Poster Reprint

ASMS 2022
Poster number TP327

Accelerated lifetime testing with real-time Early Maintenance Feedback (EMF) diagnostic monitoring on the 6475 triple quadrupole LC/MS

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Introduction

Triple quadrupole LC/MS systems have become widely accepted as a platform for targeted, large-batch, sample analysis on a day-to-day basis. A primary concern for routine/targeted analysis is instrument stability; which can vary over time due to the soiling of crucial ion optics components. While incorporating an internal standard and measuring abundance ratio may help alleviate signal drift from a data-analysis standpoint, it does not give key indications to the quality of the instrument's health.

To help alleviate concerns on instrument health and longevity, **the new Agilent 6475 triple quadrupole LC/MS system was designed with onboard intelligence that actively reports on the instrument health and status through Early Maintenance Feedback (EMF).**

EMF reports various aspects pertaining to instrument maintenance such as "last tuned", number of samples injected, number of diverter valve switches, last rough pump oil change, last gas filter change, and real time reports on detector health, nebulizer blockage, ion injector blockage, and spray stability status.

Here we present a use case to trigger Early Maintenance Feedback (EMF) events to simulate heavy instrument use through 10,000 sample injections of spiked bovine urine. The sample matrix was specifically chosen due the challenging endogenous components that may cause measurement issues (salts, metabolites, fats, proteins, etc…).

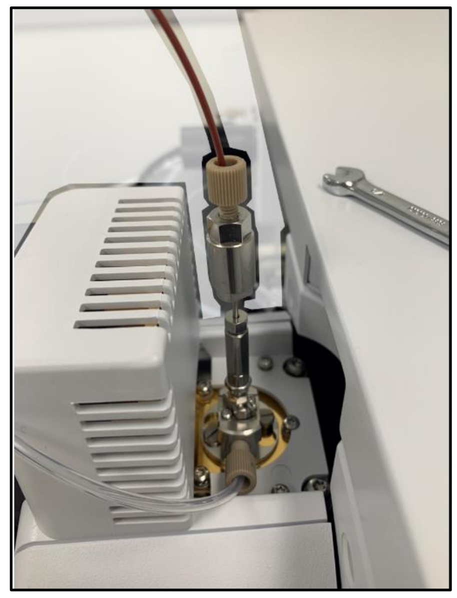
As this is not a true analytical method, the intention of this poster is primarily to stress the Early Maintenance Feedback mechanisms, test the instrument's response to heavy matrix accumulation, stability of tune parameters, and recovery of instrument tuning if out of spec.

The 6475 LC/TQ with VacShield and Early Maintenance Feedback

Experimental

Bovine urine diluted 1:1 in acetonitrile/water and were delivered to the system using an Infinity II 1290 HPLC with dual injector setup in overlapped injection mode with isocratic flow of 90:10 acetonitrile/water + 0.1% Formic acid.

To generate sufficient backpressure for stable HPLC operation and to simulate the use of an analytical HPLC column, a ZORBAX Extend-C18, 80Å, 2.1 mm, 1.8 µm, 1200 bar pressure limit, UHPLC guard column was used (821725-107), as shown in the figure below.



A ZORBAX Extend-C18, 80Å, 2.1 mm, 1.8 µm, 1200 bar pressure limit, UHPLC guard column was appended directly to the nebulizer to simulate the passing of a sample through a chromatographic column.

MRM signals of various analytes were recorded to ensure that ions were reaching the detector. This current served to "age" the Electron Multiplier horn as if it were in standard/normal operation.

Early Maintenance Feedback (EMF) provided real time monitoring of the instrument health. EMF intelligence is incorporated in the systems firmware to monitor for crucial points along the ion path such as ion injector blockage, precipitation on the nebulizer, and detector's estimated lifetime. Additionally, the instrument automatically monitored for commonly disruptive potential maintenance events such as poor spray stability and ion beam blockage events originating at the nebulizer or ion injector.

