



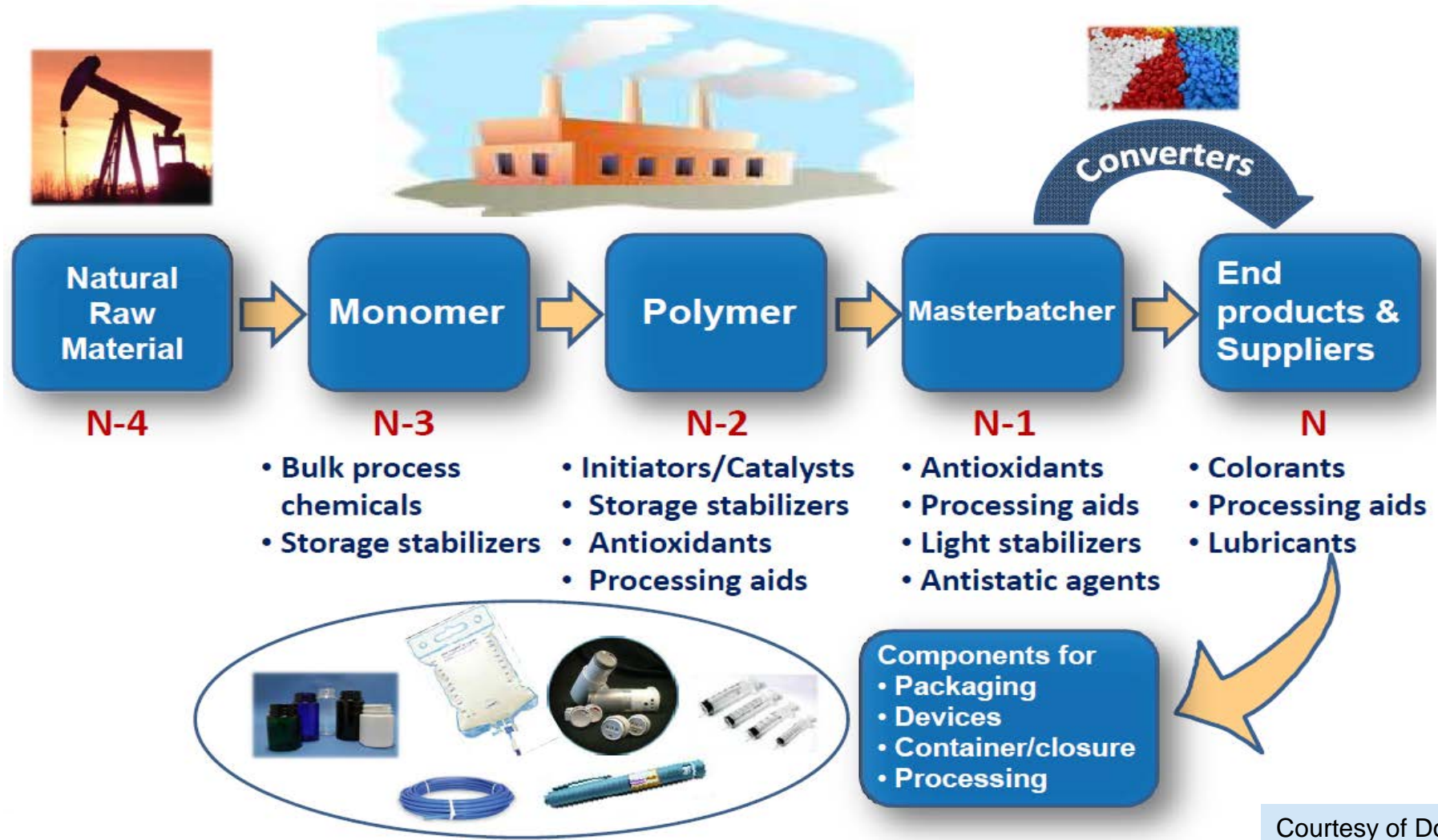
Solution for Extractables & Leachables Analysis

- Instruments, Software, Database/Spectral Library

Kate Comstock
Senior Marketing specialist
Small molecule and E&L analysis
Pharma/Biopharma Marketing, CMD

- **Introduction**
 - Definitions
 - Industries need Extractable & Leachable (E&L) analysis
 - Regulatory and industry groups
- **Thermo Fisher Scientific solution for extractable & leachable analysis**
 - Multi instrumentations and technologies
 - Data Analysis software for ID, structure elucidation, and quantitation
 - Database and spectral library

Polymer Supply Chain for Pharmaceutically Relevant Materials

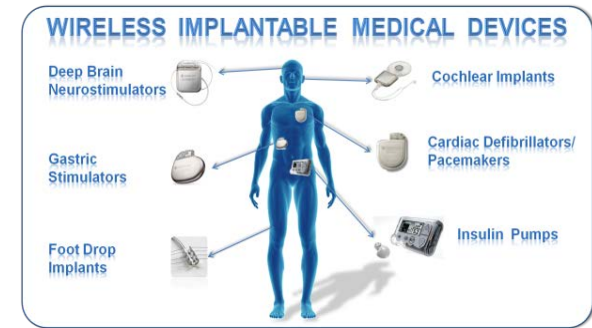


Courtesy of Doug Kiehl, Eli Lilly

The Broad Market of Extractable & Leachable Analysis



Single-use systems for bioproduction and storage



Medicine container/packaging, implant and diagnostic devices



Food package



Printing ink and adhesives



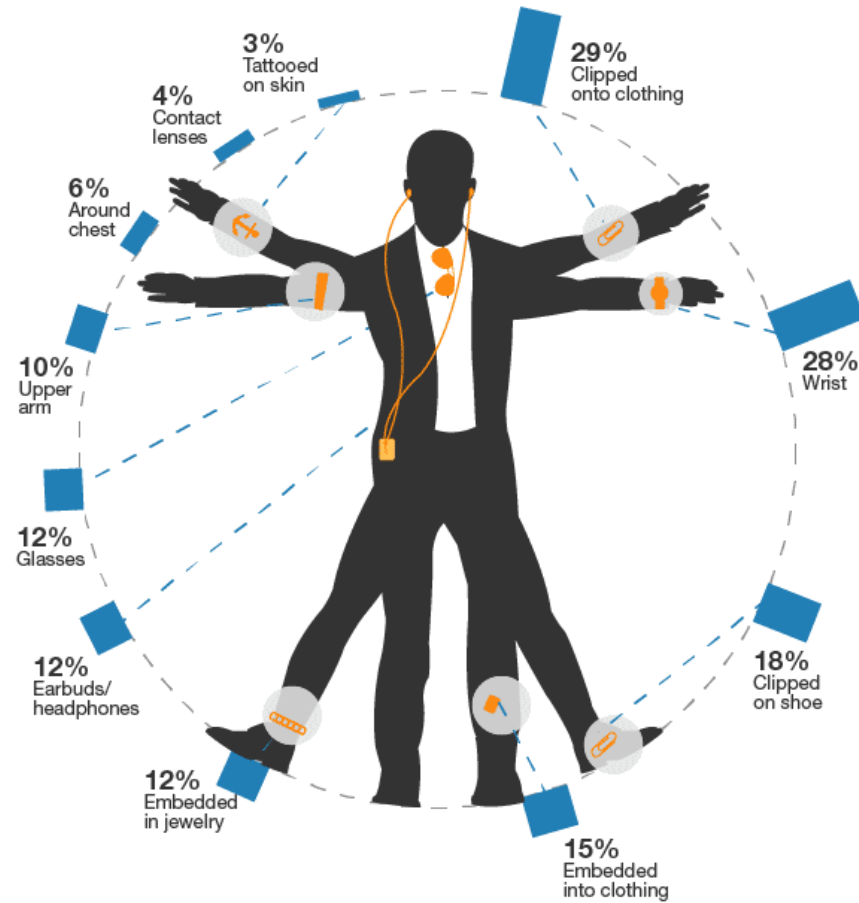
Wearable Consumer Electronic Products

Food Contact Material Migration Test is Mandatory!



Wearable Consumer Electronic Products

"How would you be interested in wearing/using a sensor device, assuming it was from a brand you trust, offering a service that interests you?"



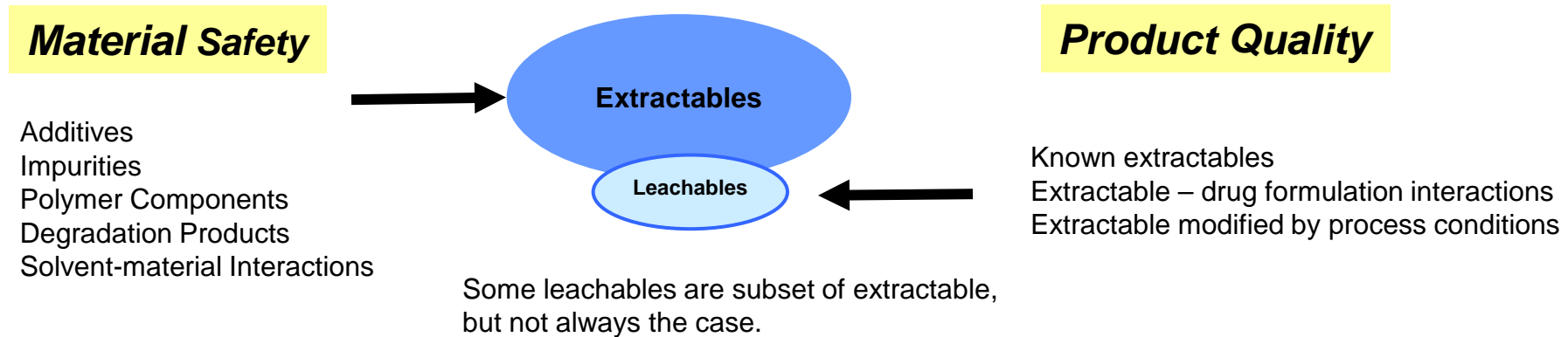
Base: 4,657 US online adults (18+)
(multiple responses accepted)

Source: North American Technographics® Consumer Technology Survey, 2013
97141

Source: Forrester Research, Inc.

The overall market for wearable technology is expected to reach USD 31.27 Billion by 2020, at a CAGR of 17.8% between 2015 and 2020.

- **Extractable (E)**
 - Compounds that migrate from the surface under more aggressive conditions of exposure (solvent, time, and temperature). Controlled extraction study
- **Leachable (L)**
 - Compounds that migrate from the contact surface to drug formulation under normal conditions of exposure. Formulated drug or simulants



Safety/risk assessment ➡ Submission to regulatory agency ➡ Market

■ Safety

- Extractables and Leachables are **Chemical Impurities**, they could contaminate medicine, food, and drink, affect product quality, and cause adverse effects for consumers.

■ Regulations

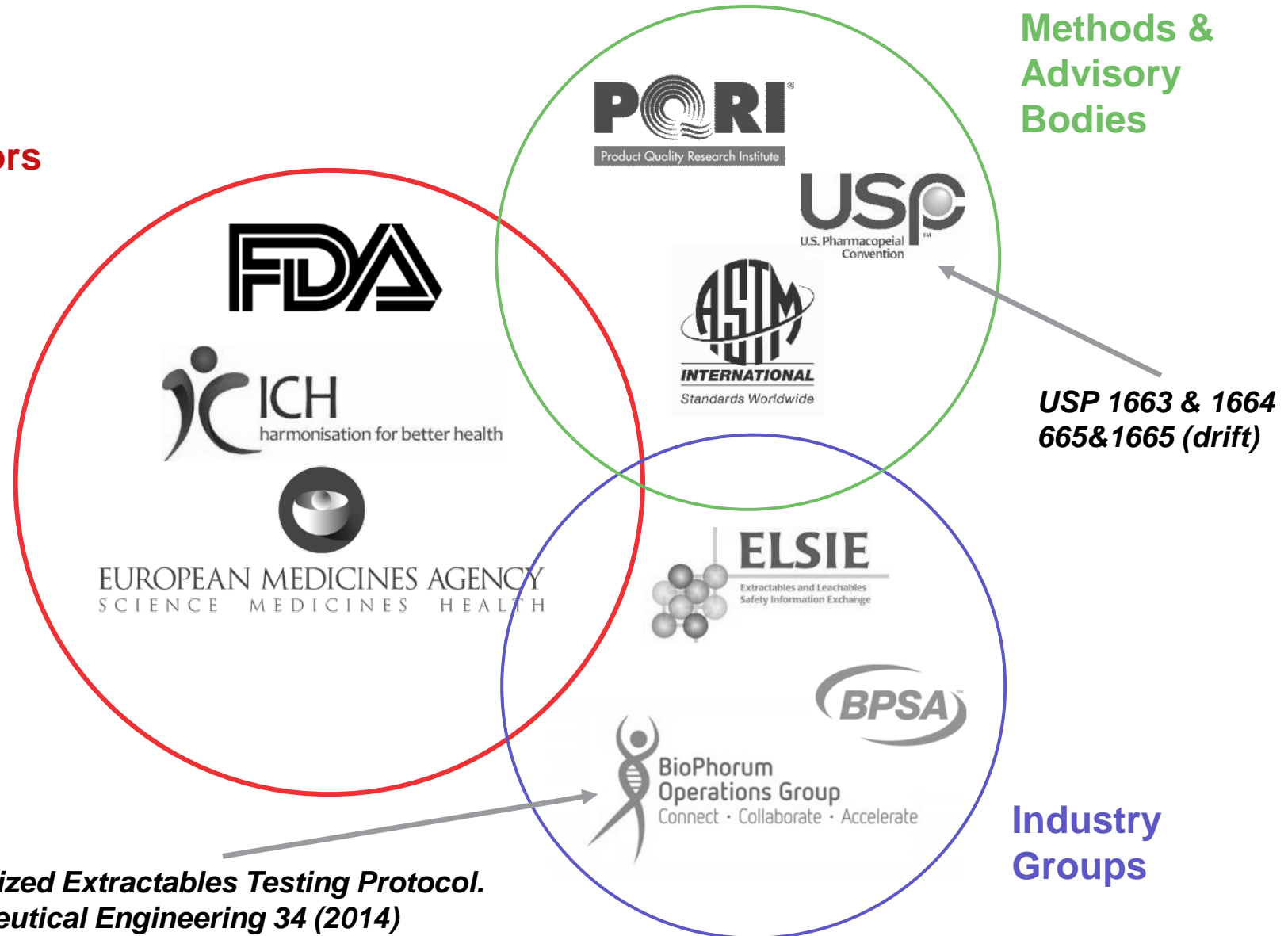
- E&L analyses are highly regulated and required for market approval of new products.
- More regulations have been made along the way and will continue into the future.

■ E&L analyses are challenging and complex

- It requires multiple instruments, expertise, data processing software, and database.
- It needs both identification and quantitation. Unknown structure elucidation is challenging.
- It must start at early stage to be ready for product launch.

E&L Regulatory and Method landscape

National Regulators



Methods & Advisory Bodies

**USP 1663 & 1664
665&1665 (drift)**

Industry Groups

**Standardized Extractables Testing Protocol.
Pharmaceutical Engineering 34 (2014)**

- **FDA guidance**
 - Container Closure Systems for Packaging Human Drugs and Biologics (May 1999)
 - 21 CFR 211.94
- **EMA guideline**
 - Guideline on plastic media packaging, EMEA/205/04
- **ICH guidelines**
 - Test procedures and acceptance criteria for new drug substances and drug products (Q6A,B)
 - Pharmaceutical development (ICH Q8)
- **PQRI leachables and extractables working group (recommendations to the FDA)**
Safety thresholds and best practices for extractables & leachables in orally inhaled and nasal drugs
- **USP Chapters**
 - Chapter 87,88 (materials direct or indirect in contact with patients biological reactivity test in vitro, in vivo)
 - Chapter 661 (Containers – Plastics)
 - Chapter 1663 Extractables Associated with Pharmaceutical Packaging/Delivery Systems
 - Chapter 1664 Drug Product Leachables Associated with Pharmaceutical Packaging Delivery Systems
 - Chapter 1665_draft Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products.
- **ISO 10993 parts (medical devices)**
- **Japan, China, and other countries healthy authorities...**

<http://bpsalliance.org/>

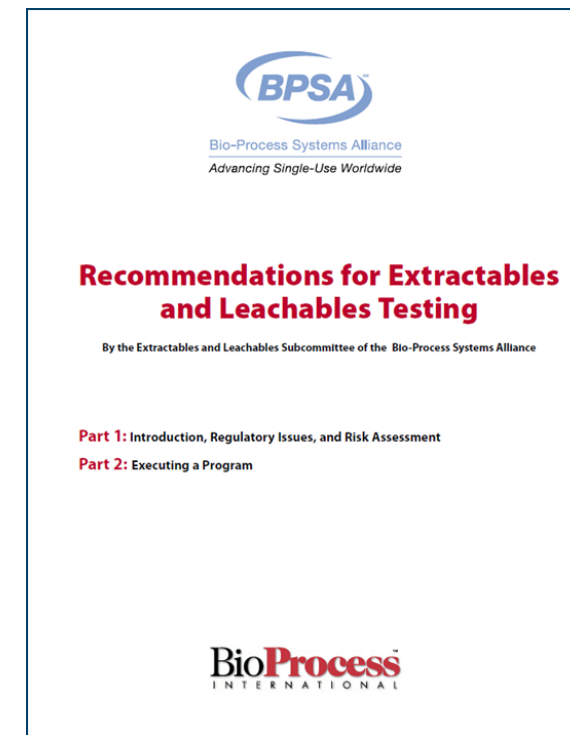


BPSA members are industry-led corporate member of single use manufactures. BPSA is encouraging and accelerating the adoption technologies used in the production of biopharmaceuticals and vaccines.

