



ThermoFisher
S C I E N T I F I C

**High Resolution Accurate Mass GC-MS based on Orbitrap
Technology - A new chapter in GC-MS**

Webinar on 25 November 2016

- Introduction to the new Thermo Scientific™ Orbitrap™ GC-MS family
- Insight into the GC-MS system based on Orbitrap technology
- Analytical performances and advantages of the Orbitrap technology for GC-MS
- Main workflows for targeted and untargeted analyses
- Most relevant analytical fields for GC-MS systems based on Orbitrap technology and examples of key applications

Q Exactive GC system

Unprecedented Depth in Analysis

RP 120,000 (FWHM @ m/z 200)

EI/CI; Full-scan, Timed-SIM

MS/MS capability



Orbitrap GC-MS Family



Redefining Routine GC-MS
RP 60,000 (FWHM @ m/z 200)
EI/CI; Full-scan; Timed-SIM
Exactive GC system



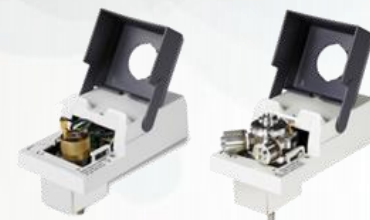
Q Exactive GC system
Unprecedented Depth in Analysis
RP 120,000 (FWHM @ m/z 200)
EI/CI; Full-scan, Timed-SIM
MS/MS capability



Insight into the Orbitrap GC-MS Systems



Insight into the Orbitrap GC-MS Systems

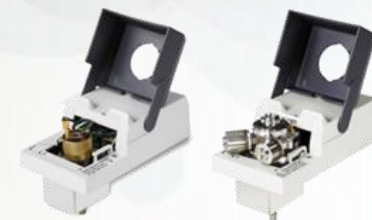


**Thermo Scientific™
TRACE™ 1310 GC
system**

**Unique modular
injector and detector
design**

Short cycle time

Insight into the Orbitrap GC-MS Systems



TRACE 1310 GC system

Unique modular injector and detector design

Short cycle time

Thermo Scientific™ ExtractaBrite™ ion source technology

Routine grade robustness

Patented RF lens

Removable without breaking vacuum through VPI

Vacuum-free column replacement through VPI



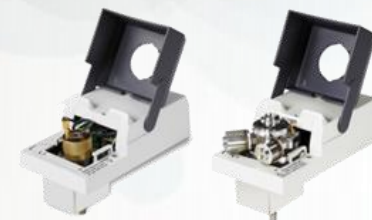
Insight into the Orbitrap GC-MS Systems



Orbitrap mass analyzer

Incredible HRAM performance

Extended Dynamic Range



TRACE 1310 GC system

Unique modular injector and detector design

Short cycle time

Thermo Scientific™ ExtractaBrite™ ion source technology

Routine grade robustness

Patented RF lens

Removable without breaking vacuum through VPI

Vacuum-free column replacement through VPI



Insight into the Orbitrap GC-MS Systems

Resolving Power

Up to
120,000 at
 m/z 200

- Maximum selectivity
- Fast enough for GC

Mass Accuracy

< 1ppm

- Every scan
- All concentrations
- In complex matrix
- Across the mass range
- Everyday!

Sensitivity

ppt

- In full-scan
- High selectivity
- High spectral fidelity

Dynamic Range

>6 orders

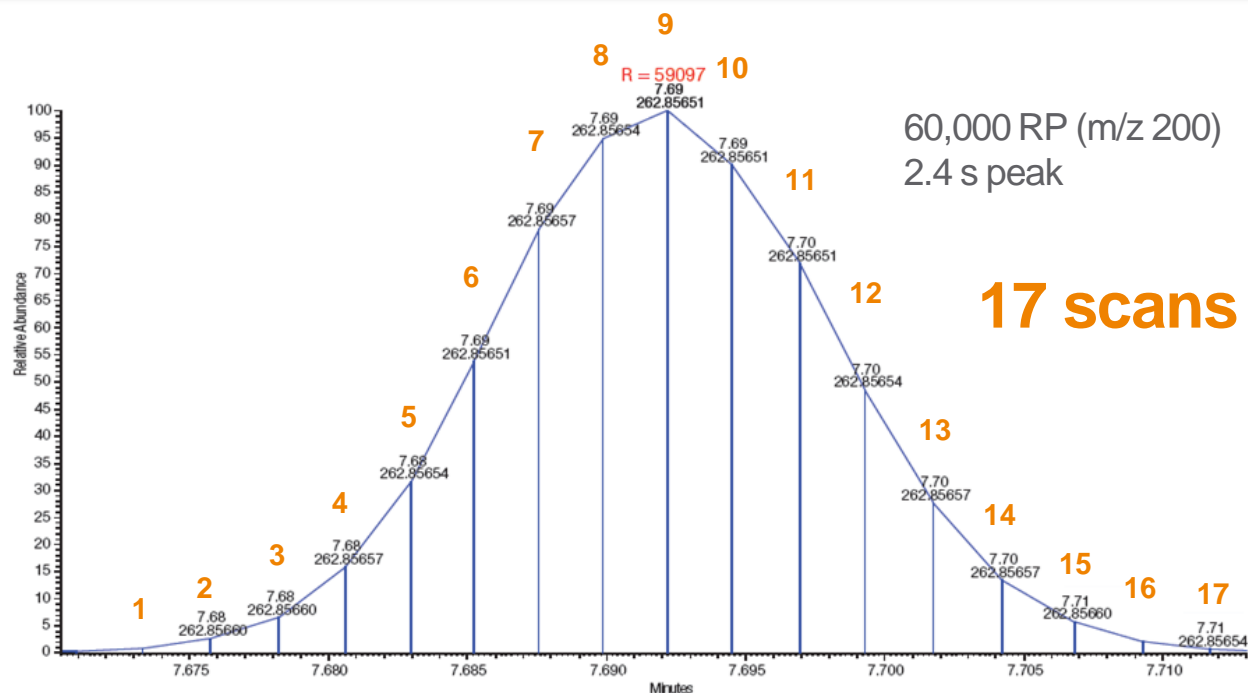
- Excellent coverage in sample profiling
- “Triple quad grade” quantitation in full-scan

High resolving power & fast acquisition

Fast acquisitions

- Important for accurate profiling of narrow GC peaks
- Full scan with resolving power of 60 (FWHM @ m/z 200) generates **17 scans**
- Fast enough for GC!

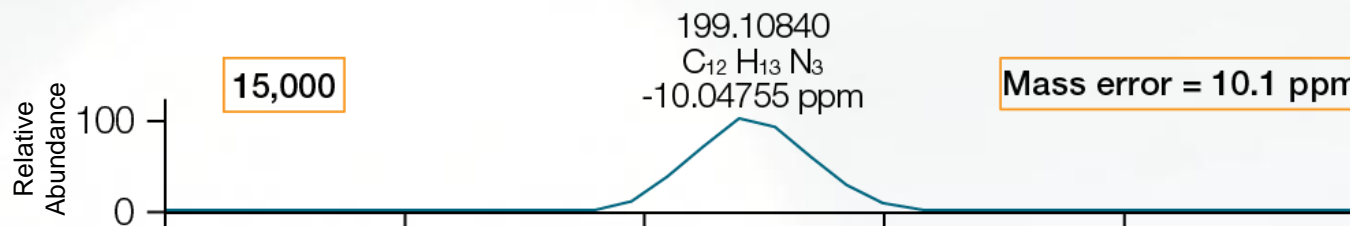
XIC of dieldrin in baby food (m/z 262.85642) 100ppb



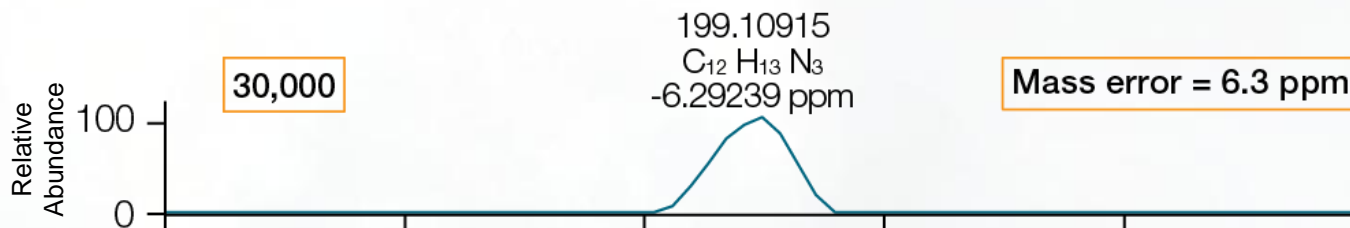
Resolving Power: Selectivity

Pyrimethanil in leek at 10 µg/Kg

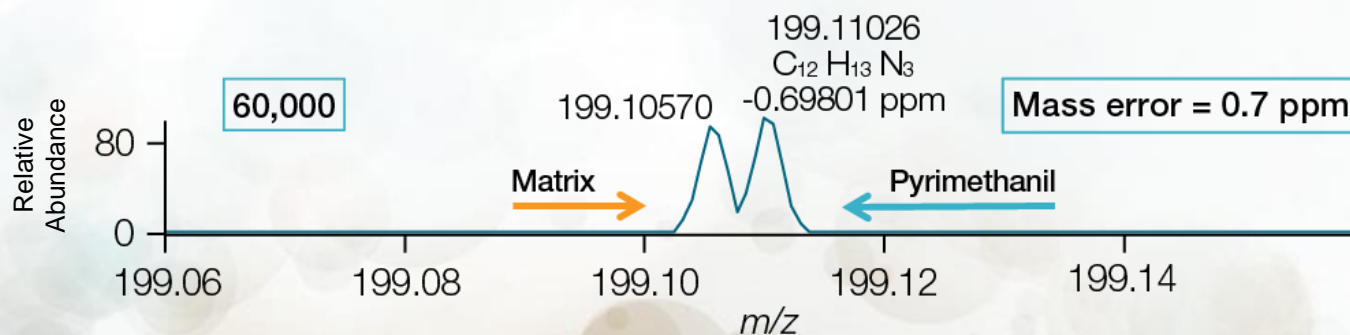
< 5 ppm ID criteria



False negative



False negative



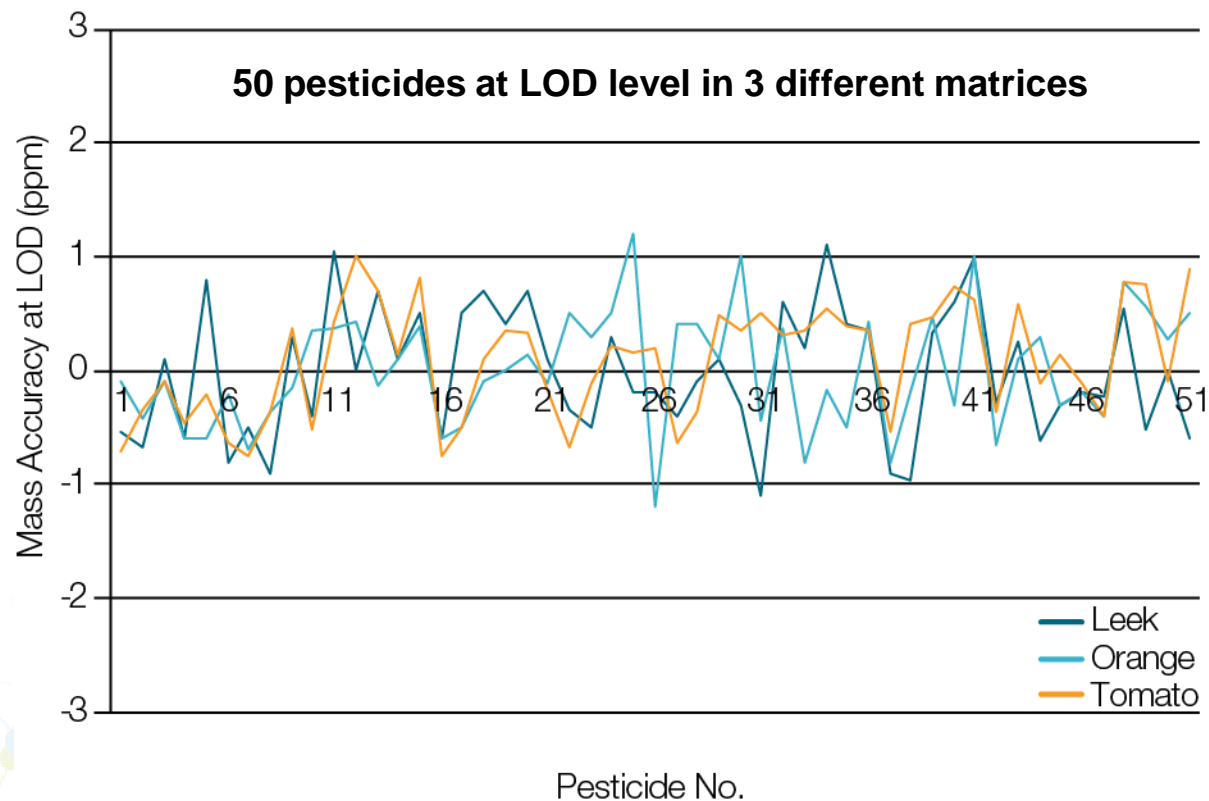
Positive
Detection

High selectivity, high sensitivity and confidence in identification

Consistently excellent mass accuracy

< 1ppm

- Scan-to-scan
- **Low level in matrix** →
- Over full mass range
- Over full concentration range
- No need for continuously calibrating in sequence



