

Poster Reprint

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# Growing MS adoption: A “Self-Driving” Mass Spectrometer Designed for Non- Experts Enhance your Chromatography Results with Mass Detection for Unambiguous Confirmation of Analytes using Agilent’s InfinityLab LC/MSD iQ Single Quadrupole

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## Introduction

HPLC with UV detection is the most widely used analytical technique in pharmaceutical laboratories. Whether a lab is seeking to understand reaction kinetics, perform routine in-process control, or release testing of starting material, intermediates, and API's, HPLC is at the core of their operations.

Chromatographers are constantly pushing their HPLC runs with shorter gradients to maximize efficiency. To obtain fast results with high confidence, mass selective detection can be added for unambiguous confirmation of analytes with enhanced specificity and sensitivity to confirm and monitor even the most elusive compounds.

Mass spectrometry (MS) brings a sense of confidence and certainty to compound analysis. Historically, many laboratories were unable to add mass detection due to the complexity of operation, steep learning curve, large instrument footprint, and cost of ownership, which made it unattainable for most routine chromatography labs. The recent development of the Agilent InfinityLab LC/MSD iQ mass selective detector overcomes these barriers to adoption, opening access to mass information and facilitating adoption of this analytical technology. The new hardware and software design of the InfinityLab LC/MSD iQ provides a self-operating MS detection system that significantly minimizes the learning curve and provides confident mass confirmation.

## Experimental



Figure 1. InfinityLab LC/MSD iQ with an InfinityLab II Prime HPLC system in the InfinityLab Flex Bench MS

## InfinityLab LC/MSD iQ Overview

Agilent's LC/MSD iQ mass selective detector has been designed from the ground up with ease-of-use, and added flexibility, while maintaining robust and reliable operation. Optimal MS parameters are automatically set based on the LC conditions to maximize efficiency and provides chromatographers worry-free mass detector operation.

A modular hardware design allows for fast maintenance without the need to remove the single quadrupole from the HPLC stack.

## Instrumentation

- Agilent LC/MSD iQ Single Quadrupole (G6160AA)
- Agilent 1290 Infinity II High-Speed Pump (G7120A)
- Agilent 1290 Infinity II Vial Sampler (G7129B)
- Agilent 1290 Infinity II Multi Column Compartment (G7116B)
- Agilent 1290 Infinity II Diode Array Detector (G7117B)