Many Technical Guides on their website

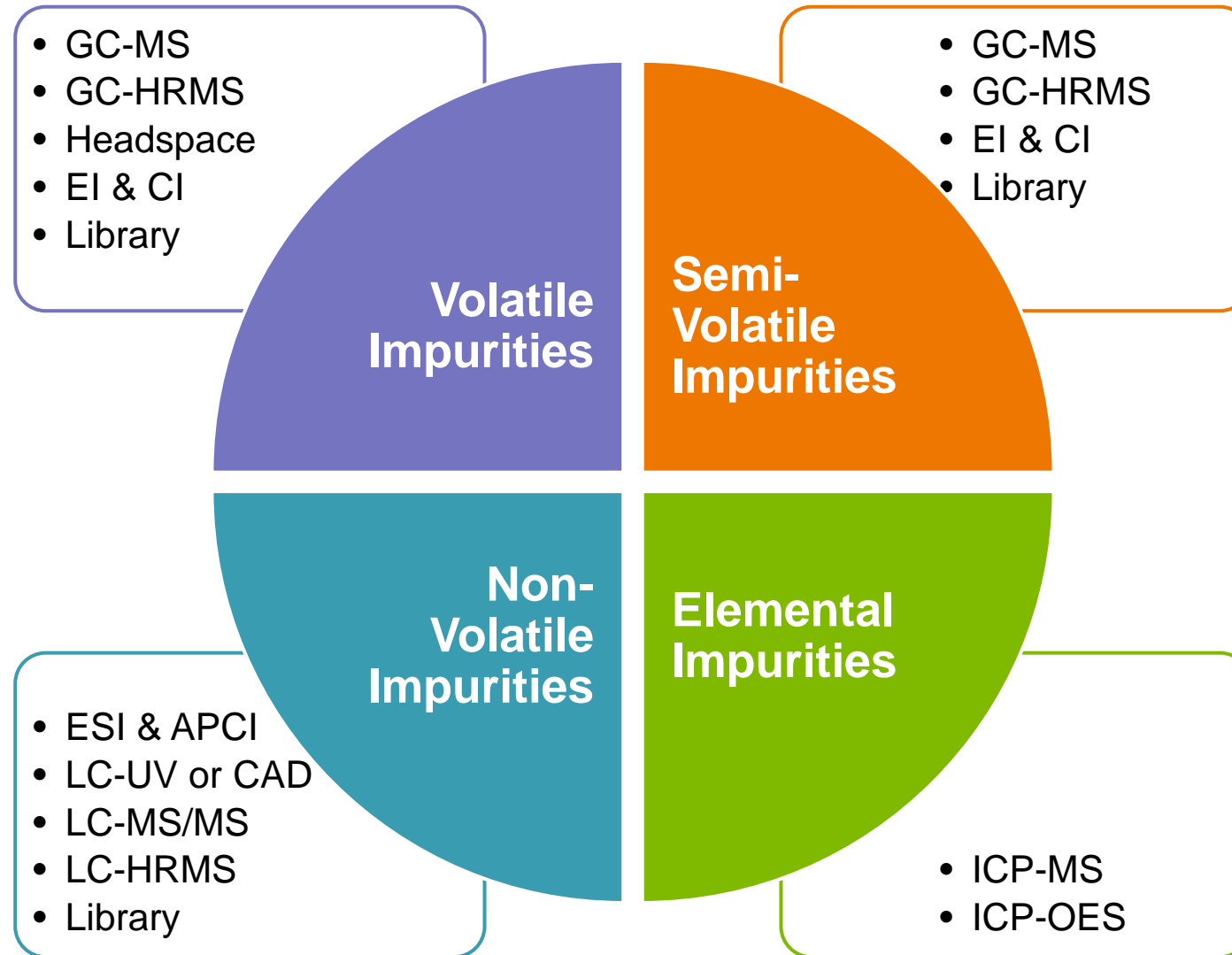
<http://bpsalliance.org/>

BPSA Members



Extractable & Leachable Analysis

Analysis of Extractables & Leachables



Thermo Scientific Instruments and Software for Impurity ID and E&L Analysis



ASE



FTIR



Q Exactive GC-MS/MS



GCMS -Single Quad



GCMS-Triple Quad



IC



ICPMS



Vanquish UHPLC



Charged Aerosol Detector



Triple Quad



Benchtop HRMS
Q Exactive



Hybrid HRMS



Orbitrap Fusion Tribrid MS



U3000 UHPLC



Software & Database



Thermo Scientific™ ISQ™ Single Quadrupole GC-MS/MS



Thermo Scientific™ TSQ™ 8000 Evo Triple Quadrupole GC-MS/MS



Thermo Scientific™ Q Exactive™ GC Orbitrap GC-MS/MS and Thermo Scientific™ TRACE™ 1310 GC

Solid Phase Microextraction (SPME)

Thermo Scientific™ Q Exactive Plus MS



Resolving Power: up to 280K @ m/z 200
Scan Range: 50-6,000

Thermo Scientific™ Q Exactive™ MS



Resolving Power: 140K @ m/z 200
Scan Range: 50-6,000

Thermo Scientific™ Q Exactive™ Focus



Resolving Power: 70K @ m/z 200
Scan Range: m/z50-2,000

Thermo Scientific™
iCAP™ 7000 Plus Series ICP-OES



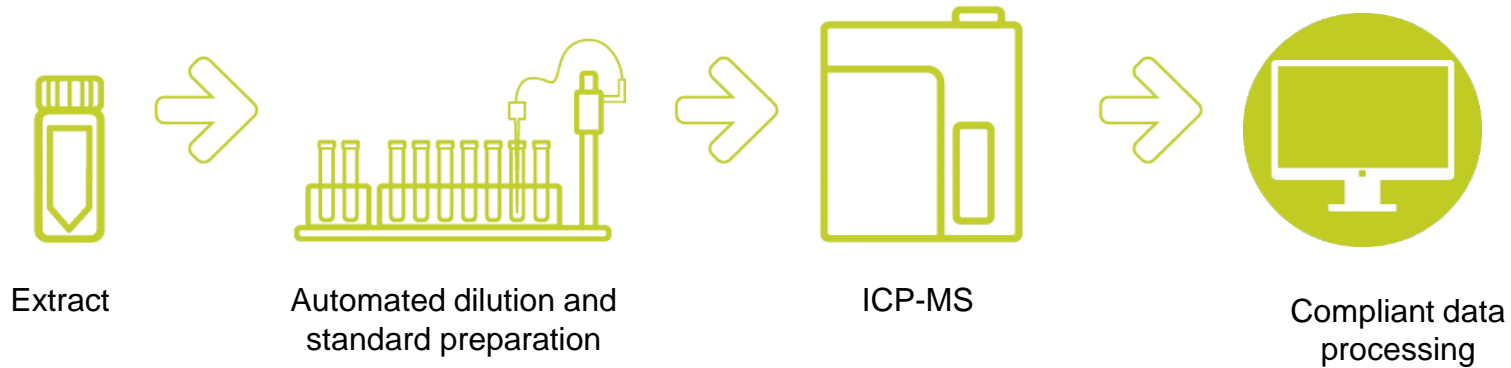
Thermo Scientific™ iCAP Q™ ICP-MS



Thermo Scientific™ iCAP™ RQ ICP-MS Series



Thermo Scientific iCAP RQ ICP-MS and Thermo Scientific Qtegra Software



Thermo Scientific™ iCAP™ RQ ICP-MS Series

Fully compliant Thermo Scientific™ Qtegra™ ISDS software

Full USP 233 & ICH Q3D method capabilities

The current compliance deadline for USP 232 and 233 is January 1, 2018

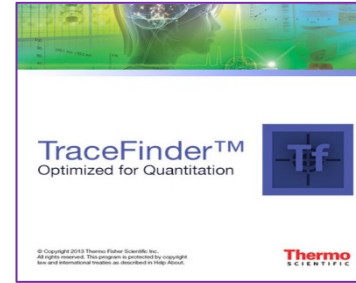
USP <232>/<233>: Be Prepared for the Changes to Come



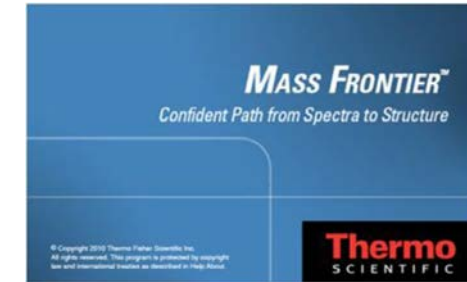
Data Analysis Software, Database and Spectral Library for E&L Analysis



Thermo Scientific™
Compound Discoverer™ 2.1



Thermo Scientific™ TraceFinder™
targeted screening and Quan



Thermo Scientific™ Mass Frontier™
spectral interpretation software



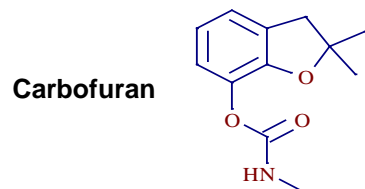
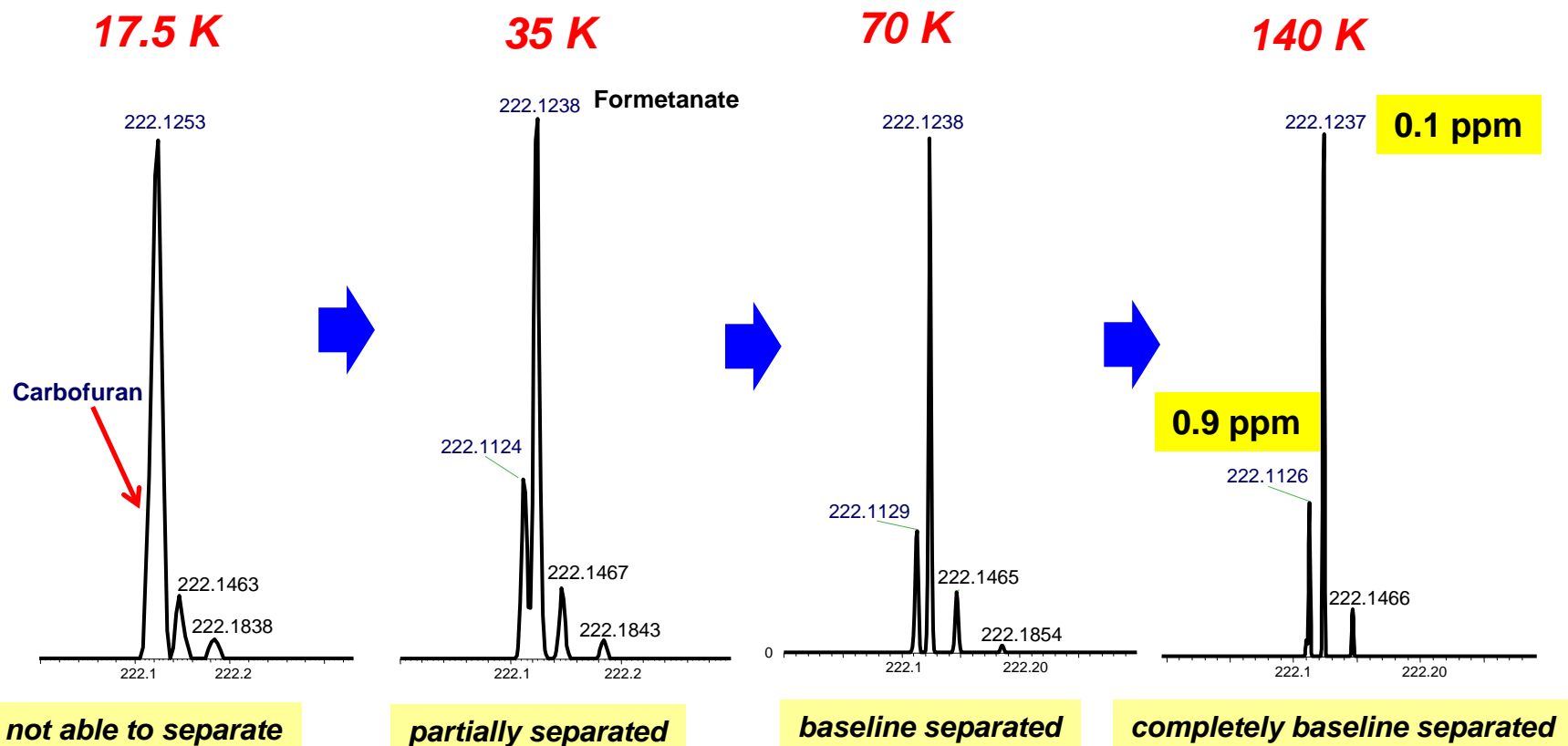
Thermo Scientific™ mzVault 2.0
Library Search and Manager



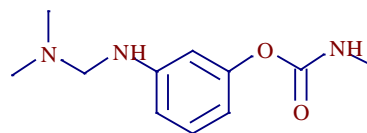
E&L Compound Database

High Resolution Mass Spectrometer for E&L Analysis

The Power of High Resolution



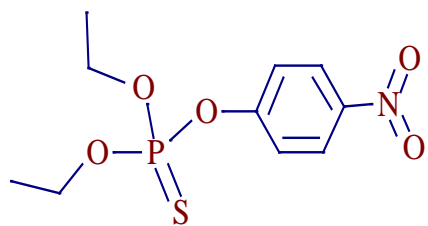
$\Delta M = 0.0109$ Da



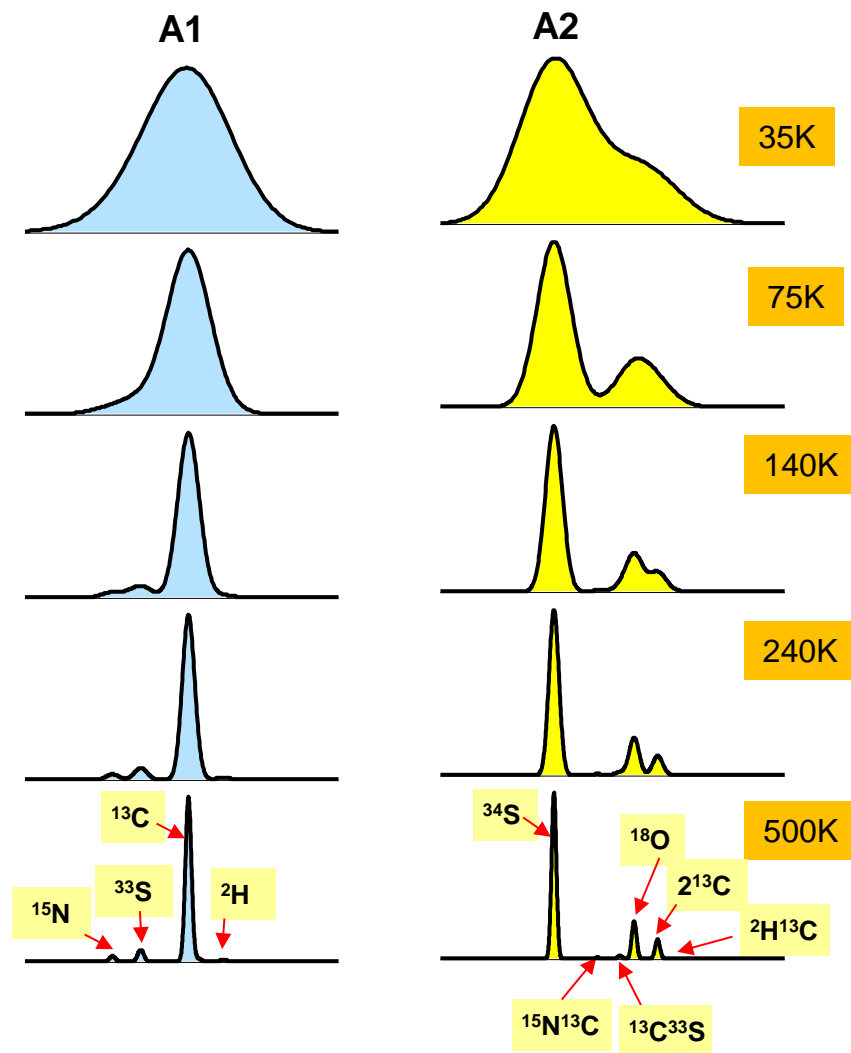
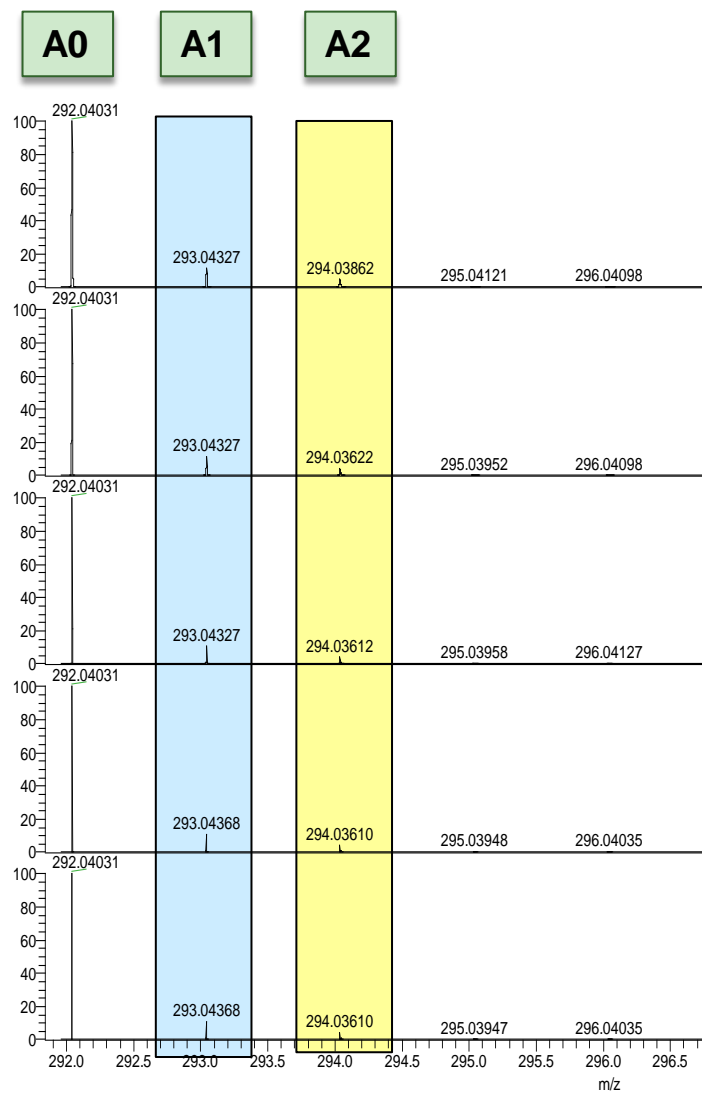
Formetanate

Name	Molecular Formula	[M+H] ⁺
Carbofuran	C ₁₂ H ₁₅ NO ₃	222.1125
Formetanate	C ₁₁ H ₁₅ N ₃ O ₂	222.1237

Very High Resolution Shows Isotope Fine Structure



Parathion
 $C_{10}H_{15}O_5NPS$
 $[M+H]^+ = 292.04031$



- **Mass Accuracy**
- **Isotopic Pattern Fidelity**
- **MSⁿ Capabilities**

Instrument of Choice: Thermo Scientific™ Orbitrap™ MS

Orbitrap MS High Resolution Accurate Mass (HRAM) data enable confident

- Component identification
- Elemental composition determination
- Structure characterization
- HR Quantitation

Thermo Scientific Q Exactive MS - First Benchtop Orbitrap Mass Spectrometer



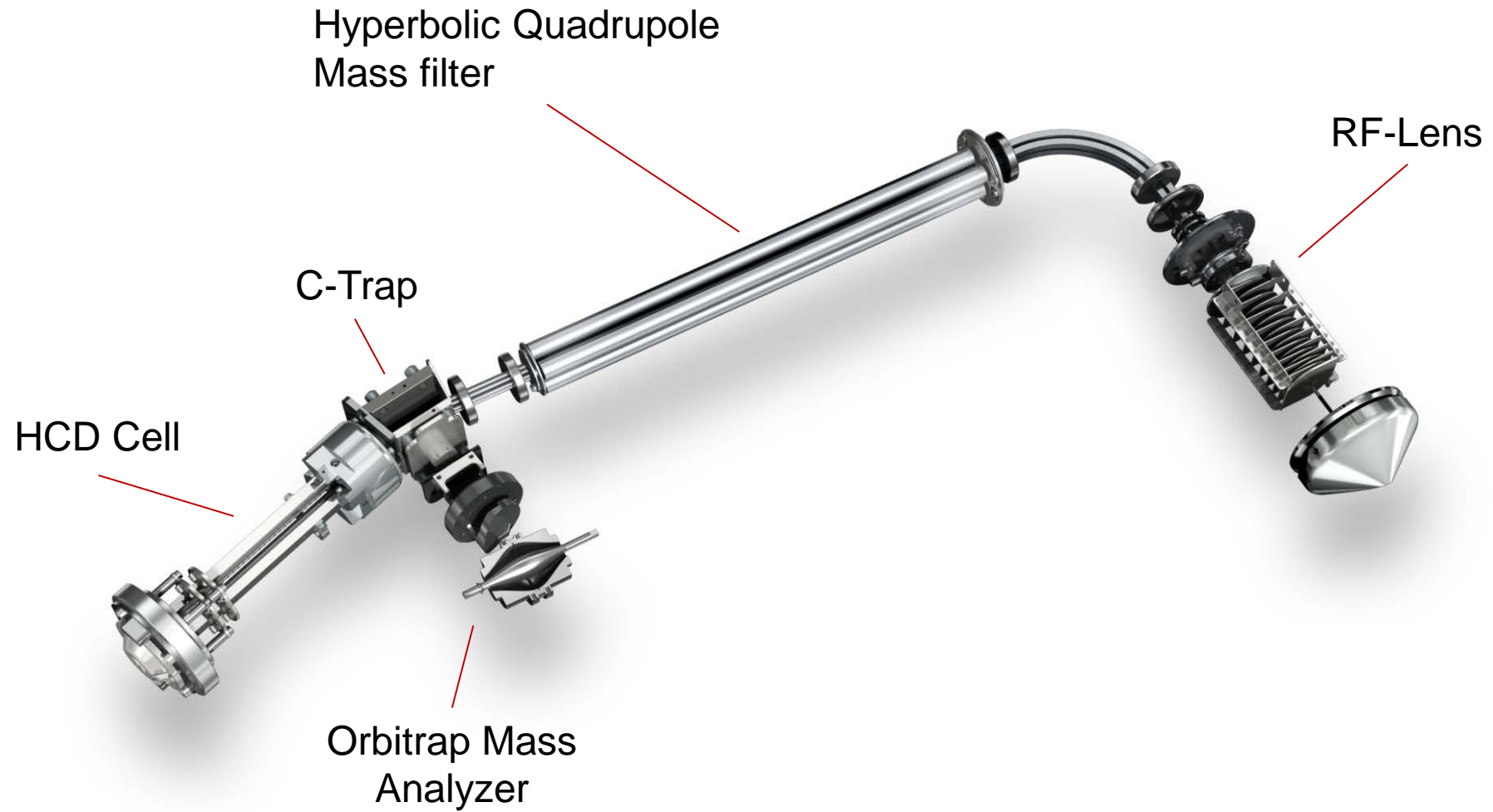
High Performance

- Resolving power
- Sensitivity
- Acquisition speed
- Mass accuracy
- Dynamic range
- Rapid polarity switching
- Multiple ionization modes

