thermo scientific

Be sure

LC-MS Medical Devices for Laboratory Developed Tests

For In Vitro Diagnostic Use

ThermoFisher SCIENTIFIC

Increase efficiency, throughput, and cost savings

Performing laboratory developed tests by liquid chromatography-mass spectrometry

Comprehensive and reliable LC-MS systems powered by a complete suite of software conforming to *in vitro* diagnostic (IVD) requirements and offering an *optional* laboratory information system (LIS) connection enabling clinical diagnostic laboratories to reach their business and scientific goals for laboratory developed tests (LDTs).

Liquid Chromatography-Mass Spectrometry (LC-MS) represents a complementary technology to typically used chemistry and immunoassay and offers greater specificity, speed, analyte range, throughput and multiplexing capabilities coupled with a lower cost per sample and reduced sample volumes.

Performing LDTs by LC-MS enables clinical diagnostic laboratories to replace expensive chemistry or immunoassays run on random-access automated lines with more economic batch testing. In addition, multiplex LC-MS can offer identification and quantification of several analytes simultaneously.

Positive immunoassay screens are typically followed by LC-MS confirmation and quantitation. But where positive rates are high, switching solely to identification and quantitation by LC-MS often makes economic and operational sense.

There remains a need for LC-MS medical devices that can meet a wide range of throughput and sensitivity needs. There is also a need for “middleware” capable of providing bidirectional communication with the Laboratory Information System (LIS).

The portfolio of Thermo Scientific™ LC-MS Medical Devices provides laboratories with a comprehensive and flexible choice of platforms suited to sensitivity and productivity needs, powered by a complete software suite, to ensure confident results and data integrity.

Ease, efficiency, and flexibility for laboratory developed tests

Flexible options to meet sensitivity and throughput needs

The comprehensive portfolio of Thermo Scientific LC-MS Medical Devices for laboratory developed tests offers the clinical diagnostic laboratory six unique choices to address a wide range of throughput and sensitivity needs. This portfolio consists of three High Pressure Liquid Chromatography (HPLC) systems differentiated by *throughput* and two Mass Spectrometers (MS) differentiated by *sensitivity*:

HPLC options

- Thermo Scientific™ Vanquish™ MD HPLC system
- Thermo Scientific™ Prelude MD™ HPLC system
- Thermo Scientific™ Prelude LX-4 MD™ HPLC system

Mass spectrometer options

- Thermo Scientific™ TSQ Quantis™ MD Series triple-stage quadrupole mass spectrometer
- Thermo Scientific™ TSQ Altis™ MD Series triple-stage quadrupole mass spectrometer

In addition, the new portfolio of Thermo Scientific LC-MS Medical Devices for LDTs enables laboratories to:

- Protect investments by addressing *in vitro* diagnostic requirements
- Eliminate the need to purchase additional software by including Thermo Scientific™ TraceFinder™ LDT software
- Overcome the limitation of manual data entry with an *optional* bi-directional LIS connection

HPLC THROUGHPUT

MS SENSITIVITY

Thermo Scientific LC-MS Sensitivity vs Throughput	Vanquish MD HPLC (Single Channel)	Prelude MD HPLC (Dual Channel)	Prelude LX-4 MD HPLC (Four Channel)
TSQ Altis MD Series Mass Spectrometer	Enhanced sensitivity with good throughput	Enhanced sensitivity with better throughput	Enhanced sensitivity with highest throughput
TSQ Quantis MD Series Mass Spectrometer	Routine sensitivity with good throughput	Routine sensitivity with better throughput	Routine sensitivity with best throughput

