

Agilent InfinityLab LC/MSD iQ

An intuitive and self-aware mass selective detector for unambiguous mass confirmation to enhance chromatographic results

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Introduction

High-performance liquid chromatography (HPLC) with ultraviolet (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 active pharmaceutical ingredient (API), 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 (MSD) 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 overcomes these barriers to adoption, opening access to mass information and facilitating adoption of this analytical technology. The hardware and software design of the InfinityLab LC/MSD iQ provides a self-operating MSD system that significantly minimizes the learning curve, and provides confident mass confirmation.

Overview

The InfinityLab LC/MSD iQ has been designed with a focus on ease-of-use and added flexibility, while maintaining robust and reliable operation. To maximize efficiency and provide chromatographers with an intuitive mass detector, the MS parameters are automatically set based on the LC method and the mass of the target compounds. Moreover, with intuitive data analysis and reporting tools, the results can be obtained quickly to streamline analysis and move projects forward efficiently. Software feedback predicts and notifies users about the need for routine instrument maintenance operations such as tune or Ion Injector change. A modular hardware design provides fast maintenance or service without the need to remove the LC stack from the LC/MSD iQ.

Typical hardware setup

A typical setup for an Agilent InfinityLab LC/MSD iQ system contains the following modules:

- Agilent LC/MSD iQ Mass Selective Detector (G6160AA)
- Agilent 1290 Infinity II High-Speed Pump (G7120A)
- Agilent 1290 Infinity II Vial Sampler (G7129B)
- Agilent 1290 Infinity II Multicolumn Thermostat (G7116B)
- Agilent 1290 Infinity II Diode Array Detector (G7117B)

Add flexibility to your analytical environment

Historically, mass spectrometers have occupied a large amount of bench space and required upgrades to electrical infrastructure. To make it easier, faster, and more affordable to adopt MS, these barriers have been eliminated with the design of the InfinityLab LC/MSD iQ. The InfinityLab LC/MSD iQ is a small, robust, integrated system. The size of the InfinityLab LC/MSD iQ is the same as an LC sampler. It is designed for the LC stack to sit on top of the InfinityLab LC/MSD iQ without occupying any additional bench space.

Most mass spectrometers require high power, necessitating upgrades to laboratory electrical infrastructure. To eliminate this need, the InfinityLab LC/MSD iQ operates on the same power requirements as the LC modules, thereby plugging into existing power outlets. For example, in the USA it uses 110 V/50–60 Hz or 220 V/50–60 Hz line voltage in other regions, so there is no need to update existing lab infrastructure.

Modern lab designs are moving towards a more modular approach to accommodate rapidly changing space and layout requirements. Labs are no longer being designed with built-in, standard-height benches. To support this trend, Agilent designed the InfinityLab Flex Bench MS, which allows you to keep your InfinityLab LC/MSD iQ system in one stack with easy access to all modules. It improves the lab environment with an integrated solution for waste management and a noise reduction cover to minimize noise coming from the rough pump. Finally, it can easily be moved to other locations as needed.

The flexibility of the portable Flex Bench MS and the InfinityLab LC/MSD iQ combined with the ability to operate it anywhere in the lab means you can take the system to where it is needed most.

The InfinityLab LC/MSD iQ mass detector uses Agilent OpenLab CDS for seamless data acquisition, analysis, and reporting all in one application. Open access operation is enabled through Agilent MassHunter Walkup software.

Increase confidence in your analytical results

While optical detection has supported analytical labs for decades, it is an indirect measurement that can be ambiguous. For example, compounds may not contain chromophores, or degradation products may have lost the chromophore. In addition, compounds can coelute with impurities, and

sometimes may be undetected, or otherwise require extensive reanalysis and time-consuming chromatographic optimization to resolve. To correlate the chromatographic retention time to compounds or impurities, standards are required.

Mass information adds another dimension of analysis to HPLC/UV, adding insight, efficiency, and confidence to the analytical lab. Coeluting

compounds with different masses can be distinguished without having to run lengthy chromatographic separations or run standards. For workflows such as API purity analysis, the mass of the API and its percent purity can be determined quickly. In addition, the purity can be confirmed within a single chromatographic peak, as shown in Figure 1.