## Results and Discussion

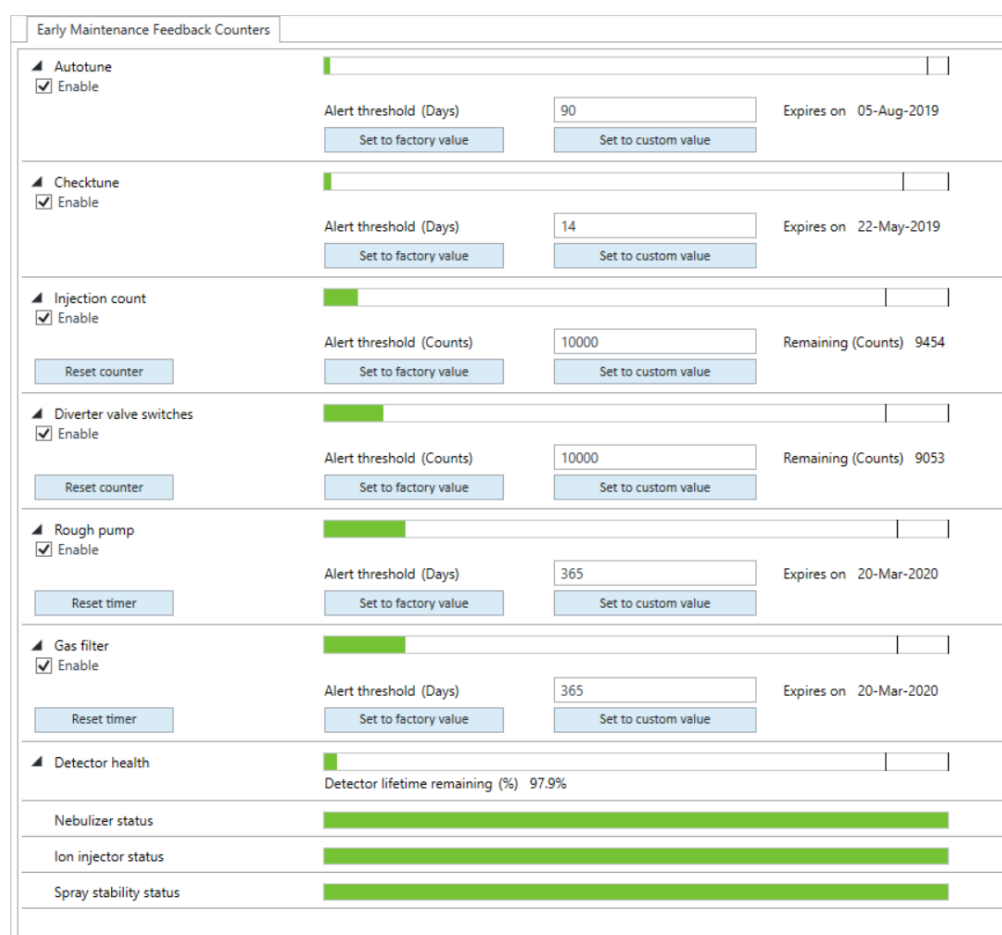


Figure 2. Instrument Early Maintenance Feedback

- Instrument early maintenance feedback predicts and notifies users about routine maintenance operations such as capillary change, detector performance, and others.

## Auto Acquire and scheduled Autotune

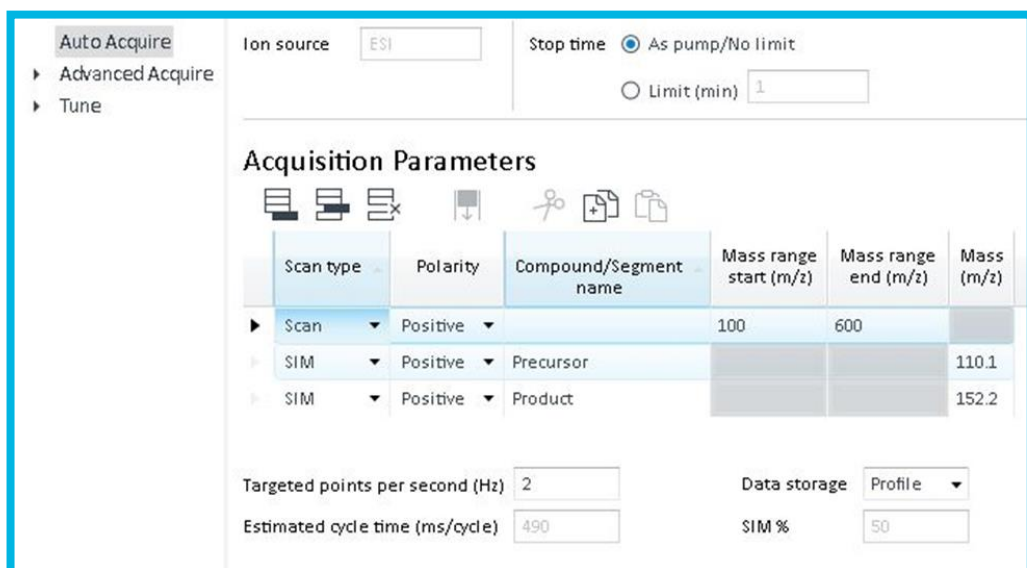


Figure 3. Auto Acquire mode

- The new Auto Acquire mode sets up MS parameters automatically based on the LC method and analytes of interest.
- Only the LC method and mass range (or mass for SIM) is required from the user, the software takes care of the rest.