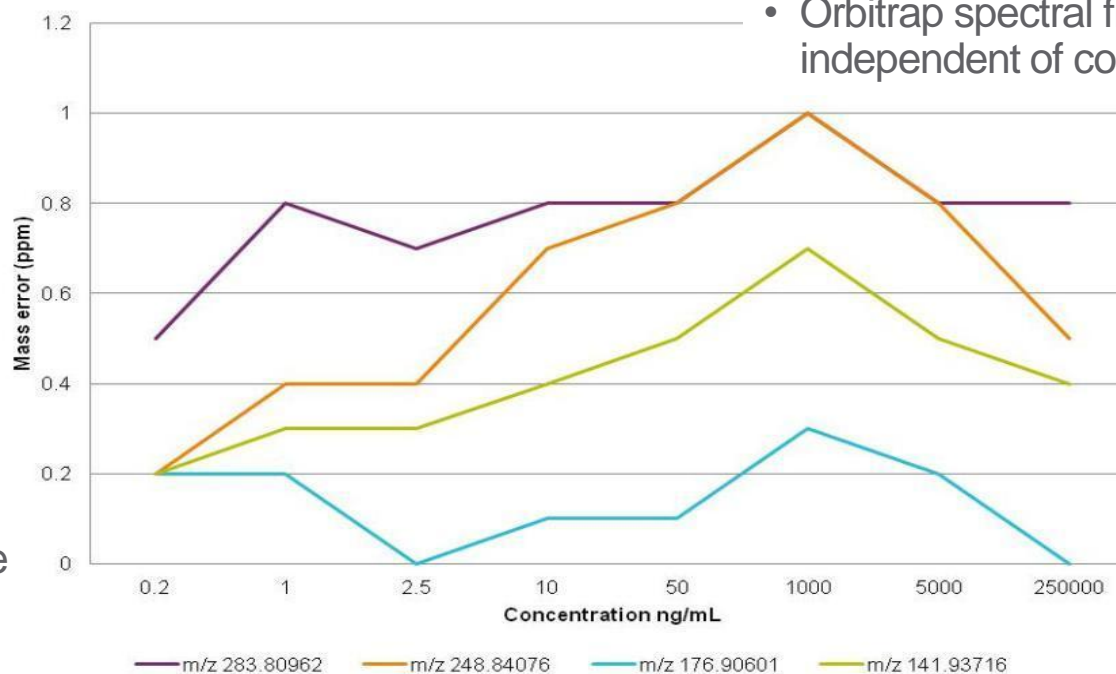
Consistently excellent mass accuracy

< 1ppm

- Scan-to-scan
- Low level in matrix
- Over full mass range
- **Over full concentration range** →
- No need for continuously calibrating in sequence

Mass accuracy over >6 orders

- Hexachlorobenzene
- 0.2 – 250,000 ng/mL
- Orbitrap spectral fidelity independent of concentration



Data courtesy of Hans Mol and Marc Tienstra, RIKILT



Unprecedented quantitation power for HR/AM GC-MS

PPT sensitivity

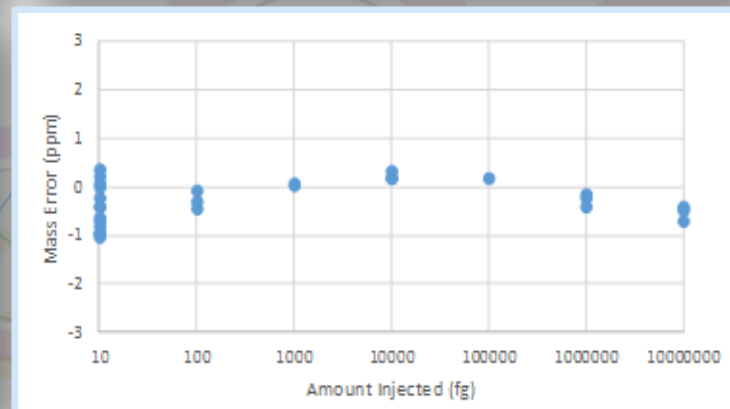
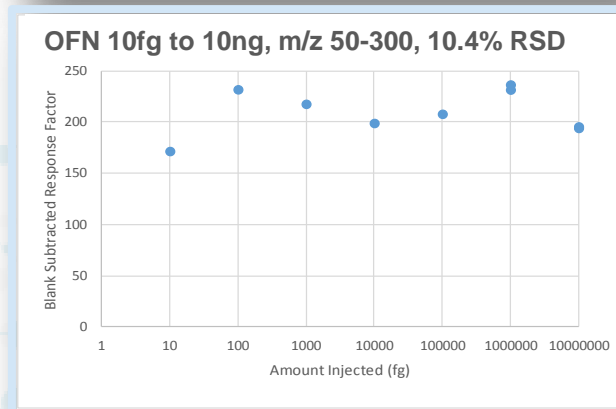
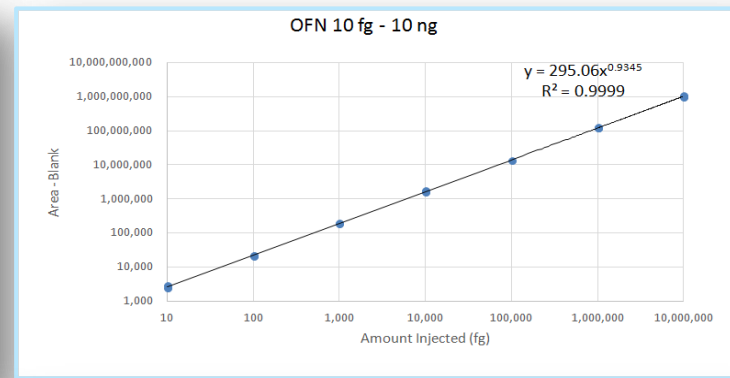
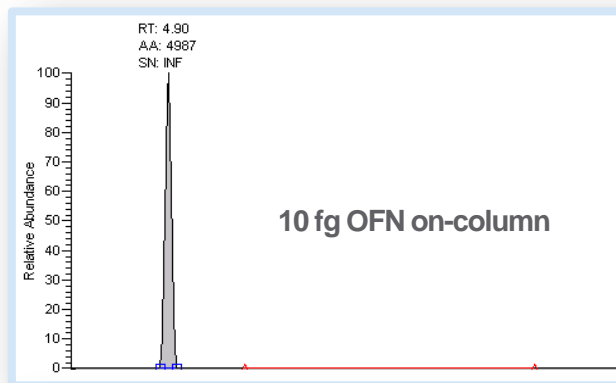
- Low fg on-column detection limits
- “triple quad grade” quantitation

Extended linear range

- > 6 Orders linear range

Excellent precision

Highest selectivity



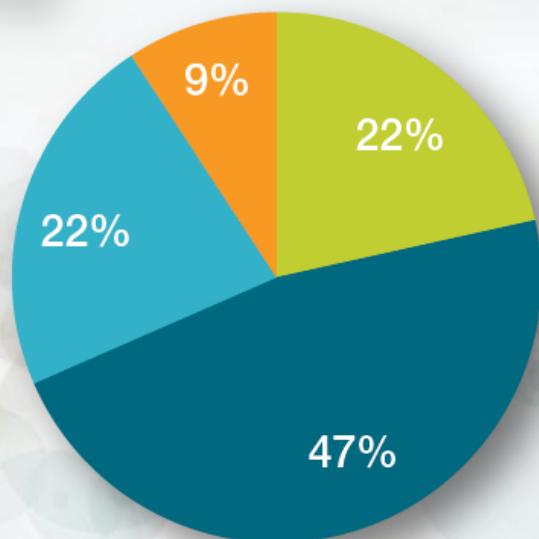
High Sensitivity

Triple quadrupole level sensitivity possible with a non-target Full Scan acquisition