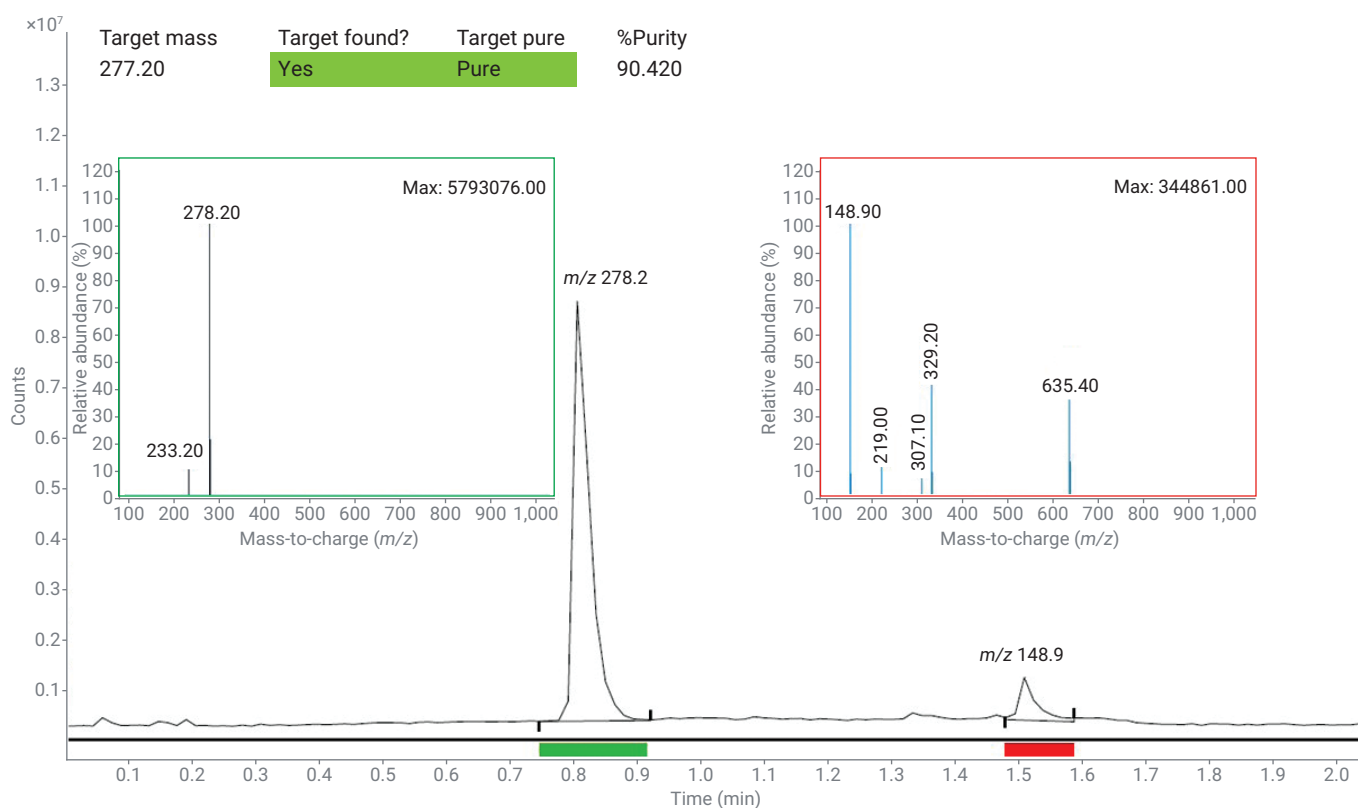


Figure 1. Automated sample purity analysis and report for amitriptyline by Agilent InfinityLab LC/MSD iQ. The target mass for amitriptyline was entered before analysis, and this report was generated automatically. The purity of amitriptyline was confirmed to be greater than 90%. The purity of the individual chromatographic peaks (RT = 0.82 and 1.51 minutes) measured by the InfinityLab LC/MSD iQ is reported by the colored bar below the peak. The first peak is pure, and contains amitriptyline. The second peak is impure, and contains multiple impurities accounting for approximately 10% of the total peak areas.

Unambiguous confirmation, even with coeluting compounds

Single-ion masses can be extracted from mass spectral data to produce an extracted ion chromatogram (EIC), which can separate coeluting, chromatographically unresolved compounds, as shown in Figure 2. An experienced chromatographer may deduce that the first UV peak must contain at least two compounds due to the peak shape. However, MS detection readily confirms and identifies the unresolved components.

The mass data clearly distinguish the two compounds. Without the mass information, additional investment is required to re-optimize the method to baseline resolve the compounds chromatographically. This is unnecessary when the coelution can be confirmed, and both compounds can be resolved based on their mass difference.