No cleaning or removal of the nebulizer, ion injector, or ion source chamber and spray shield was carried out over the course of the injection series.

Post-Experiment Investigations

Upon completion of the injection series, an examination of the ion source and desolvation assembly was carried out to identify regions of ion burn, salt accumulation, broad matrix deposition, or potential modes of failure.

Tune ion abundances that were recorded during the Checktune procedure were plotted to evaluate the effects of matrix over time.

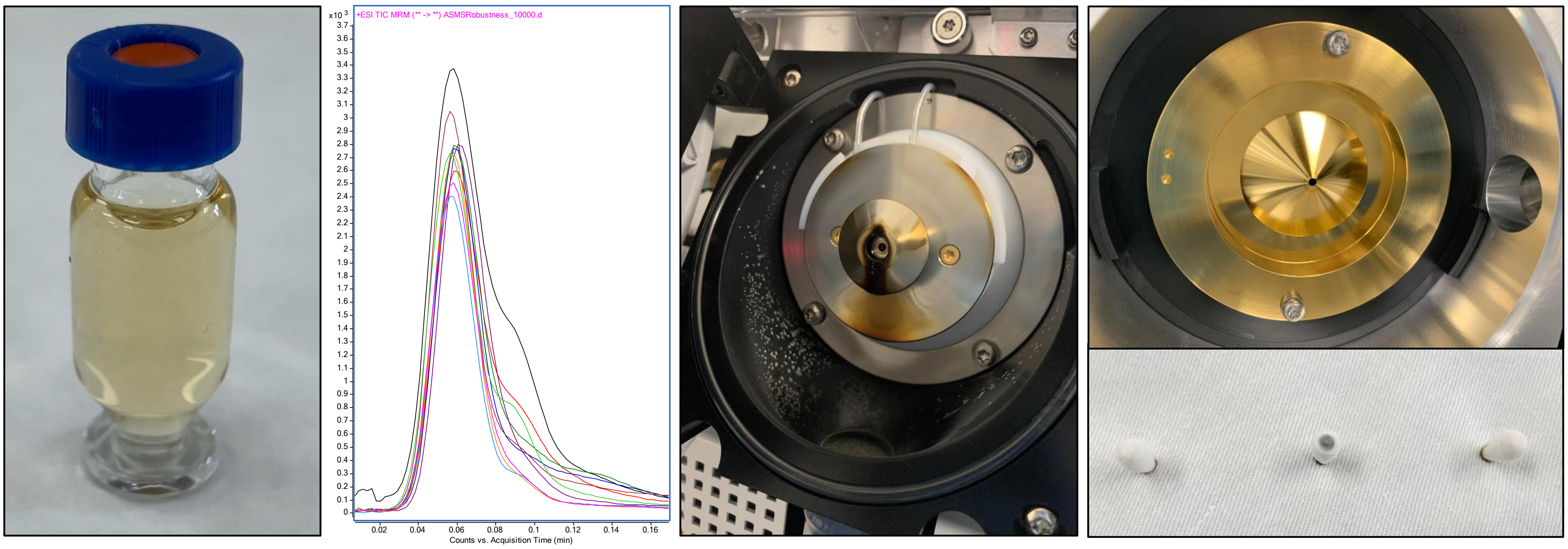
Pre-experiment to Post-experiment Physical Attributes

A) Sample vial with diluted matrix (Bovine urine 1:1 acetonitrile/water).

B) Sample overlaid MRM TIC every 1,000 injections.

