Fast screening for confident Compound ID

Food Safety • Environmental • Clinical Research
Forensic Toxicology • Drug Discovery

Thermo SCIENTIFIC

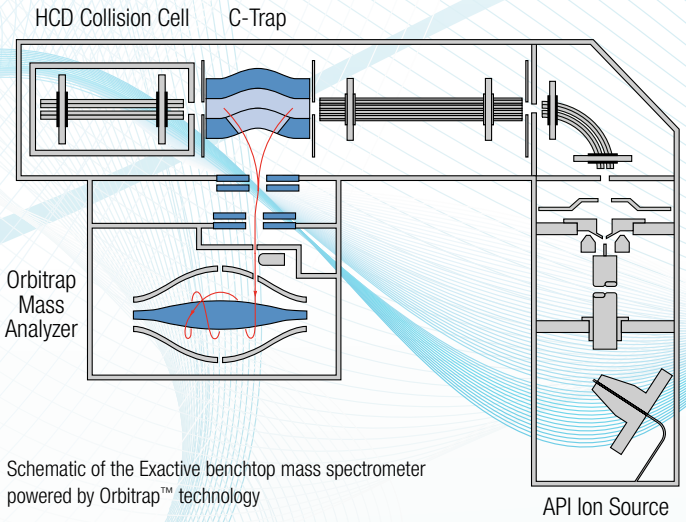
Thermo Scientific Exactive –
A New Era in Ultrahigh Resolution

The Thermo Scientific Exactive mass spectrometer begins a new era in ultrahigh resolution benchtop mass spectrometry for screening and quantifying low levels of analytes in complex samples. This easy-to-use LC-MS system delivers accurate mass for every scan without the need for data averaging. Operating at a 10 Hz scanning frequency the Exactive™ mass spectrometer is fully compatible with UHPLC and ensures exact mass measurement for fast chromatography applications.

Powered by Thermo Scientific Orbitrap technology, the Exactive mass spectrometer is ideal for compound identification and high throughput screening for both qualitative and quantitative analysis. The Exactive instrument uses high resolution accurate mass to provide fast, reproducible, precise results – without compromise.

Features of the Exactive LC-MS system

- Compound screening using high resolution accurate mass
- "All Ion Fragmentation" for structural elucidation
- Up to 100,000 resolution for complex sample analysis
- Benchtop LC-MS with FTMS performance



Schematic of the Exactive benchtop mass spectrometer powered by Orbitrap™ technology

Benchtop Mass Spectrometry

Set and forget

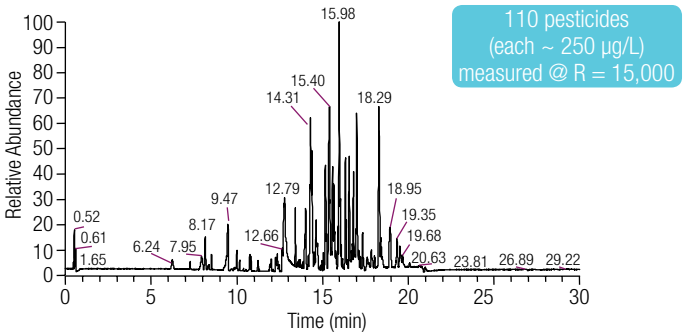
Using all resolution settings of up to 100,000, the Exactive mass spectrometer is fully compatible with fast UHPLC and delivers accurate mass information all the time – for every scan. Simply use the system in default mode and select the required scan speed …

Resolve interferences – superior resolution

for separation of isobaric compounds

While scanning at 10 Hz the Exactive LC-MS system maintains high resolution and precise mass accuracy for both full scan and HCD experiments. Rapid polarity switching enables the detection of the widest range of compound types. This allows confirmation of targeted compounds together with the ability to identify unknown species in the same analysis.

Screening can be performed for all selected chromatographic peaks in the analysis to determine elemental formulas, and this information can also be searched against specified databases.