150 pesticides in mixed vegetable matrix

GC Orbitrap

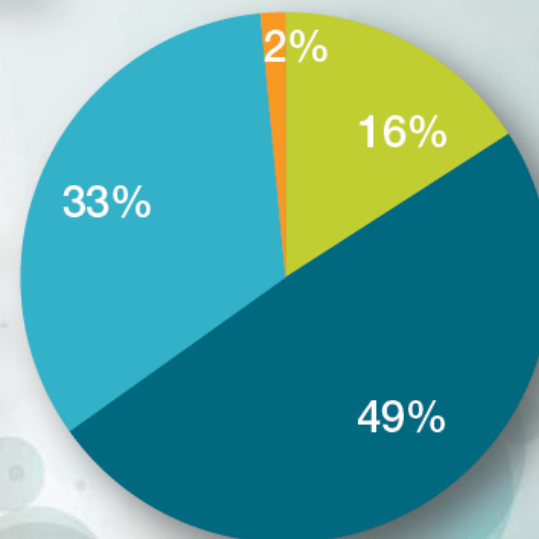
IDL ppb



Full scan

GC-MS/MS

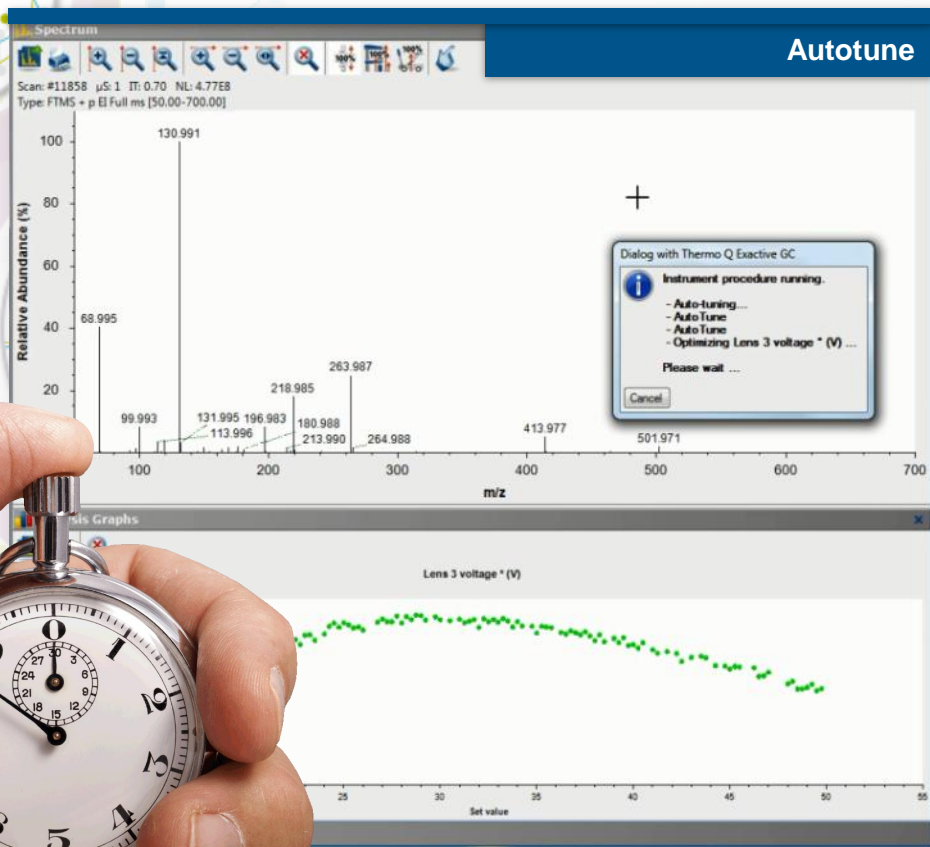
IDL ppb



SRM

Breakthrough in GC-MS Performance

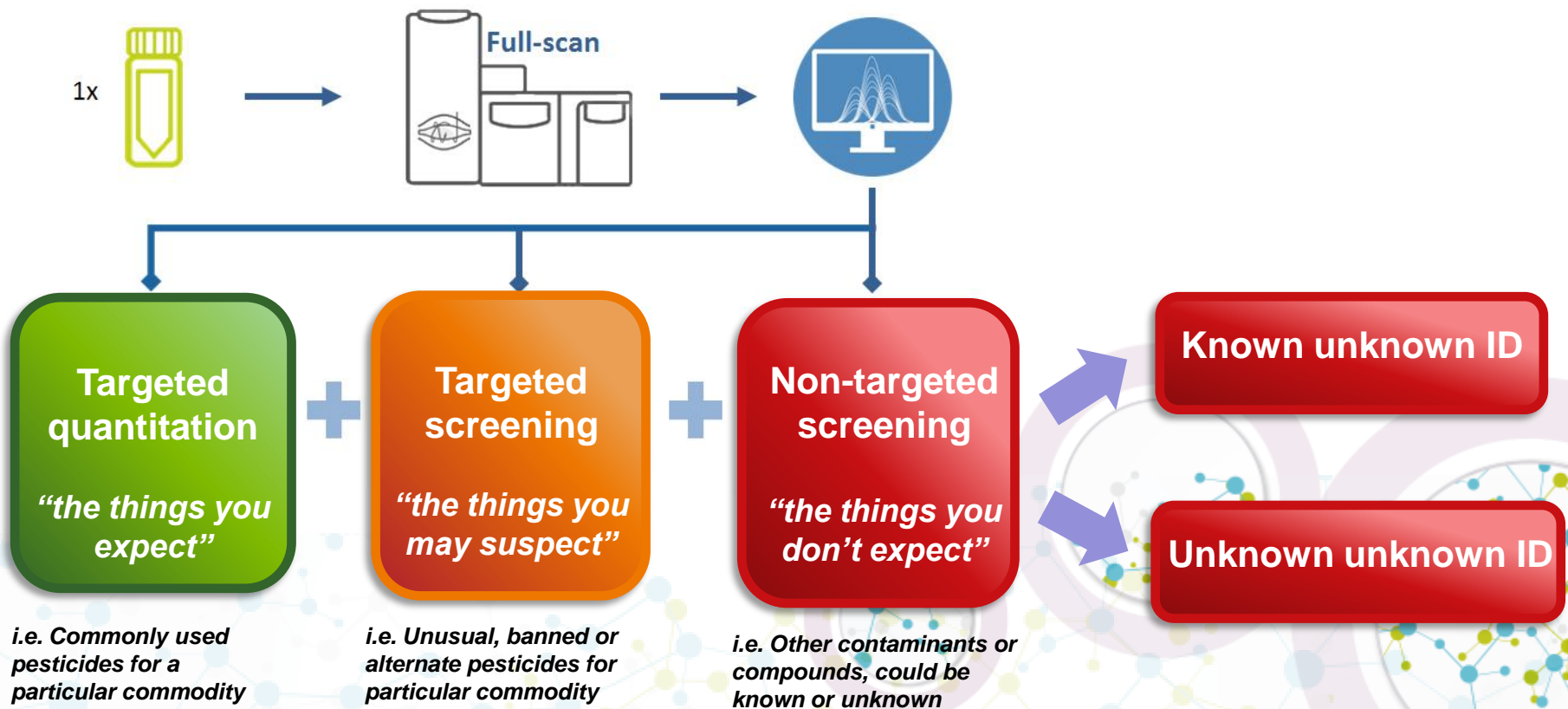
To get data this good, it's really fast and simple...



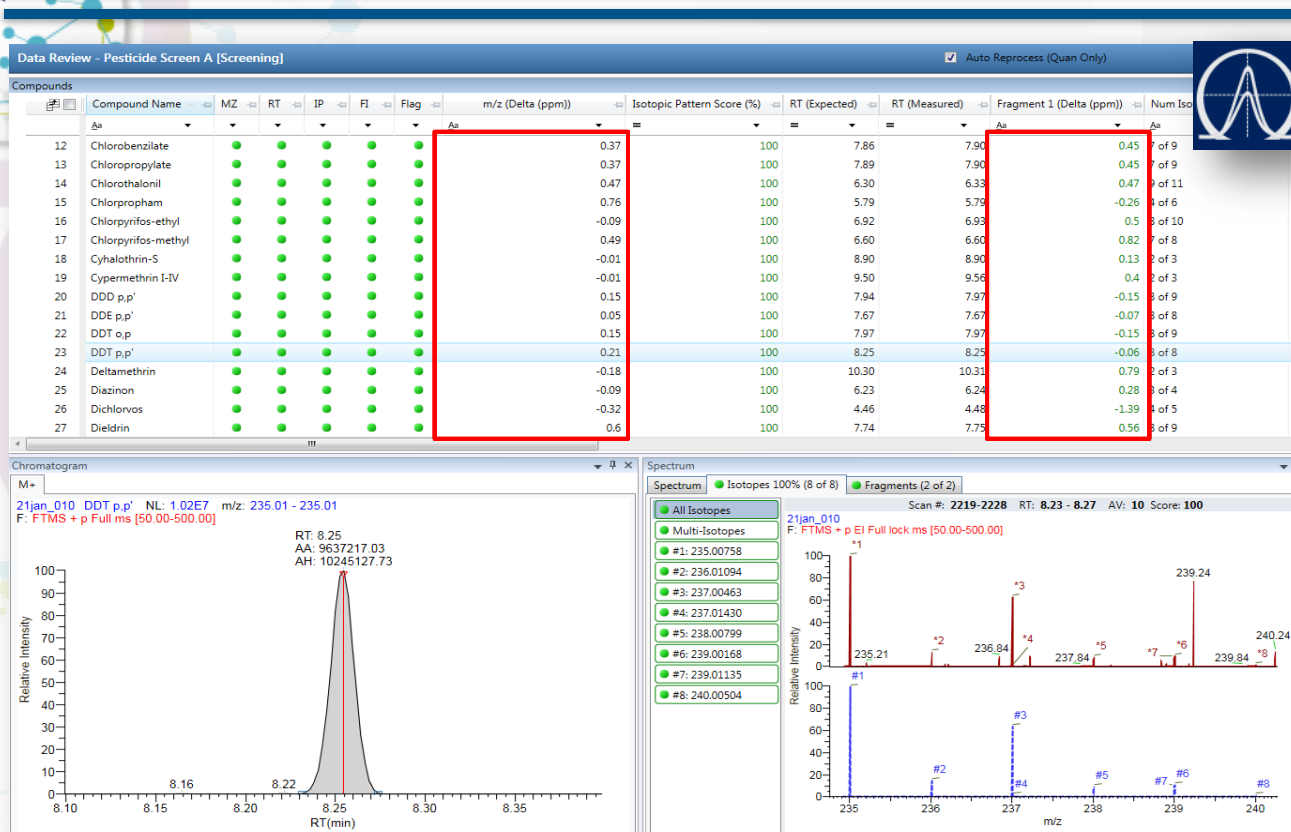
Easy set-up

- Familiar Q Exactive environment
- Simple status
- Automated leak checking
- Automated tuning & calibration
- Source and lens tuning ~25 s
- Mass calibration ~30 s
- Ready to go < 1 min

Non-targeted full scan acquisition



Targeted screening and automatic identification



- Example for p,p'-DDT
- Identification based on accurate mass (mass error < 2 ppm)
- Confirmation through isotopic pattern and detection of fragment ions
- Sub-ppm mass accuracy for both main and confirmatory ions (red boxes)

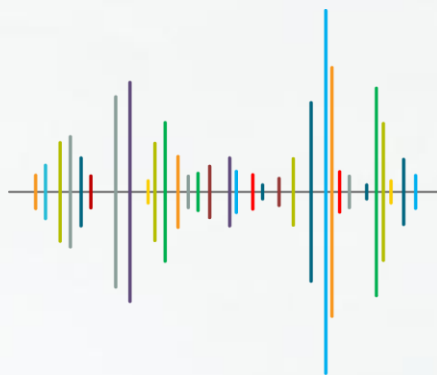
TraceFinder Non-targeted Screening Overview

1. Detect and refine



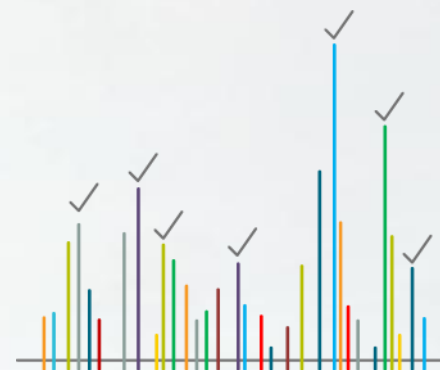
- Sensitive and selective peak detection
- High resolution spectral deconvolution
- Clean spectrum

2. Generate candidates



- Search spectra against spectral libraries
- HRAM or low resolution spectral libraries (NIST, Wiley...)
- Candidates list generated

3. Filter and identify

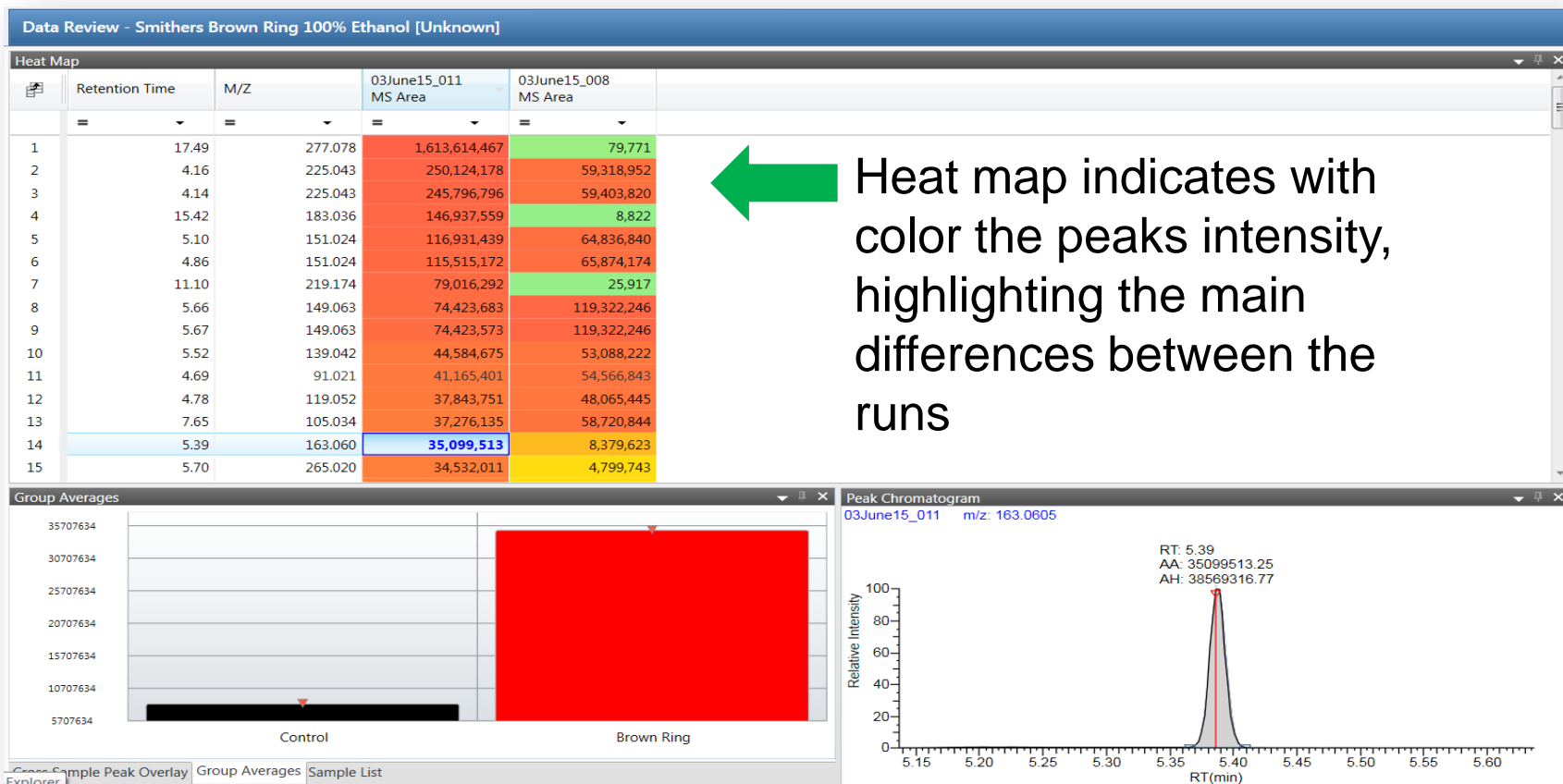


- High resolution filtering of candidates
- Putative identifications made

Automatic compound identification

Quickly Isolate the Peaks of Interest

Peaks list in the sample (S/N>30:1)



Peaks list can be sorted by fold difference compared with a reference sample or blank, to highlight the differential peaks

Identify the Compound – Searching NIST 14

26 hits from NIST are sorted based on:

- Spectral matching
- High resolution filtering (HRF) score
HRF: is the % of ions that can be explained by the elements in the proposed compound

Combined SI and HRF values give an overall score (%) to quickly and confidently identify the compound. Eliminates other hits that would be valid if only SI is used