Addressing *in vitro* diagnostic requirements

Protecting today's investment for tomorrow's testing

LC-MS Medical Device Usage	Liquid Chromatography Systems			Mass Spectrometers	
	Vanquish MD HPLC	Prelude MD HPLC	Prelude LX-4 MD HPLC	TSQ Altis MD Series Mass Spectrometer	TSQ Quantis MD Series Mass Spectrometer
Intended Use	General purpose laboratory instruments intended to separate drugs or compounds in human specimens. For *in vitro* diagnostic use only by trained, qualified laboratory personnel.			Intended to identify and quantify inorganic and organic compound in human specimens. For *in vitro* diagnostic use only by trained, qualified laboratory personnel.	
Indications for Use	Used by clinical diagnostic laboratories as a component of a laboratory developed test (LDT) method or workflow.			Used by clinical diagnostic laboratories as a component of a laboratory developed test (LDT) method or workflow.	
Contraindications of Use	For *in vitro* diagnostic tests only. The Vanquish MD HPLC, Prelude MD HPLC, and Prelude LX-4 MD HPLC are to be operated only with hardware or software approved for *in vitro* diagnostic application.			For *in vitro* diagnostic applications only. The TSQ Altis MD Series and TSQ Quantis MD Series mass spectrometers are to be operated only with hardware or software labeled for *in vitro* diagnostic use.	
Limitations of Use	Compatible with the following instruments from Thermo Fisher Scientific: TSQ Altis MD Series mass spectrometer and TSQ Quantis MD Series mass spectrometer.			Compatible with the following instruments from Thermo Fisher Scientific: Vanquish MD HPLC, Prelude MD HPLC, and Prelude LX-4 MD HPLC.	

As a component of an LDT method or workflow, validation of the LDT method or workflow is the responsibility of the clinical laboratory.

Laboratory developed tests

The U.S. regulatory background

FDA definition

"A laboratory developed test (LDT) is a type of in vitro diagnostic test that is designed, manufactured and used within a single laboratory. LDTs can be used to measure or detect a wide variety of analytes, substances such as proteins, chemical compounds like glucose or cholesterol, or DNA, in a sample taken from a human body. Some LDTs are relatively simple tests that measure single analytes, such as a test that measures the level of sodium. Other LDTs are complex and may measure or detect one or more analytes. For example, some tests can detect many DNA variations from a single blood sample, which can be used to help diagnose a genetic disease. Various levels of chemicals can be measured to help diagnose a patient's state of health, such as levels of cholesterol or sodium.

While the uses of an LDT are often the same as the uses of FDA-cleared or approved in vitro diagnostic tests, some labs may choose to offer their own test. For example, a hospital lab may run its own vitamin D assay, even though there is an FDA-cleared test for vitamin D currently on the market.

The FDA does not consider diagnostic devices to be LDTs if they are designed or manufactured completely, or partly, outside of the laboratory that offers and uses them.

LDTs are important to the continued development of personalized medicine, so it is important that in vitro diagnostics are accurate and ensure that patients and health care providers do not seek unnecessary treatments, delay needed treatments, or become exposed to inappropriate therapies."

FDA activity

"The FDA has generally not enforced premarket review and other applicable FDA requirements because LDTs were relatively simple lab tests and generally available on a limited basis. Due to advances in technology and business models, LDTs have evolved and proliferated significantly since the FDA first obtained comprehensive authority to regulate all in vitro diagnostics as devices in 1976. Some LDTs are now much more complex, have a nationwide reach and present higher risks, such as detection of risk for breast cancer and Alzheimer's disease, which are similar to those of other IVDs that have undergone premarket review.

In gathering feedback on the LDT draft guidances issued in 2014, we continuously engaged with interested stakeholders, including those groups that authored alternative proposals. We analyzed more than 300 sets of comments on the draft guidances and discussion from a subsequent public workshop held in 2015 as well as engaged in many meetings and conferences with various stakeholders. In the absence of issuing final guidance and at the request of stakeholders, we feel it is our responsibility to share our synthesis of all the feedback we have received, with the hope that it advances public discussion on future LDT oversight.

To this end, on January 13, 2017, the FDA issued a HYPERLINK "https://www.fda.gov/media/102367/download" discussion paper on LDTs. The synthesis does not represent the formal position of FDA, nor is it enforceable. We hope to simply advance the public discussion by providing a possible approach to spur further dialogue."