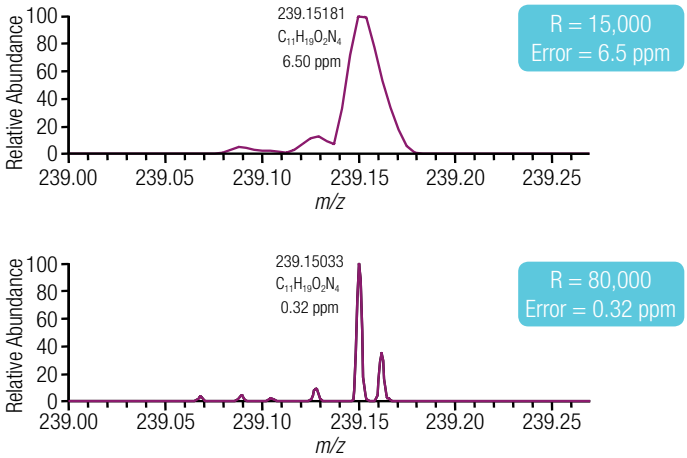
Reconstructed ion chromatogram (XIC) with 5 ppm window of about 110 pesticides (each ~ 250 µg/L) from a mixture in horse feed matrix

Unusually high mass errors are an indication of insufficient resolution resulting in unresolved doublets of isobaric peaks, frequently (as seen in the example) due to matrix interferences. The Exactive mass spectrometer allows re-analysis of the sample at higher resolution (in this case 80,000) in order to separate the isobaric peaks and thereby correctly identify the target compound (Pirimicarb) within the specified instrument mass accuracy.

Component	Elemental Composition	[M+H]	Error [ppm]
Propoxur	$C_{11}H_{15}NO_3$	210.1125	1.10
Chlortoluron	$C_{10}H_{13}ClN_2O$	213.0789	1.20
Metribuzin	$C_8H_{14}N_4OS$	215.0961	2.00
Atrazine	$C_8H_{14}ClN_5$	216.1011	2.50
Diuron	$C_9H_{10}Cl_2N_2O$	233.0243	2.00
Carbetamide	$C_{12}H_{16}N_2O_3$	237.1234	1.20
Pirimicarb	$C_{11}H_{18}N_4O_2$	239.1503	6.50*
Clomazone	$C_{12}H_{14}ClNO_2$	240.0786	0.10
Cyanazine	$C_9H_{13}ClN_6$	241.0963	0.90
Linuron	$C_9H_{10}Cl_2N_2O_2$	249.0192	1.20
Thiacloprid	$C_{10}H_9ClN_4S$	253.0309	0.70
Triadimefon	$C_{14}H_{16}ClN_3O_2$	294.1004	0.30
Paclobutrazol	$C_{15}H_{20}ClN_3O$	294.1368	1.40
Fenthion-sulfoxide	$C_{10}H_{15}O_4PS_2$	295.0222	2.00
Triadimenol	$C_{14}H_{18}ClN_3O_2$	296.1161	0.20
Imazalil	$C_{14}H_{14}Cl_2N_2O$	297.0556	1.70
Spiroxamine	$C_{18}H_{35}NO_2$	298.2741	1.20

**Unusual high error of 6.5 ppm → recheck @ higher resolution*

List of 17 selected pesticides from the mixture in horse feed matrix



The unsually high error of 6.5 ppm (top) indicates the need for higher resolution. Re-analysis performed at 80,000 (bottom) shows baseline separation of the targeted pesticide from the matrix interference