Peak Identification

Score	Matched Compound	Formula	CAS	SI	HRF Score	M+ m/z	M+	M+ Lib	% Elements
94.4	1,4-Dihydrophenacetic acid,...	C18H30O2		728	99.4959	278.22403	Yes	Yes	100
70.4	1,5-Dioxaspiro[5.6]dodeca-7,...	C18H32O2Si2		524	99.8259	336.19353	No	Yes	100
57.7	Benzoic acid, 3,5-bis(1,1-dim...	C17H26O3	1620-64-0	706	58.9058	278.18764	No	Yes	100
56.8	3,5-di-tert-Butyl-4-hydroxyph...	C17H26O3	20170-32-5	659	58.9058	278.18764	No	Yes	100
55.4	Benzenemethanol, 3,5-bis(1,1...	C17H26O3	14387-17-8	591	58.9058	278.18764	No	Yes	100
51.3	Monoallyl phthalate, TBDMS ...	C17H24O4Si		517	52.4488	320.14383	No	No	100
44.5	2,6-Bis(tert-butyl)phenol, TMS...	C17H30OSi	10416-73-6	514	35.6312	278.20604	No	Yes	100
42.4	12-Cyclohex-3-enyl-3-methyl...	C23H24N2O		533	29.2285	344.18831	No	Yes	100
41.6	6-Oxo-5-phenyl-2,3,5,6-tetra...	C16H13N3O	87365-22-8	525	27.7606	263.10531	No	Yes	100

Chemical ionization for molecular ion detection

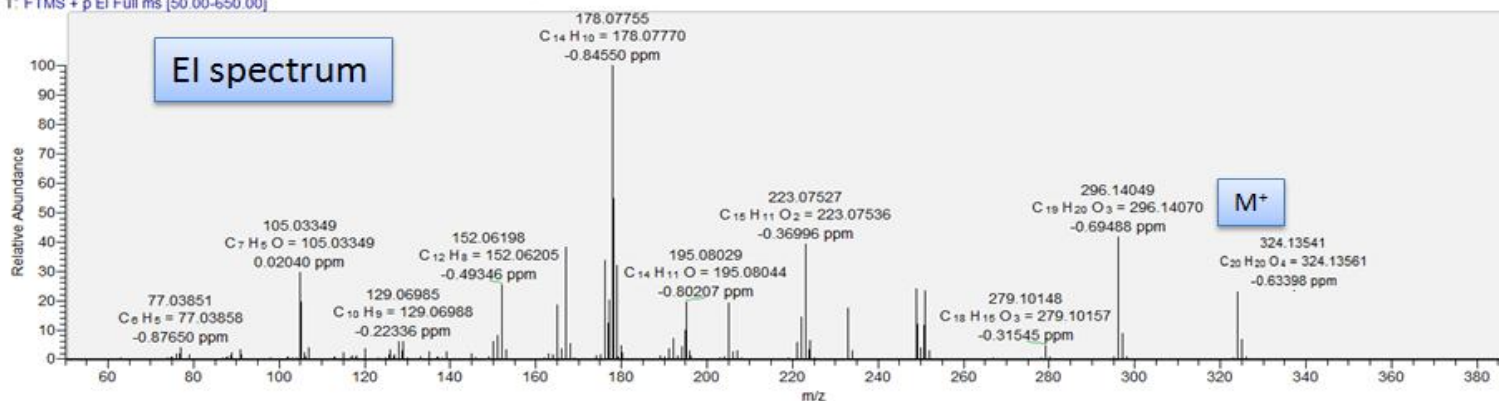
In case of low score no clear match with libraries ...



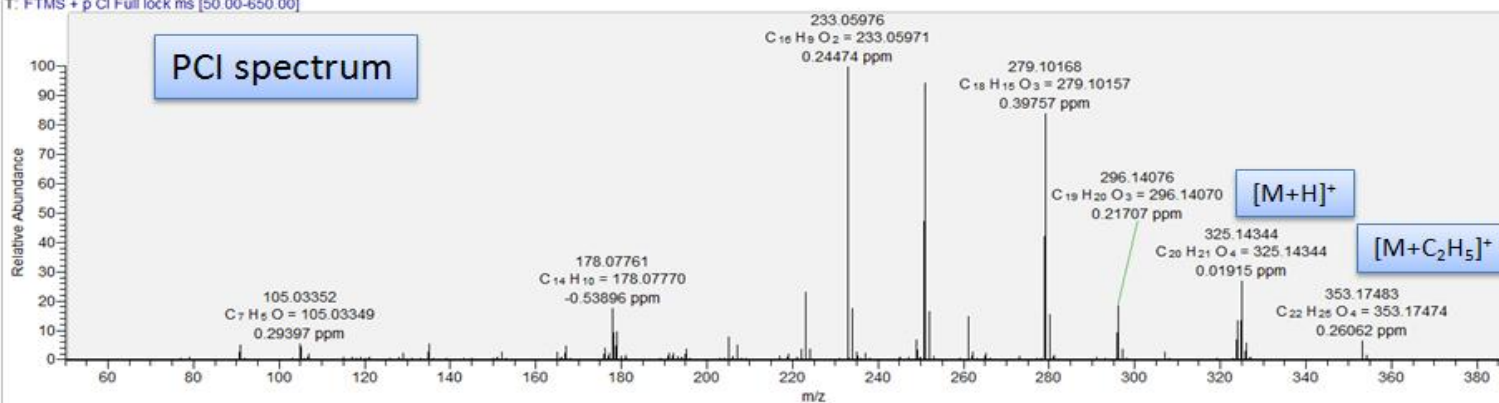
..... Remove the ionization source or switch to CI source in 2 minutes without breaking vacuum

GC-Orbitrap EI and PCI spectrum

03june15_015 #4674-4683 RT: 15.16-15.18 AV: 10 SB: 32 17.97-17.99, 18.19-18.24 NL: 3.98E9
T: FTMS + p EI Full ms [50.00-650.00]

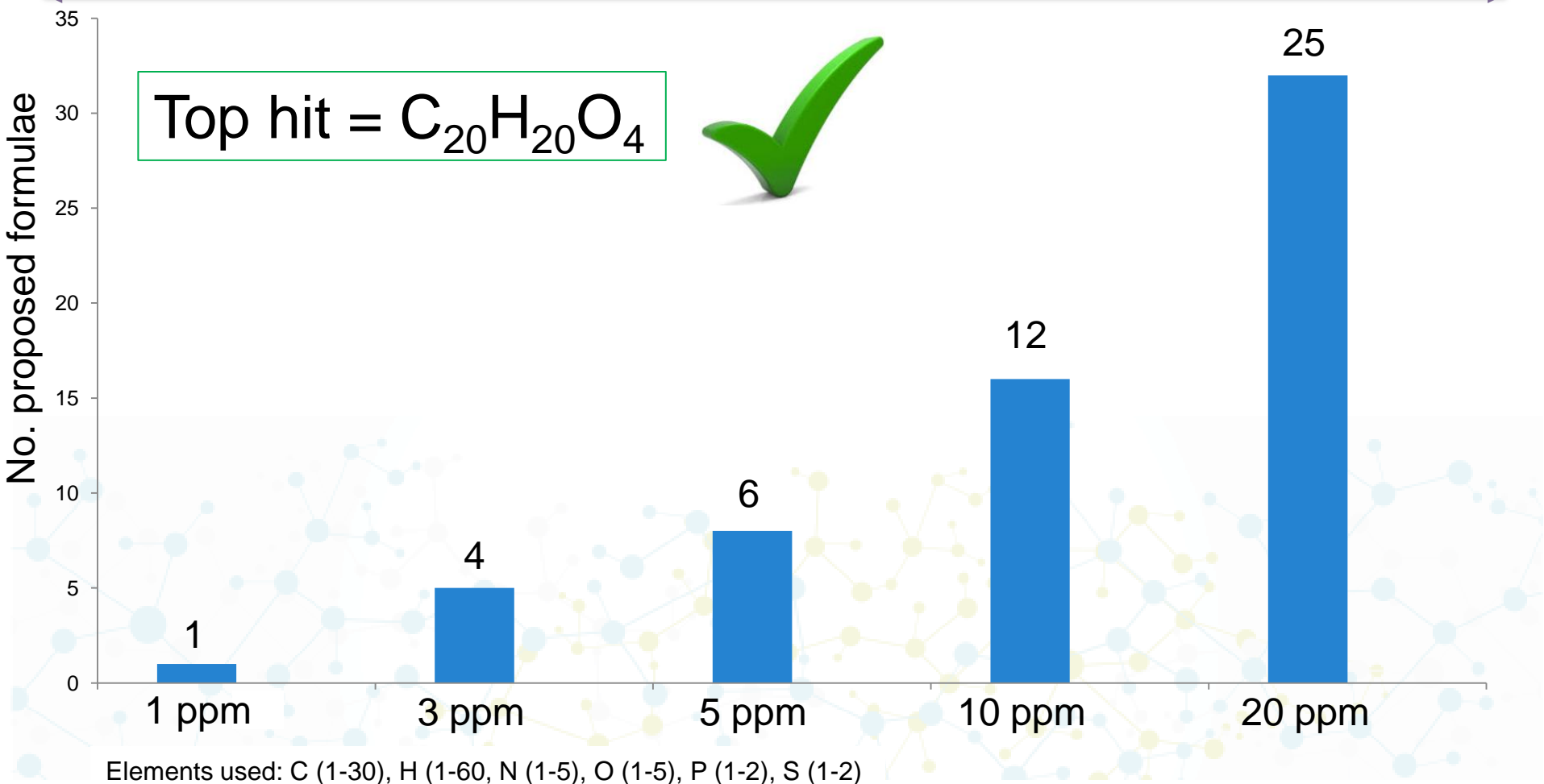


03june15_024 #4655-4676 RT: 15.15-15.20 AV: 22 SB: 26 17.97-17.99, 18.19-18.23 NL: 6.36E7
T: FTMS + p CI Full lock ms [50.00-650.00]

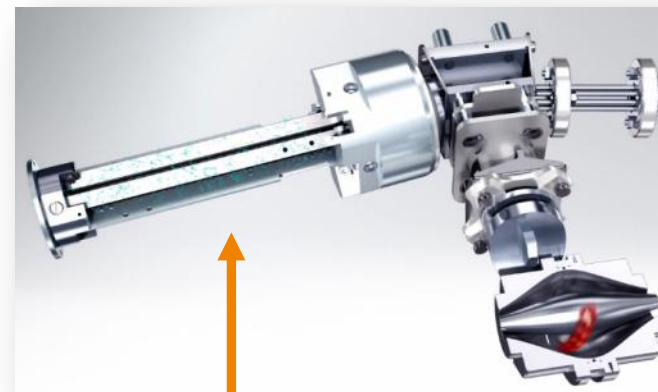
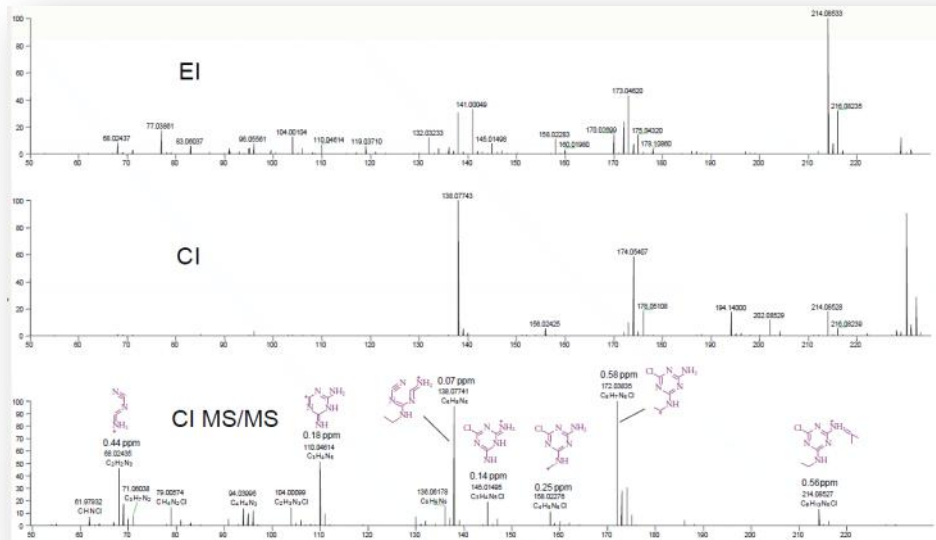


Non-targeted Screening – Unknown Compounds Identification

Importance of mass accuracy for unknown ID



CI + MS/MS for additional structural information



HCD Fragmentation Cell

- Sub ppm mass accuracy for greater confidence in the identification of fragments to support proposed formula
- Thermo Scientific™ Compound Discoverer™ software for structural interpretation

Essential research tool for leading edge applications



Metabolomics

Untargeted metabolomics
Targeted metabolomics
Metabolism studies



Food & Beverage

Pesticide screening
General contaminant screening
Targeted contaminant analysis
Food profiling
Adulteration, authenticity & origin
NIAS : Extractables & leachables