Source: https://www.fda.gov/medical-devices/vitro-diagnostics/laboratory-developed-tests

Choose from a unique portfolio of compatible LC-MS devices for LDTs

INCREASING HPLC THROUGHPUT AND PRODUCTIVITY

Prelude LX-4 MD HPLC System

Four automated HPLC channels deliver up to four different separations to a single mass spectrometer, reducing mass spectrometer idle time. Increase productivity by deploying efficient, easy to use LC-MS instruments, more effectively.

Prelude MD HPLC System

Automated sample cleanup and **two channels of HPLC separation** for better productivity and certainty in test results. **Thermo Scientific™ TurboFlow™ technology** can automate many sample cleanup tasks, greatly reducing error-prone manual steps that result in variability.

Vanquish MD HPLC System

When analyte resolution is more critical than sample throughput and batch turnaround time, the more powerful **single channel Vanquish MD HPLC system**, with a smaller footprint, meets analytical needs, as well as space and budget limitations.

A unique choice of flexible options to meet a wide range of sensitivity and throughput needs for LDTs.

TraceFinder LDT Software

An integral component of the TSQ Altis MD Series mass spectrometer and TSQ Quantis MD Series mass spectrometer, which is used to run samples, acquire and process data, as well as generate reports.

TSQ Series II Altis MD and Quantis MD Software

An integral component of the TSQ Altis MD Series and TSQ Quantis MD Series mass spectrometers, which is used to "tune" the mass spectrometer, enable diagnostic capabilities, and develop test methods.

TSQ Altis MD Series Mass Spectrometer

Provides enhanced sensitivity for demanding quantitative analyses with remarkable speed and robustness. The **TSQ Altis MD Series mass spectrometer** will be used by clinical diagnostic laboratories to address their *more sensitive requirements* for laboratory developed tests.

TSQ Quantis MD Series Mass Spectrometer

Provides the sensitivity needed for routine quantitative analyses with remarkable speed and robustness. The **TSQ Quantis MD Series mass spectrometer** will be used by clinical diagnostic laboratories to meet their *routine requirements* for laboratory developed tests

The B-Link Connector

Optional downloadable software package capable of providing **bi-directional communication** between TraceFinder LDT software and the Laboratory Information Systems (LIS) or other middleware. Installed on the same computer as TraceFinder LDT software.

INCREASING MS SENSITIVITY

Vanquish MD HPLC System

Better separation, results, and ease-of-use

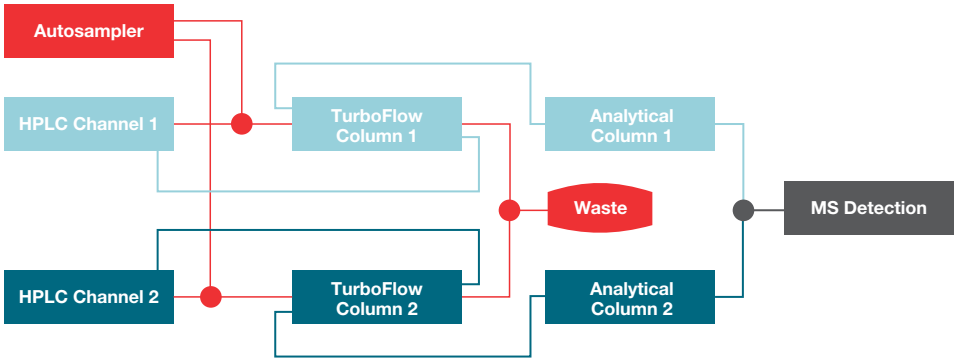
The *single channel* Vanquish MD HPLC meets critical analytical needs, while addressing space and budget limitations for laboratories where sample throughput and batch turnaround time do not require two or four channel solutions.