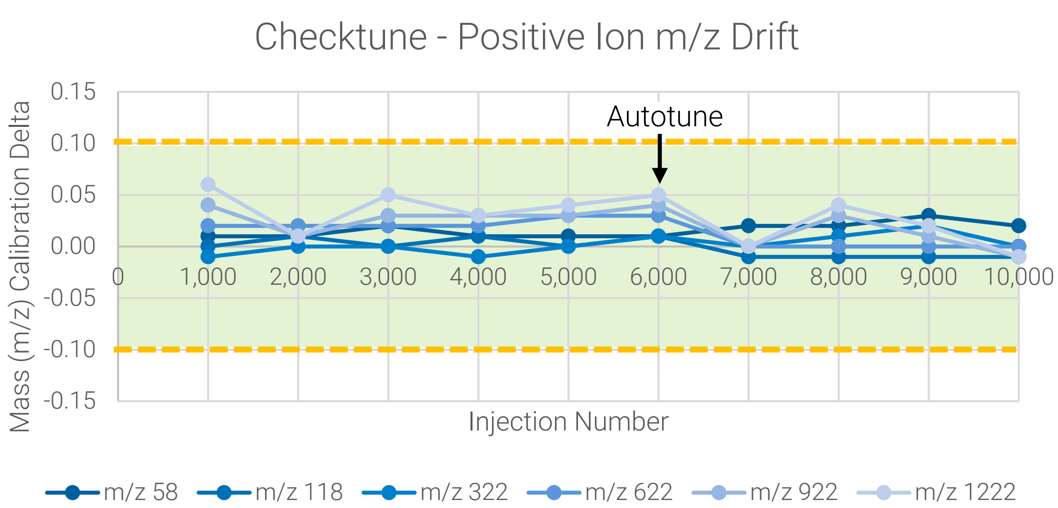
C) MS inlet after 10,000 injections. Spray shield and capillary cap with heavy contamination while maintaining ion injector performance

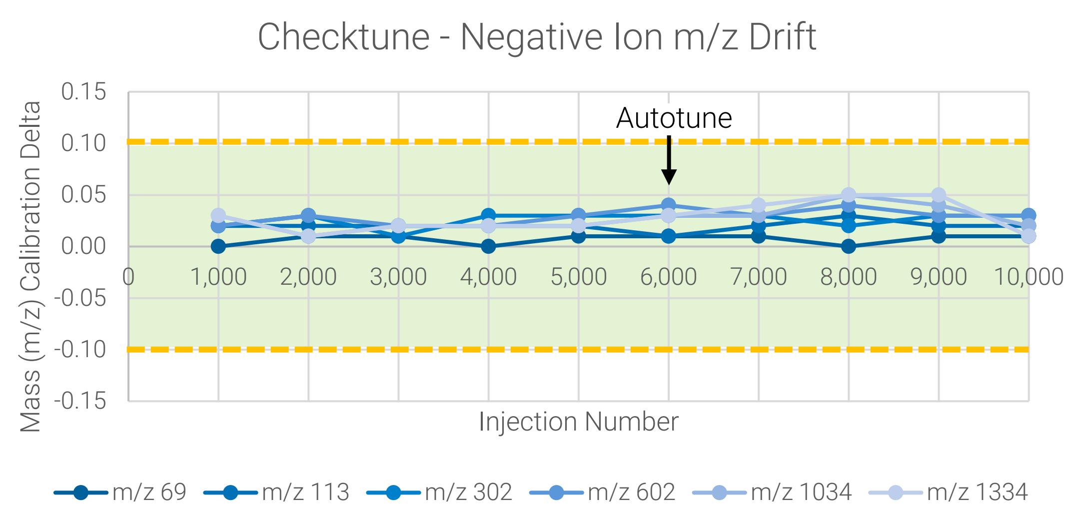
D) Skimmer with desolvation assembly removed. Cotton swabs with IPA to highlight matrix contamination in vacuum region after ion injector (front of skimmer, back of skimmer, octopole).

