

AET

AET

40

40

30

30

20

20

10

10

µg

ThermoFisher
SCIENTIFIC

Analytical Workflows for Extractable and Leachable Impurities

Pharma & Biopharma Tours | 2016

Introduction



- What is required for extractables testing?

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- Overview of analytical capabilities for 4 extractable and leachable analysis workflows

- What is required for extractables testing?
- Overview of analytical capabilities for 4 extractable and leachable analysis workflows
- Introduce NEW technology for identification and quantification of unknown impurities

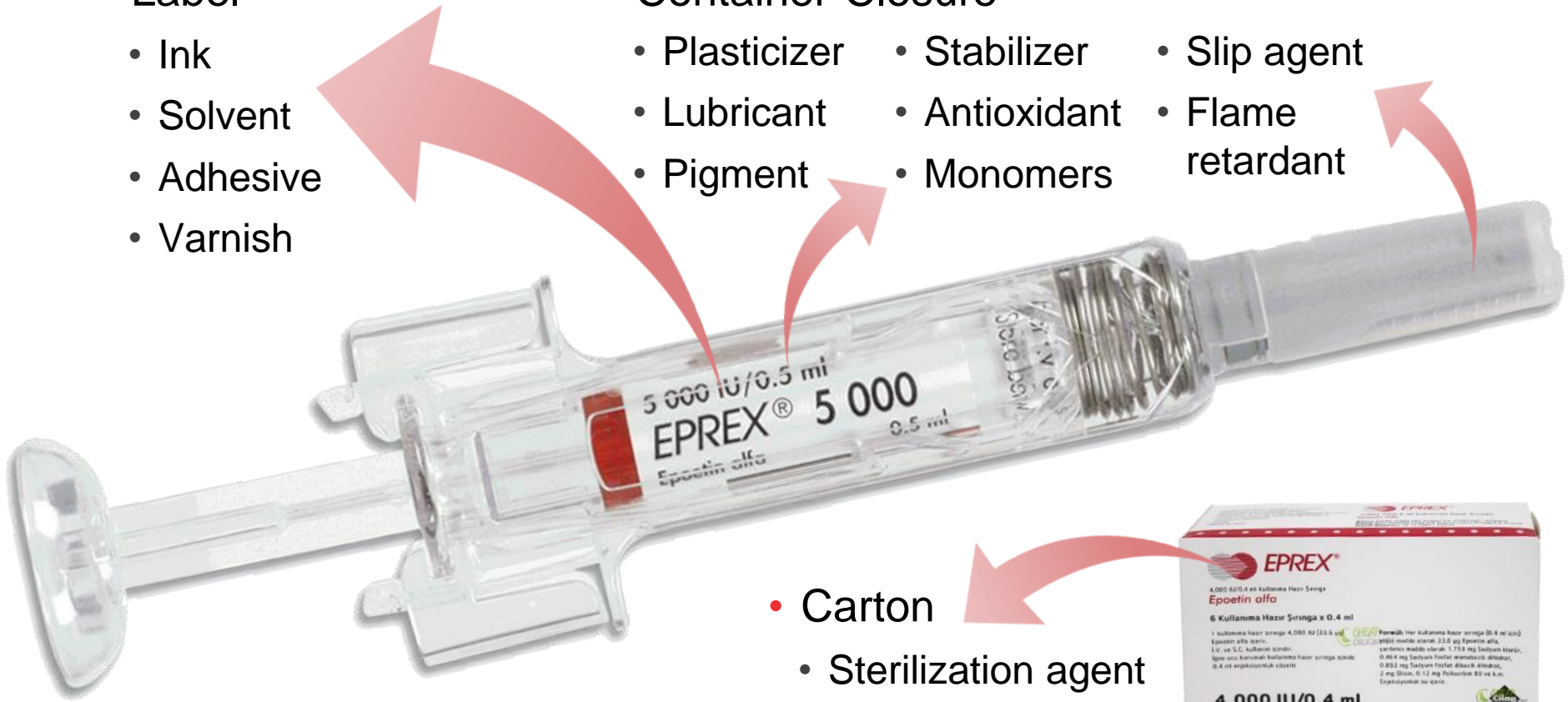
What is there to leach?