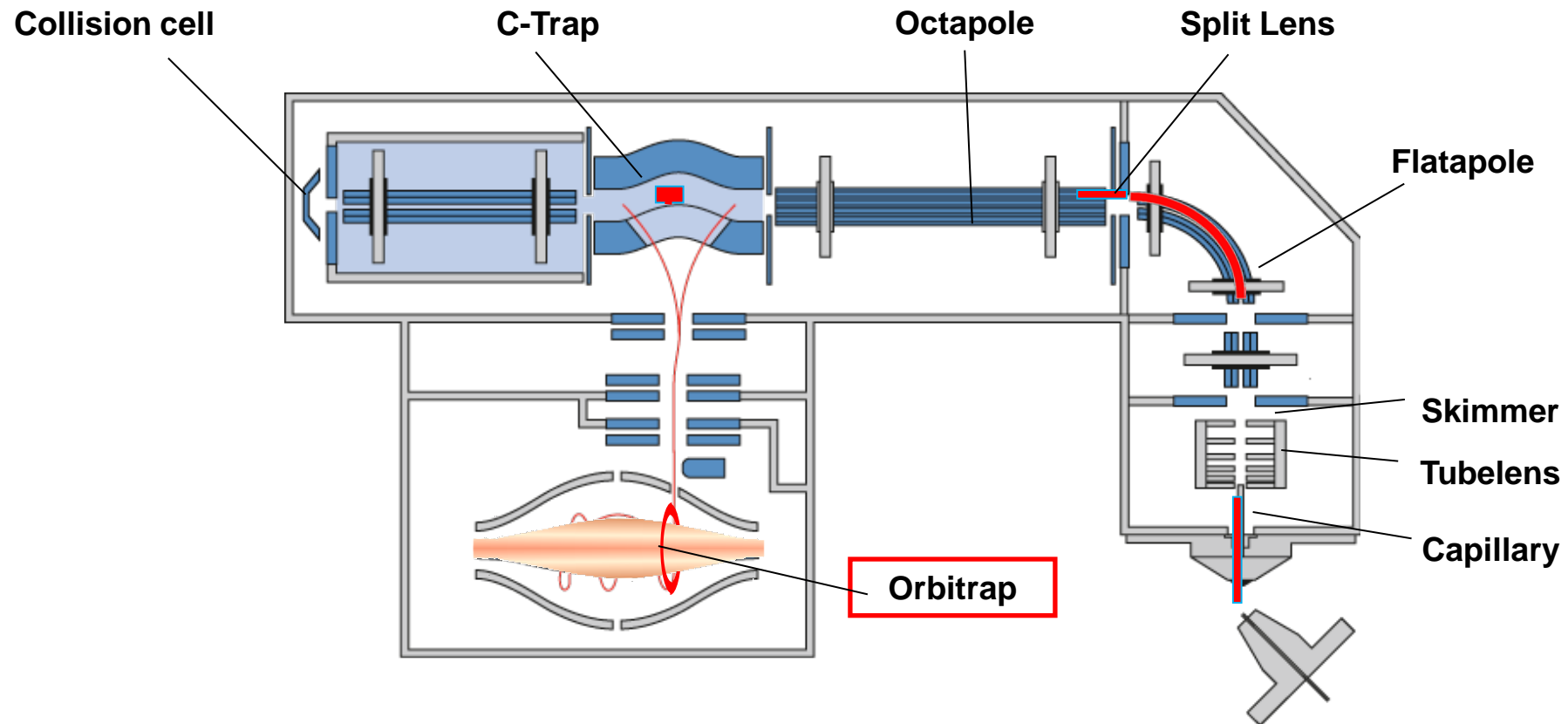
Easy to use

- Bench top
- Tune Wizard
- Method templates
- Drag and drop
- Robust
- Plug and play

Thermo Scientific Q Exactive MS Schematics



Thermo Scientific Orbitrap MS – Principle of Operation

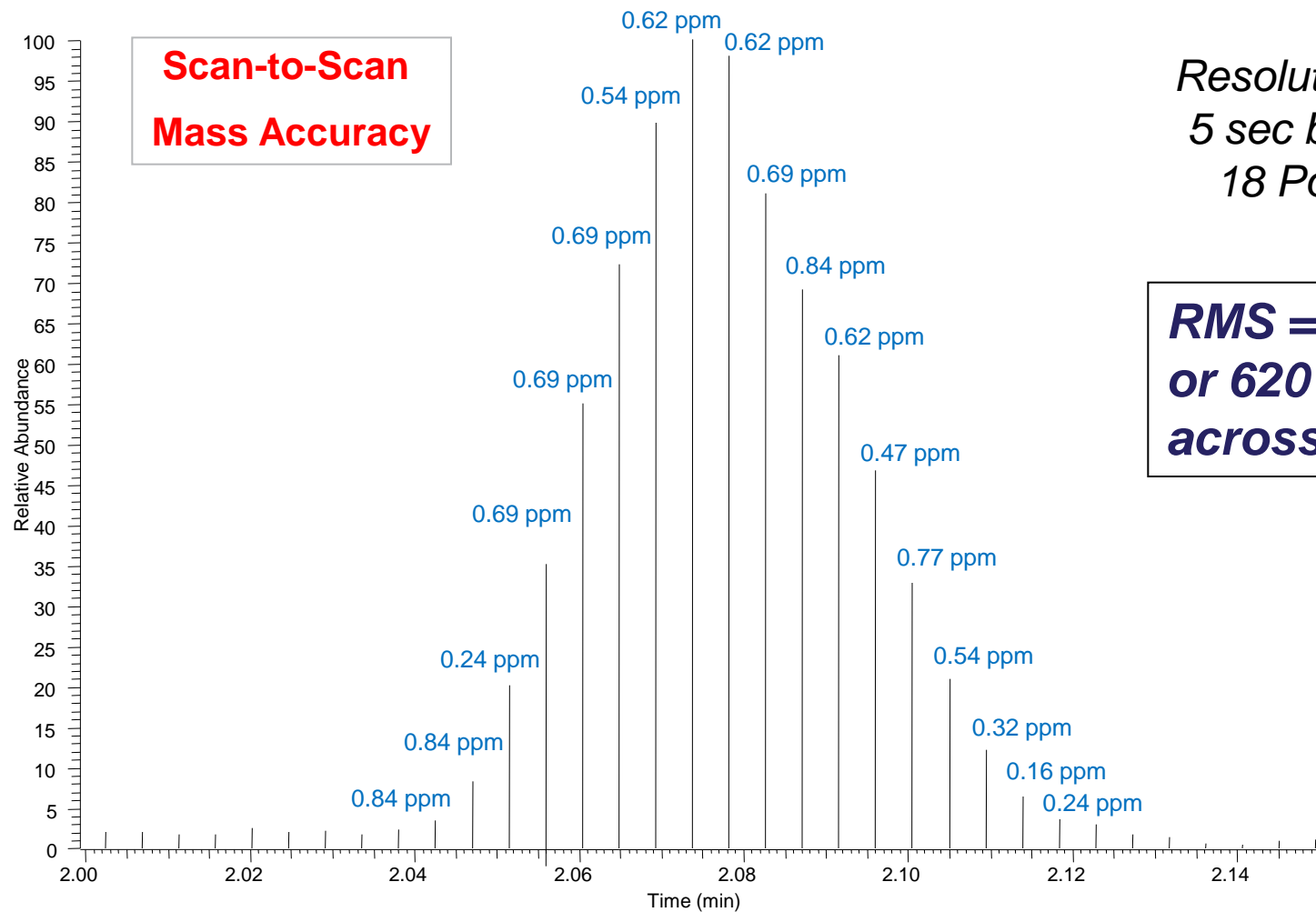


1. Ions are injected through the source
2. ...and trapped in the C-trap and squeezed into a smaller cloud
3. ...then a voltage pulse across C-trap ejects ions towards the Orbitrap
4. ...where they are trapped and detected

- **Max Resolution**
 - 140,000 at m/z 200
- **Max Scan Speed**
 - Up to 12 Hz (at 17,500)
- **Mass Accuracy**
 - < 3 ppm external
 - < 1 ppm internal
- **Mass Range:** m/z 50 – 6,000
- **Intra-scan Dynamic Range:** > 5000:1
- **Sensitivity**
 - Full MS: 500 fg Buspirone on column S/N 100:1
 - SIM: 50 fg Buspirone on column S/N 100:1
- **Polarity Switching**
 - One full cycle in < 1 sec (one full scan positive mode and one full scan negative mode at resolution setting of 35,000)

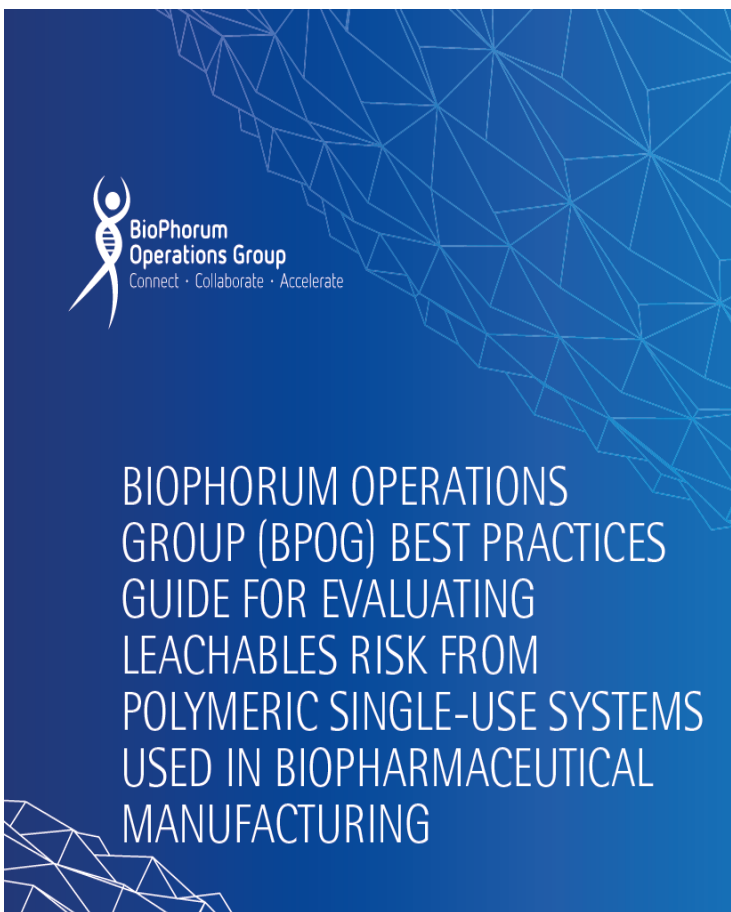
Resolution at m/z 200	Max. Scan Speed (Hz)
17,500	12
35,000	7
70,000	3
140,000	1.5

Scan-to-Scan Mass Accuracy | Carbaryl, C₁₂H₁₁NO₂



*Resolution @ 70k
5 sec base peak
18 Pos scans*

***RMS = 0.62 ppm
or 620 ppb
across the peak***

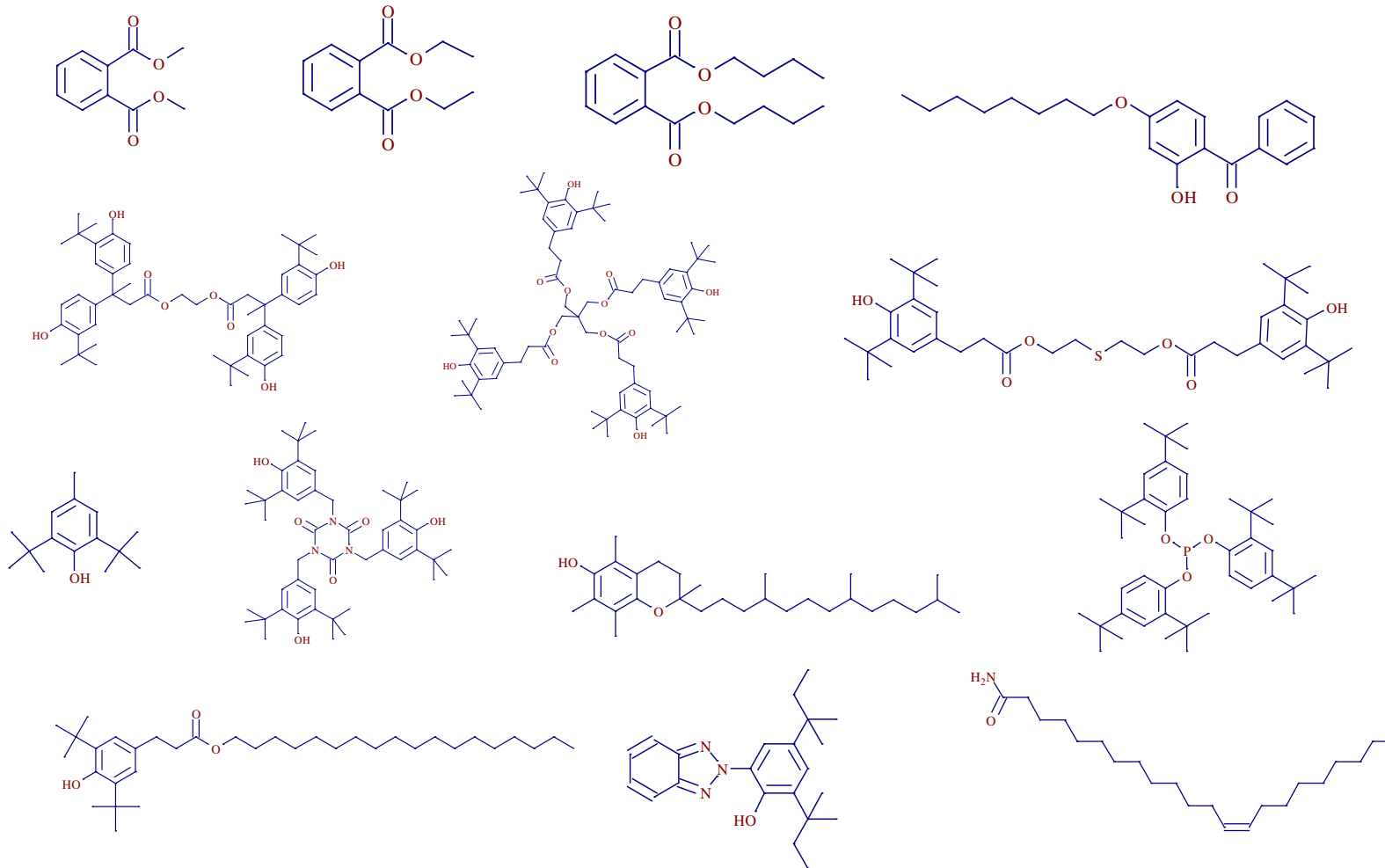


5.4 Analytical methods

- Know what you need from the data before approaching a CRO to perform leachables studies.
- Define the limits of detection (LOD) and limits of quantitation (LOQ) of your analytical methods. Persist in getting required data from vendors.
- Validate/qualify the analytical methods appropriately in consideration of the test objective.
- Use standard/control samples at the beginning and the end of each run.
- Use accurate mass detectors, even if only conducting a screening study.
- Use appropriate matrix controls to account for degradation of matrix components that could be mistaken for leachables.
- Non-specific analyses are typically not useful for leachables studies.
- Do not make assumptions without data; generate required data.
- Matrix interference from protein/excipients/process components can be significant; ensure that such effects on the methods planned are well understood before performing analysis.
- Determine analytical evaluation thresholds (AET) for your target compounds.
- Where possible, use an MS (or MSn) library to aid in the identification of compounds.

Additives and Their Unknown Degradants are Common Extractables

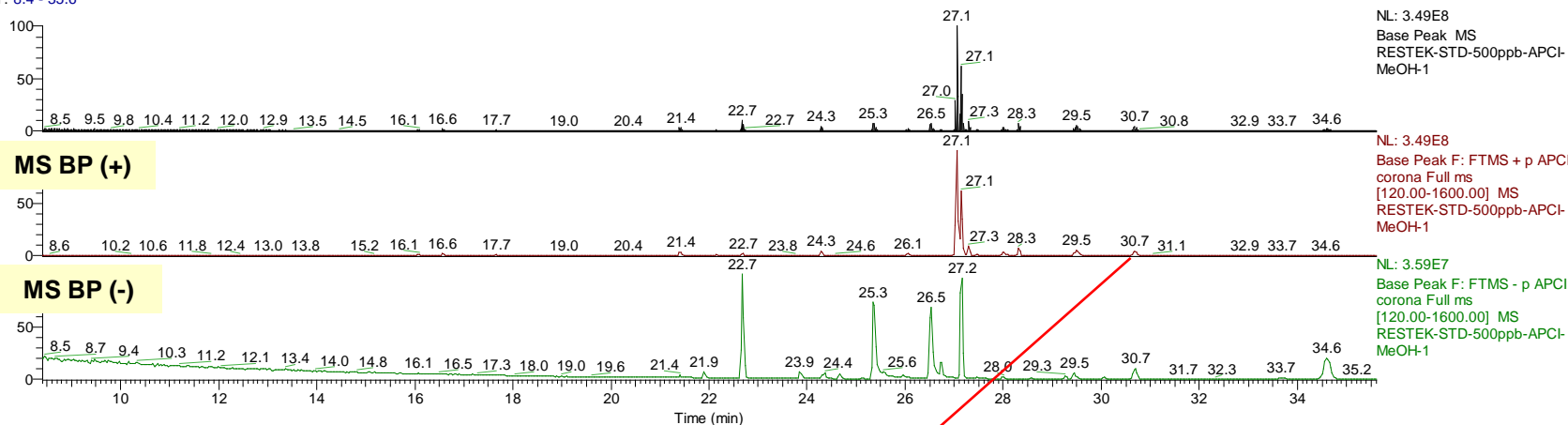
Antioxidant, plasticizer, slipping agent, light stabilizer... also monomer, oligomer.



