.995 on both ion injectors. Accuracy at the 10 and 100 ppb levels were assessed and showed passing criteria on both ion injectors (Figure 3). Passing criteria for accuracy was from 80 to 120 % of target concentration. Precision at the 10 and 100 ppb levels also passed acceptance criteria, which was <5 %RSD. Instrument detection limits (IDL) at the 10 ppb spiking level were comparable and of the same order of magnitude (Figure 4).

The only exception was that FLU had an IDL of 0.83 on the RoHS injector vs 3.87 on the Legacy injector.

RoHS and Legacy Ion Injector Comparison on the Ultivo (G6465B)

Ten autotunes were run on each ion injector and showed no significant difference in how the tune algorithm applied physical parameters to the instrument. Human urine is a complex matrix that was chosen to challenge the instrument and ion injector. The Ultivo is a sensitive instrument, so a trace level calibration range, relevant to current applications, was chosen. An eight-point calibration curve ranging from 5 to 1000 ppt was made and all R^2 values were > 0.995 on both ion injectors. LOD, LOQ, Accuracy and Precision were examined to compare the RoHS and Legacy ion injector (Figure 5).

Results and Discussion

LOD values were < 2.6 ppt for all analytes, which was below the calibration range. LOD was highly comparable between both ion injectors showing that the urine matrix did not affect detection limits on either injector. LOQ was < 7.7 ppt for all compounds and in several cases below the calibration range. Similar to LOD, LOQ values were comparable between both ion injectors. For this experiment LOD and LOQ were determined statically using the standard deviation of replicate injections. The low-level LOD and LOQ values show a high level of reproducibility from injection to injection. This is also seen in the precision at 10 and 100 ppt where all RSD values are < 10 %RSD, which was the criteria of acceptability given the low level of detection expected. Further accuracy at the 10 and 100 ppt level was comparable and reproducible on both ion injectors. The acceptance criteria for accuracy were 80 to 120 %, however in the current study accuracy on both injectors fell between 90 to 110 %.

Conclusions

- The RoHS ion injector shows similar performance to the legacy capillary.
- No appreciable differences in performance were observed on two different MS platforms.
- The RoHS capillary will be offered as a replacement for current Legacy ion injectors in the future.

More Information

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