- Label

- Ink
- Solvent
- Adhesive
- Varnish

- Container-Closure

- Plasticizer
- Lubricant
- Pigment
- Stabilizer
- Antioxidant
- Monomers
- Slip agent
- Flame retardant



- Carton

- Sterilization agent
- Preservatives
- Sealant & Ink



Extractables & Leachables

- **EXTRACTABLE**

- Chemical released from process equipment, packaging or delivery system; **under laboratory extraction conditions.**

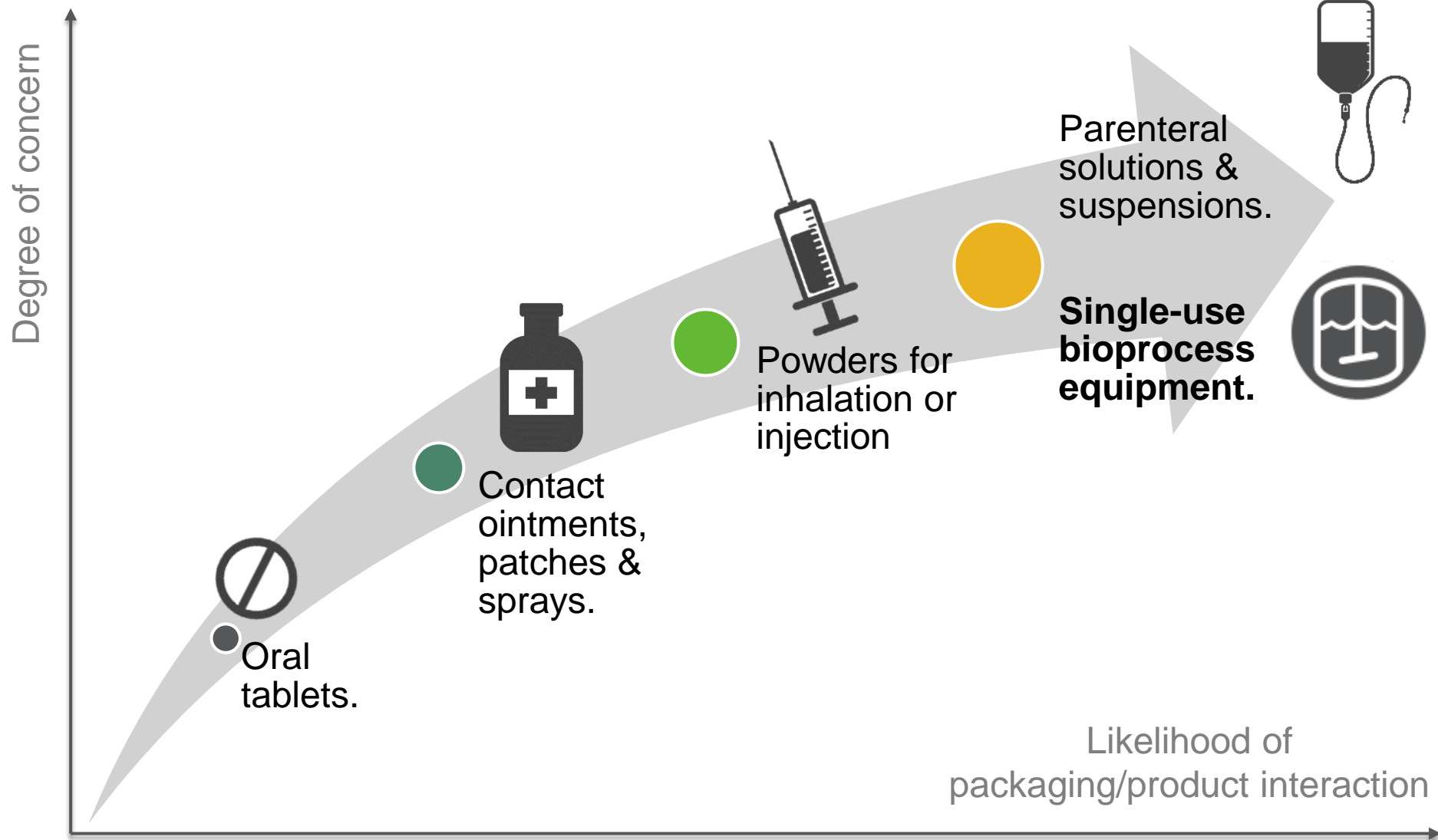


- **LEACHABLE**

- Chemical that **migrates** from process equipment, packaging or delivery system; into drug formulation **under normal usage conditions.**