- Increased analytical speed and reliability—necessary for targeted quantitation analyses performed by clinical laboratories focused on laboratory developed tests
- Increased flexibility—industry leading 2 × 3 solvent channels for maximized method flexibility
- Increased confidence—excellent flow accuracy and precision by ultra-precise piston drives
- Outstanding robustness—enabled by highest system up-time and low total cost of ownership

Prelude MD HPLC System

Confidence in results with ease and efficiency

Run up to *two times* the samples while maintaining selectivity and sensitivity. Multichannel optimization of two parallel HPLC channels maximizes MS utilization and improves sample throughput.

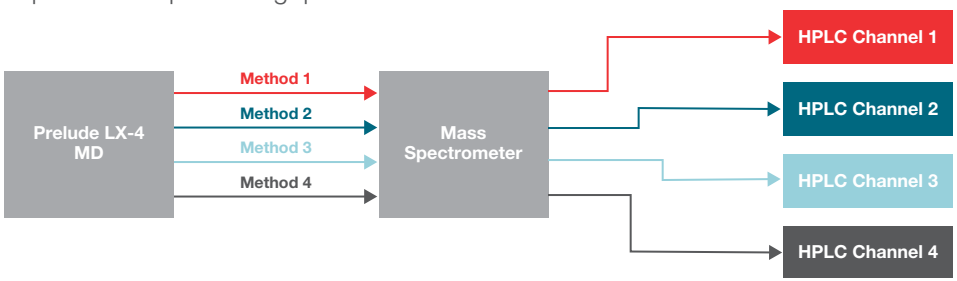


The autosampler injects samples into the TurboFlow columns for cleanup. The HPLC pump then delivers the analytes of interest to the analytical columns for separation. After separation, analytes are delivered to the MS for detection.

Prelude LX-4 MD HPLC System

Achieve the highest productivity with ease

Run up to *four times* the samples while maintaining selectivity and sensitivity. Multichannel optimization of four parallel HPLC channels maximizes MS utilization and improves sample throughput.



When coupled with a single mass spectrometer, the Prelude LX-4 MD HPLC can approach the throughput of four HPLC systems.

Comprehensive software for performing LDTs with confidence

Easy to use, built-in mass spectrometry software

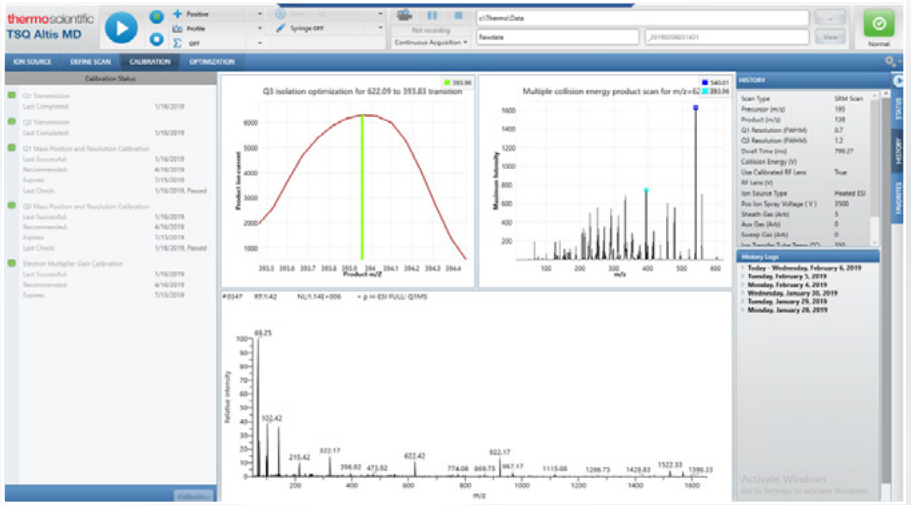
"Tune" the mass spectrometer and develop test methods with the integral TSQ Series II Altis MD and Quantis MD Software. Control of the mass spectrometer is conveniently provided through two application packages: **Tune** and **Method Editor**.