Compound Identification

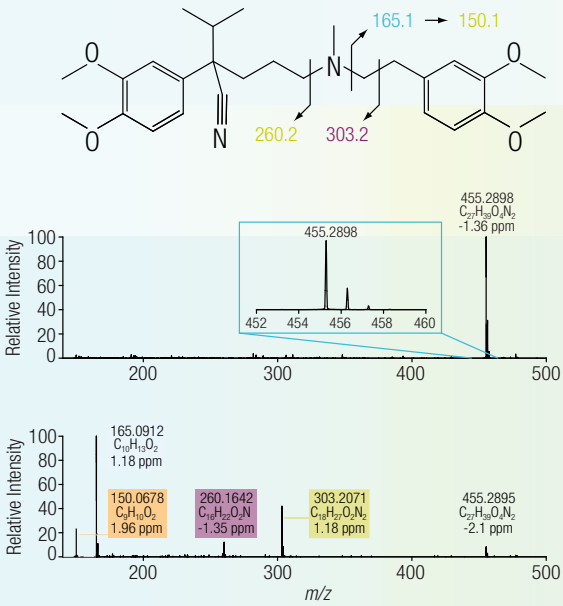
The key to faster, unambiguous results

is high resolution and accurate mass

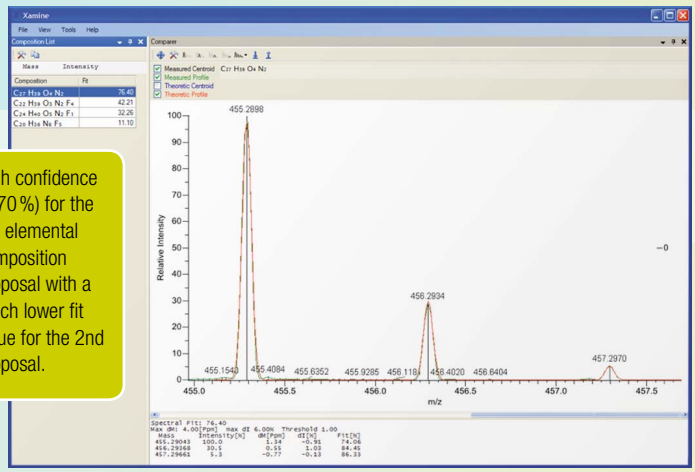
New software to calculate elemental compositions uses a special isotopic pattern and intensity algorithm to refine the list of potential candidates and, in most cases, deliver a single answer without pre-defining the set of elements.

In combination with this intelligent software processing, the Exactive LC-MS system provides fully automated elemental compositions.

A typical method setup for the identification of unknown compounds uses alternating full MS and HCD scans. This experiment provides accurate masses of the precursor and fragment ions (as shown for Verapamil), enabling structural identification of both target and unknown compounds.



Verapamil positive full scan MS and HCD spectra at resolution of 30,000



High confidence (>70 %) for the 1st elemental composition proposal with a much lower fit value for the 2nd proposal.

The software features a special algorithm that uses isotopic information to determine elemental composition with greater confidence

Mass	Composition	Error [ppm]	Probability [%]
150.0678	$C_9H_{10}O_2$	1.96	72.3
165.0912	$C_{10}H_{13}O_2$	1.18	83.3
260.1642	$C_{16}H_{22}O_2N$	-1.35	80.9
303.2071	$C_{18}H_{27}O_2N_2$	1.18	79.3
455.2898	$C_{27}H_{39}O_4N_2$	-1.36	76.4

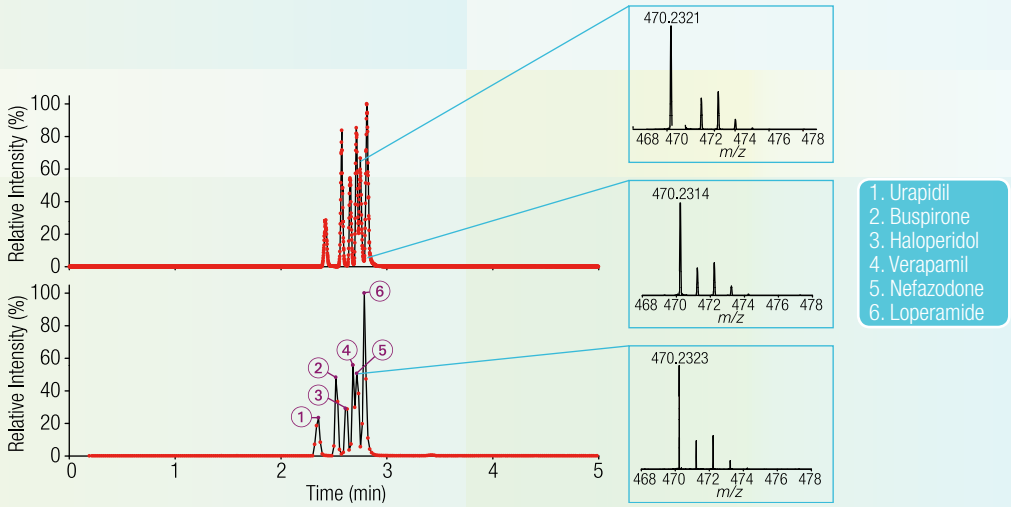
List of elemental compositions for Verapamil and its fragment ions as determined using the new software algorithm (highest probability is assigned to the correct elemental composition in all cases)

Fast Scan Speed

Maintain high quality data at any scan speed

One challenge for MS analysis is to provide compound identification when coupled to a fast UHPLC system. The resulting chromatographic peak widths may be less than 1 second at half height. The Exactive mass spectrometer delivers up to 10 data points across such narrow LC peaks – with every scan giving analytical mass data with the correct identity and elemental composition.