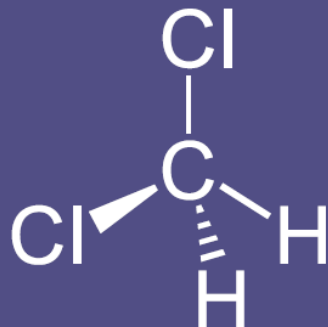


Where are is the greatest concern for leachables?



Analysis of Extractables & Leachables

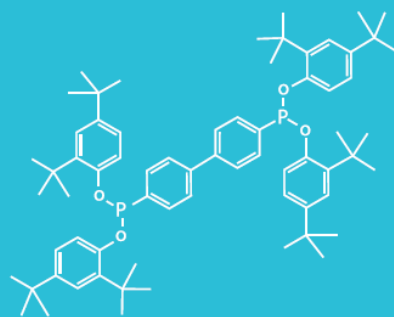
Unknowns
come in all
shapes and
sizes



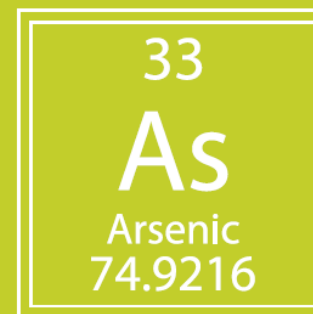
Volatile



Semi-volatile



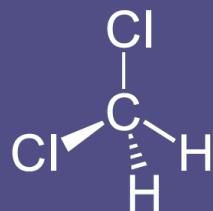
Non-volatile



Elemental

Analysis of Extractables & Leachables

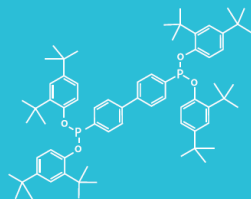
- GC-MS
- GC-HRMS
- Headspace
- EI & CI
- Library



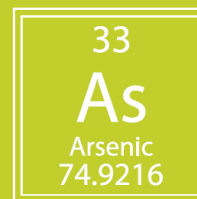
Volatile



Semi-volatile



Non-volatile



Elemental

- ESI & APCI
- LC-UV or CAD
- LC-MS/MS HRAM
- IC-MS
- Library

- GC-MS
- GC-MS/MS HRAM
- EI & CI
- Library

- LC-ICP-MS
- IC-ICP-MS
- ICP-MS
- ICP-OES

Complete solution for Extractables & Leachables

Preparation



Accelerated solvent extraction technology

Consumables



MS certified vials, columns and ultra-pure solvents

Volatiles



Headspace sampling and compliant GC-MS

Semi-volatiles



Advanced Orbitrap-based HRAM GC-MS/MS

Non-Volatiles



Advanced Orbitrap-based HRAM LC-MS/MS

Elemental



Robust, compliant ICP-MS

EXTRACTION

ANALYSIS AND REPORTING

Sample preparation



Principle and Best Practices Recommended

Regulatory guidelines:

- USP Chapter <1663> & <1664>
- Product Quality Research Institute (PQRI)
- BioPhorum Operations Group (BPOG)

“Controlled extraction studies should;

- ***Employ vigorous extraction with multiple solvents of varying polarity***
- ***Incorporate multiple extraction techniques”***



Heated agitation
(2-30 days)



Sonication
(2-5 days)



Soxhlet
(24 Hours)