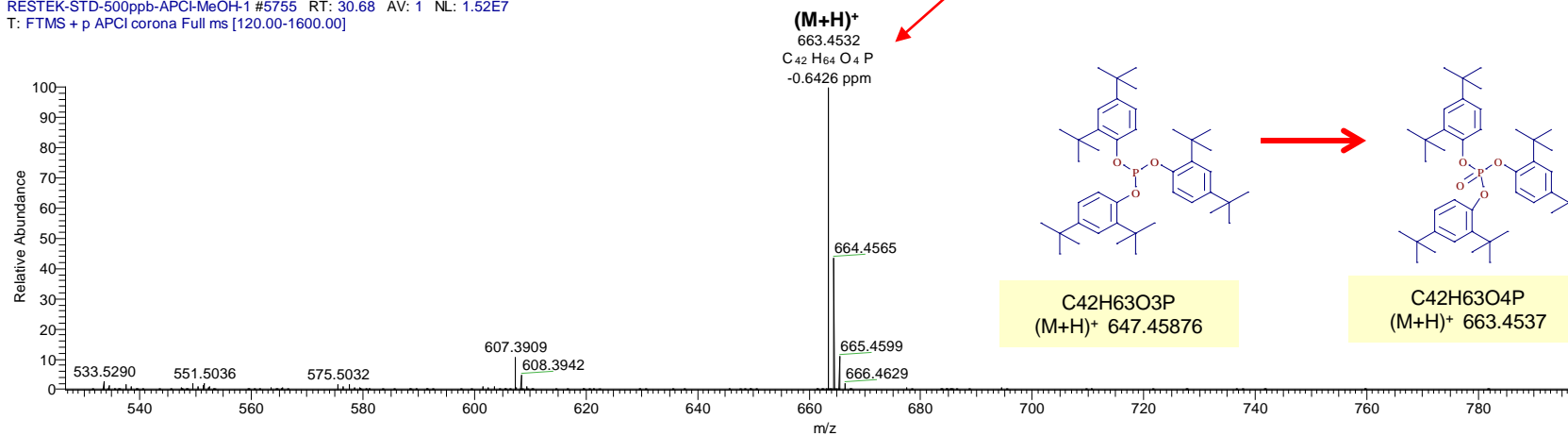
Irgafos 168 (Oxidation Product)

RESTEK-STD-500ppb-APCI-MeOH-1 02/02/16 19:09:40
 APCI Accucore C18 2.1X100 2.6 um A: H2O/0.05% HAc/5mMNH4Ac B: MeOH

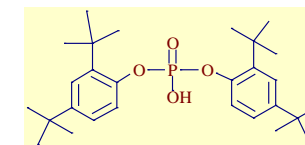
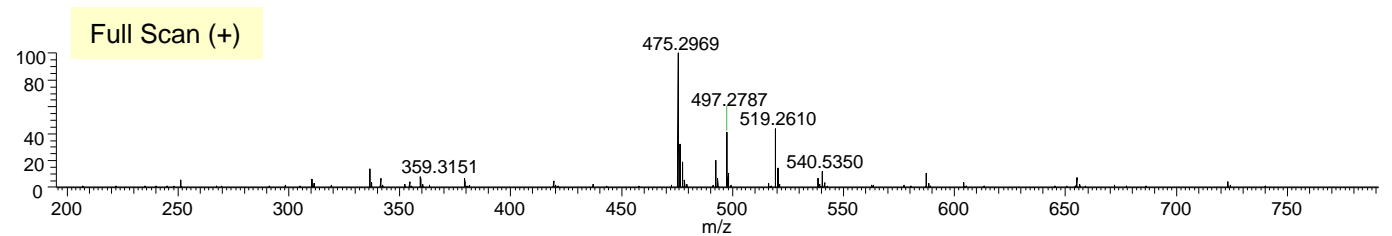
RT: 8.4 - 35.6



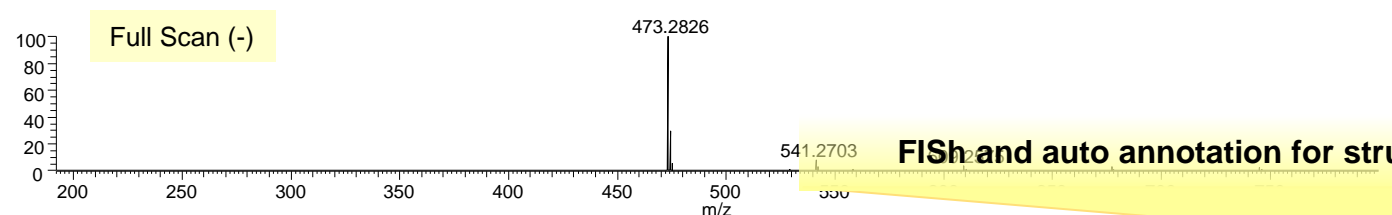
RESTEK-STD-500ppb-APCI-MeOH-1 #5755 RT: 30.68 AV: 1 NL: 1.52E7
 T: FTMS + p APCI corona Full ms [120.00-1600.00]



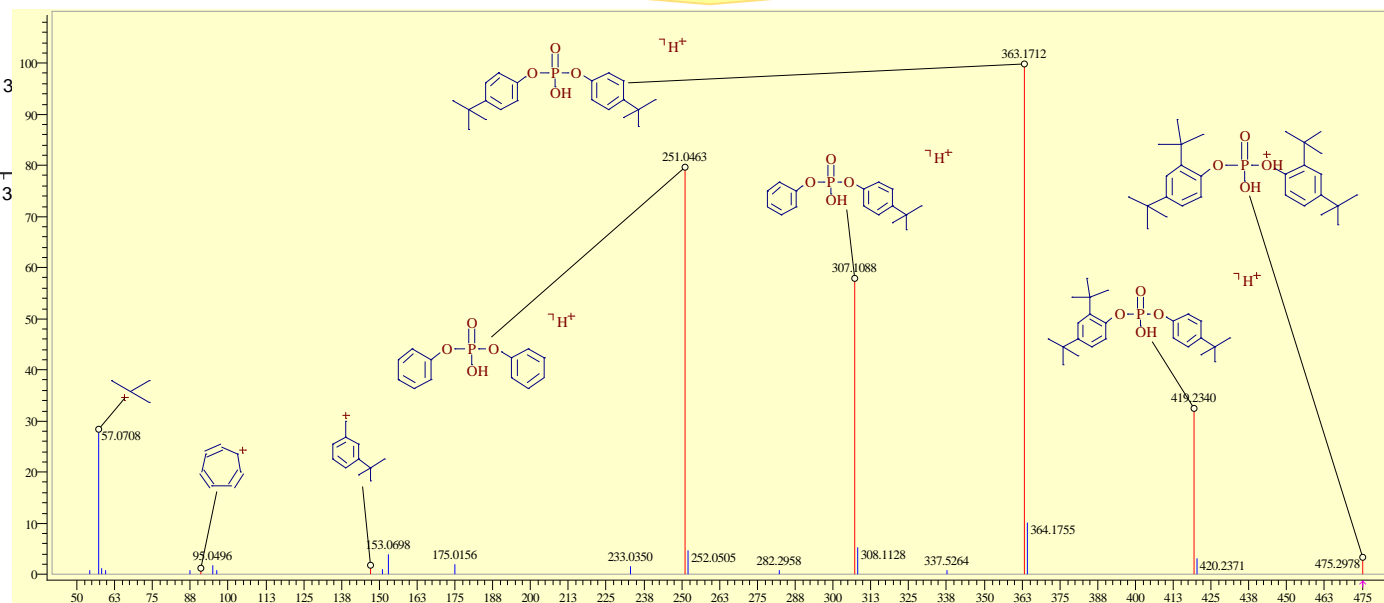
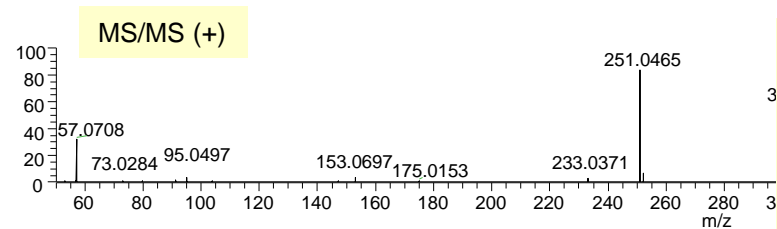
Irgafos 168 Degradant ID by Full Scan (+/-) and MS/MS Spectra



C₂₈H₄₃O₄P
(M+H)⁺ 475.2971
(M-H)⁻ 473.2826

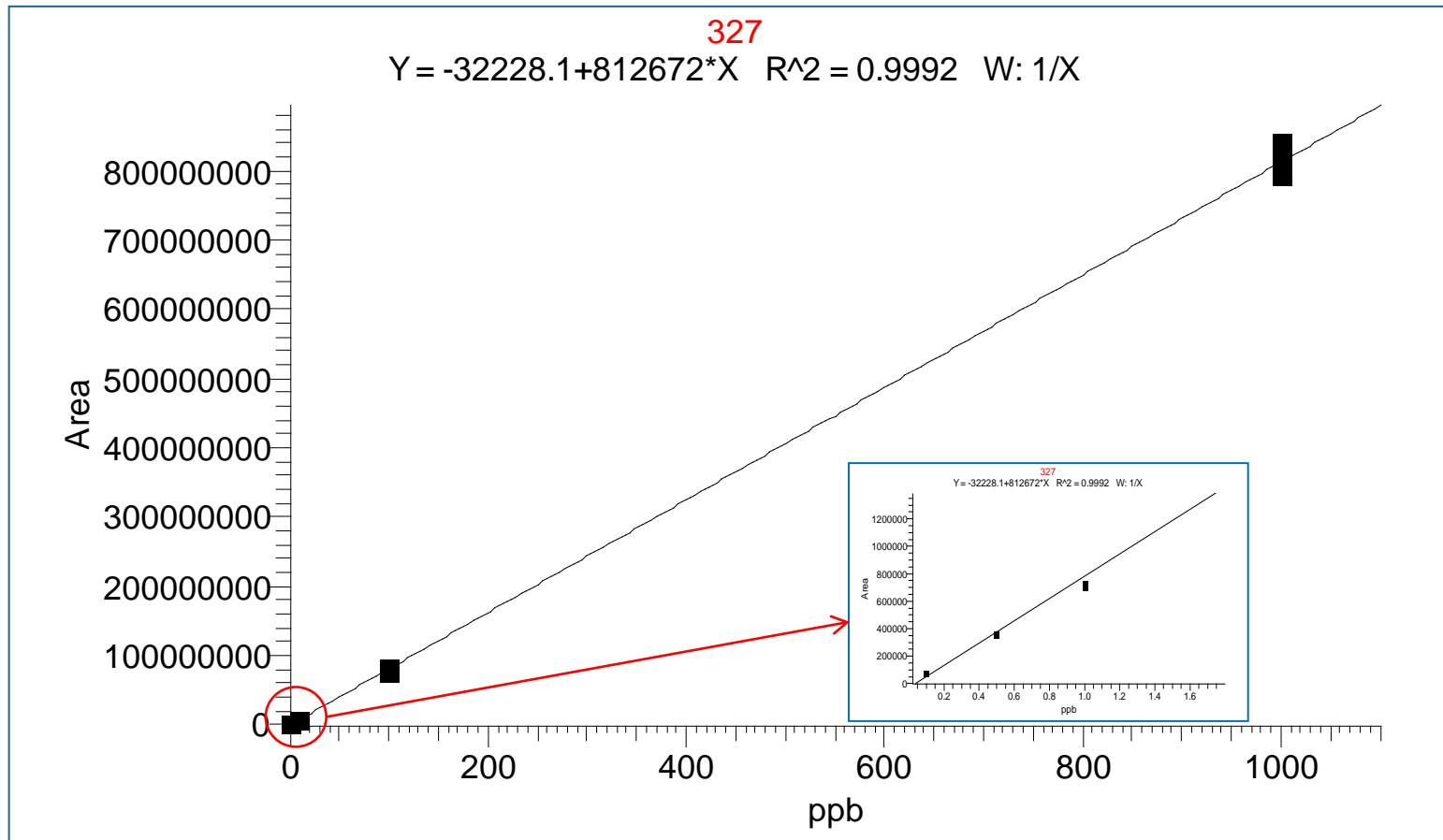
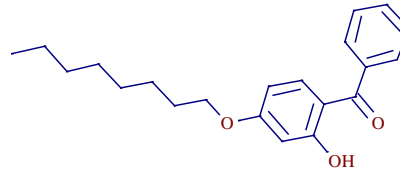


FISH₂ and auto annotation for structure elucidation of Irgafos 168 Degradant



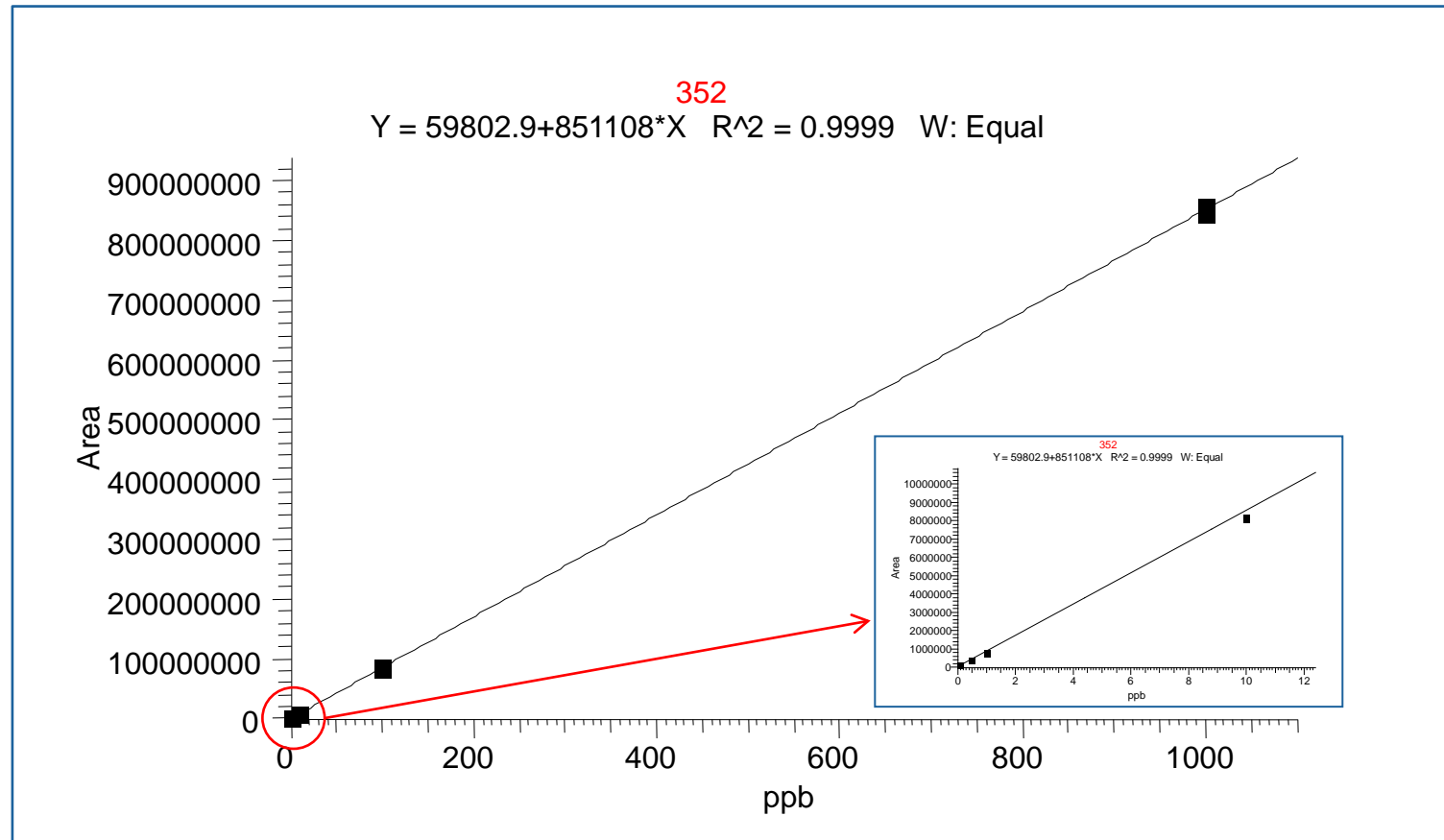
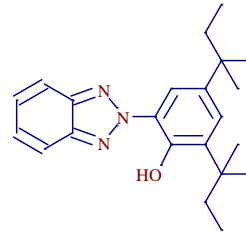
Quantitation of Octabenzene on Thermo Scientific Q Exactive Focus MS

Octabenzene
Cas# 1843-05-6
C₂₁H₂₆O₃
(M+H)⁺ 327.18092

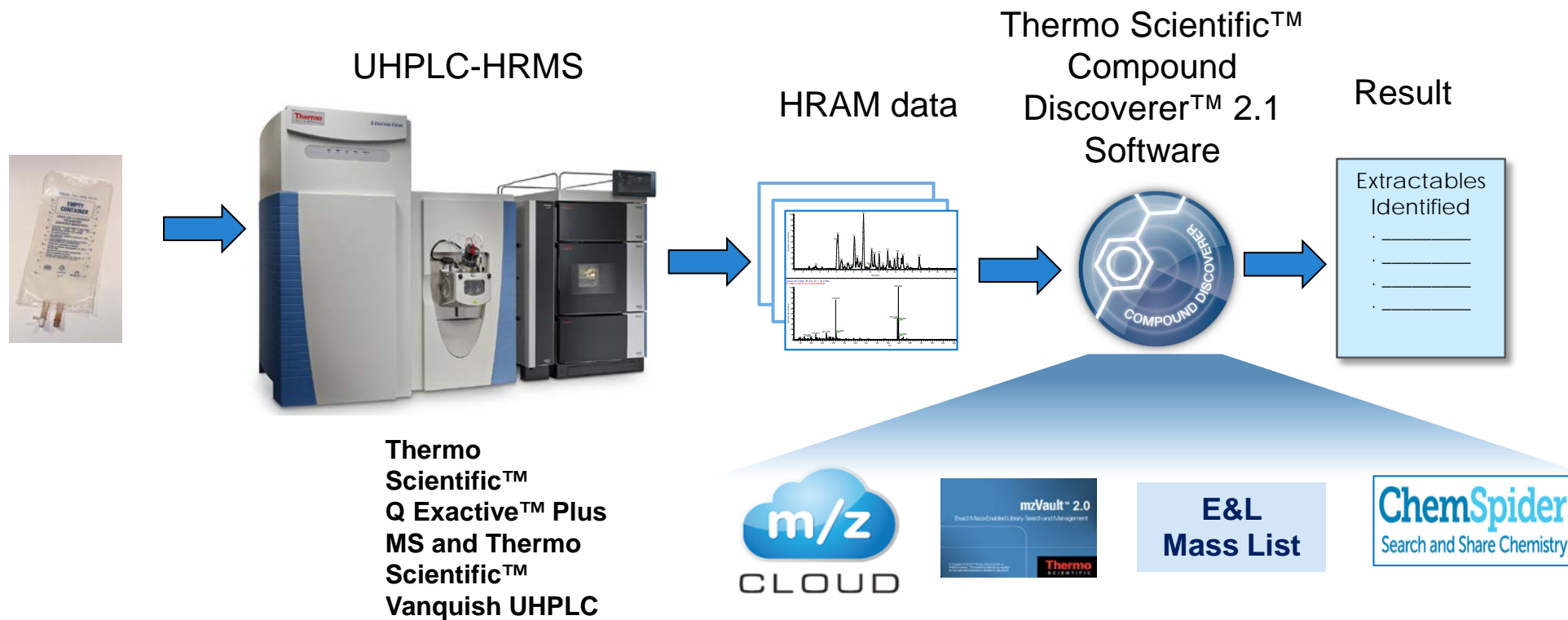


Quantitation of Tinuvin 328 on Thermo Scientific Q Exactive Focus MS

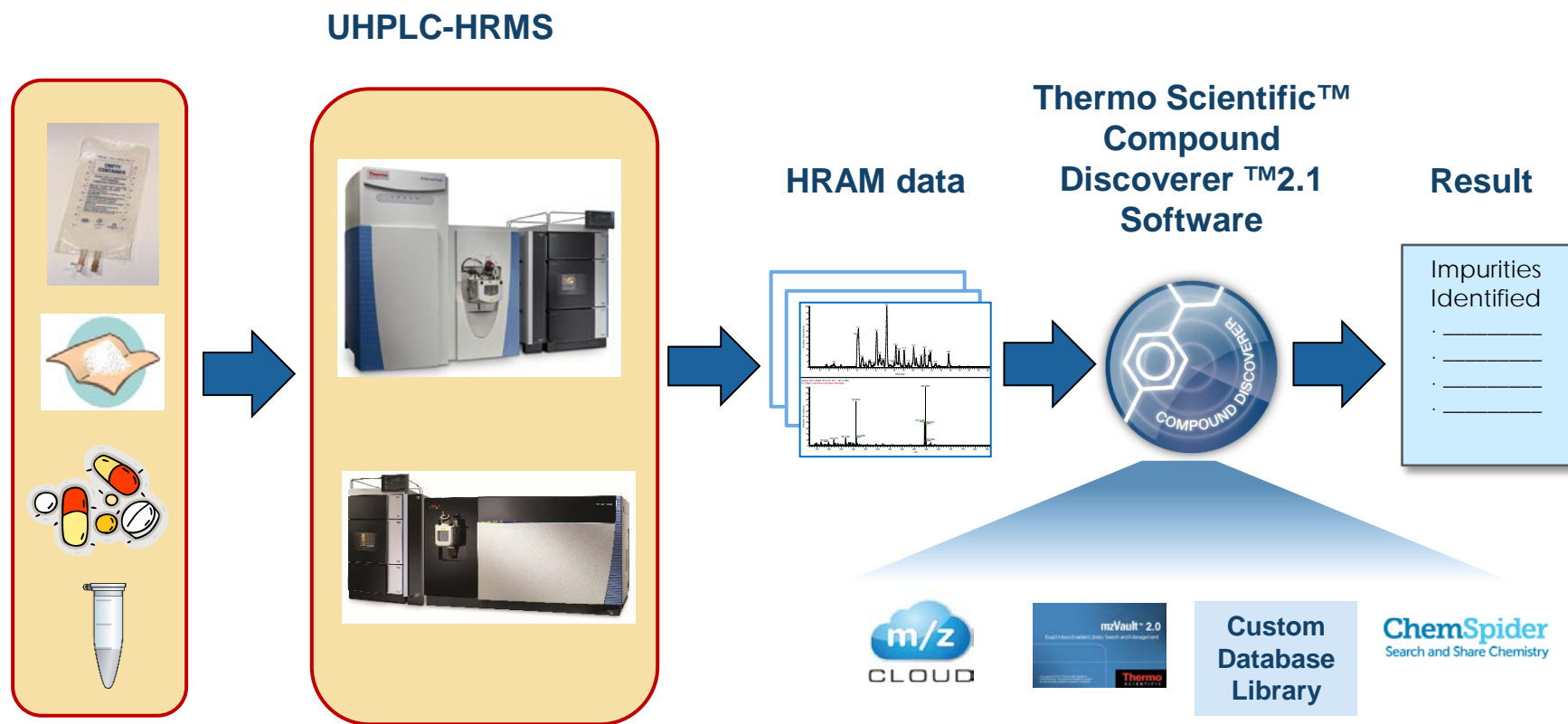
Tinuvin 328
Cas# 21615-49-6
C₂₂H₂₉N₃O
(M+H)⁺ 352.23834



LC-HRMS Analysis for IV Bag Extractables



General Workflow for Small Molecule Impurity ID and E&L Analysis



General Workflow for API Impurity and Extractable & Leachable Analysis

MS Method: High Resolution Accurate Mass Untargeted Screening

- **HRAM untargeted screening with polarity switching**
- ESI/APCI full scan MS and data-dependent top 3 MS/MS data with polarity switching using 70K & 17.5K resolution for FMS and HCD MS² respectively. Stepped NCE: 30, 45, 60.