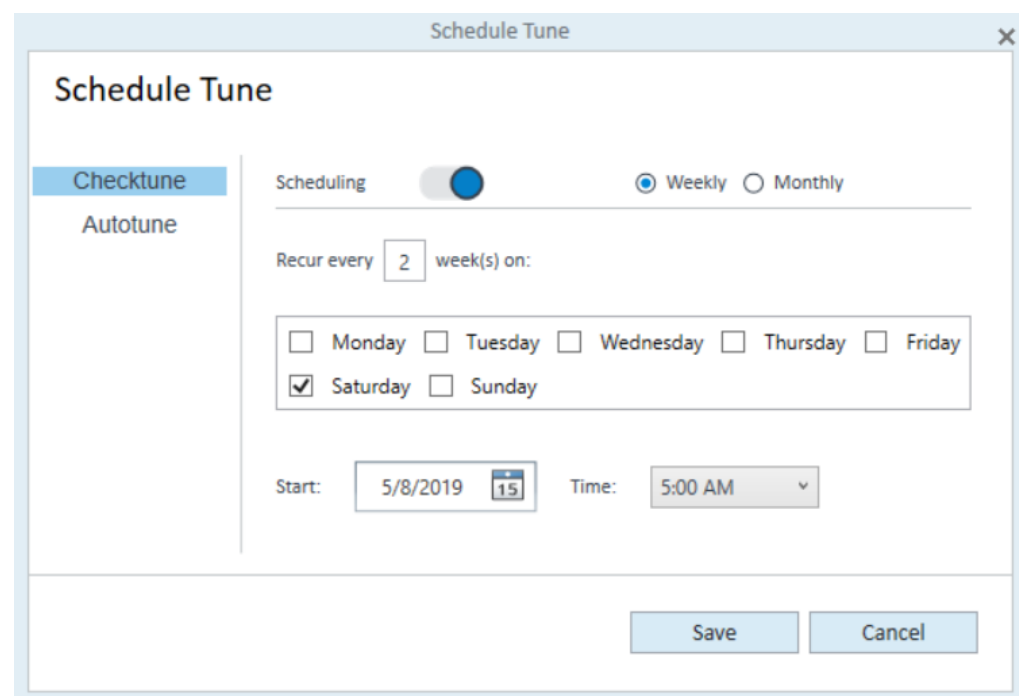


Figure 4. Automatic Tune Scheduler

- A Checktune can now be automatically scheduled to automate the performance verification.
- Calibrant solution is housed in the mass spectrometer and delivered through the calibrant delivery system valve so there is no need to prepare or set up a calibration mix.
- An Autotune can also be scheduled. Autotune calibrates the mass axis and optimizes performance. All ion optic, mass filter, and detector voltages are optimized to meet stringent criteria for the calibrant peaks and takes less than five minutes for both positive and negative mode.

## MS improves sensitivity and selectivity

In an evolving regulatory landscape with requirements becoming more stringent, UV detection may not be sensitive enough for many applications. For example, in the case of mutagenic impurities, which have a very low detection threshold, a mass detector is invaluable for detecting compounds which are present in the sample at low concentration. (Fig. 5)

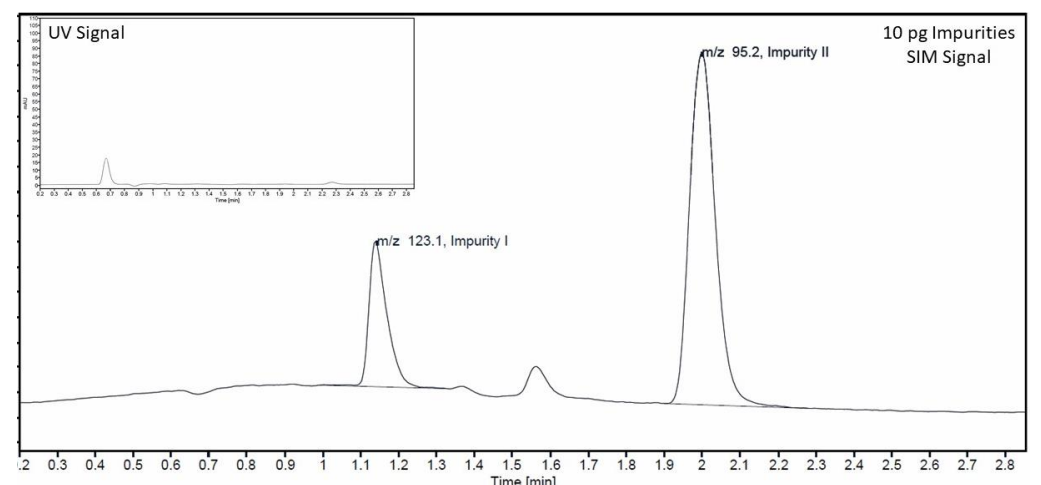


Figure 5. 10 pg of impurities were monitored by UV and mass detection. Impurities were not detected in the UV signal (inlay) but are clearly shown in the SIM signal.

- Mass detection is over 100x more sensitive than UV detection.
- For Selected Ion Monitoring (SIM) mode, the MS spends more time filtering only select masses, greatly enhancing sensitivity.