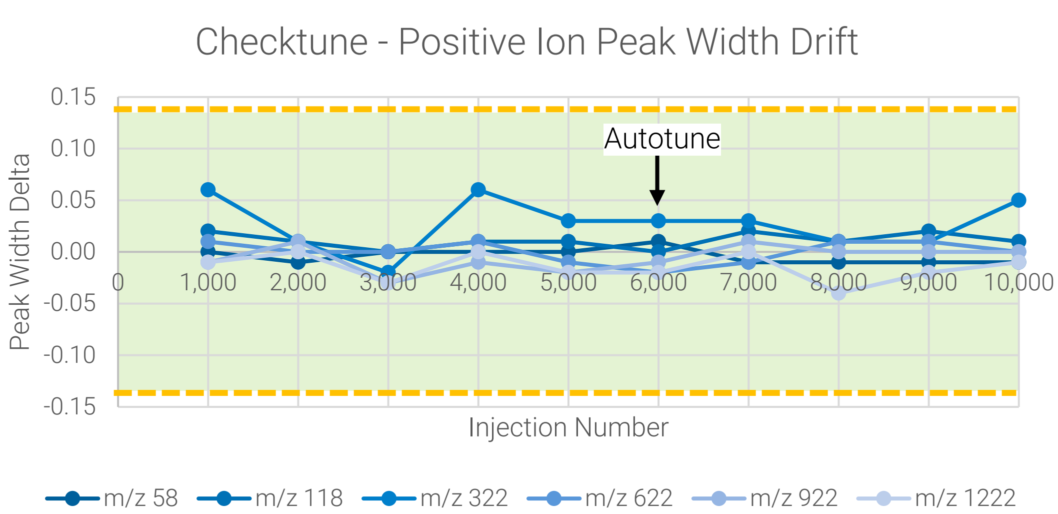


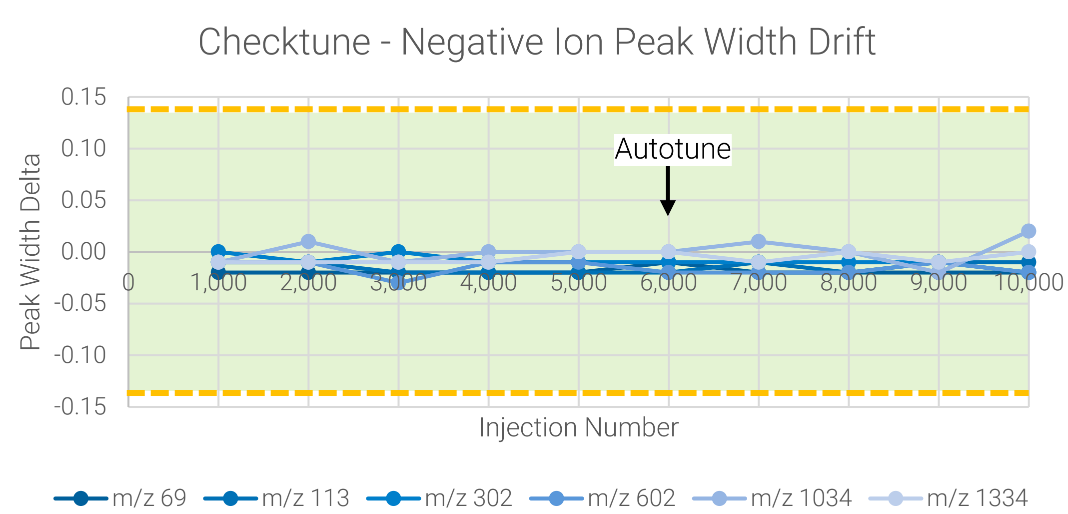
Tune ion tolerances as matrix components accumulated onto the spray chamber

Checktunes were performed every 1,000 injections with no cleaning of the nebulizer or ion injector. Despite heavy front-end contamination, mass calibration (m/z drift) and mass spectral peak width (FWHM) remained within tolerance and stable over the 10,000 injections. Tolerances for m/z<1000, mass calibration must remain within ±0.1 Da, while peak width must remain ±0.14 Da. Over the course of injection series, the instrument reported an "Out of Tolerance" event at injection 6,000; this was remedied by running the Autotune procedure before proceeding to the next series of injections.