Tune features:

- Constantly monitor instrument parameters and operating status
- Tune and calibrate critical features for maximum performance
- Easily troubleshoot using diagnostic functions
- Generate reports for diagnostic purposes

Method Editor features:

- Set up and run experiments using optimized scan types established in Tune mode
- Design customized sequences of scans for complicated samples
- Specify peripheral device controls as part of an experiment



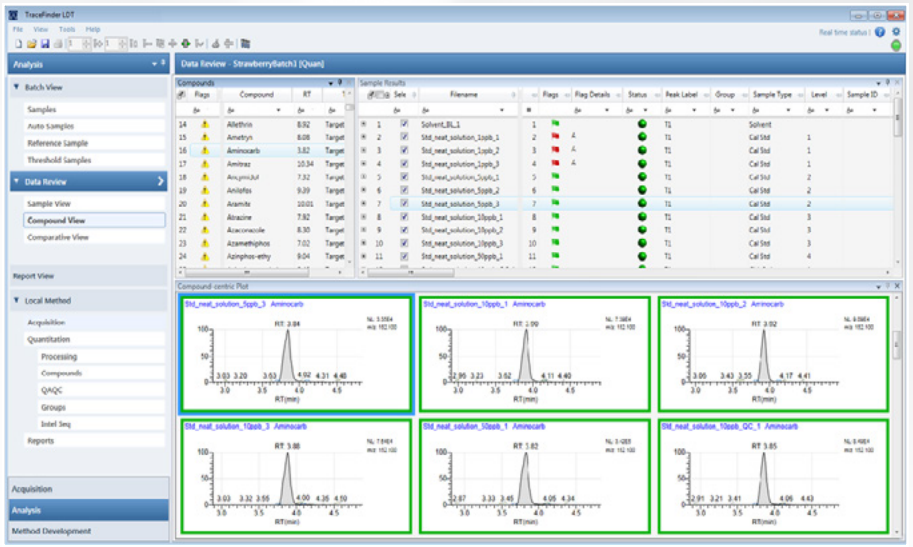
Calibrate the instrument for maximum performance with a variety of scan types, scan modes, ion polarities, scan rates, and resolution settings.

Quantitate with the integral TraceFinder LDT software

TraceFinder LDT software provides a seamless approach to high-throughput quantitation. Automate and accelerate the processes of creating methods, loading samples, generating data, manually reviewing and editing results, and finalizing the data review and reporting process for a quick start-up. Comprehensive processing methods provide improved handling of ion ratio calculations, reviewing, reporting, and comparison of mass spectra and data integration.

Key features:

- Manage user-based permissions, data repositories, and auditing
- Configure reports, detection and acquisition defaults, and customize columns and flags
- Develop instrument methods, and set processing, error flag parameters, and report options
- Acquisition mode for creating and submitting samples
- Results mode with batch views, data review, local method views, and report views



Comprehensive processing methods provide improved handling of ion ratio calculations, reviewing, reporting, comparison of mass spectra and data integration.