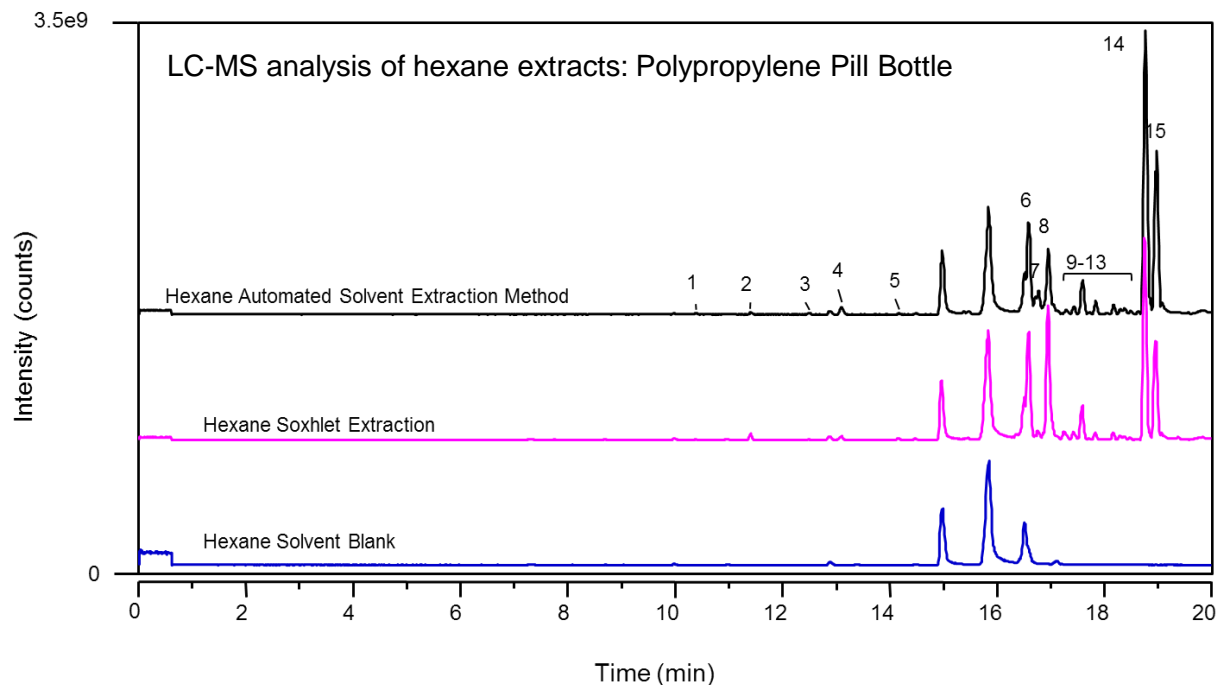


Accelerated solvent
extraction technique
(30 minutes)

Accelerated Solvent Extraction Technique

- Automates sample preparation for solid and semi-solid samples
- Extracts above the boiling point of solvent using elevated pressure
- Extraction time <30 min/sample
- Compliant Chromeleon software control