Results and Discussion

No critical Early Maintenance Feedback events were triggered over the course of this investigation

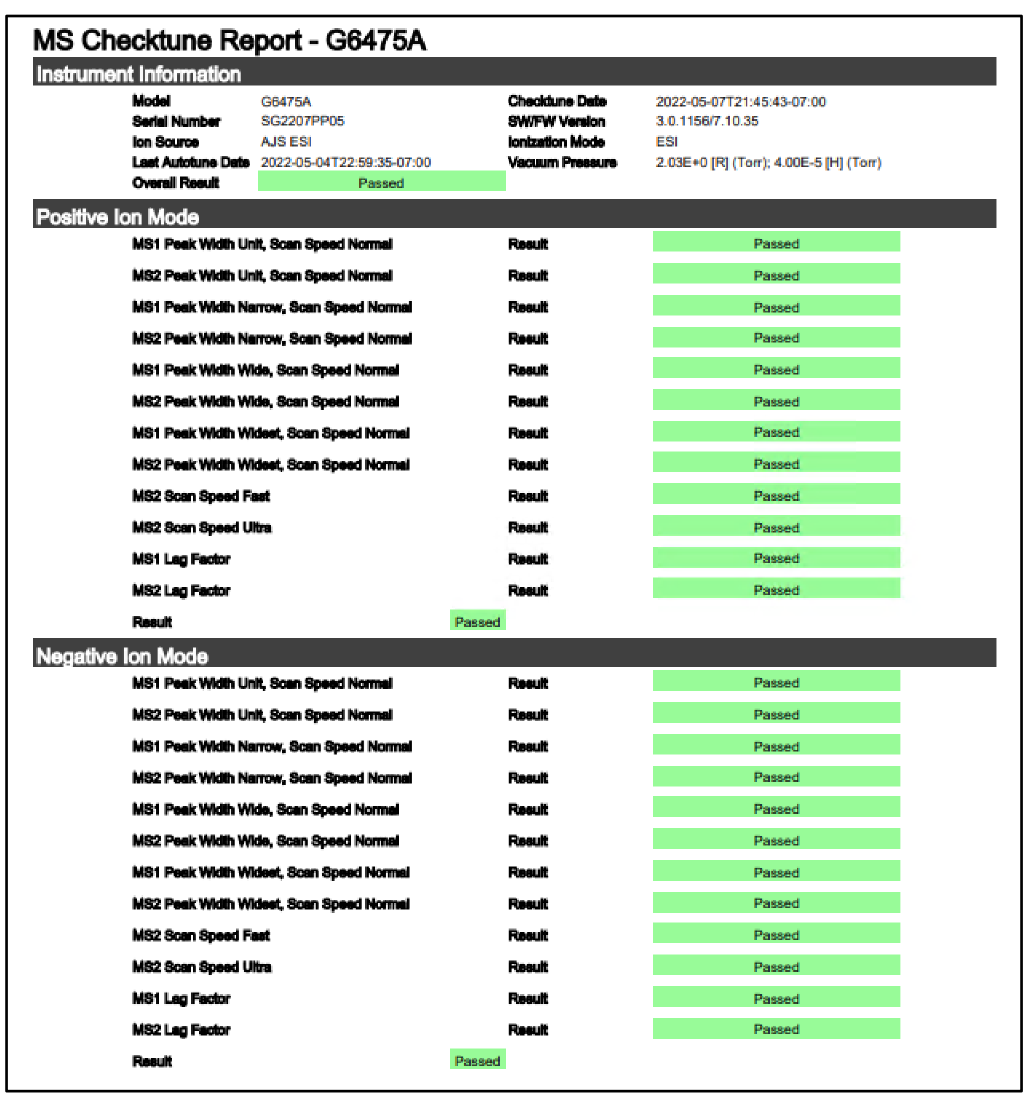
Early Maintenance Feedback continuously monitors for the most common sources of addressable issues pertaining to heavy routine analysis use. Over the course of this investigation, none of these events were triggered with the exception of "Injection Count" set to a threshold of 10,000 injections.