Increase sensitivity with mass detection

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 impurities that must be detected at low concentration, a mass detector is invaluable for detecting compounds at the required low concentration. Figure 3 shows a small molecule compound (trazodone) monitored by UV and mass detection. Trazodone was not detectable by UV detection below 10 pg, and had a very low signal at 100 pg. Trazodone can easily be detected by the InfinityLab LC/MSD iQ below 1 pg.

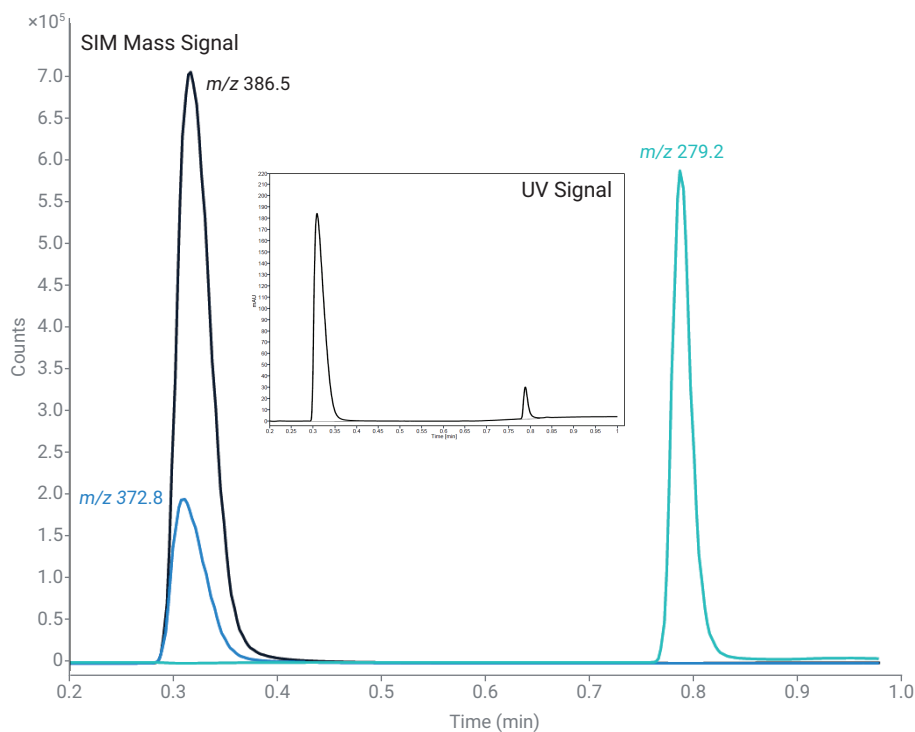


Figure 2. Coeluting compounds can easily be identified by mass detection. Only two peaks are present in the UV signal (inset), where there are three confirmed compounds in the mass signal.