The screenshot displays the ThermoFisher software interface for configuring a mass spectrometry method. The main window shows a method overview with a timeline and a diagram of the MS workflow. The workflow diagram illustrates a Full MS scan followed by a ddMS² scan, with arrows indicating the data flow between the two stages. The interface is divided into two columns: Positive and Negative, each showing a set of properties for the method.

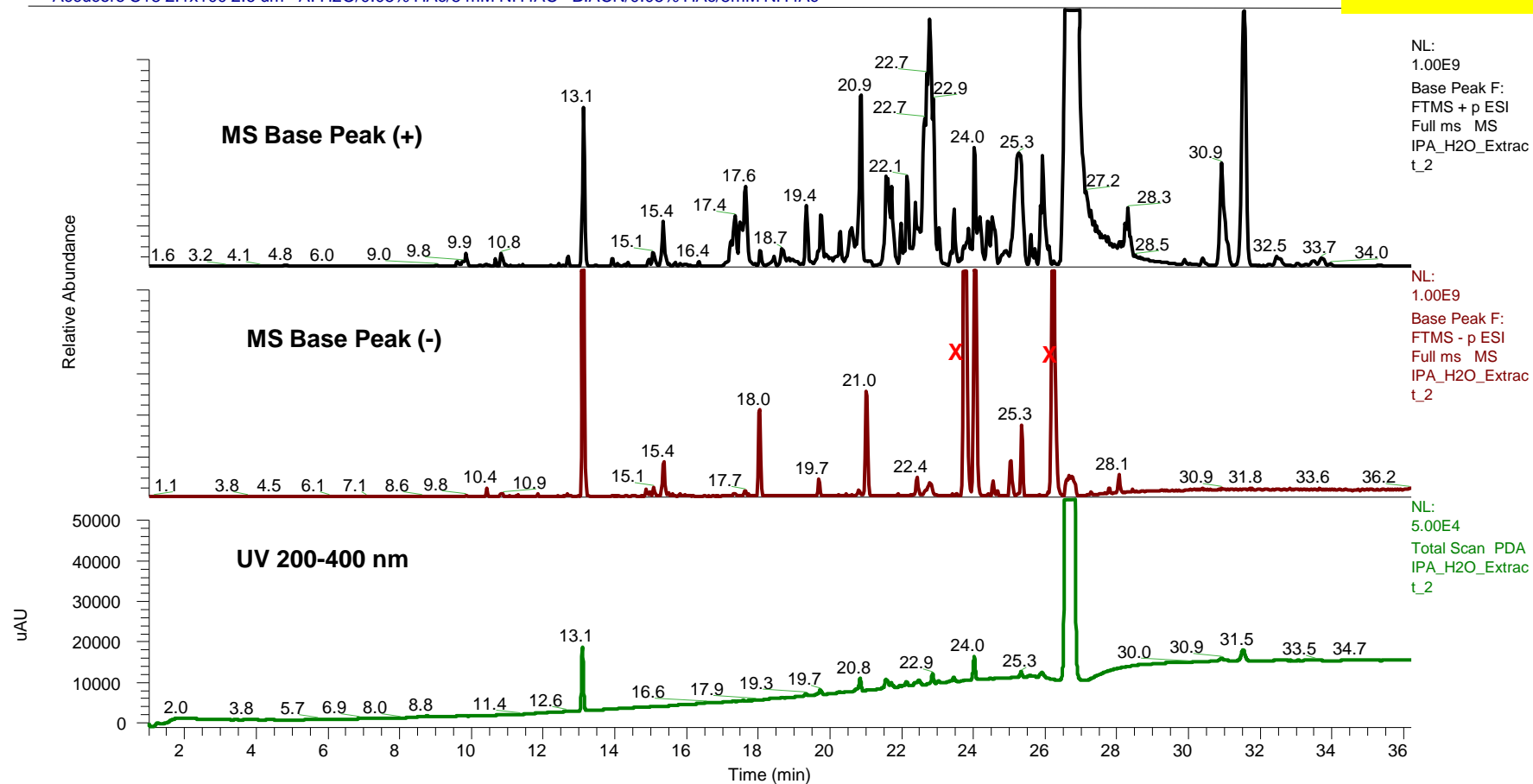
Positive		Negative	
Properties		Properties	
Properties of the method		Properties of the method	
Global Settings		Global Settings	
User Role	Advanced	User Role	Advanced
Use lock masses	off	Use lock masses	off
Lock mass injection	—	Lock mass injection	—
Chrom. peak width (FWHM @ s)	—	Chrom. peak width (FWHM @ s)	—
Time		Time	
Method duration	42.00 min	Method duration	42.00 min
Customized Tolerances (+/-)		Customized Tolerances (+/-)	
Properties of Full MS / dd-MS² (TopN)		Properties of Full MS / dd-MS² (TopN)	
General		General	
Runtime	0 to 41 min	Runtime	0 to 41 min
Polarity	positive	Polarity	negative
In-source CID	0.0 eV	In-source CID	0.0 eV
Default charge state	1	Default charge state	1
Inclusion	—	Inclusion	—
Exclusion	—	Exclusion	—
Tags	—	Tags	—
Full MS		Full MS	
Microscans	1	Microscans	1
Resolution	70,000	Resolution	70,000
AGC target	3e6	AGC target	3e6
Maximum IT	100 ms	Maximum IT	100 ms
Number of scan ranges	1	Number of scan ranges	1
Scan range	120 to 1500 m/z	Scan range	120 to 1500 m/z
Spectrum data type	Profile	Spectrum data type	Profile
dd-MS² / dd-SIM		dd-MS² / dd-SIM	
Microscans	1	Microscans	1
Resolution	17,500	Resolution	17,500
AGC target	1e5	AGC target	1e5
Maximum IT	50 ms	Maximum IT	50 ms
Loop count	3	Loop count	3
MSX count	1	MSX count	1
TopN	3	TopN	3
Isolation window	1.6 m/z	Isolation window	1.6 m/z
Isolation offset	0.0 m/z	Isolation offset	0.0 m/z
Fixed first mass	50.0 m/z	Fixed first mass	50.0 m/z
NCE / stepped NCE	20, 40, 60	NCE / stepped NCE	20, 40, 60
Spectrum data type	Profile	Spectrum data type	Profile
dd Settings		dd Settings	
Underfill ratio	5.0 %	Underfill ratio	5.0 %
Intensity threshold	1.0e5	Intensity threshold	1.0e5
Apex trigger	2 to 3 s	Apex trigger	2 to 3 s
Charge exclusion	—	Charge exclusion	—
Peptide match	—	Peptide match	—
Exclude isotopes	on	Exclude isotopes	on
Dynamic exclusion	5.0 s	Dynamic exclusion	5.0 s

IV Bag IPA-H2O Extract - MS Base Peak Chromatogram and UV

D:\ISGS-E&L\ISGS-IVBag\IPA_H2O_Extract_2

Accucore C18 2.1x100 2.6 um A: H2O/0.05% HAc/5 mM NH4AC B: ACN/0.05% HAc/5mM NH4AC

Zoom-in View



X = present in the blank

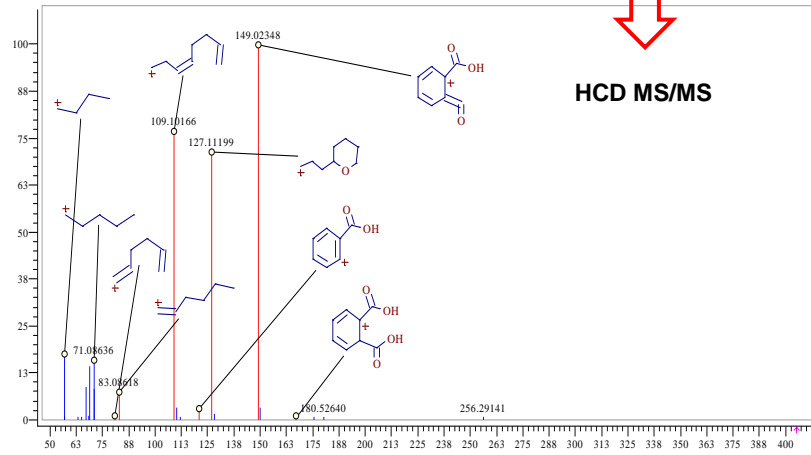
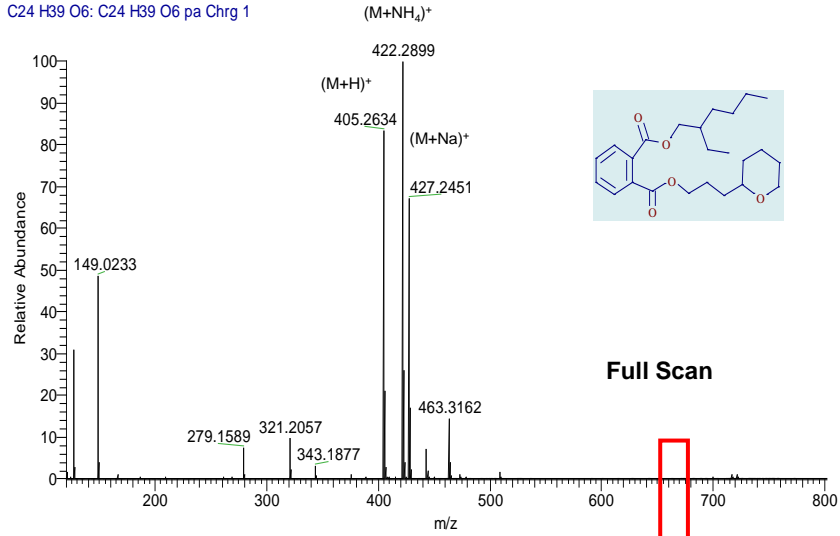
Full Scan and HCD MS/MS Data for Component ID and Structure Elucidation

G:\Old Passport\...NPA_H2O_Extract_1

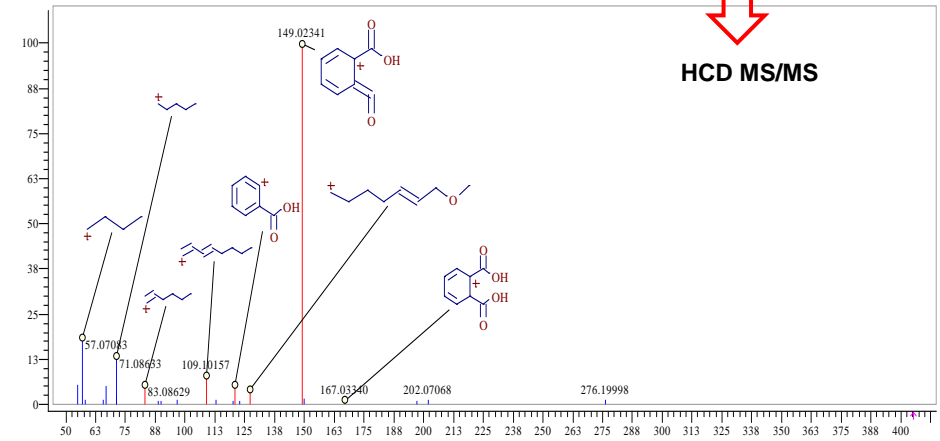
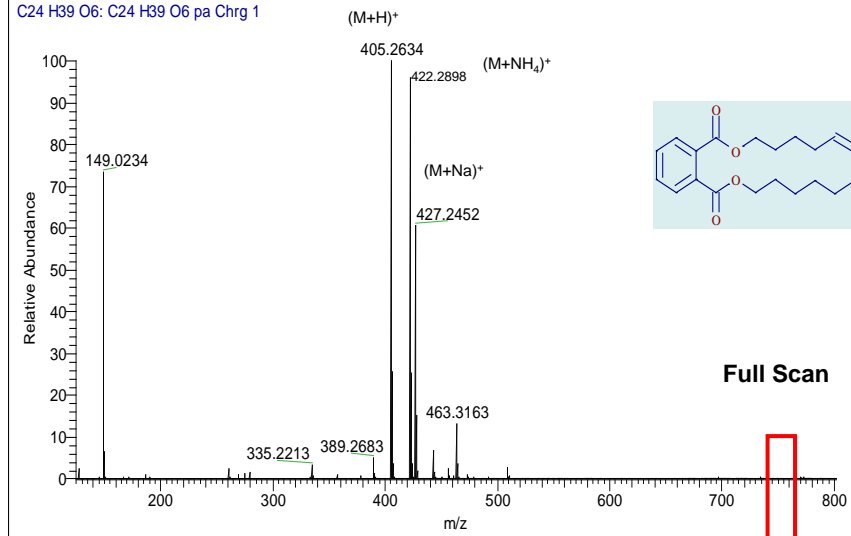
01/18/16 07:08:13

Accucore C18 2.1x100 2.6 um A: H2O/0.05% HAc/5 mM NH4AC B: ACN/0.05% HAc/5mM NH4AC

C24 H39 O6: C24 H39 O6 pa Chrg 1

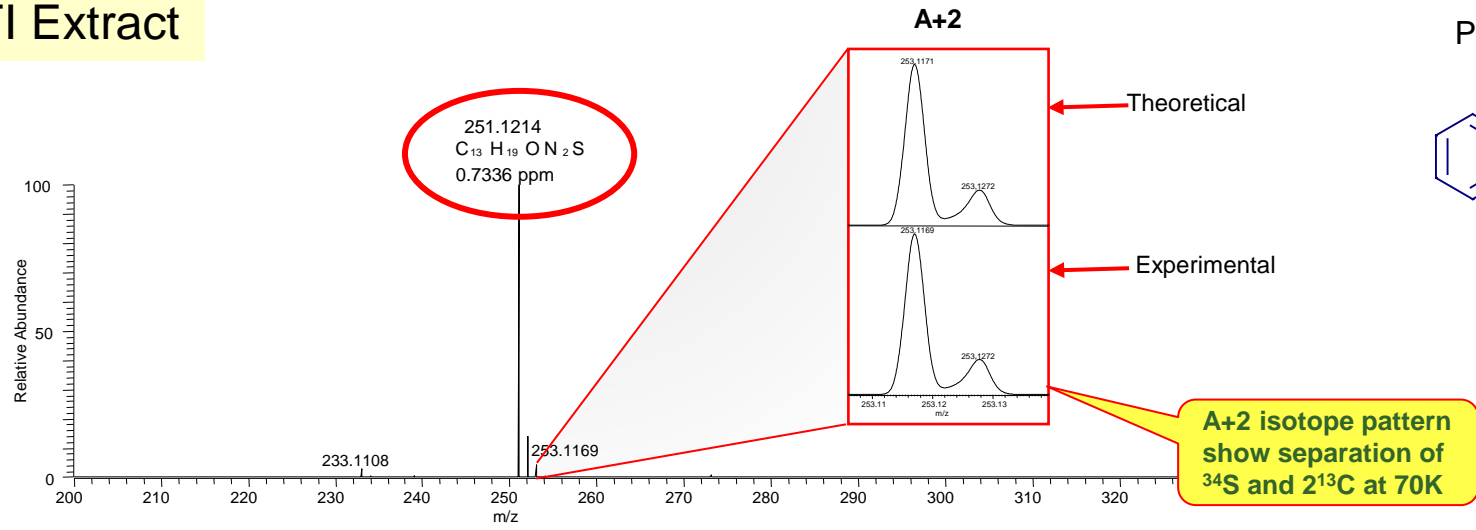


C24 H39 O6: C24 H39 O6 pa Chrg 1

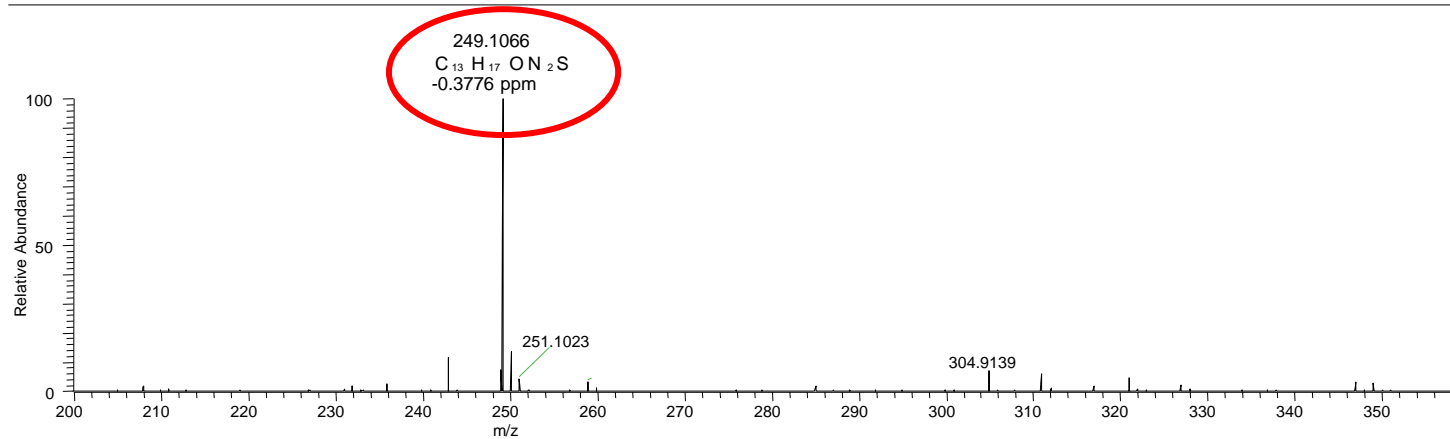
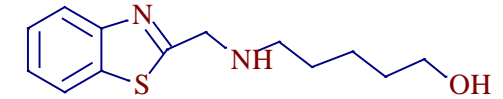