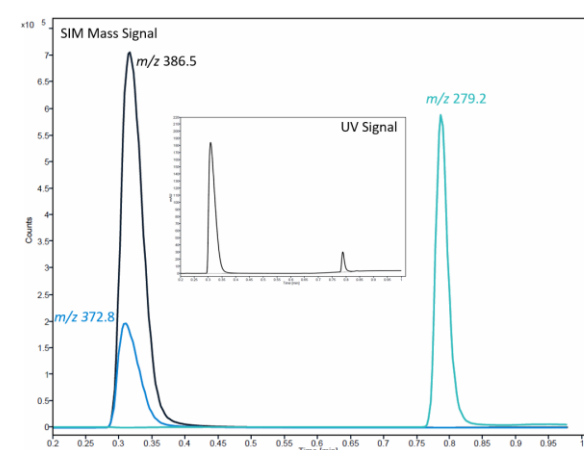


Figure 6. Co-eluting compounds can be easily identified by extracted ion chromatograms or SIM mode. Only two peaks are present in the UV signal (inlay), where there are three confirmed compounds in the mass signal.

- Extracted ion chromatograms (EIC) show how much of a chromatographic peak is made up of a select mass, enhancing selectivity.
- By selecting the masses of three Sulfa compounds, the coeluting peak in Fig. 6 is separated into two peaks.

## OpenLab CDS – acquisition, data analysis and reporting all in one package

OpenLab CDS software was designed with automation in mind and has a user-friendly interface that is intuitive and quick to learn. (Fig. 7) Instrument status, method input, and sample submission is all accessible from tabs in data acquisition. Data analysis and reporting is included and fully integrated with acquisition so processing and reporting of data can be executed automatically with a sample submission. OpenLab CDS provides full compliance features that support data integrity with US FDA 21 CFR Part 11, EU Annex 11, and other similar regulations.

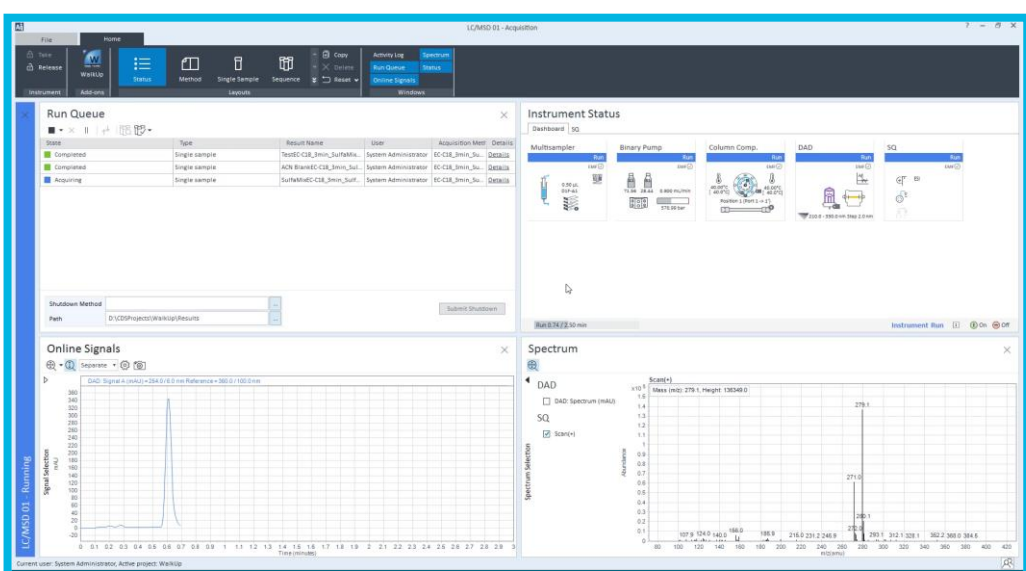


Figure 7. OL CDS data acquisition screen.

- OL CDS provides an intuitive interface that is easy to learn.
- Data analysis is built-in and can be launched directly from the run queue in data acquisition
- An single processing method will automatically process data and generate a report as soon as a run is complete as shown in Fig. 8 below.