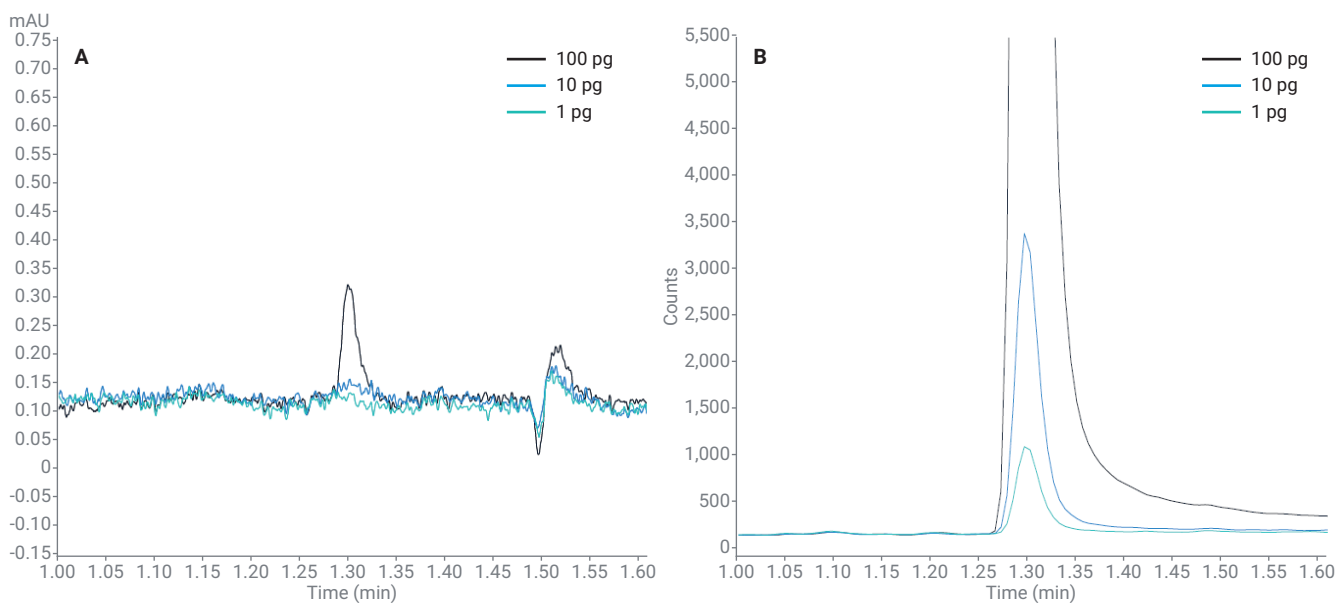


Figure 3. Trazodone was monitored by UV (A) and mass (B) detection. Trazodone was not detectable by UV detection below 10 pg, and had a very low signal at 100 pg. Trazodone can easily be detected with the LC/MSD iQ at below 1 pg levels.

Instrument intelligence designed to flatten the learning curve for MS

While typical mass spectrometers require experience and knowledge to operate, the InfinityLab LC/MSD iQ eliminates the complexity of MS method setup. The Auto Acquire mode sets the MS parameters automatically based on the LC method and analytes of interest (Figure 4). Users can simply choose their LC method and enter an MS scan range or SIM ions, and the InfinityLab LC/MSD iQ intelligence determines the MS parameters automatically.

Auto Acquire

- ▶ Advanced Acquire
- ▶ Tune

Ion source: ESI

Stop time: As pump/No limit
 Limit (min)

Acquisition Parameters

Scan type	Polarity	Compound/Segment name	Mass range start (m/z)	Mass range end (m/z)	Mass (m/z)
▶ Scan	Positive		100	600	
▶ SIM	Positive	Precursor			110.1
▶ SIM	Positive	Product			152.2

Targeted points per second (Hz):

Estimated cycle time (ms/cycle):

Data storage: Profile

SIM %:

Figure 4. Auto Acquire automatically sets the MS parameters based on the user inputs highlighted in green, along with the LC flow rate in the method.

Early maintenance feedback tracks instrument health and adds predictability to lab operations

Even the most reliable systems require occasional maintenance to maintain optimal performance. To make this process predictable and maximize uptime, the InfinityLab LC/MSD iQ includes real-time diagnostics, known as early maintenance feedback. The Early Maintenance Feedback panel is easily accessed by right clicking the single quadrupole instrument module in data acquisition.

Key maintenance processes are recorded, and maintenance notifications are generated. The ion source stability, ion injector performance, and detector health of the InfinityLab LC/MSD iQ are monitored. Key usage metrics and Autotune intervals are also tracked. (Figure 5). Thresholds can be set for warning notifications before maintenance is required, and the status bar shows the key thresholds with the component's current health status. This visual display provides the user with an easy-to-interpret view of the system state.

Automatic tuning ensures that your instrument is working as expected every day

To ensure optimal robustness and reliability, MS performance must be checked and recalibrated periodically by an automated process called Autotune. The InfinityLab LC/MSD iQ is highly stable, so this typically only needs to be performed every few months. This was previously initiated by an experienced MS user, with the interval based on experience.