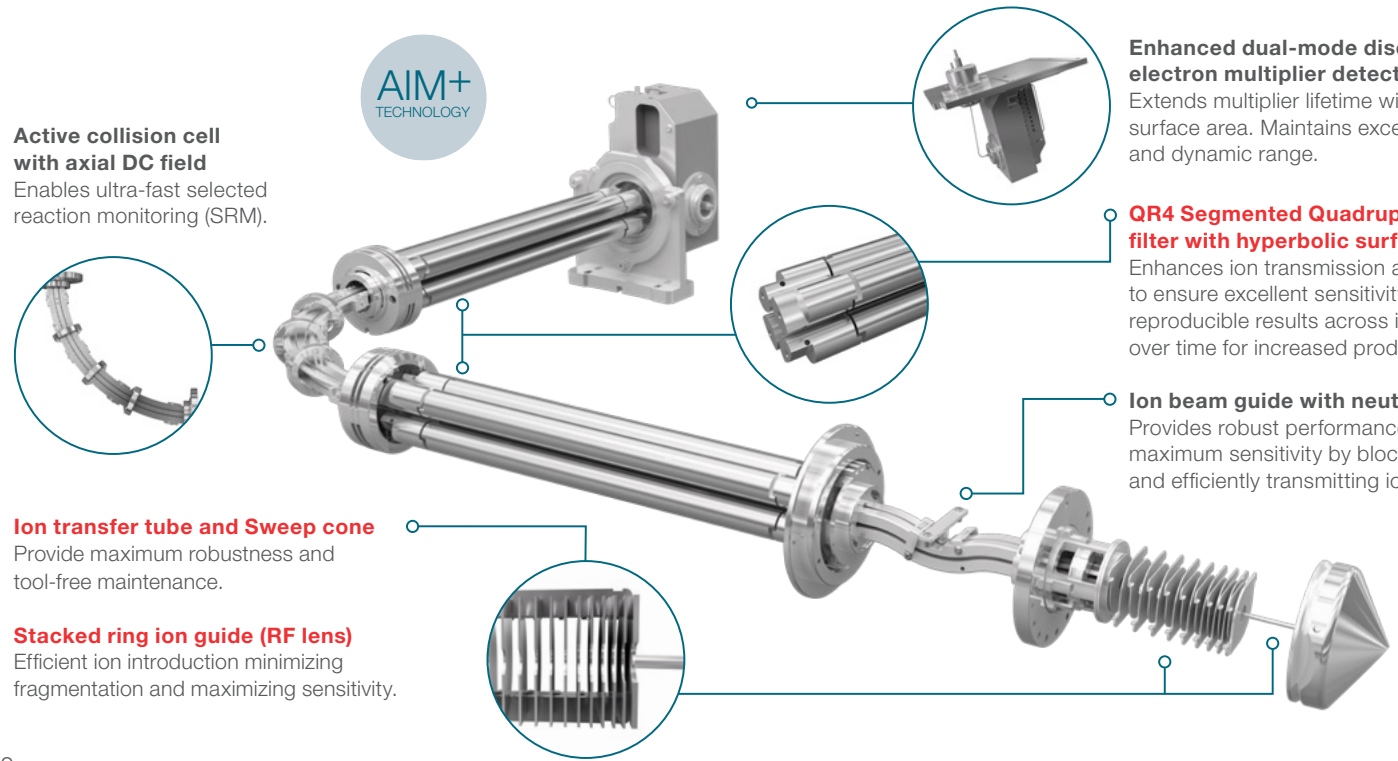
TSQ Quantis MD Series mass spectrometer

IVD compliance with sensitivity, remarkable speed, and robustness for routine laboratory developed tests

The TSQ Quantis MD Series triple-stage quadrupole mass spectrometer offers the sensitivity needed for routine, everyday quantitative analyses together with remarkable speed and robustness. The TSQ Quantis MD Series mass spectrometer will be used by clinical diagnostic laboratories to meet their routine requirements for laboratory developed tests.

With Thermo Scientific™ Active Ion Management (AIM+) technology, the TSQ Quantis MD Series confidently delivers routine analyses day after day.

Mass Range (Daltons)	*m/z* 5–3000
Resolution (FWHM)	0.4 Da
Sensitivity 5 µL Injection of a 200 fg/µL Reserpine Solution	Minimum signal-to-noise ratio of 200,000:1



Active collision cell with axial DC field
Enables ultra-fast selected reaction monitoring (SRM).

Enhanced dual-mode discrete-dynode electron multiplier detector
Extends multiplier lifetime with increased surface area. Maintains excellent linearity and dynamic range.