Industrial

Fine and specialties characterization
Flavors & fragrances
Process impurity analysis
Agrochemical metabolism
Product profiling
Product authenticity
Petroleomics



Environmental

Contaminant screening
Environmental fate studies
Disinfection by-products characterization
Emerging compounds research



Pharmaceutical

Impurity analysis
Extractables & leachables



Clinical & Toxicology

Anti-doping
Designer substances
Forensic toxicology

Pesticides Analysis in Food

Fast Screening, Identification, and Quantification of Pesticide Residues in Baby Food Using GC Orbitrap MS Technology

Cristian Cojocariu,¹ Dominic Roberts,¹ Michael T. Helmanski,² Richard J. Fussell,² and Paul Silcock¹
¹Thermo Fisher Scientific, Runcorn, UK
²Food and Environment Research Agency (FERA), York, UK

Application Note 10440



High Efficiency, Broad Scope Screening of Pesticides Using Gas Chromatography High Resolution Orbitrap Mass Spectrometry

Dominic Roberts,¹ Hans Mol,² Marc Tienstra,² Cristian Cojocariu,¹ and Paul Silcock¹
¹Thermo Fisher Scientific, Runcorn, UK
²RIKILT – Wageningen UR, Wageningen, The Netherlands

Application Note 10448



thermoscientific

APPLICATION NOTE

Routine Quantitative Method of Analysis for Pesticides using GC Orbitrap Mass Spectrometry in accordance with SANTE/11945/2015 Guidelines

No. 10509



Fast Screening, Identification, and Quantification of Pesticide Residues in Baby Food Using GC Orbitrap MS Technology

Cristian Cojocariu,¹ Dominic Roberts,¹ Michael T. Helmanski,² Richard J. Fussell,² and Paul Slocok¹
¹Thermo Fisher Scientific, Runcorn, UK
²Food and Environment Research Agency (FERA), York, UK

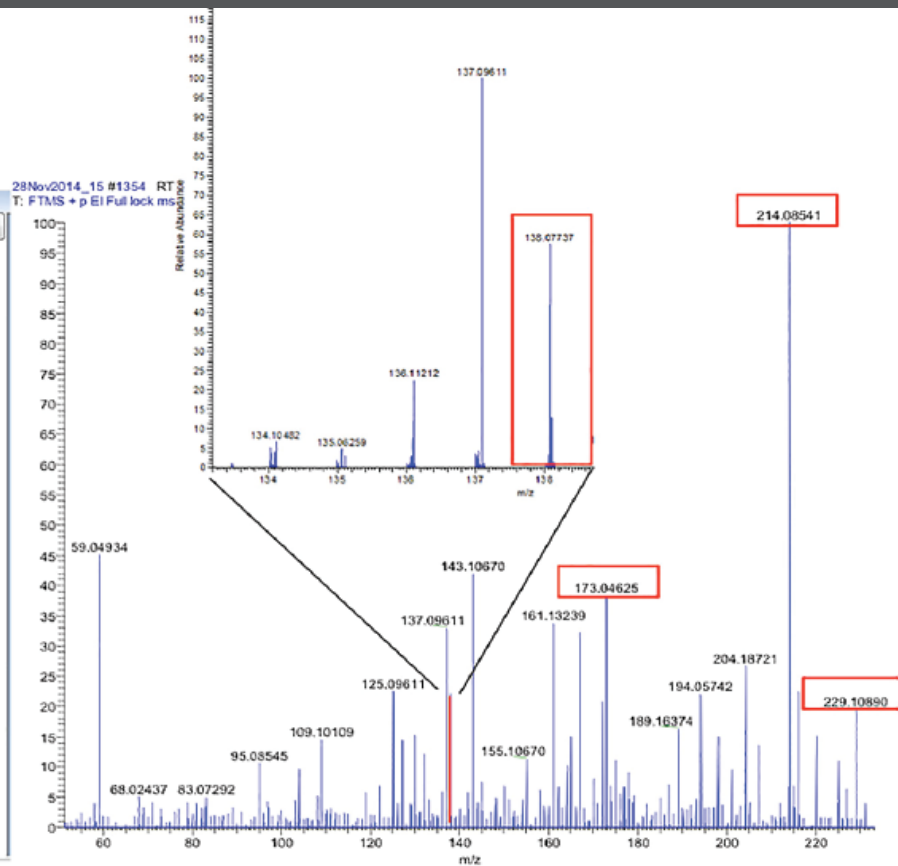
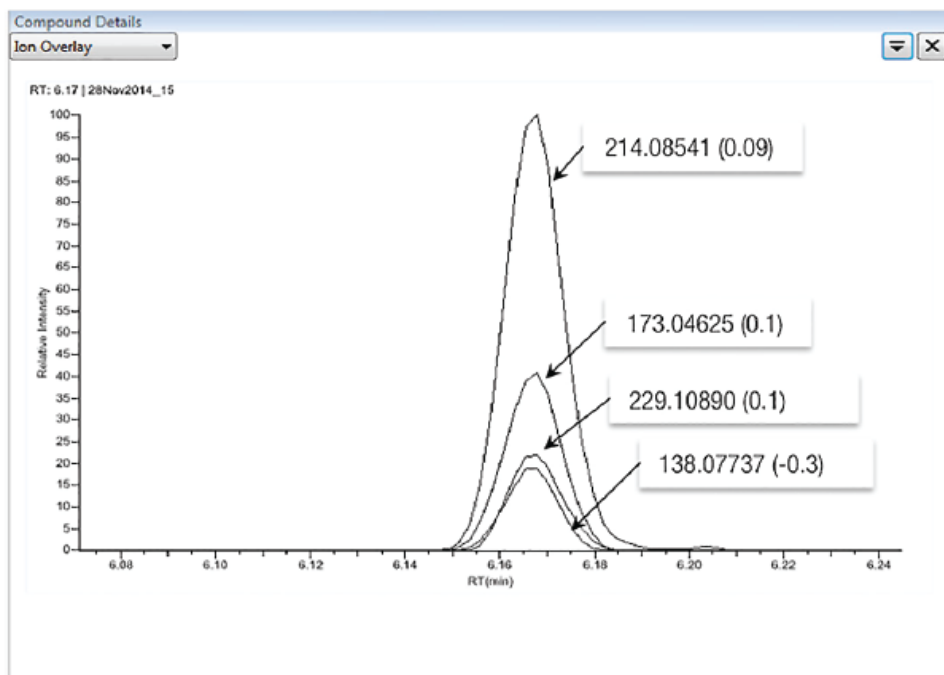
Application Note 10449



- Quantitative performance of the Q Exactive GC system for compound quantification was tested for all 132 pesticides
- Matrix-match calibration curve 0.5–100 ng/g (or 1.0–200 ng/g)
- System sensitivity, linearity, and peak area reproducibility were evaluated
- Additionally, mass accuracy of the target pesticides was assessed across the concentration levels

Pesticides Analysis in Baby Food - Sensitivity

Terbutylazine at 0.5 ng/g



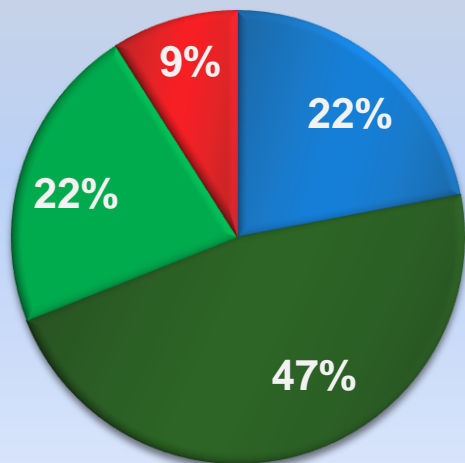
All pesticides were detected in the lowest calibration matrix-matched standard 0.5 (or 1.0) ng/g

Pesticides Analysis in Baby Food – Estimated IDL and RSD%

- IDL determined on 10 repeated injections of 5 ng/g matrix-matched standard, using the Student's-*t* critical values at 99% confidence
- Average % RSD for absolute peak area reproducibility is 6% (n=10) at 5 pg injected on column
- Q Exactive GC sensitivity is comparable to that of the Thermo Scientific™ TSQ™ 8000 Evo triple quadrupole GC-MS, with 91% of pesticides having an IDL < 2 ng/g

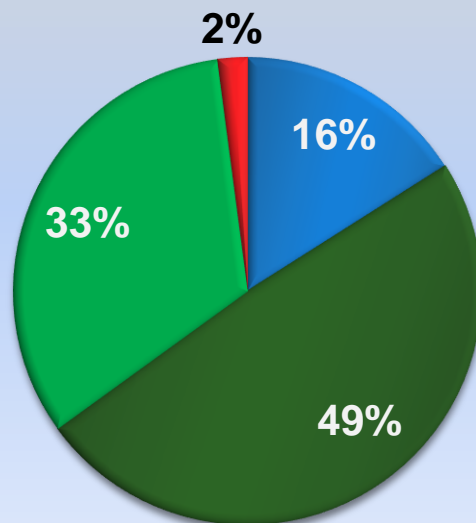
QExactive GC

■ <0.5 ■ 0.5-1.0 ■ 1.0-2.0 ■ 2.0-4.0



TSQ 8000 EVO

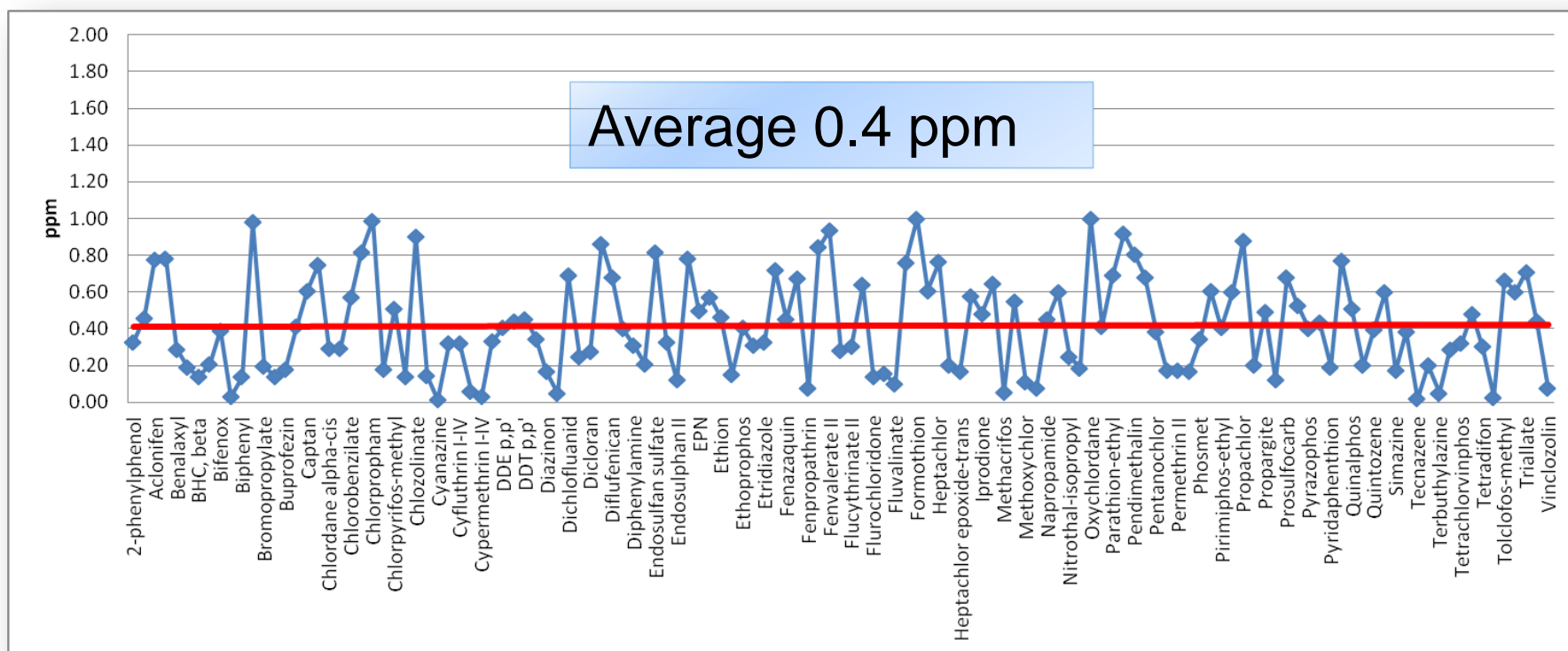
■ <0.5 ■ 0.5-1.0 ■ 1.0-2.0 ■ 2.0-4.0



Percentage of pesticides and corresponding IDL interval (on total of 132 target compounds)