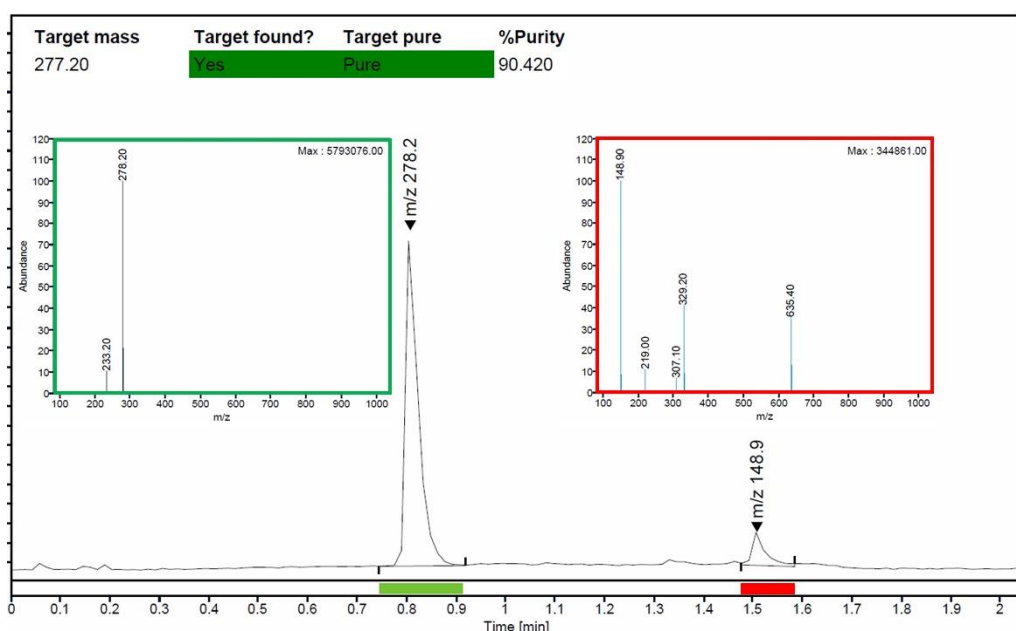


Figure 8. Automated sample purity analysis and report for amitriptyline by LC/MSD iQ. The target mass for amitriptyline (277.20) was entered before analysis and this report was generated automatically.

## Impurity analysis: is there a difference between brand name and generic OTC drugs?

An experiment utilizing OL CDS and the LC/MSD iQ was performed to compare the impurities in a brand name versus generic product of an acetaminophen. Fig. 9 shows the impurity standards detected in SIM mode at the 5 ng level. A brand name and generic acetaminophen drug tablet was dissolved in methanol and the percentage of detected impurities is shown in Table 1 below.

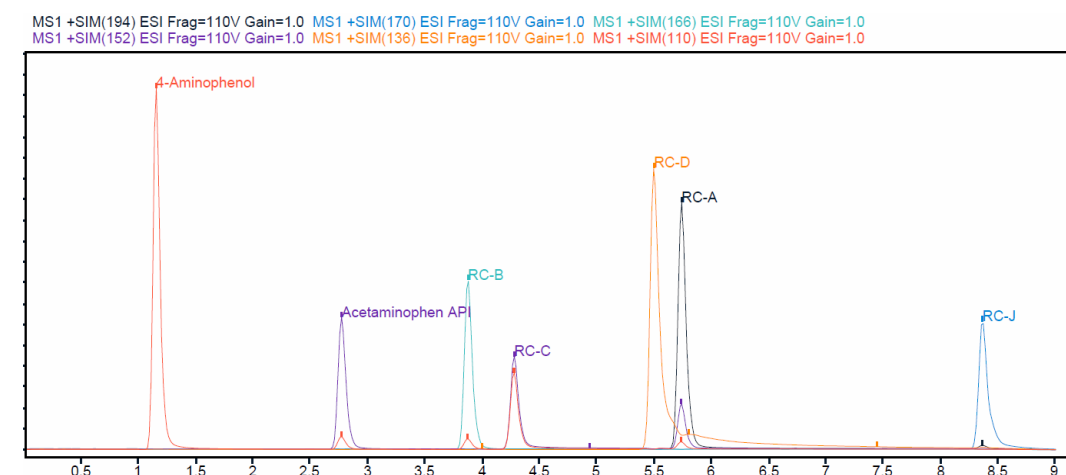


Figure 9. Targeted analysis of 5 ng on column of impurity standards for acetaminophen.

Impurity	Brand	Generic
A	0.0024%	0.0029%
B	0.0017%	0.0057%
D	0.0050%	0.0004%

Table 1. Percentage of detected impurities in relation to the acetaminophen API.

- The LC/MSD iQ was able to detect impurities at thousands of a percent compared to the API.
- There is indeed a difference in the concentration of impurities between a brand name and generic product.

## Conclusions

- Agilent's new InfinityLab LC/MSD iQ provides new users with an intuitive mass spectrometer to maximize confidence in their analytical results.
- The instrument was designed with the chromatographer in mind, reducing the complexity of the mass spectrometer without compromising ease of use, robustness and reliability.
- In conjunction with OpenLab CDS software, adding a mass detector to your HPLC stack is now easier than ever!