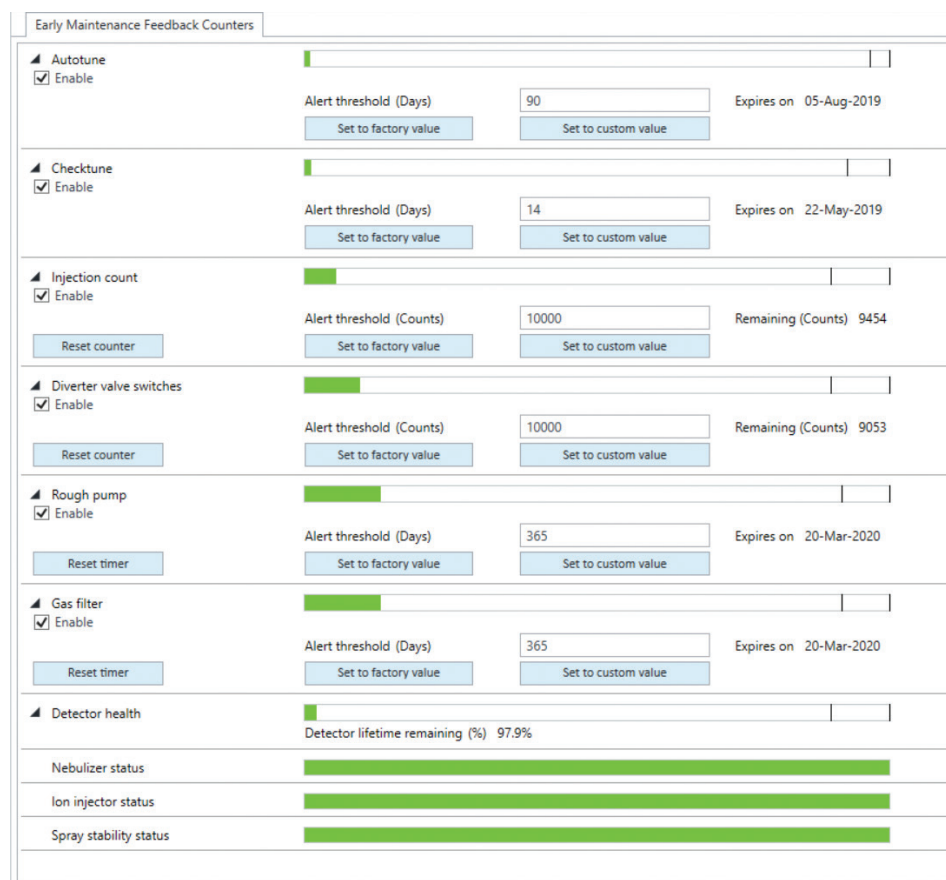


Figure 5. The Early Maintenance Feedback panel tracks and reports the current health of the MS components. It notifies the user that the MS is working as expected or reports a potential issue in advance, enabling predictability in maintenance.

To maximize uptime, and simplify the process, Checktune and Autotune can now be scheduled to occur during idle instrument periods (Figure 6). For example, Checktune can be scheduled every couple of weeks before scientists arrive, and it only takes a few minutes. Checktune will validate the mass axis, peak full width at half maximum (FWHM), and abundance of calibrant ions. Calibrant solution is housed in the mass spectrometer, and is delivered through the calibrant delivery system valve so it is not necessary to prepare or set up a calibration mix. The system is stable for many months, so in the rare case that Checktune fails, Autotune should be run. Autotune adjusts all ion optic, mass filter, and detector voltages to meet stringent criteria for the calibrant peaks, and takes less than five minutes for both positive and negative mode.

Save time and reduce complexity with built-in automation, from data acquisition to reporting

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

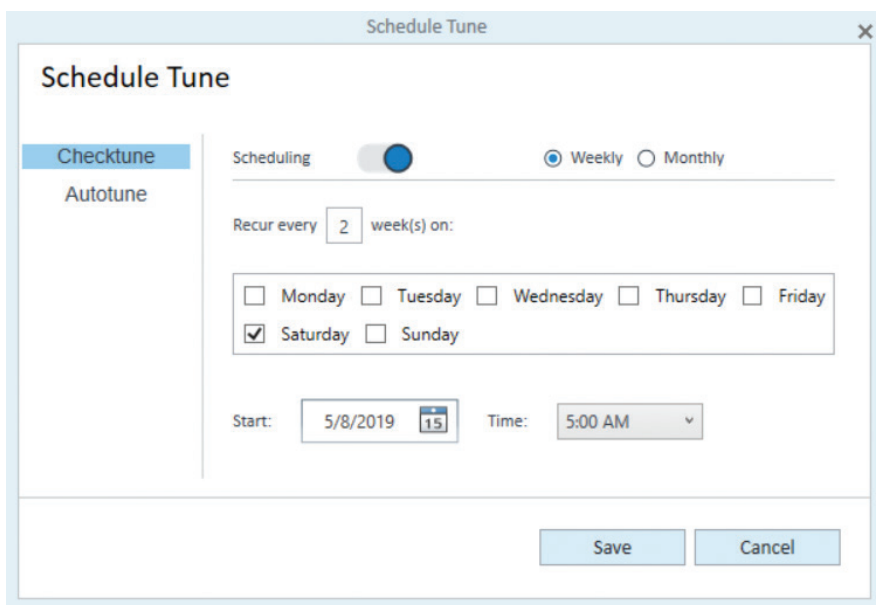


Figure 6. Checktune and autotune measure and re-establish optimal MS settings, and can be scheduled to run automatically during instrument idle time to maximize instrument use for sample analysis, and maintain optimal performance.