Thermo Scientific™ Dionex™ ASE™ 350
Accelerated Solvent Extractor System

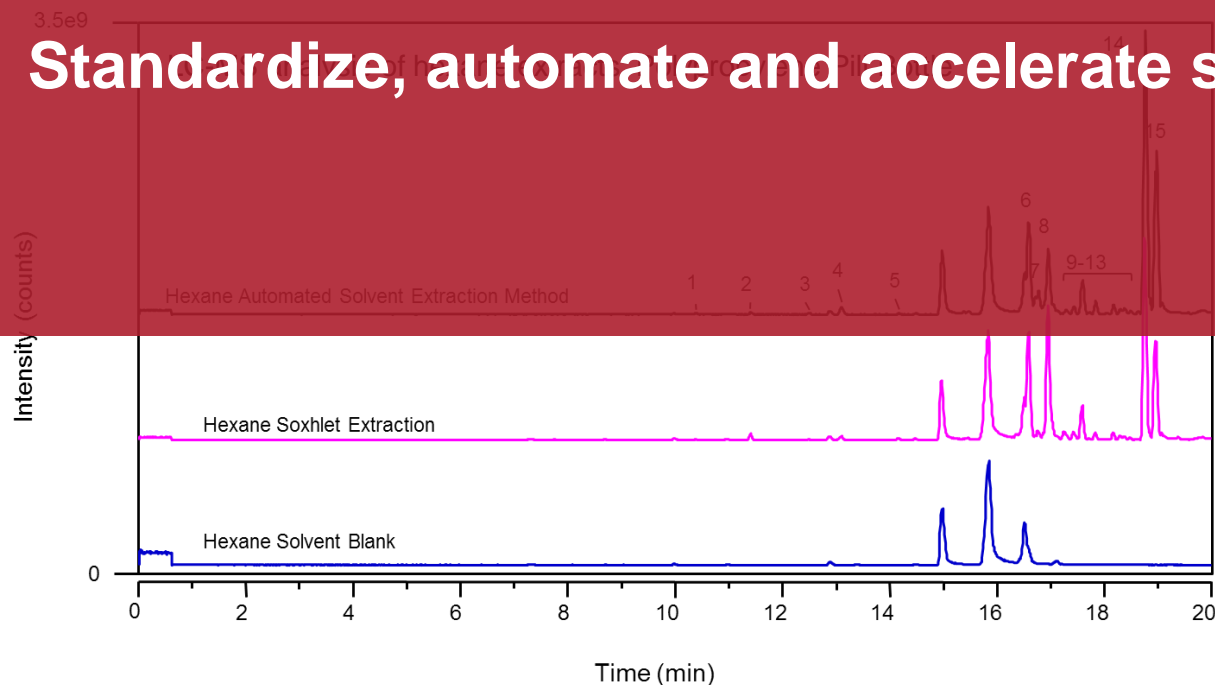


Accelerated Solvent Extraction Technique

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- Extraction time <30 min/sample
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Thermo Scientific™ Dionex™ ASE™ 350
Accelerated Solvent Extractor System

Standardize, automate and accelerate sample preparation

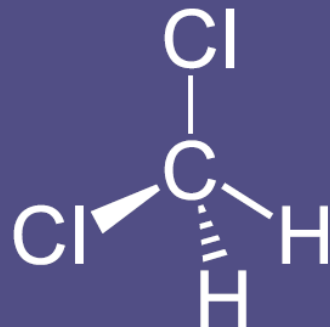


Comparison of Soxhlet vs. Dionex ASE 350 System

Parameter	Soxhlet	Dionex ASE 350 System
Extract solvent used per sample (mL)	160	<30
Total extraction time per sample (min)	1440	<30
Extracted compounds	Same	Same
Extracts peak Intensity Ratio Accelerated Solvent Extraction/Soxhlet		1.4x to 90x