Despite constant bombardment of ions, detector health was observed to be stable and did not change to a considerable degree, the nebulizer and ion injector remained unclogged, and the spray stability remained consistent.

Detector EMV	Positive Mode	Negative Mode
Start	1212 V	1232 V
End	1198 V	1232 V

Checktune results per 1,000 Injections

Checktune report after 10,000 injections shown below with passing result. Results for both positive and negative, MS1 and MS2, as well as various scan speeds and peak widths shown in a single page report (detailed also available).


MS Checktune Report - G6475A

Instrument Information

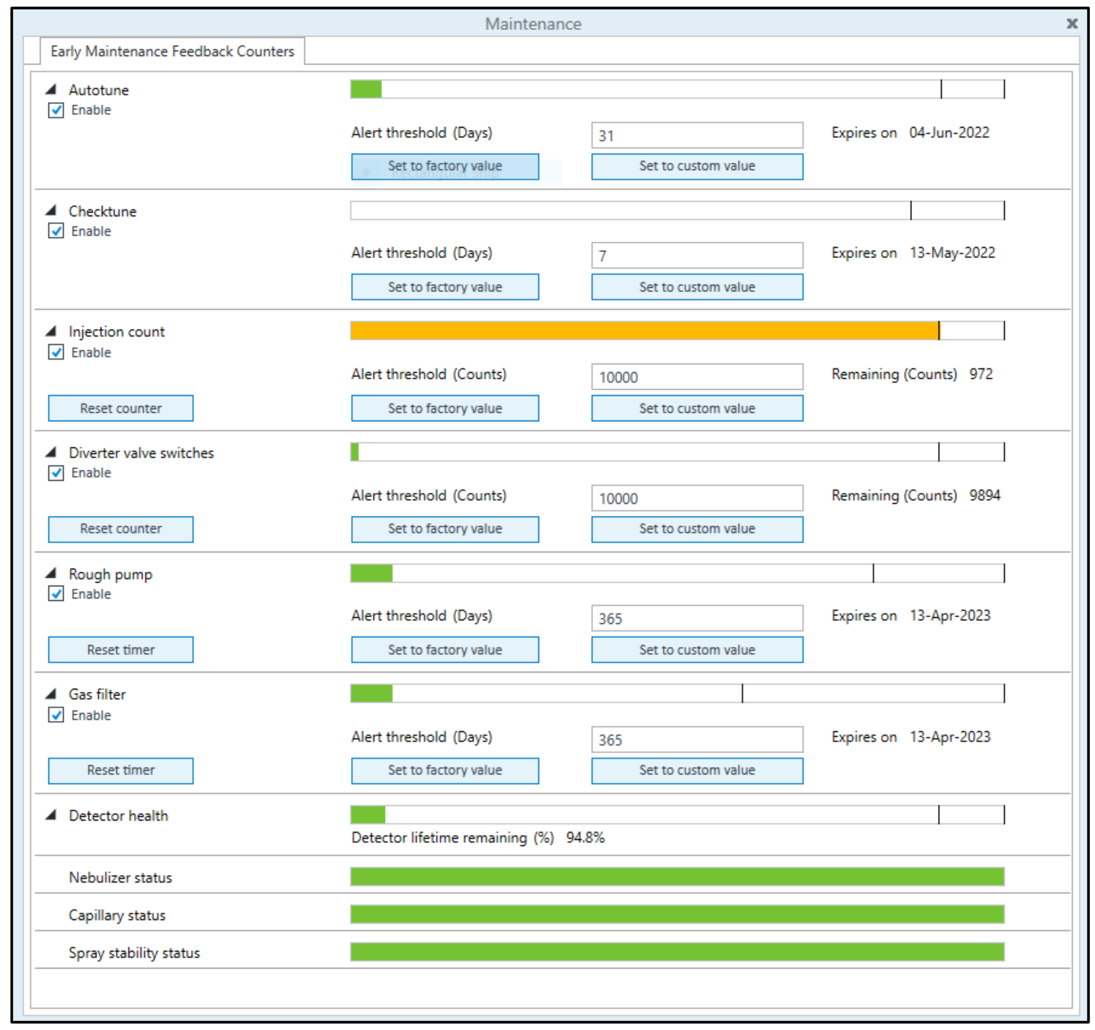
Model	G6475A	Checktune Date	2022-05-07T21:45:43-07:00
Serial Number	SG2207PP05	SW/FW Version	3.0.1156/7.10.35
Ion Source	AJS ESI	Ionization Mode	ESI
Last Autotune Date	2022-05-04T22:59:35-07:00	Vacuum Pressure	2.03E+0 [R] (Torr); 4.00E-5 [H] (Torr)
Overall Result	Passed		