Pos/Neg Switching Maintain High Mass Accurate Mass and Fine Isotope Pattern

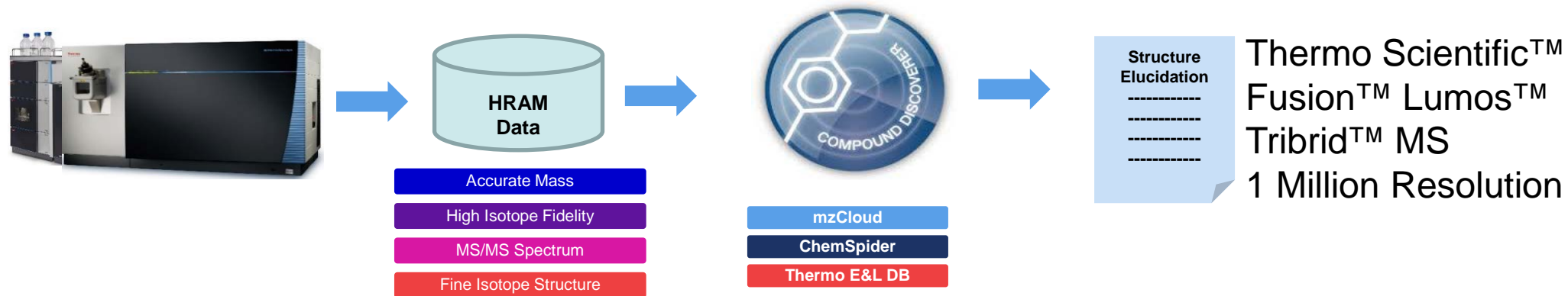
From O-Ring WFI Extract



Proposed Structure



Ultra High Resolution MS Reveals Fine Isotope Structure



CD 2.1 Result - Predicted Compositions for a unknown component in cosmetic product IPA/H2O extract

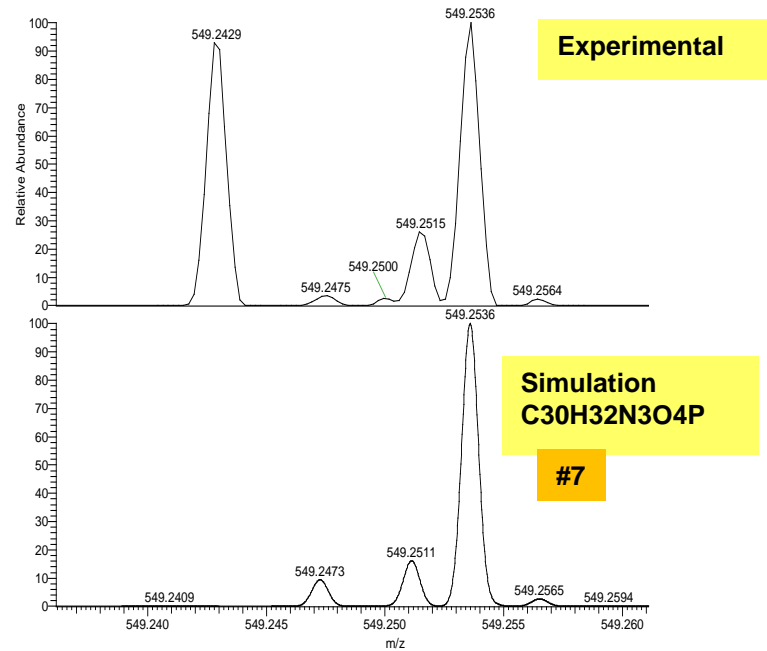
Checked	Name	Formula	Annotation Sc	FISH Coverage	Molecular Weig	RT [min]	Area (Max.)	# ChemSpider Results	# mzCloud Results	mzCloud Best Match
53		C27 H36 N3 O4 P S			529.21404	11.708	2857456	119	0	

Check	Compound Match	Formula	Molecular Weight	ΔMass [Da]	ΔMass [ppm]	RDBE	H/C	Rank	# Matched Iso.	# Missed Iso.	# Matched F	SFit [%]	Pattern Cov. [%]	MS Cov. [%]	MSMS Cov. [%]	In ChemSpider	
1	<input type="checkbox"/>	<input type="checkbox"/>	C27 H36 N3 O4 P S	529.21641	-0.00238	-4.49	12.0	1.3	1	7	0	23	78	100.00	99.97	99.64	
2	<input type="checkbox"/>	<input type="checkbox"/>	C24 H35 N O12	529.21593	-0.00189	-3.57	8.0	1.5	7	5	0	18	54	100.00	96.51	95.64	X
3	<input type="checkbox"/>	<input type="checkbox"/>	C29 H31 N5 O3 S	529.21476	-0.00072	-1.37	17.0	1.1	2	7	0	22	72	100.00	99.97	98.57	X
4	<input type="checkbox"/>	<input type="checkbox"/>	C28 H37 N O5 P2	529.21470	-0.00066	-1.25	12.0	1.3	5	4	0	20	85	100.00	96.48	97.90	
5	<input type="checkbox"/>	<input type="checkbox"/>	C23 H32 N9 O2 P S	529.21373	0.00031	0.58	13.0	1.4	10	5	2	22	39	97.17	95.98	99.48	
6	<input type="checkbox"/>	<input type="checkbox"/>	C28 H35 N O7 S	529.21342	0.00061	1.16	12.0	1.2	3	8	0	23	63	100.00	100.00	99.64	X
7	<input type="checkbox"/>	<input type="checkbox"/>	C30 H32 N3 O4 P	529.21304	0.00099	1.88	17.0	1.1	6	4	0	19	76	100.00	96.48	96.84	
8	<input type="checkbox"/>	<input type="checkbox"/>	C22 H36 N5 O6 P S	529.21239	0.00164	3.11	8.0	1.6	4	7	0	23	60	100.00	99.97	99.64	
9	<input type="checkbox"/>	<input type="checkbox"/>	C32 H37 N P2 S	529.21219	0.00184	3.48	16.0	1.2	9	7	0	6	65	100.00	99.97	11.05	

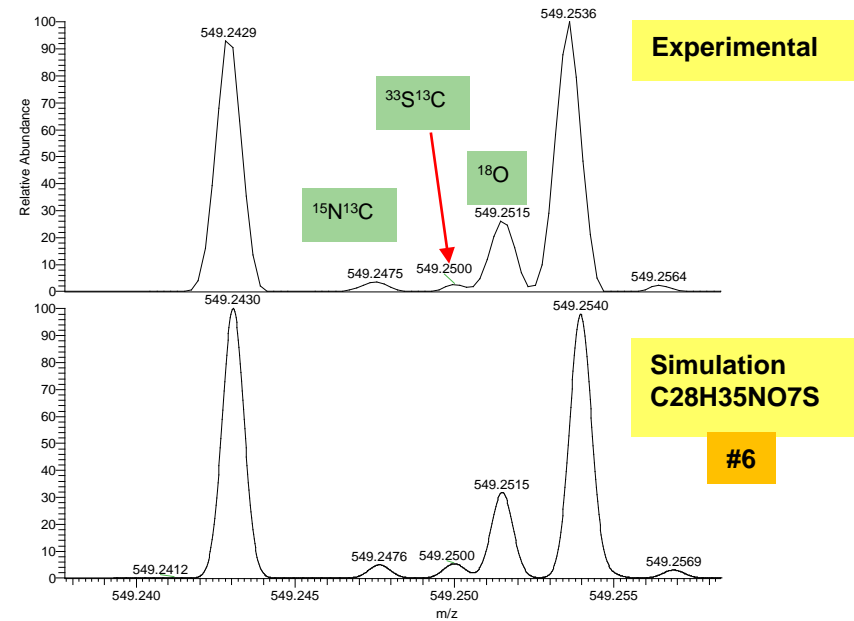
#6 and #7

A2 Isotope Fine Structure Validates Correct Elemental Composition

The incorrect formula doesn't match the result.



The correct formula matches the ana fine isotope structure.



The above results demonstrate that the fine isotope structure made available by ultra high resolution mass spectrometer greatly enhances the ability to confidently determine the correct unknown elemental composition.

mzCloud - HR Mass Spectral Database



mzCloud™

- Advanced high resolution mass spectral database (Free)
- Very high quality data: standardized acquisition, highly curated data
- Search through spectrum, structure, substructure, m/z, ...
- Identifying compounds even when they are not present in the library through substructure search



<https://www.mzcloud.org>

Free and cloud-based

The screenshot shows the mzCloud website interface. At the top, there is a navigation bar with the logo and the text "Advanced Mass Spectral Database". A search bar is located in the top right corner. Below the navigation bar, there is a main content area with a description of the database, a video player showing a screenshot of the software interface, and a "New mzCloud App!" button with Google Play and App Store icons. A search bar for compounds by name or ID is also present. At the bottom, there is a statistics section with the following data:

Category	Count	Change
compounds	6,730	(+57)
trees	10,537	(+85)
spectra	2,309,264	(+63,477)
QM models	704,266	(+0)

view more statistics

(+ added in the last 14 days)

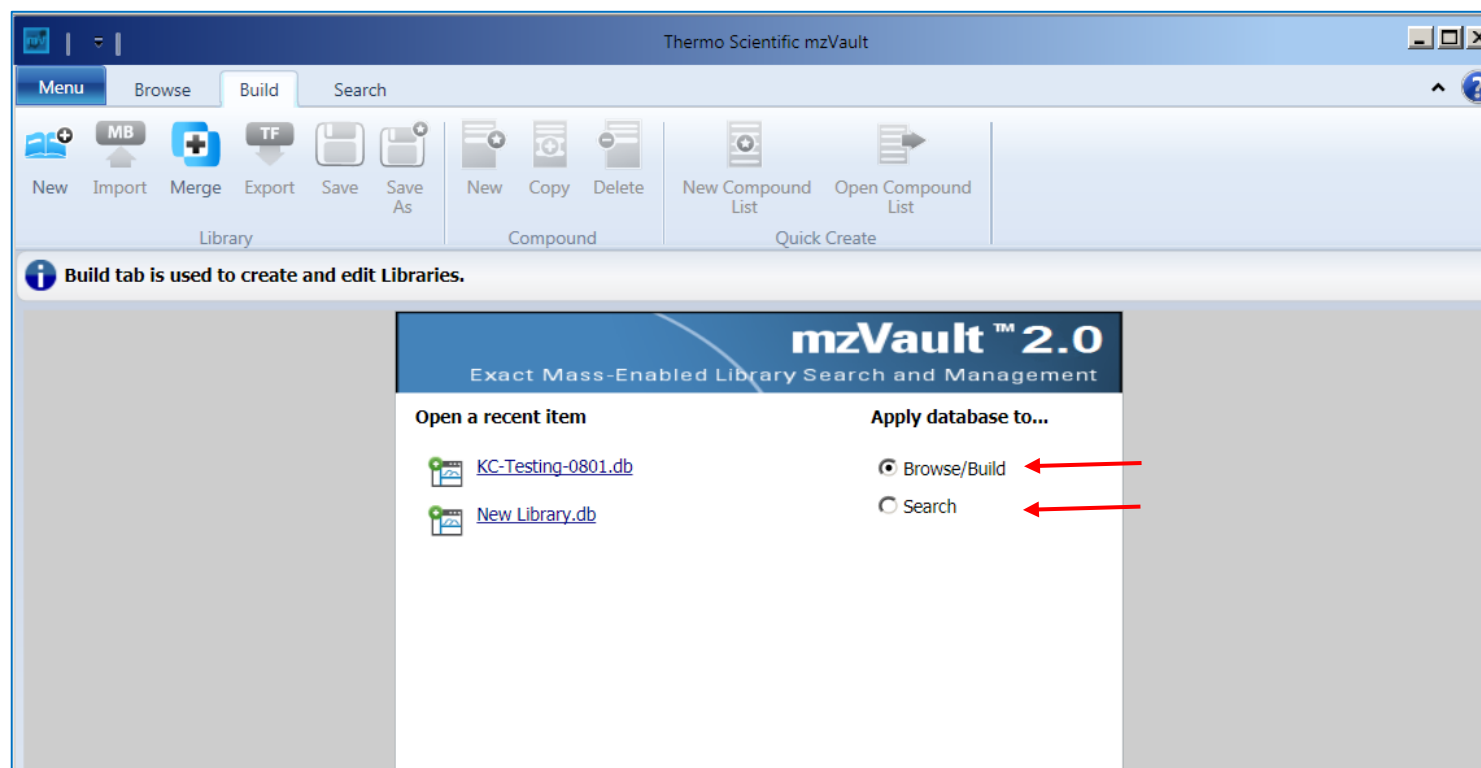
The screenshot displays the mzCloud Spectral Library interface. On the left, a navigation sidebar includes 'Views', 'Libraries', and 'Search' (highlighted with a red box). The 'Search' dropdown menu is open, showing options like 'Spectrum', 'Tree', 'Structure', 'Monoisotopic Mass', 'Peak', 'Precursor', and 'Name'. A callout 'Search by different terms' points to this menu. The main area shows a 'Reference Library' with search results for 'Irganox 1035', 'Accelerator BBTS', and '5-Chloro-2-hydroxy-4-methylbenzophenone'. A callout 'Metadata available for selected library entry' points to the entry details. The 'Spectral Tree' section shows a tree of spectra with a callout 'Spectral tree'. The 'Recalibrated Spectrum' section displays a mass spectrum with chemical structures and peak annotations, with a callout 'Recalibrated spectra fragment ions annotation'. The 'Breakdown Curves' section shows multiple colored curves representing different ions, with a callout 'Breakdown curves'. A callout 'Permanent citable links for entry, tree, and spectra' points to the bottom of the interface.

Thermo Scientific mzVault 2.0



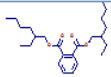
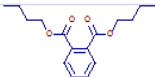
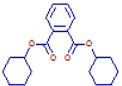
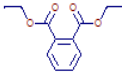

Exact Mass-Enabled Library Search and Management

- local mzCloud
- Creating customer library
- Searching library



E&L Compound Database the “E&L Mass List” in CD 2.1

This Excel sheet database contains ~2000 common E&L related compounds. This is a “living document” and new E&L related compounds are added periodically.

Commercial Name	Chemical Name	Class	CAS No.	Chemical Formula	Formula weight	[M-H] ⁻	(M-H) ⁻	M+NH ₄ ⁺	M+Na ⁺	M+K ⁺	Structure	mzCloud link
dioctyl phthalate	ethylhexylphthalate	PL	117-81-7	C ₂₄ H ₃₈ O ₄	390.27701	391.28429	389.26973	408.31083	413.26623	429.24017		https://mzcloud.org/DataViewer.aspx#CReference2
Dibutyl phthalate	Dibutyl phthalate	PL	84-74-2	C ₁₆ H ₂₂ O ₄	278.1518	279.15908	277.14452	296.18562	301.14102	317.11496		https://mzcloud.org/DataViewer.aspx#CReference2
	Dicyclohexyl phthalate		84-61-7	C ₂₀ H ₂₆ O ₄	330.18311	331.19039	329.17583	348.21693	353.17233	369.14627		https://mzcloud.org/DataViewer.aspx#CReference2
	Diethyl phthalate		84-66-2	C ₁₂ H ₁₄ O ₄	222.08921	223.09649	221.08193	240.12303	245.07843	261.05237		https://mzcloud.org/DataViewer.aspx#CReference2
	Dimethyl phthalate		131-11-3	C ₁₀ H ₁₀ O ₄	194.05791	195.06519	193.05063	212.09173	217.04713	233.02107		https://mzcloud.org/DataViewer.aspx#CReference2

This database has been added to Thermo Scientific™ Compound Discoverer™ as “E&L Mass List”.

Thermo Scientific Compound Discoverer 2.1 Software for Compound ID and Structure Elucidation



- **Component extraction and elemental composition prediction**
 - HRAM data
 - Isotope pattern
 - *fine isotope structure*
 - MS/MS fragments

- **Unknown identification through multiple databases searching in parallel**
[Known unknown compound ID](#)

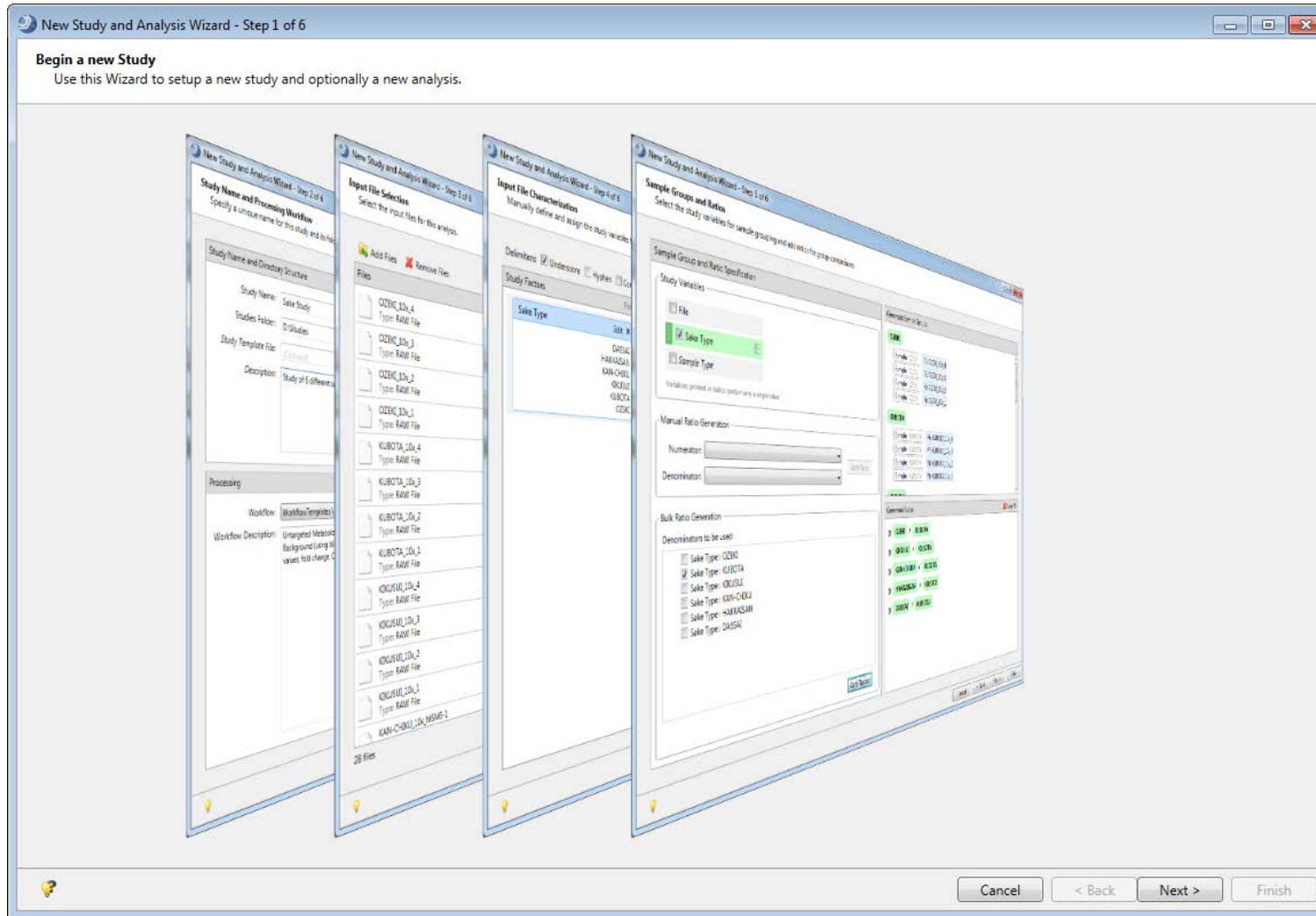
- **Unknown compound structure elucidation using “Structure Proposals”**
 - Predicted Compositions
 - MS/MS fragment ions
 - The similarity search identify the fragment ions or substructures in mzCloud, which facilitated unknown structure elucidation.
[De Novo ID](#) [Most Challenge Task](#) [Need Chemistry knowledge and expertise](#)

- **Validity check of the proposed structure**
 - using “FISh Scoring” feature by searching the embedded “HighChem Fragmentation Library”.