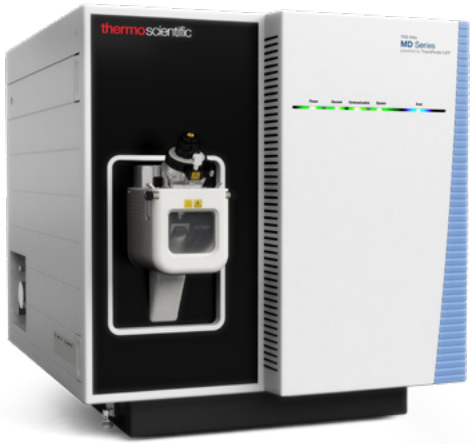
QR4 Segmented Quadrupoles mass filter with hyperbolic surfaces:
Enhances ion transmission and consistency to ensure excellent sensitivity and reproducible results across instruments and over time for increased productivity.

Ion beam guide with neutral blocker
Provides robust performance and maximum sensitivity by blocking neutrals and efficiently transmitting ions.

Ion transfer tube and Sweep cone
Provide maximum robustness and tool-free maintenance.

Stacked ring ion guide (RF lens)
Efficient ion introduction minimizing fragmentation and maximizing sensitivity.

Thermo Scientific™ OptaMax™ NG ion source APCI ready
Automates all gas and voltage connections for ease-of-use. Provides optimizable spray position for ultimate performance in HESI or APCI mode.