Dionex ASE 350 system delivers faster extractions using less solvent

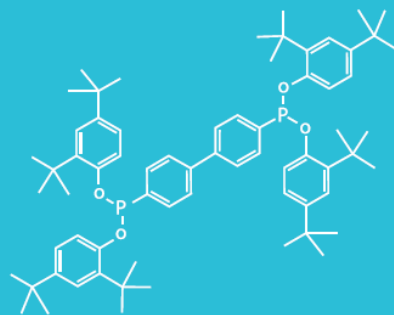
Volatiles



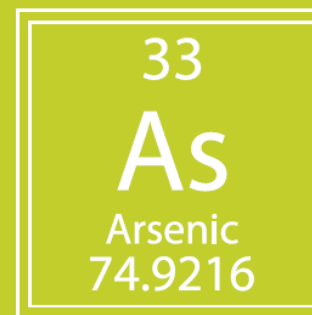
Volatile



Semi-volatile

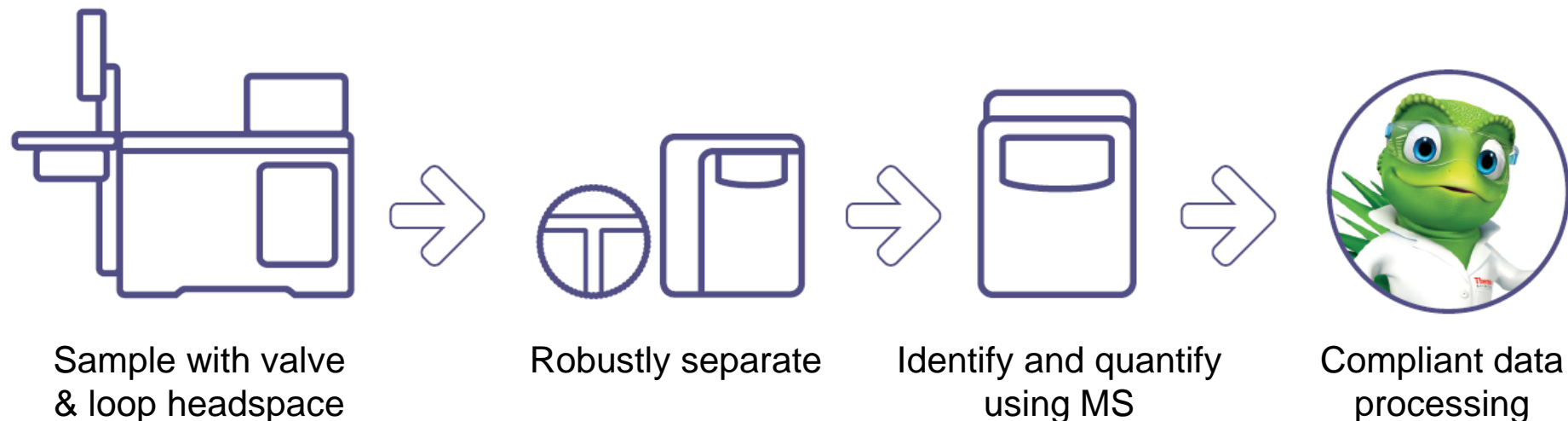


Non-volatile



Elemental

Volatile impurities workflow



- Analogous to **USP 467** Residual solvents workflow
- Molecules are generally known, or simple to identify
- **Routine compliant quantification**



Complete technologies for volatile impurities



Thermo Scientific™ TriPlus™ 300 headspace sampler



Thermo Scientific™ Trace 1310 GC



Thermo Scientific™ TraceGOLD™ TG-624SiIMS GC Columns



Thermo Scientific™ ISQ™ Series GC-MS



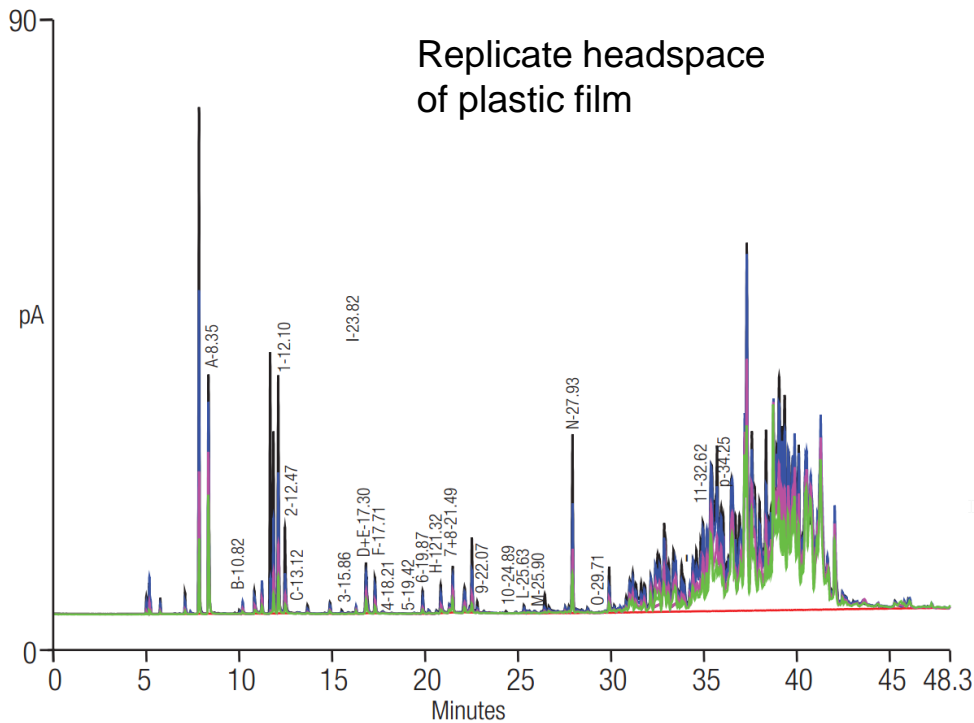
Thermo Scientific™ Dionex™ Chromeleon™ CDS