Excellent mass accuracy (< 2 ppm) is obtained at all scan speeds using external mass calibration. Equally good results are achieved at the base of the HPLC peak and at the peak top, which is important for ensuring accurate mass results with fast chromatography. This unique performance characteristic allows the use of single scans rather than averaging several scans across a chromatographic peak.



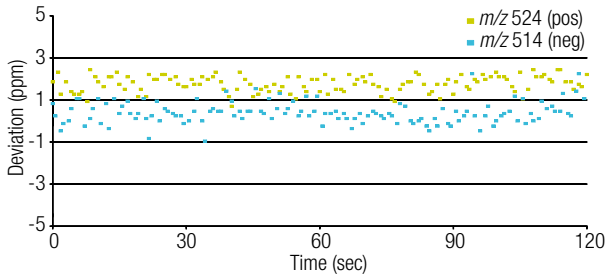
Scan speed comparison: Top trace displays 10 scans per second at R = 10,000; bottom trace shows 1 scan per second at R = 100,000

Polarity Mode Switching

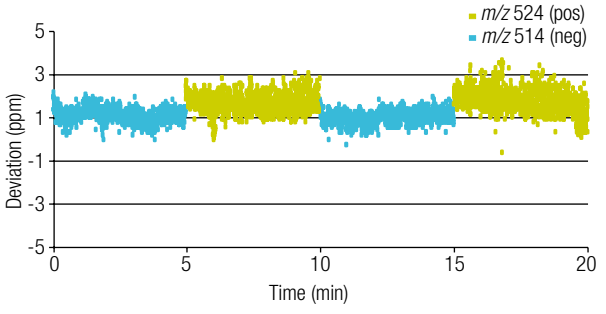
Highest flexibility without compromise

For applications such as pesticide screening or drug discovery it is important to be able to ionize samples in both polarity modes in order to detect the widest range of diverse compound types. Fast positive/negative switching mode, with accurate mass performance, is essential for maximum screening coverage in LC-MS analyses.

The Exactive mass spectrometer provides full scan cycles with polarity switching in less than one second. The mass accuracy is precise in both polarities independent of the type of experiment (alternating scanning for LC-MS or polarity change after a given time segment in the LC-MS experiment), demonstrating no loss of mass accuracy even with external mass calibration.



Fast polarity switching: 256 scans (positive and negative alternating) in 120 seconds externally mass calibrated



Polarity switching: Every 5 minutes (external mass calibration)

Set Up and Analyze

Thermo Scientific ExactFinder workflow software

for routine targeted and general unknown screening and quantitation

The ExactFinder™ software unifies qualitative and quantitative workflows in a single, intuitive software package. With simplified method setup and data review, plus automated data processing and reporting, the ExactFinder software substantially increases laboratory productivity in a range of applications, from food and environmental safety to forensic toxicology.

For unprecedented confidence in screening results, the ExactFinder software integrates multiple forms of compound identification and verification, including its unique HRAM (High Resolution Accurate Mass) spectral library and library search and ChemSpider database queries.

Advanced algorithms such as automated component detection, isotopic pattern matching, and parameter less peak detection increase throughput and facilitate throughput in complicated sample analyses.

The ExactFinder software eliminates the bottleneck of data mining with comprehensive database and library searching. ExactFinder software includes a novel LC-MS/MS HRAM library of thousands of mass spectra from over a thousand compounds, enabling better matching for confirmation, and increased confidence in results.