Positive Ion Mode

MS1 Peak Width Unit, Scan Speed Normal	Result	Passed
MS2 Peak Width Unit, Scan Speed Normal	Result	Passed
MS1 Peak Width Narrow, Scan Speed Normal	Result	Passed
MS2 Peak Width Narrow, Scan Speed Normal	Result	Passed
MS1 Peak Width Wide, Scan Speed Normal	Result	Passed
MS2 Peak Width Wide, Scan Speed Normal	Result	Passed
MS1 Peak Width Widest, Scan Speed Normal	Result	Passed
MS2 Peak Width Widest, Scan Speed Normal	Result	Passed
MS2 Scan Speed Fast	Result	Passed
MS2 Scan Speed Ultra	Result	Passed
MS1 Lag Factor	Result	Passed
MS2 Lag Factor	Result	Passed
Result	Passed	

Negative Ion Mode

MS1 Peak Width Unit, Scan Speed Normal	Result	Passed
MS2 Peak Width Unit, Scan Speed Normal	Result	Passed
MS1 Peak Width Narrow, Scan Speed Normal	Result	Passed
MS2 Peak Width Narrow, Scan Speed Normal	Result	Passed
MS1 Peak Width Wide, Scan Speed Normal	Result	Passed
MS2 Peak Width Wide, Scan Speed Normal	Result	Passed
MS1 Peak Width Widest, Scan Speed Normal	Result	Passed
MS2 Peak Width Widest, Scan Speed Normal	Result	Passed
MS2 Scan Speed Fast	Result	Passed
MS2 Scan Speed Ultra	Result	Passed
MS1 Lag Factor	Result	Passed
MS2 Lag Factor	Result	Passed
Result	Passed	



Conclusions

- Instrument robustness over 10,000 injections was demonstrated using a heavy matrix (bovine urine) sample.
- Checktunes were recorded to verify instrument stability. Tune ion Mass Calibration and Peak Widths were recorded every 1,000 injections and were within tolerance criteria for good performance.
- Nebulizer spray, ion injector capillary, and spray stability triggered no adverse events.
- Constant ion bombardment through MRM acquisition did not age the detector in a significant manner

References

[1]Robustness of the Agilent Ultivo Triple Quadrupole LC/MS with the ESI Source, Agilent Technologies, Inc. 2019, 5994-0671EN.

[2]Metzger, Benedikt; Willmann, Lucas; Simplify your Method Development using the Agilent 1260 Infinity Prime LC System and InfinityLab LC/MSD iQ, Agilent Technologies, Inc. 2020, 5994-2124EN

[3]Sartain, Mark; Sosienski, Theresa; Yang, Dan-Hui Dorothy; Robustness of the Agilent Ultivo Triple Quadrupole LC/MS for Routine Analysis in Food Safety, Agilent Technologies, Inc. 2017, 5991-8741EN

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DE48683824

Published in USA, May 20, 2022

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