Pesticides Analysis in Baby Food - Accurate Mass

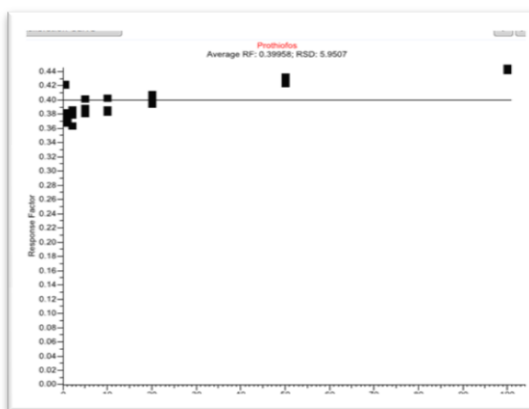
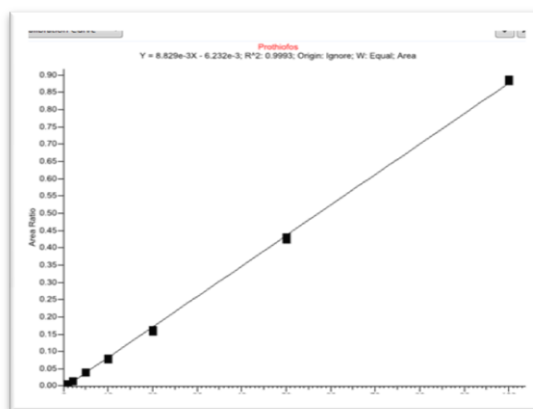
Accurate mass measurements (average of n = 10) for the pesticides indentified in the baby food sample at 5 (or 10) ng/g level



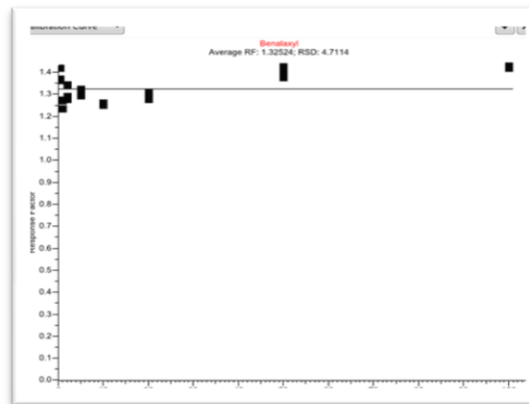
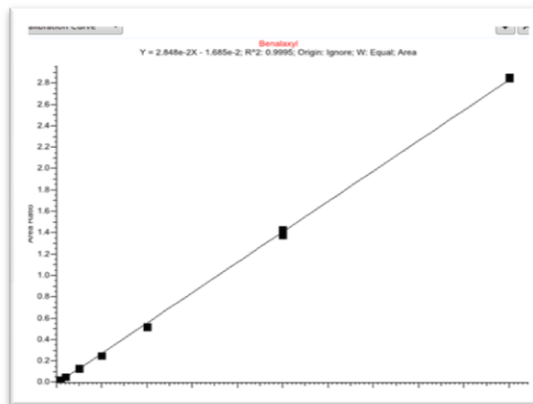
Pesticides Analysis in Baby Food - Linearity

- Linearity assesses for 3x repeat injections per calibration point for range of 0.5–100 ng/g (or 1-200 ng/g)
- In all cases the coefficient of determination (R^2) was >0.99 with an average value of $R^2 = 0.997$ and with residual values from the regression line of $<25\%$

Prothiofos



Benalaxyl



Drugs of Abuse in Biological Matrix

High Confidence, Non-Targeted Screening for Drugs of Abuse in Urine

Dominic Roberts,¹ Andrea Steuer,² Michael Poetzsch,² Thomas Kraemer² and Paul Silcock¹

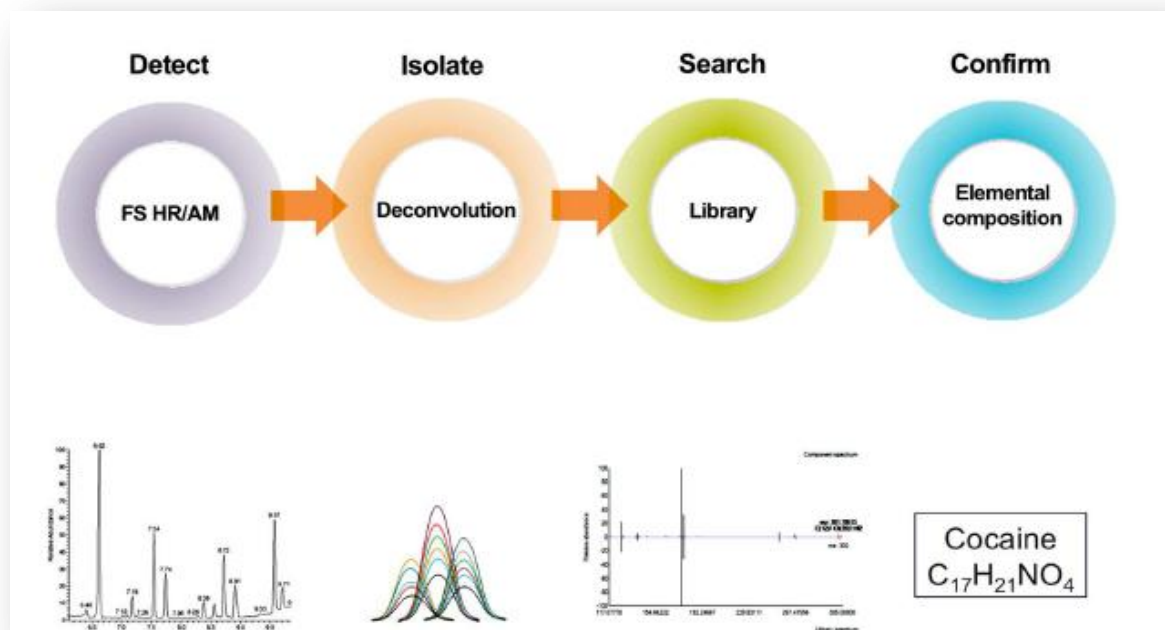
¹Thermo Fisher Scientific, Runcorn, UK

²Department of Forensic Pharmacology and Toxicology, Zurich Institute of Forensic Medicine, University of Zurich, Zurich, Switzerland

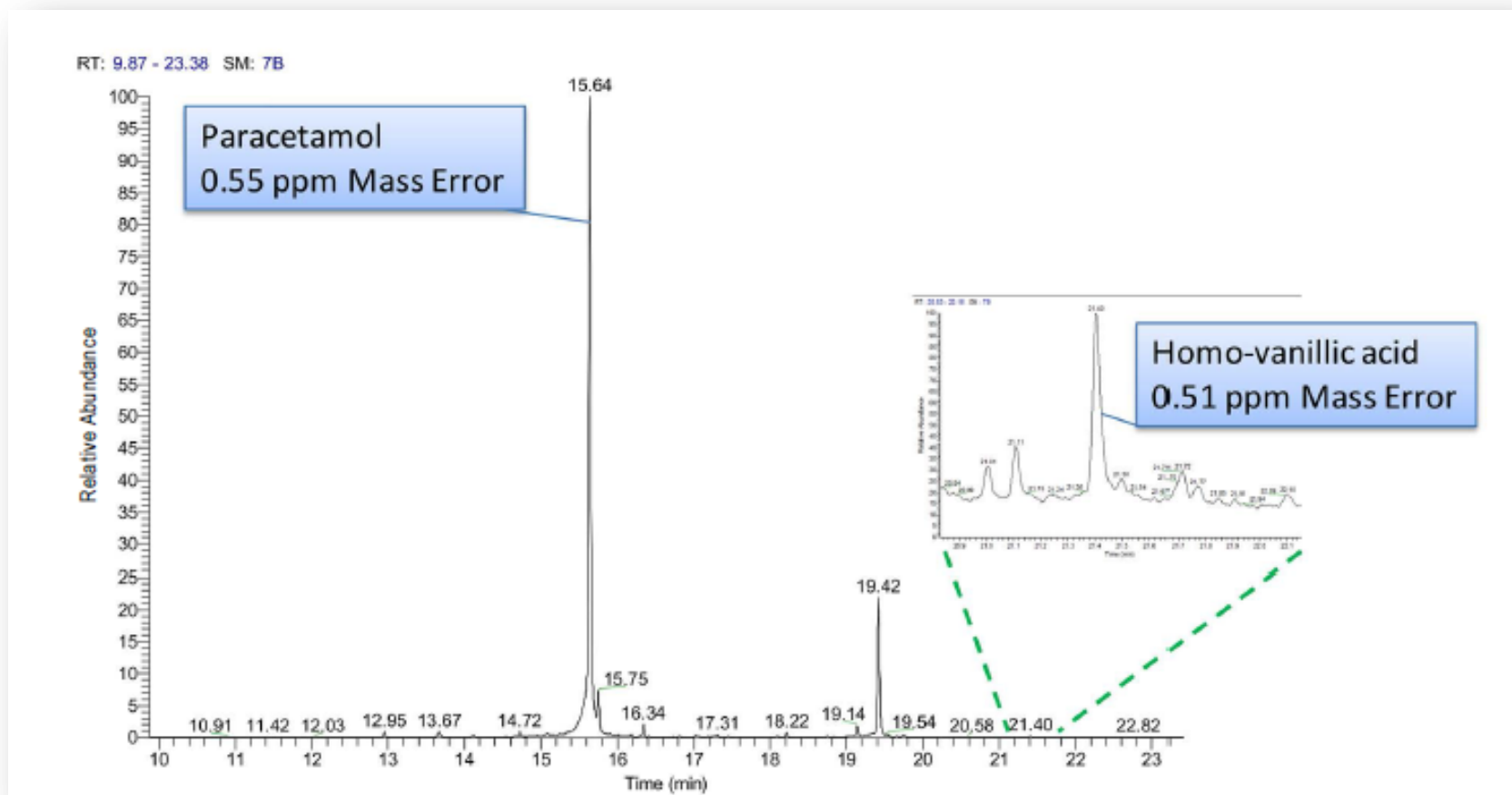
Application Note 10495



- Objective: Analyze the acetylated urine samples using a non target full scan experiment
- Screen the samples against a spectral library



Drugs of Abuse in Biological Matrix - Wide Dynamic Range



In screening for drugs in urine the compounds of interest can be present at both very high and ultra trace concentrations.

Untargeted Metabolomics Using Orbitrap-Based GC-MS

Stefan Weidt,² Bogusia Pesko,² Cristian Cojocariu,¹ Paul Silcock,¹ Richard J. Burchmore,² and Karl Burgess²

¹Thermo Fisher Scientific, Runcorn, UK

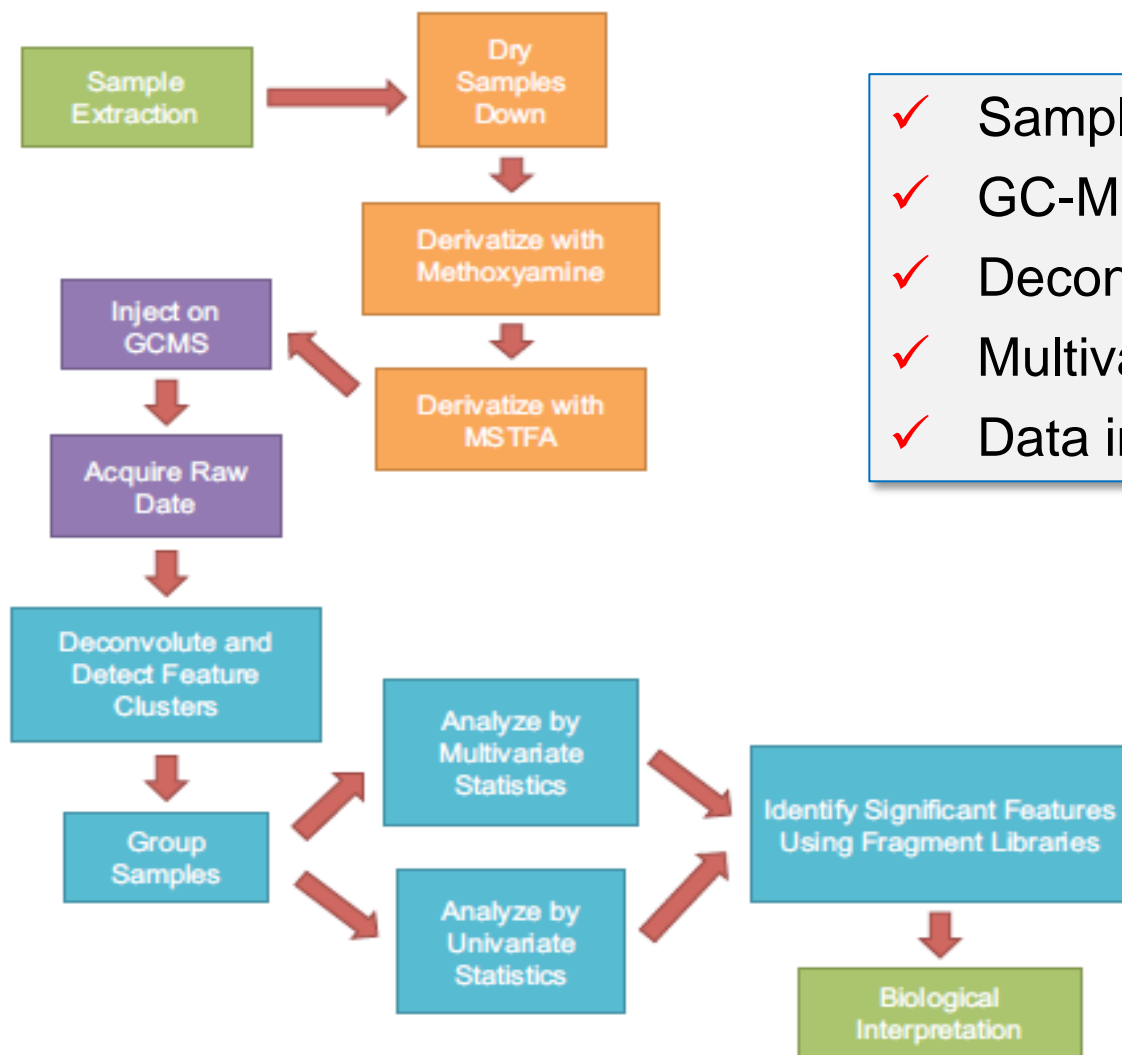
²Glasgow Polyomics, University of Glasgow, Glasgow, UK