- **Differential Analysis for different lots, batch, or type samples analyses.**

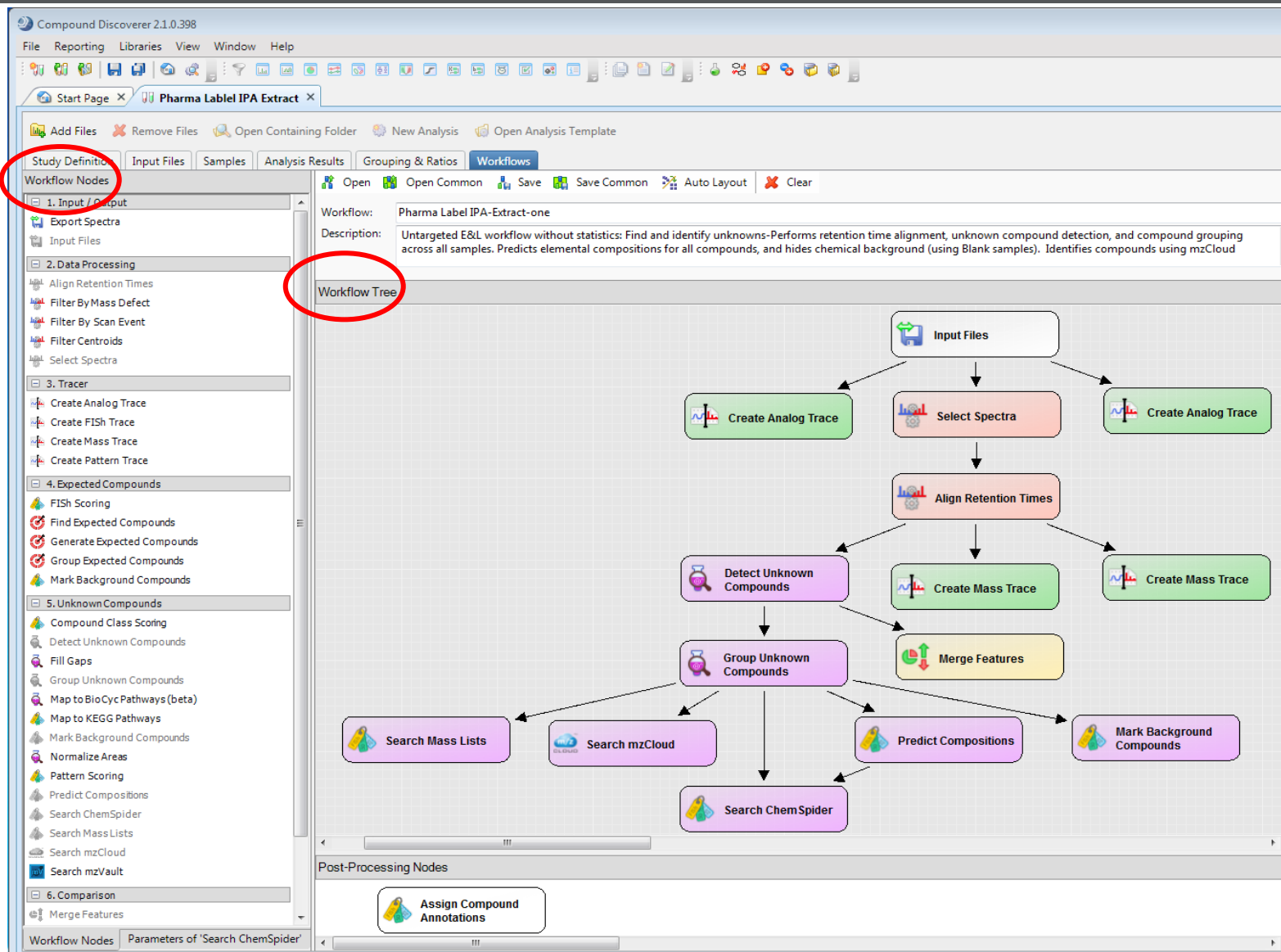
FISh stands for “Fragment Ion Search”

Thermo Scientific Compound Discoverer 2.1 Software Study and Analysis Wizard



Creating a study and analysis use the guided “New Study and Analysis wizard”

Pharma Label Extractable Study - Nodes-based Processing Workflow



Result View – Data Interpretation

The screenshot displays the Compound Discoverer 2.1.0.398 interface. The top panel shows a chromatogram with a peak at 7.618 minutes. The middle panel shows a mass spectrum with a base peak at m/z 391.22949. The bottom panel shows a table of compounds with the following data:

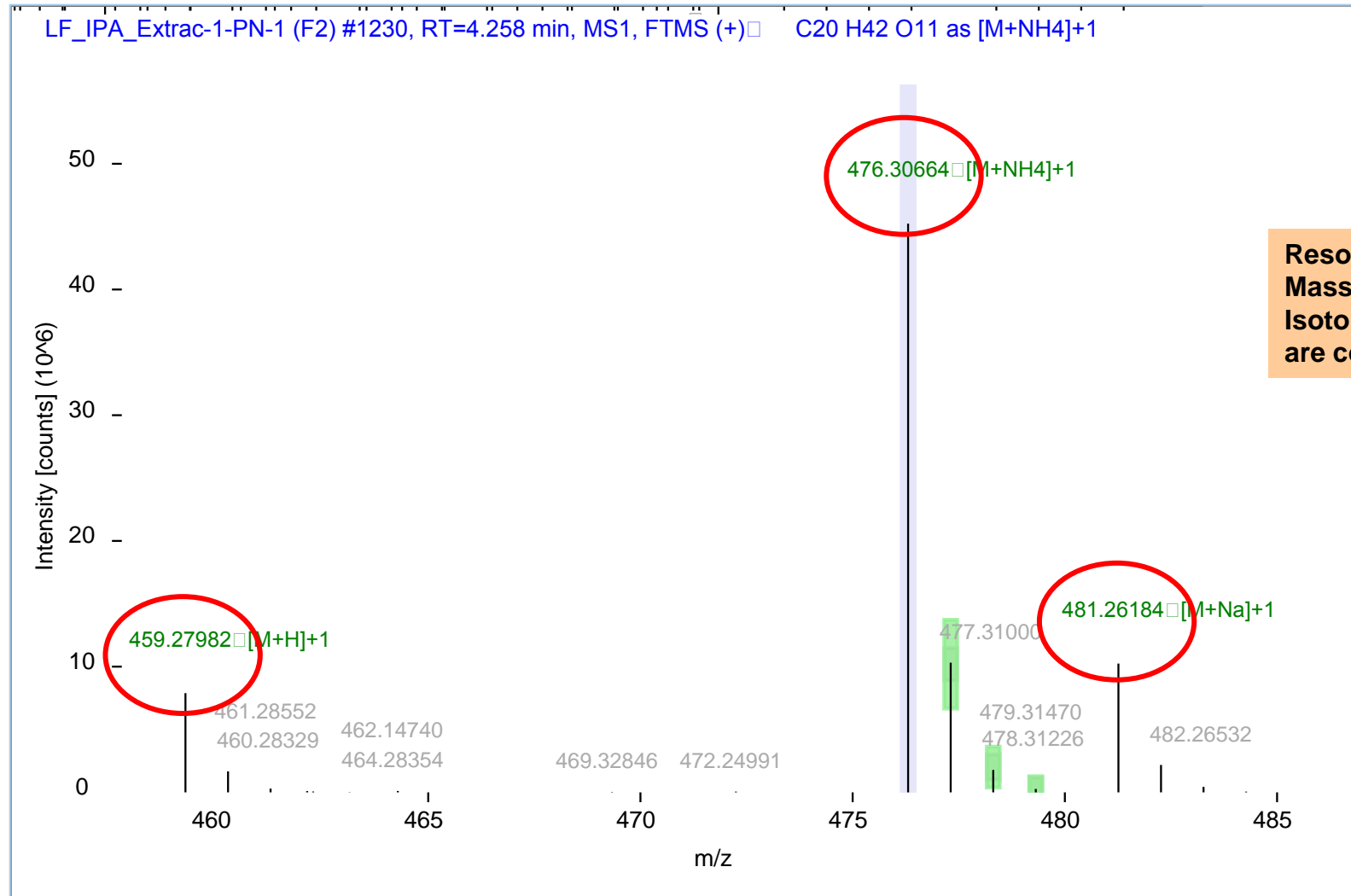
Checked	Name	Formula	Annotation Sc	FISH Coverage	Molecular Weight	RT [min]	Area (Ma	# ChemSpider Re	# mzCloud F	mzCloud Best Mat	Mass List	mzCloud
<input type="checkbox"/>	Oleamide	C18 H35 N O	■■■		264.24510	17.335	146255525	112	4	98.5		
<input type="checkbox"/>	Melamine	C3 H6 N6	■■■		126.06560	0.472	106680600	7	5	100.0		
<input checked="" type="checkbox"/>	Hexamethoxymethyl melamine	C15 H30 N6 O6	■■■		390.22225	7.621	106255412	3	3	98.7		
<input type="checkbox"/>	Eicosapentaenoic acid	C20 H30 O2	■■■		302.22429	16.490	96918439	710	10			
<input type="checkbox"/>	6-Propyl-2-naphthol	C13 H14 O	■■■		186.10445	9.903	89008975	397	12			
<input type="checkbox"/>	Methamphetamine	C10 H15 N	■■■		149.12048	1.070	87923353	297	4	93.7		
<input type="checkbox"/>	pro-ser-arg	C14 H26 N6 O5	■■■		358.19619	7.621	82384299	4	6			

Below the main table, there is a sub-table with the following data:

Checked	Molecular Weight	RT [min]	FWHM [min]	Max. # MI	# Adducts	Area	Study File ID
<input type="checkbox"/>	390.22219	7.619	0.045	4	2	106255412	F6
<input type="checkbox"/>	390.22232	7.624	0.048	4	2	98027607	F3

sub-tables →

Component Detection with Adducts Grouping



Result Filters - Flexible Result Review

The screenshot shows a software window titled "Result Filters" with a sidebar on the left and a main workspace on the right. The sidebar contains a list of filter categories, each with an "ON" button and a radio button. The "Compounds" category is selected, indicated by a green dot. The main workspace displays a tree view under the heading "Compounds". A yellow box labeled "AND" is connected to two filter rules. The first rule is "Background is false" with a "Remove" button. The second rule is "Area (Max.) is greater than or equal to 5000000.00" with a "Remove" button. Below the workspace are several control buttons: "Show all tables" (checkbox), "Load", "Save", "Save As...", "Clear All", "Clear", and "Apply Filters".

Filtering the result based on your need

Multiple Database Searching in Parallel to Identify Known Unknowns

The screenshot displays the Compound Discoverer 2.1.0.398 interface. The top section shows a chromatogram with a peak at 7.618 minutes. The middle section shows a mass spectrum with a base peak at m/z 177.08813. The bottom section shows a table of search results.

Checked	Name	Formula	Annotation Sc	FISH Coverage	Molecular Weight	RT [min]	Area (Ma)	# ChemSpider Re	# mzCloud f	mzCloud Best Mat	Mass List	mzCloud Bes	Group Areas	Group CV [%]
<input type="checkbox"/>	Oleamide	C18 H35 N O	■■■		264.24510	17.335	146255525	112	4	98.5			1.23e4 1.38e8	29 9
<input type="checkbox"/>	Melamine	C3 H6 N6	■■■		126.06560	0.472	106680600	7	5	100.0			1.06e8 4.17e4	1 10
<input checked="" type="checkbox"/>	Hexamethoxymethyl melamine	C15 H30 N6 O6	■■■		390.22225	7.621	106255412	3	3	98.7			1.93e3 1.02e8	1 6
<input type="checkbox"/>	Eicosapentaenoic acid	C20 H30 O2	■■■		302.22429	16.490	96918439	710	10			83.0	2.50e3 9.34e7	1 5
<input type="checkbox"/>	6-Propyl-2-naphthol	C13 H14 O	■■■		186.10445	9.903	89008975	397	12			84.9	4.01e7 8.40e7	22 8

Checked	Compound Match	Structure	Name	Formula	Molecular Weight	ΔMass [Da]	ΔMass [ppm]	Type	Scan #	Match	Best Match	Best Sim. Match	mzCloud ID
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		Hexamethoxymethyl melamine	C15 H30 N6 O6	390.22268	0.00043	1.11	Identity	3394	98.5	98.7	98.2	2645

Mirror plot for each mzVault hit: observed MS2 vs. library MS2

- Matches collision energy between raw file MS/MS and reference MS/MS

Sub table show detailed info for compound

Add Chemspider Search Result to “Structure Proposal and Apply FISH” for Unknown ID

The screenshot displays the Compound Discoverer 2.1.0.398 interface. The main window is divided into several panes: Chromatograms, Mass Spectrum, and a table of search results. A red box highlights the 'Add to Structure Proposals and Apply FISH Scoring' option in the context menu. A red arrow points from this option to the 'Specify FISH Scoring Settings' dialog box, which is also highlighted with a red box. The dialog box shows settings for FISH scoring, including 'Annotate full spectrum tree', 'Use general rules', 'Use fragmentation libraries', 'Allow aromatic cleavage', 'Max. Depth', 'High accuracy mass tolerance', 'Low accuracy mass tolerance', and 'S/N threshold'. A red arrow points from the 'Specify FISH Scoring Settings' dialog box to the 'FISH Scoring Queue' pane, which shows the progress of the scoring process for the selected compound.

Chromatograms

Group By: Solvent Type (2/2), Sample Type (1/1), File (2/2)

Filter By: Solvent Type, Sample Type, File

Mass Spectrum

IPAH₂O_Extract_2 (F1) #9355, RT=35.342 min, MS1, FTMS (+)
C32H64N2O2 as [M+H]⁺

F1 #9355, RT=35.342 min, M:
F1 #9363, RT=35.371 min, M:
F1 #9364, RT=35.375 min

Intensity (counts) (10⁶)

m/z

Specify FISH Scoring Settings

Annotate full spectrum tree
 Use general rules
 Use fragmentation libraries
 Allow aromatic cleavage
5 Max. Depth

High accuracy mass tolerance: 2.5 mmu
Low accuracy mass tolerance: 0.5 Da
S/N threshold: 3

OK Cancel

FISH Scoring Queue

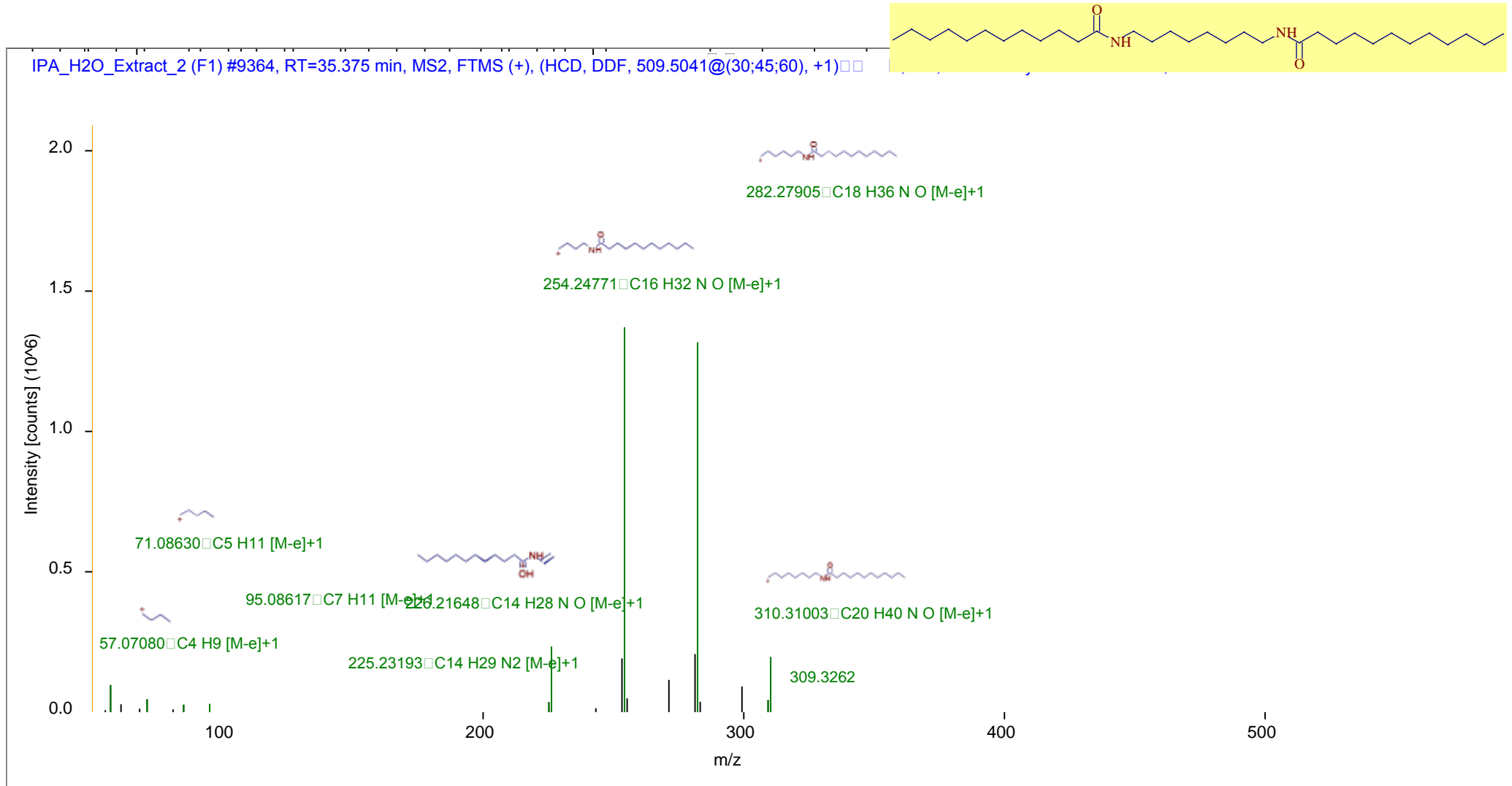
Name: N,N'-1,8-Octanediyldi
MW [Da]: 508.49678
Processing Since: 5 ms
State: Processing

Checked	Name	Molecular Weight	RT
<input type="checkbox"/>	Dimethyl 2,13-	1046.73669	
<input type="checkbox"/>	3-Methoxy pro	386.26670	
<input checked="" type="checkbox"/>	N,N'-1,8-Octan	508.49683	
<input type="checkbox"/>	N-[2-(Cyclohex	556.30295	
<input type="checkbox"/>		754.48604	