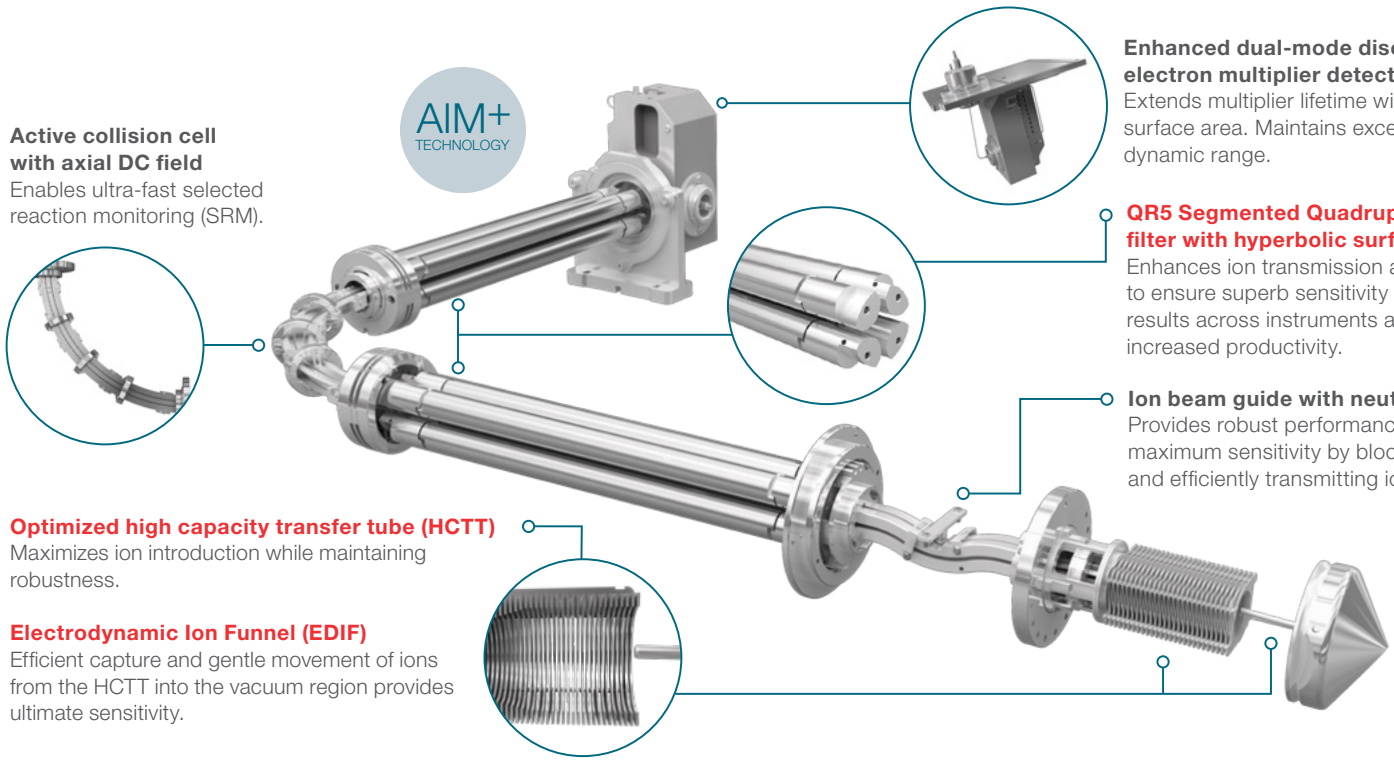
TSQ Altis MD Series mass spectrometer

Enhanced sensitivity with remarkable speed and robustness for laboratory developed tests

The TSQ Altis MD Series triple-stage quadrupole mass spectrometer offers enhanced sensitivity for demanding quantitative analyses together with remarkable speed and robustness. The TSQ Altis MD Series will be used by clinical diagnostic laboratories to address their more sensitive requirements for laboratory developed tests.

With AIM+ technology, the TSQ Altis MD Series confidently delivers ultimate performance in human specimens at low levels of analyte.

Mass Range (Daltons)	*m/z* 5–2000
Resolution (FWHM)	0.2 Da
Sensitivity 5 µL Injection of a 200 fg/µL Reserpine Solution	Minimum signal-to-noise ratio of 500,000:1



Active collision cell with axial DC field
Enables ultra-fast selected reaction monitoring (SRM).

Enhanced dual-mode discrete-dynode electron multiplier detector
Extends multiplier lifetime with increased surface area. Maintains excellent linearity and dynamic range.

QR5 Segmented Quadrupoles mass filter with hyperbolic surfaces
Enhances ion transmission and consistency to ensure superb sensitivity and reproducible results across instruments and over time for increased productivity.

Ion beam guide with neutral blocker
Provides robust performance and maximum sensitivity by blocking neutrals and efficiently transmitting ions.

Optimized high capacity transfer tube (HCTT)
Maximizes ion introduction while maintaining robustness.

Electrodynamic Ion Funnel (EDIF)
Efficient capture and gentle movement of ions from the HCTT into the vacuum region provides ultimate sensitivity.

OptaMax NG ion source APCI ready
Automates all gas and voltage connections for ease-of-use. Provides optimizable spray position for ultimate performance in HESI or APCI mode.

thermo scientific

Bi-Directional LIS Connection

Expedited by the *optional* B-Link LIS/LIMS Connector

B-Link® is a Universal LIS/LIMS Connector validated for TraceFinder LDT software. Comprised of a downloadable software package of "middleware" capable of providing bidirectional communication between TraceFinder software and the Laboratory Information System (LIS), the B-Link LIS/LIMS Connector software is installed on the TSQ Altis MD Series data system or TSQ Quantis MD Series data system—there is no need for any additional hardware.

This turnkey middleware solution facilitates data-sharing between:

- The LIS/LIMS and B-Link (ASTM-1394-91 and ASTM 1381-95); and,
- B-Link and TraceFinder LDT software (.csv)

Since the .csv input and output of the mass spectrometer do not conform to the requirements of the typical Laboratory Information System, laboratories performing LC-MS are often challenged by data management issues, such as:

- Downloading test requests to the mass spectrometer
- Uploading test reports to the Laboratory Information System

The B-Link LIS/LIMS Connector resolves these data management issues by converting data to the appropriate format and providing bi-directional communication:

- Between LIS/LIMS and B-Link Connector
- Between B-Link Connector and TraceFinder LDT software

Bi-Directional LIS Connection

Find out more at **thermofisher.com/BeSure**

IVD In Vitro Diagnostic Medical Device

ThermoFisher SCIENTIFIC