Application Note 10457



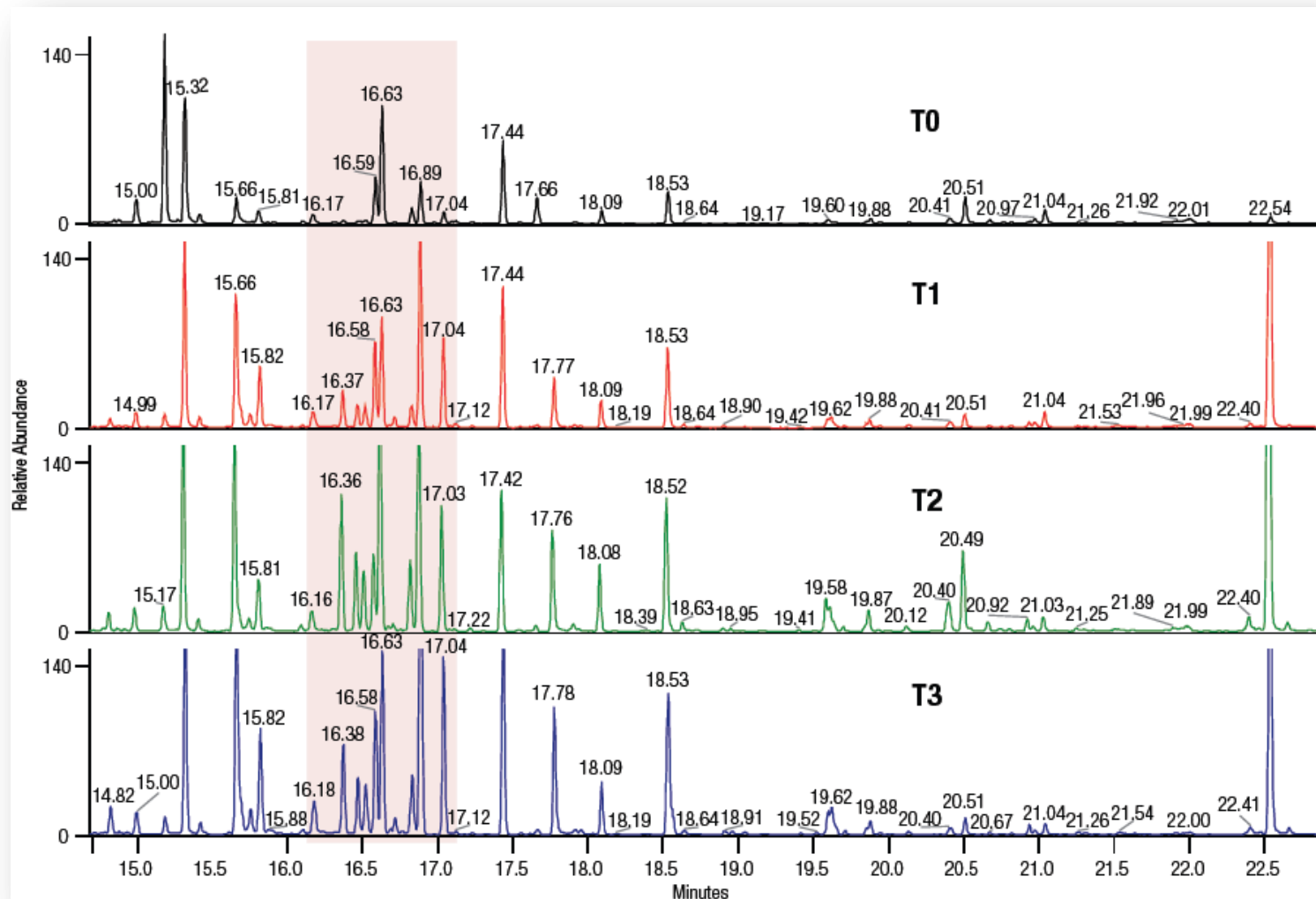
- Objective: Detect biomarkers for time of death in a rat model
- Rat thigh muscle tissue sections were sampled from eight rats post mortem at increasing times of decomposition

Untargeted Metabolomics - Workflow

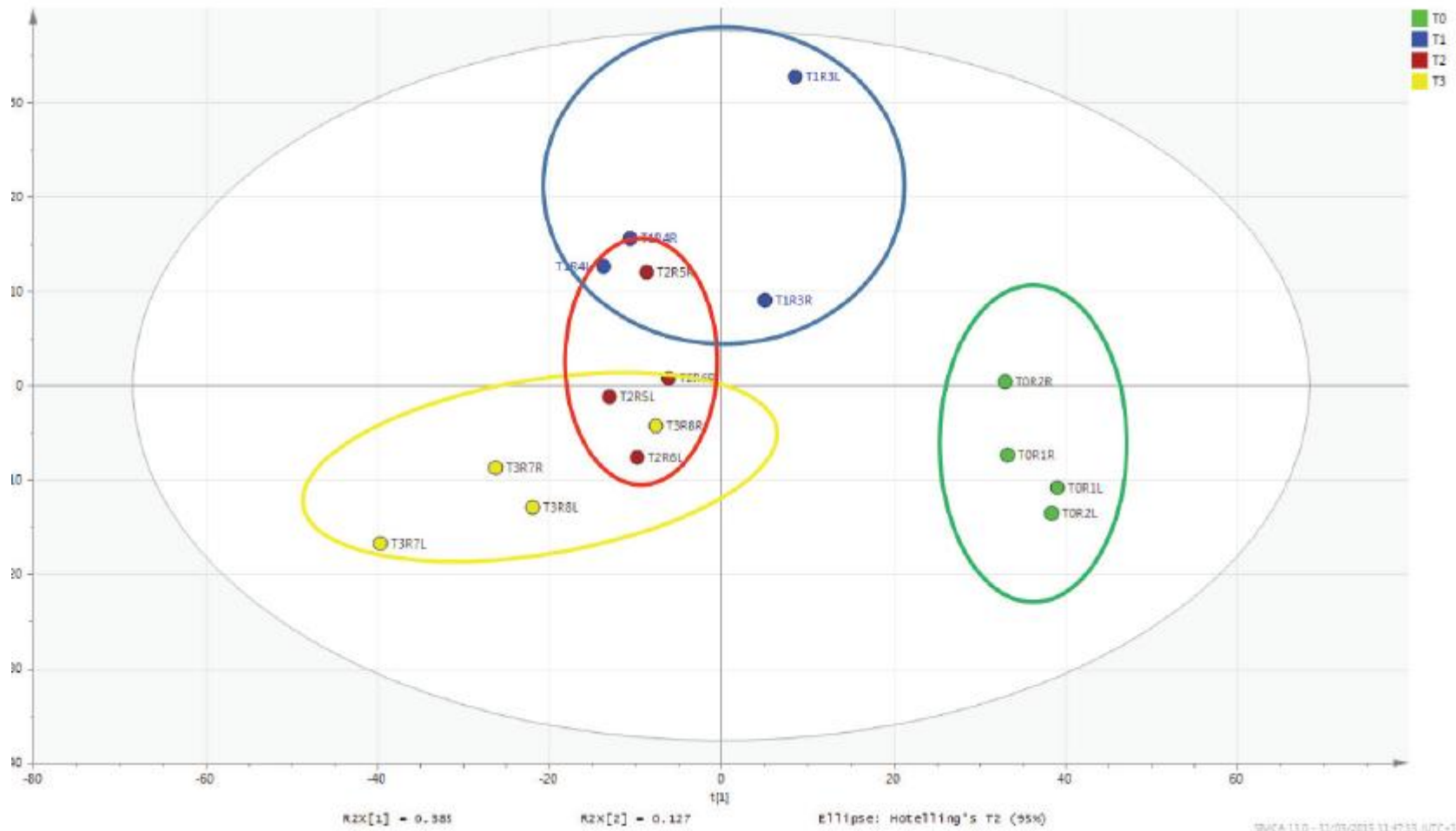


- ✓ Sample preparation
- ✓ GC-MS acquisition
- ✓ Deconvolution and ID
- ✓ Multivariate analysis
- ✓ Data interpretation

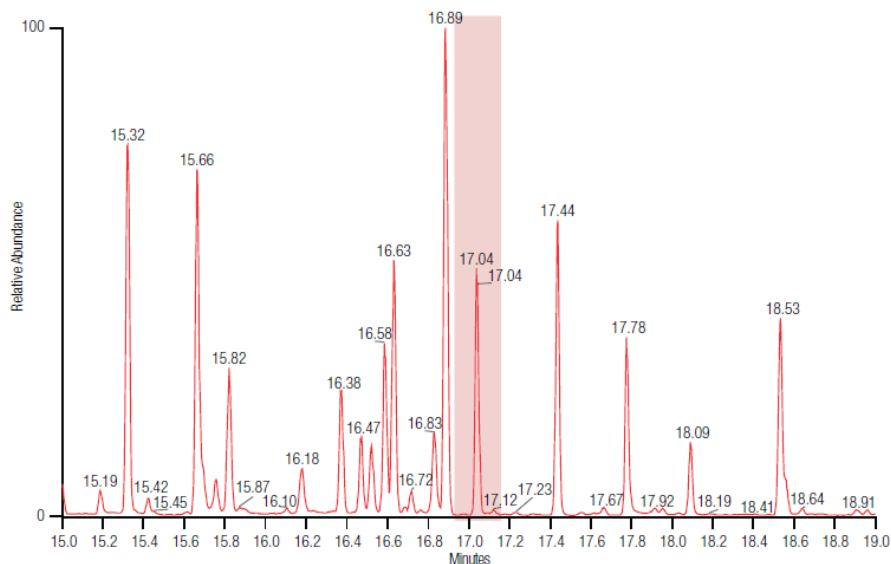
Untargeted Metabolomics - Discovery Phase



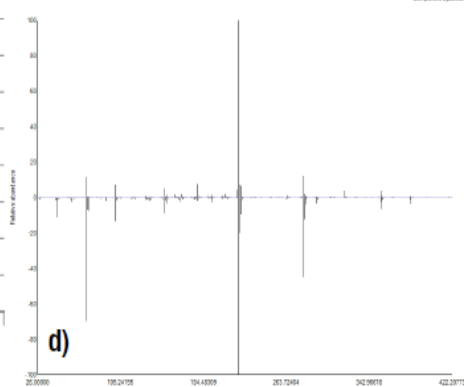
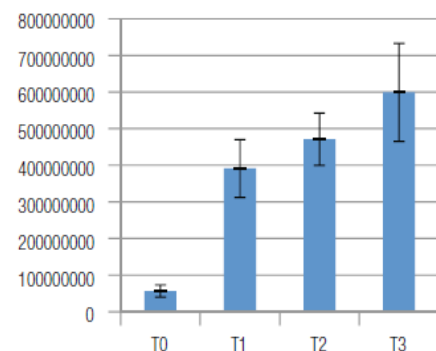
Untargeted Metabolomics - Data Interpretation



Untargeted Metabolomics - Identification Phase



Base Peak Mass	RT	Max Intensity	T0	T1	T2	T3	Ttest: T0	Ttest: T1	Ttest: T2	Ttest: T3
217.09554	17.04	746000000	1.0	6.9	8.3	10.6	1.000	0.003	0.001	0.004



Tyrosine – Trimethylsilyl Ester – Match: 818, R Match: 891, Prob. 82.8%

Putative Compound ID	RT (min)	NIST Forward Match	Fold Increase Compared to T0	Base Peak Fragment Elemental Composition	ppm Accuracy (Base Peak)	ppm Accuracy (Molecular Ion)
L-Threonine, 3TMS	10.71	795	2.8	$C_9H_{24}ONSi_2$	0.27	0.13
L-Aspartate, 3TMS	11.78	707	7.0	$C_9H_{22}NO_2Si_2$	0.18	0.34
L-Methionine, 2TMS	12.40	749	15.0	$C_7H_{18}NSSi$	0.24	0.04
L-Glutamine-3TMS	15.32	815	2.0	$C_7H_{14}NOSi$	0.53	0.21
Putrescine, 4TMS	16.18	870	2.0	$C_7H_{20}NSi_2$	0.05	N/A
Lysine, 4TMS	16.88	732	5.1	$C_8H_{18}NSi$	0.19	0.05

Targeted and Non-targeted Screening in Tap Water

Discovery of Emerging Disinfection By-Products in Water Using Gas Chromatography Coupled with Orbitrap-based Mass Spectrometry

Cristian Cojocariu,¹ Cristina Postigo,² Susan D. Richardson,³ Damia Barcelo,^{2,4} and Paul Silcock¹

¹Thermo Fisher Scientific, Runcorn, UK

²Institute of Environmental Assessment and Water Research, (IDAEA-CSIC) Water and Soil Quality Research Group, Department of Environmental Chemistry, 08034 Barcelona, Spain

³University of South Carolina, Department of Chemistry and Biochemistry, Columbia, SC 29208, U.S.A.