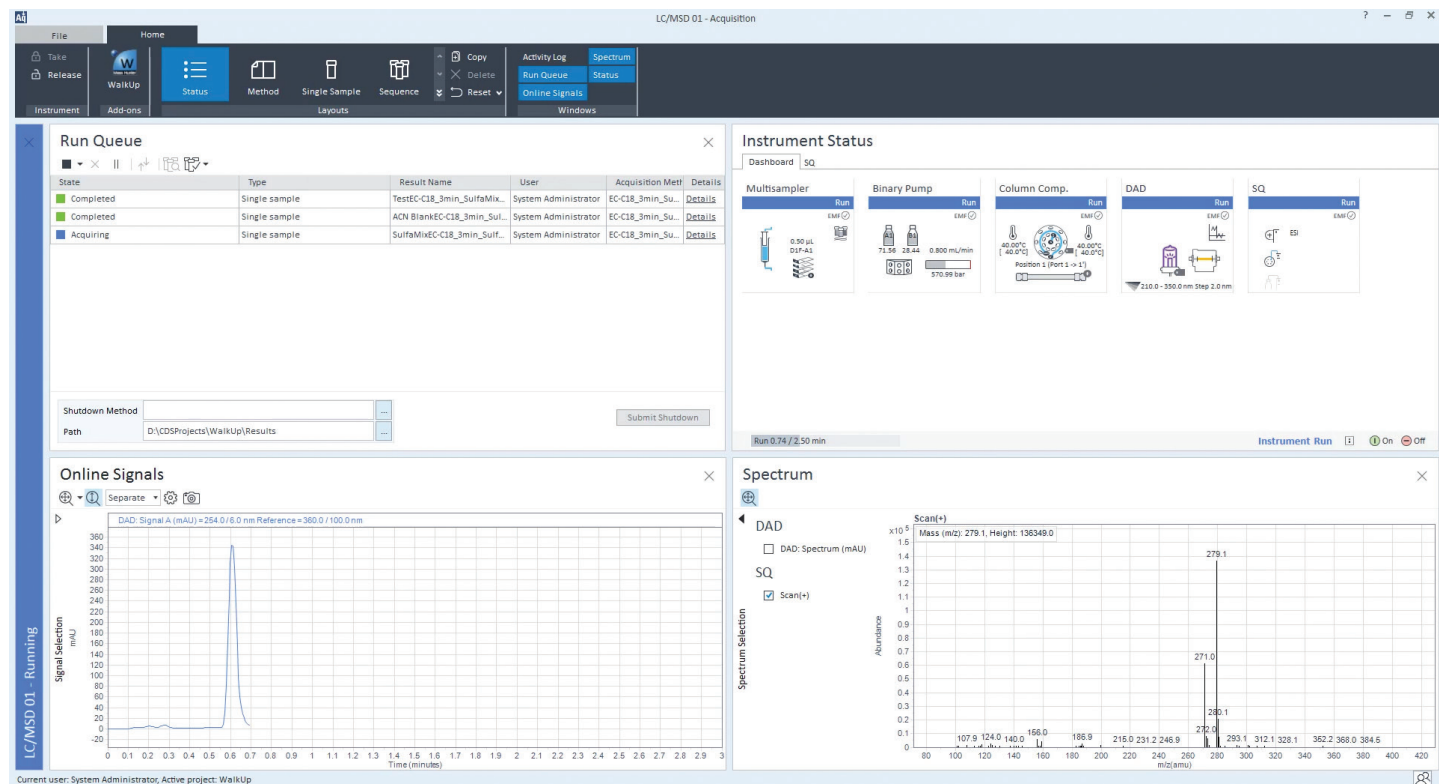


Figure 7. Agilent OpenLab CDS software makes data acquisition, analysis, and reporting accessible all from one program, and was designed to be intuitive and easy to learn for all types of users.

Conclusion

The Agilent 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 MS without compromising ease-of-use, best-in-class robustness, and reliability. In conjunction with Agilent OpenLab CDS software, adding a mass selective detector to your HPLC stack is now easier than ever.

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