Easy setup of targeted and general unknown screening data-processing methods

Fast, information-rich data review

Simplified reporting

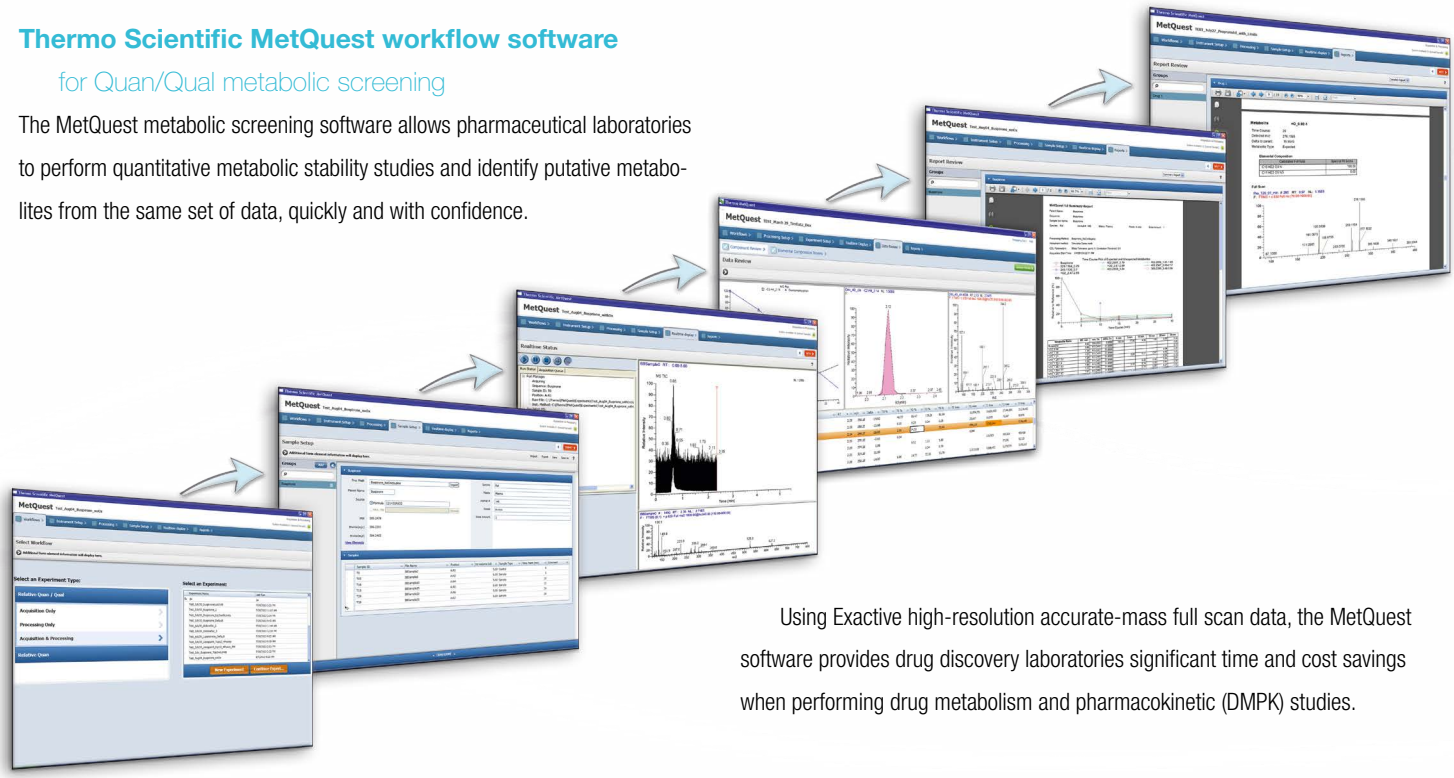
Regardless of your application, method development, data review and reporting are simplified for maximum laboratory productivity. Create your processing method, review your data, and print your report.

Thermo Scientific Software

Thermo Scientific MetQuest workflow software

for Quan/Qual metabolic screening

The MetQuest metabolic screening software allows pharmaceutical laboratories to perform quantitative metabolic stability studies and identify putative metabolites from the same set of data, quickly and with confidence.



Using Exactive high-resolution accurate-mass full scan data, the MetQuest software provides drug discovery laboratories significant time and cost savings when performing drug metabolism and pharmacokinetic (DMPK) studies.

The Perfect Match

Screening and Quantifying Software

with Exactive LC-MS

Possessing an instrument which provides routine high resolution and mass accuracy is the critical starting point. It is the coupling of sophisticated hardware technology and advanced software such as ExactFinder and MetQuest, that creates workflow-oriented, application-specific systems. The right combination of hardware and software enables scientists to easily analyze samples using familiar approaches while also searching for the right answers. In new ways ExactFinder and MetQuest software complete the workflow solutions driven by the unique and powerful capabilities of the Exactive instrument.

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