⁴Catalan Institute for Water Research (ICRA), Parc Científic i Tecnològic de la Universitat de Girona, 17003 Girona, Spain

Application Note 10490



- Detection and accurate mass identification of emerging iodinated DBPs in chlorinated and chloraminated water samples
- Data were acquired in Full Scan (EI) and processed in Trace Finder Software for spectral deconvolution and compound identification using NIST Library and High-Resolution Filtering (HRF) of the candidates
- >2500 peaks were found in the chloraminated water extract
- An exact mass filter was used to isolate only the compounds containing iodine (m/z 126.90392)
- For emerging contaminants not having a match in the MS Libraries, the EI spectra were interrogated with a pre-determined set of elements, and PCI was used to confirm the accurate mass of the molecular ion
- The consistent sub-ppm mass accuracy measurements delivered unambiguous determination of the elemental composition and subsequent structural elucidation of unknown chemicals

Targeted and Non-targeted Screening in Tap Water

Iodo-DBPs identified and confirmed in disinfected NL NOM Waters

RT (min)	Identity	Elemental Composition	Chemical Structure	Theoretical m/z (EI)	Measured m/z (EI)	Δ (ppm)	Theoretical m/z $[M+H]^+$	Measured m/z $[M+H]^+$	Δ (ppm)
3.71	Iodomethane	CH ₃ I	<chem>C—I</chem>	141.92739	141.92745	0.4	142.93522	142.93522	0.0
5.36	Chloriodomethane	CH ₂ ClI	<chem>Cl—C—I</chem>	175.88842	175.88839	0.2	176.89625	176.89620	0.3
5.76	Iodoacetaldehyde	C ₂ H ₃ IO	<chem>O=C—C—I</chem>	169.92231	169.92234	0.2	170.93013	170.93014	0.06
7.36	Diiodomethane	CH ₂ I ₂	<chem>I—C—I</chem>	267.82404	267.82424	0.8	268.83186	268.83192	0.2
8.03	Ethyl iodoacetate	C ₄ H ₇ IO ₂	<chem>CCOC(=O)C—I</chem>	213.94852	213.94840	0.6	214.95635	214.95627	0.4
8.14	ethyl β -iodopropionate	C ₂ H ₉ IO ₂	<chem>CCOC(=O)CC—I</chem>	n.d.	n.d.	—	228.97200	228.97198	0.07
8.77	Chlorodiiodomethane	CHClI ₂	<chem>Cl—C—I</chem>	301.78507	301.78509	0.1	301.78507	301.78511	0.1
9.85	Bromodiiodomethane	CHBrI ₂	<chem>Br—C—I</chem>	345.73455	345.73459	0.1	345.73455	345.73446	0.3

Targeted and Non-targeted Screening in Tap Water

N-Nitrosodimethylamine in tap water

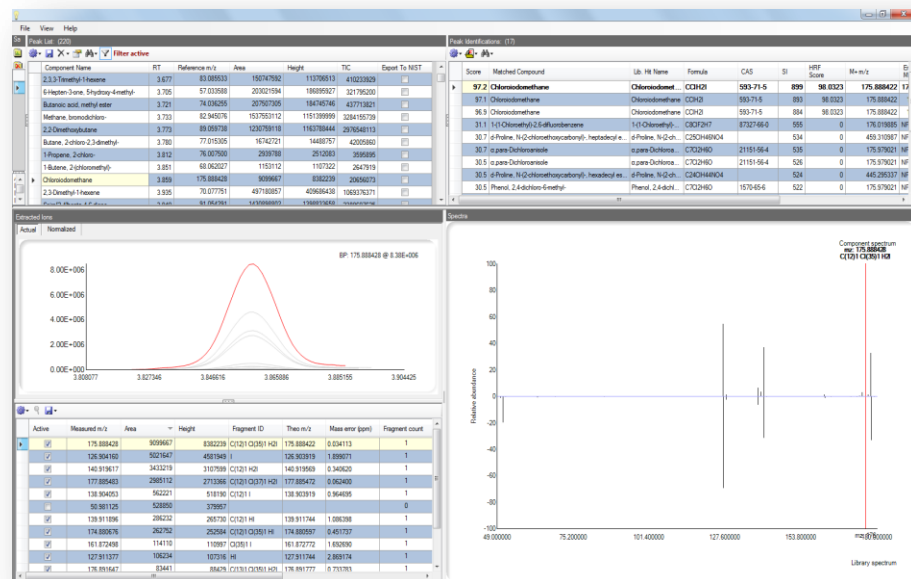
- Full Scan acquisition and quantitation of nitrosamine



Sample	% recovery d6-NDMA	Calculated NDMA concentration (ng/L)	Mass error [ppm]
M1A	107	1.1	0.7
M1B	105	0.98	0.01
M5A	111	4.7	0.01
M5B	104	4.3	0.01
M10a	88	8.4	0.2
M10b	99	8.1	0.1

- Identification of additional classes of contaminants by deconvolution, NIST Library matching and HRF score

- **Halogenated organics**
 - e.g. chloriodomethane, tetrachloroethylene
- **Pharmaceuticals**
 - e.g. Clindamycin, Felbamate
- **Monoterpenes and phthalates**



Confident Identification of Leachable Impurities from Pharmaceutical Container Closure Materials using Orbitrap-Mass-Spectrometer-Based GC-MS

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¹Thermo Fisher Scientific, Runcorn, UK

²Smithers Rapra, Shawbury, UK

Application Note 10488



Impurity Profiling of Pharmaceutical Starting Materials Using Gas Chromatography Coupled with High-Resolution Accurate Mass Spectrometry

Cristian Cojocariu and Paul Silcock
Thermo Fisher Scientific, Runcorn, UK

Application Note 10494



Leachable Impurities in Four O-ring Samples

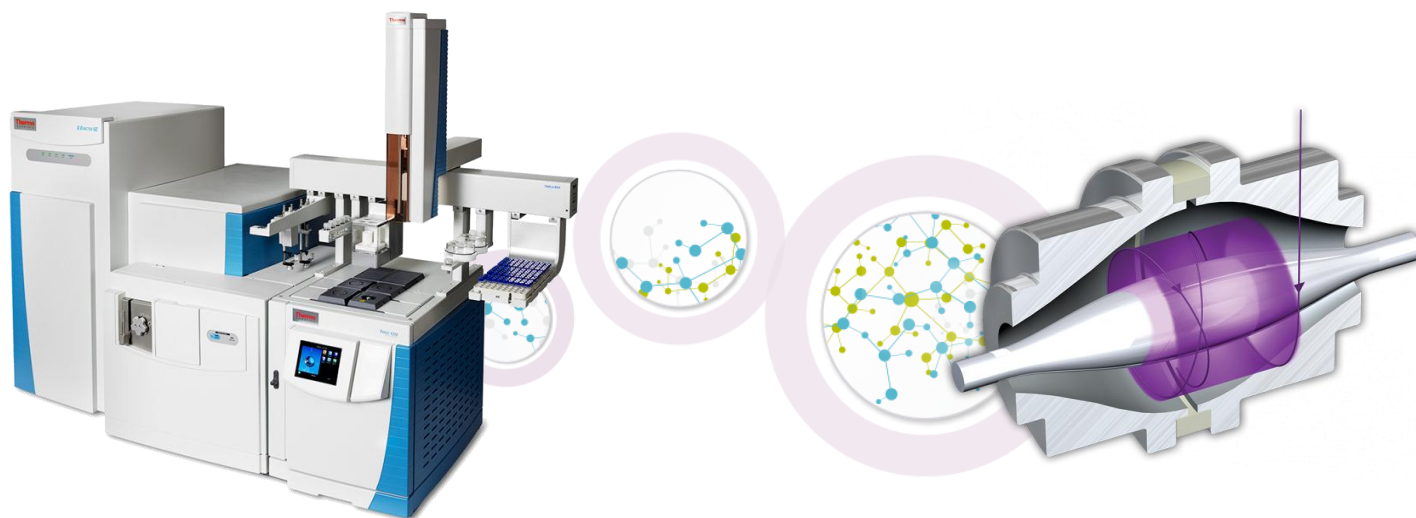
Sample	RT (min)	Base Peak (m/z)	Search Index	Compound Name	Formula	Base Peak Mass Accuracy (ppm)	Molecular ion Mass Accuracy (ppm)
Black O-Ring	15.17	178.07754	No match	$C_{20}H_{20}O_4$	$C_{20}H_{20}O_4$	0.88	0.66
	15.29	178.07754	No match	$C_{20}H_{20}O_4$	$C_{20}H_{20}O_4$	0.11	0.22
	18.08	171.13806	673	Tetraethylene glycol bis (2-ethylhexanoate)	$C_{24}H_{46}O_7$	0.64	-
	23.47	219.17435	777	Irganox 1076	$C_{35}H_{62}O_3$	0.03	1.02
	14.94	280.10939	536	ethyl 1-hydroxy-2,3-diphenylcycloprop-2-ene-1-carboxylate	$C_{18}H_{16}O_3$	0.39	0.39
	16.50	126.09145	652	9-Octadecenamide	$C_{18}H_{35}NO$	0.87	0.63
Brown O-Ring	17.48	277.07790	806	Triphenylphosphine oxide	$C_{18}H_{15}OP$	0.85	0.06
	15.42	183.03595	831	Triphenylphosphine	$C_{18}H_{15}P$	0.68	0.91
	11.10	219.1743	796	4-tert-butyl-2,6-diisopropylphenol	$C_{16}H_{26}O$	0.18	0.21
	11.35	149.02341	831	Diethyl phthalate	$C_{12}H_{14}O_4$	0.60	0.9
	13.57	185.04198	813	Diphenyl sulfide	$C_{12}H_{10}S$	0.21	0.05
White O-Ring	11.93	263.20074	711	1,4-Dihydrophenacetic acid, 3,5-di- <i>t</i> -butyl, ethyl ester	$C_{18}H_{30}O_2$	0.72	0.43
	7.65	101.02344	781	Butanedioic acid, diethyl ester	$C_8H_{14}O_4$	0.54	-
Red O-Ring	10.44	163.07549	775	Ethanone, 1-[4-(1-hydroxy-1-methylethyl)phenyl]	$C_{11}H_{14}O_2$	0.85	0.38
	15.09	87.044	740	Methyl stearate	$C_{10}H_{20}O_2$	1.26	0.06
	16.00	155.07025	690	di(butoxyethyl)adipate	$C_{18}H_{34}O_6$	0.13	1.02

Sub 1 ppm mass accuracy
+
Excellent sensitivity
=
Confident identification

Resolving power
+
Dynamic range
=
Eliminate interferences
and increase confidence in
complex matrix

Conclusion

- Thermo Scientific Q Exactive and Exactive GC systems are **easy-to-use**, dedicated HRAM GC-MS platforms that provides **highly sensitive, routine grade performance** in both targeted and untargeted screening experiments.
- The quantitative performances are matching the Triple Quad **MS/MS sensitivity in Full Scan** acquisition, with **consistent NIST searchable spectra** over a wide concentration range.
- Thanks to the **superior resolving power, accurate mass** measurements and extended **linear dynamic range**, the Orbitrap GC-MS systems provide a **greater confidence** in the discovery, identification and quantification of compounds for the **ultimate sample analysis workflow**.





Do you have additional questions or do you want to talk to an expert from Thermo Fisher Scientific?

Please send an E-Mail to analyze.eu@thermofisher.com and we will get back to you.

Find out more about our Q Exactive GC Orbitrap GC-MS and GC-MS/MS systems on:

<http://info1.thermoscientific.com/OrbitrapGCMS>