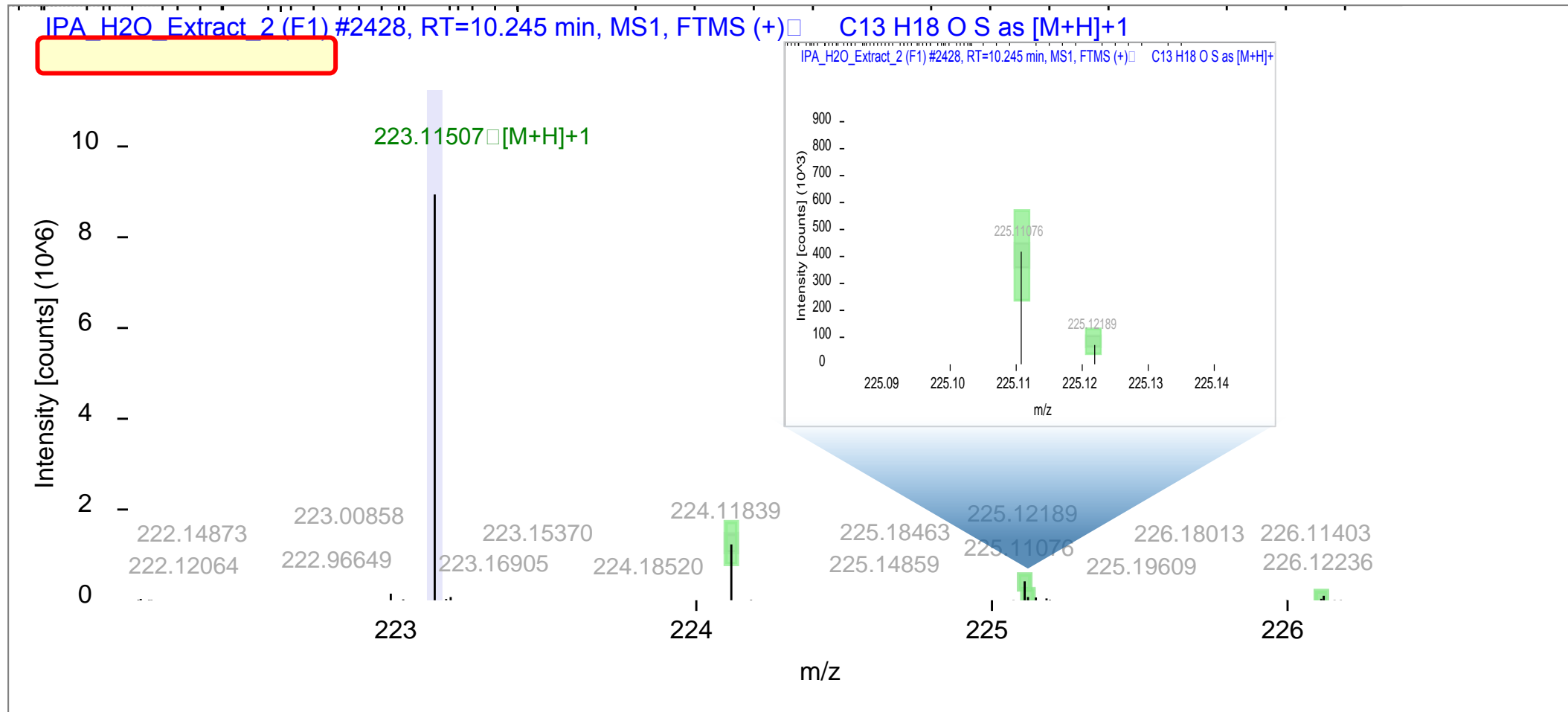
Found Match	Structure	Formula	Molecular Weight	ΔMass [Da]	ΔMass [ppm]	CSID	# References	
		N,N'-1,8-Octanediyldidodecanamide	C32H64N2O2	508.49676	-0.00007	-0.13	2523028	6

FISH stands for “Fragment Ion Search”

FISh Scoring Result: Fragment Ion Matching and Fragment Structure Annotation



Unknown Structure Elucidation Based on CD 2.1 "Predicted Compositions"



Unknown Structure Elucidation Using Compound Annotation Editor and FISh Scoring

Compound Annotation Editor

Description FISh Scoring

Formula: C13 H18 O S

Formula to fit:

Molecular weight / error in Da: 222.10784 -0.00005

Molecular weight to fit: 222.10789

Name:

ChemSpider... Apply FISh scoring Save Cancel

Propose structure based on
“Predicted Composition”
and MS/MS fragments



Compound Annotation Editor

Description FISh Scoring

Annotate full spectrum tree High accuracy mass tolerance: 2.5 mmu

Use general rules

Use fragmentation libraries Low accuracy mass tolerance: 0.5 Da

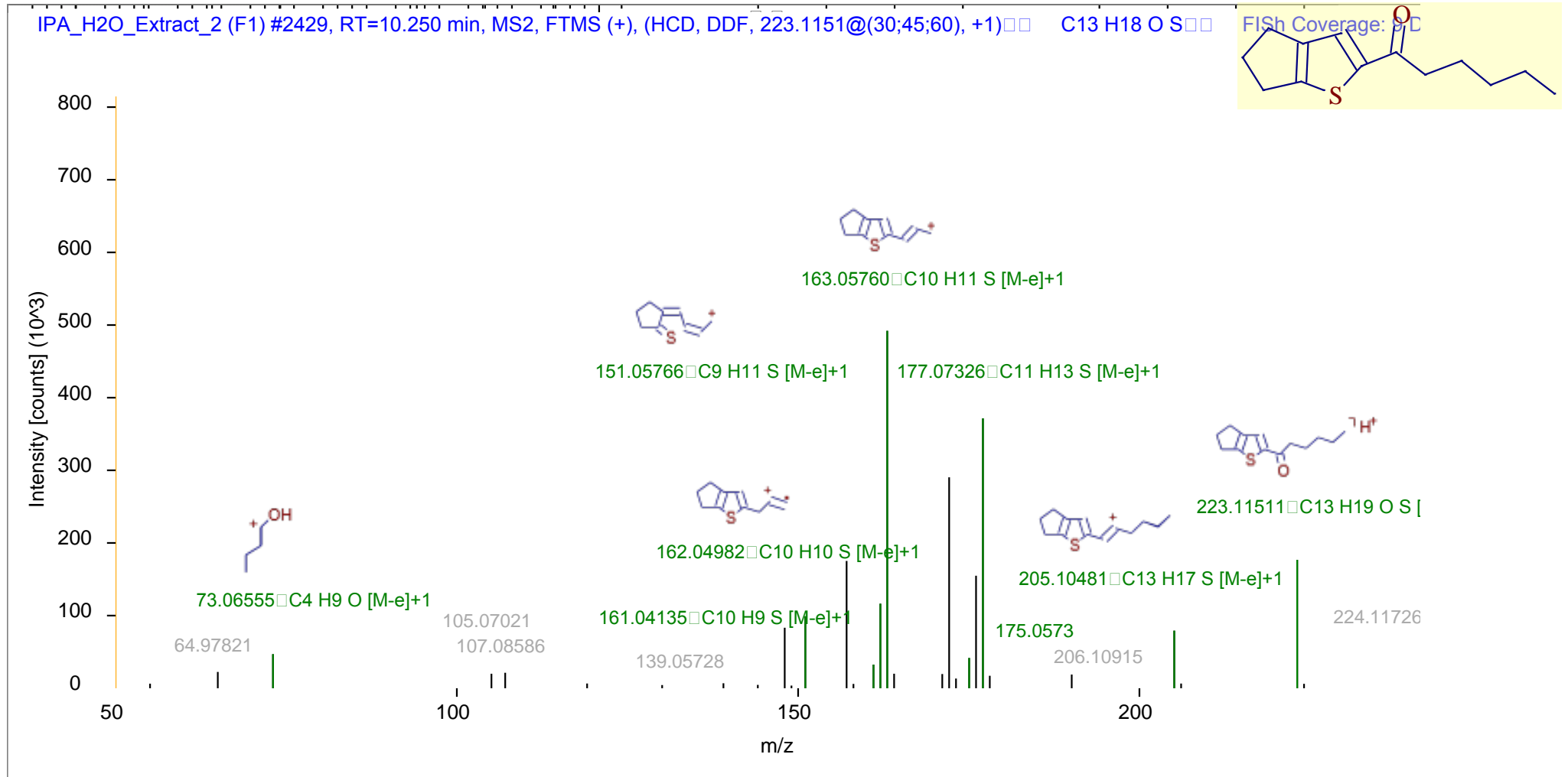
Allow aromatic cleavage

5 Max. Depth S/N threshold: 3

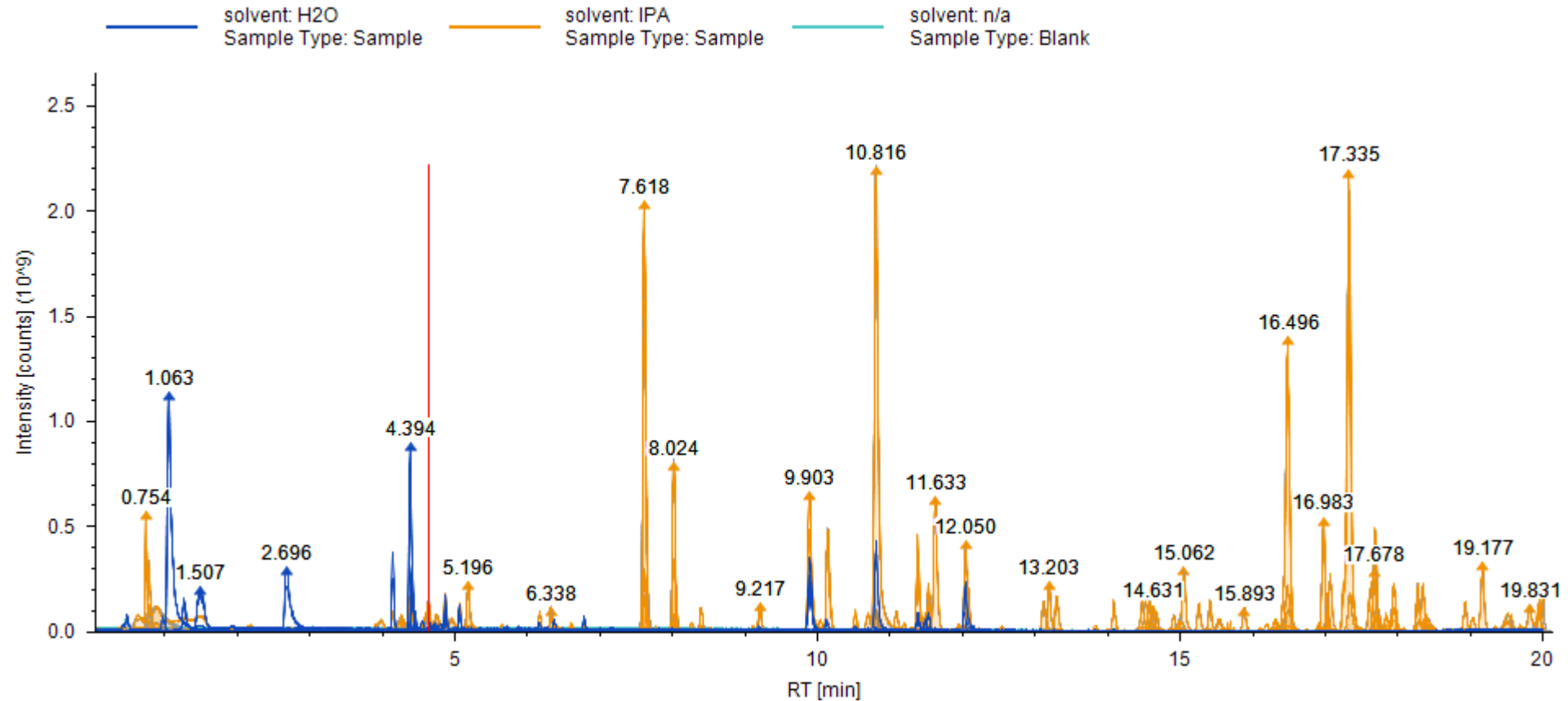
ChemSpider... Apply FISh scoring Save Cancel

Apply “FISh Scoring”
to search the embedded
“HighChem Fragment Library”

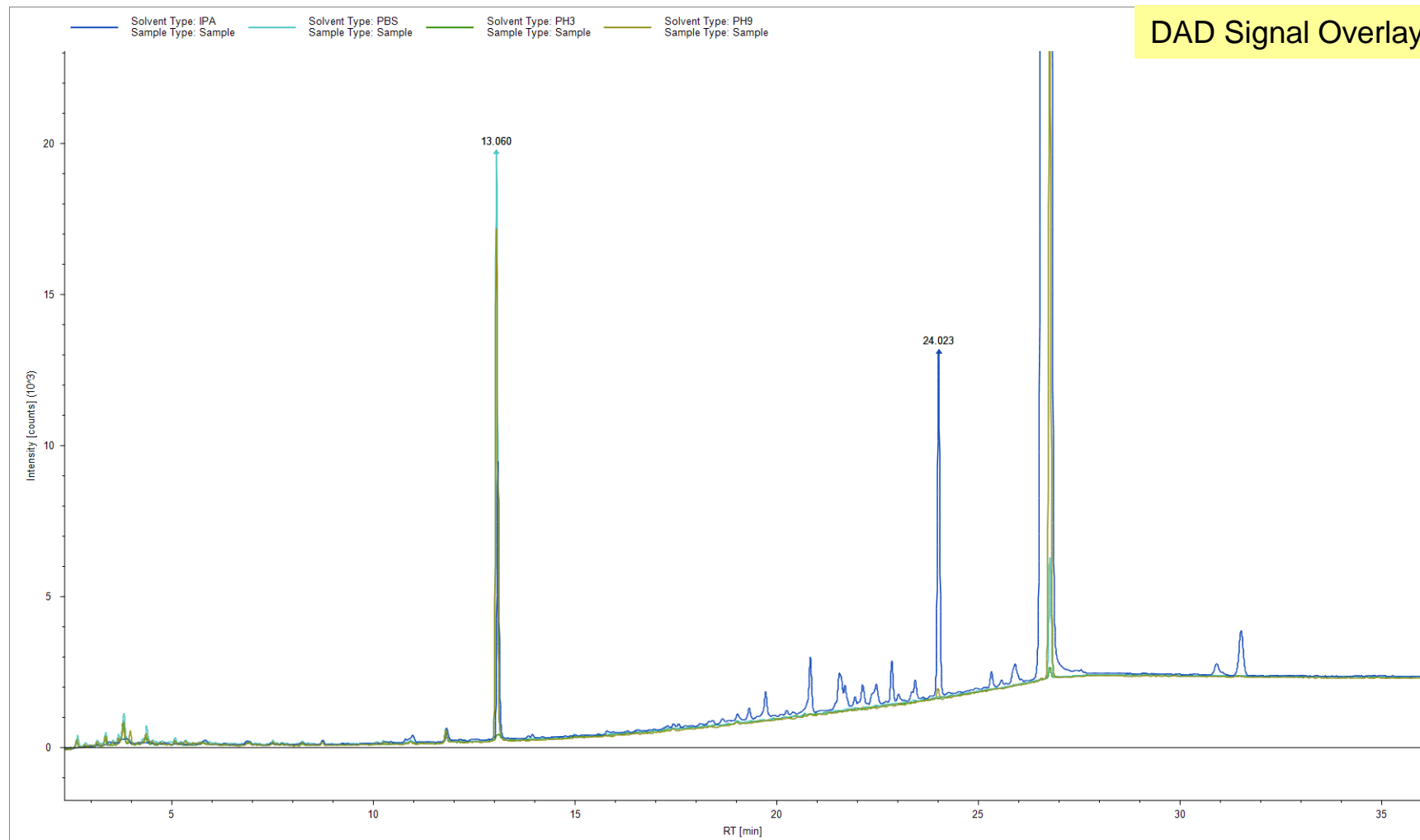
FISh Scoring Result: Fragment Ion Matching and Fragment Structure Annotation



Specialized Traces

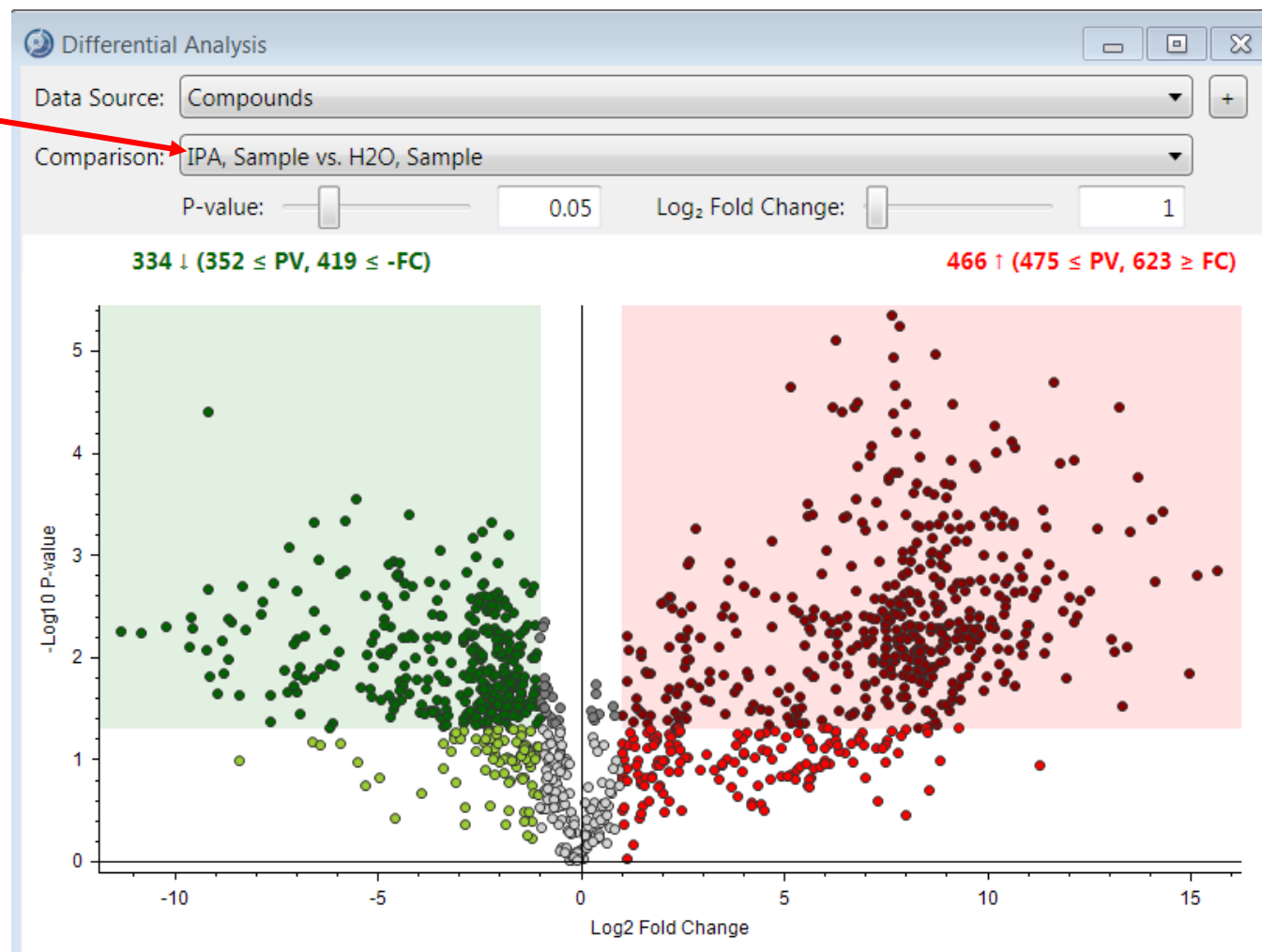


Specialized Traces Provide Additional Information




CD 2.1 Differential Analysis Feature: Volcano Plot

Using the interactive volcano plot to find compounds that are significantly different between two sample groups

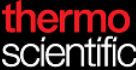


<http://mycompounddiscoverer.com>



Compound Discoverer

Integrated solutions for small molecule structure identification



- HOME
- WHAT IS COMPOUND DISCOVERER?
- HELP BUTTON
- REQUEST FEATURE...
- RESOURCES
- TUTORIALS

Compound Discoverer 2.1 Released! Get your Demo here.

JUL 31 Posted by [Tim Stratton](#)

For current Compound Discoverer 2.0 users:
The electronic upgrade to Compound Discoverer 2.1 is free! Follow the download instructions below and use the instructions for the CD 2.0 to CD 2.1 upgrade.

For new users:
To download the Compound Discoverer 2.1 Demo (CD 2.1 demo), go to the Thermo Scientific Software Portal (Flexera) and download it from the "Compound Discoverer 2.1 Demo" folder.
[CLICK HERE FOR DETAILS.](#)

Posted in [Welcome](#)

Tags: [Information](#) Comments Off

Compound Discoverer at ASMS 2017

APR 14 Posted by [Tim Stratton](#)

Thanks to everyone who was able to join us at this years Compound Discoverer Users Meeting and parallel Node Developer Workshop at ASMS this year!

We've already heard great feedback from several people and, because of that, we plan to make these meetings a regular occurrence and improve them even more in the future.

Thank you!

www.thermofisher.com/learnleachables

Kate.comstock@thermofisher.com

Some of the Common Additives

- Plasticizers
- Flame Retardants
- Impact Modifiers
- Antioxidants
- Antimicrobials
- UV Stabilizers
- Colorants
- Lubricants & processing aids