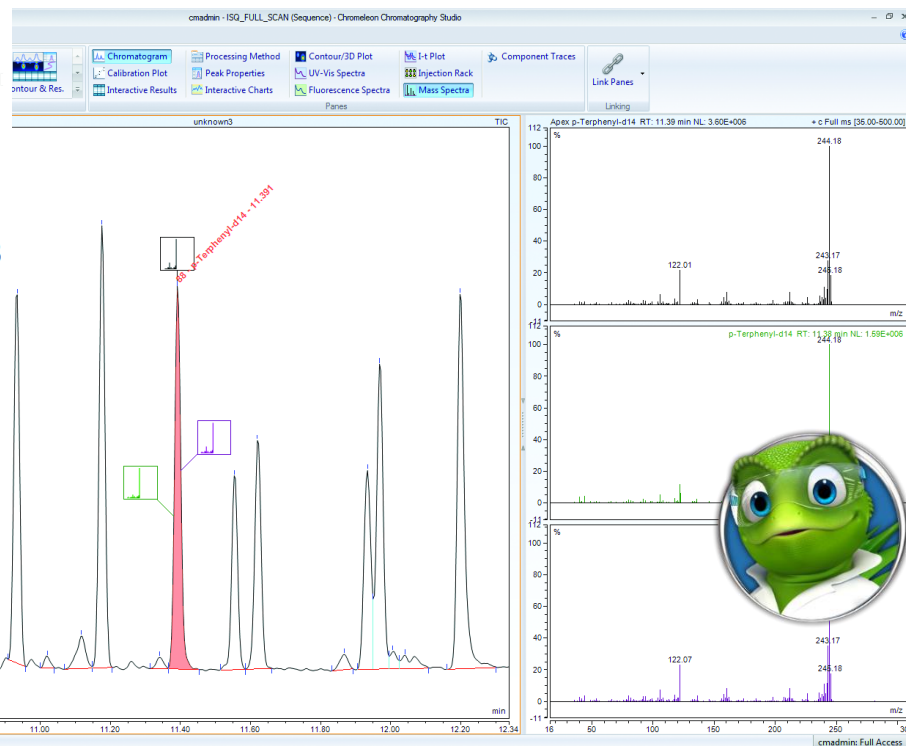
Thermo Scientific™ AppsLab Library™



Volatiles headspace analysis



- Methods available on AppsLab
- One click Chromeleon eWorkflow
- Full **quantitative** and **qualitative** mass spectral analysis

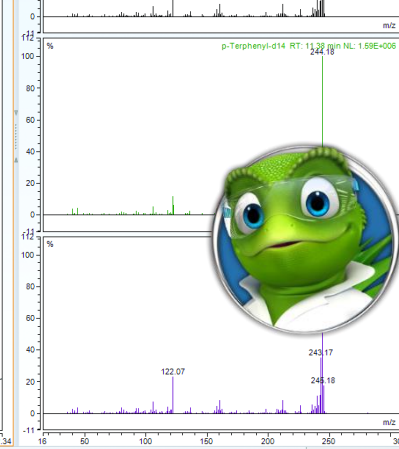
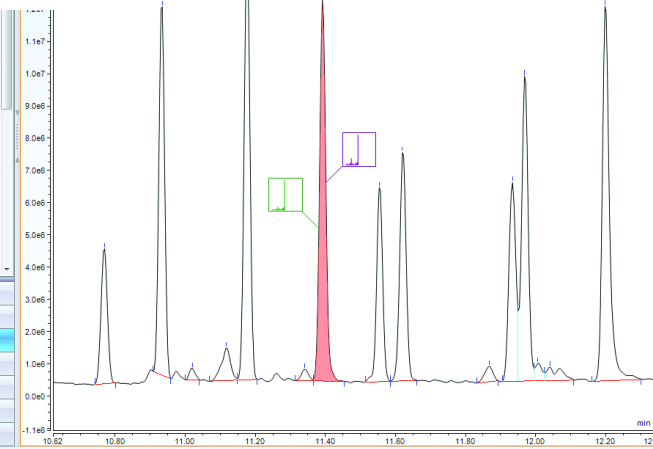


10 unknown2
11 unknown3

Channels
MS Quantitation
TIC

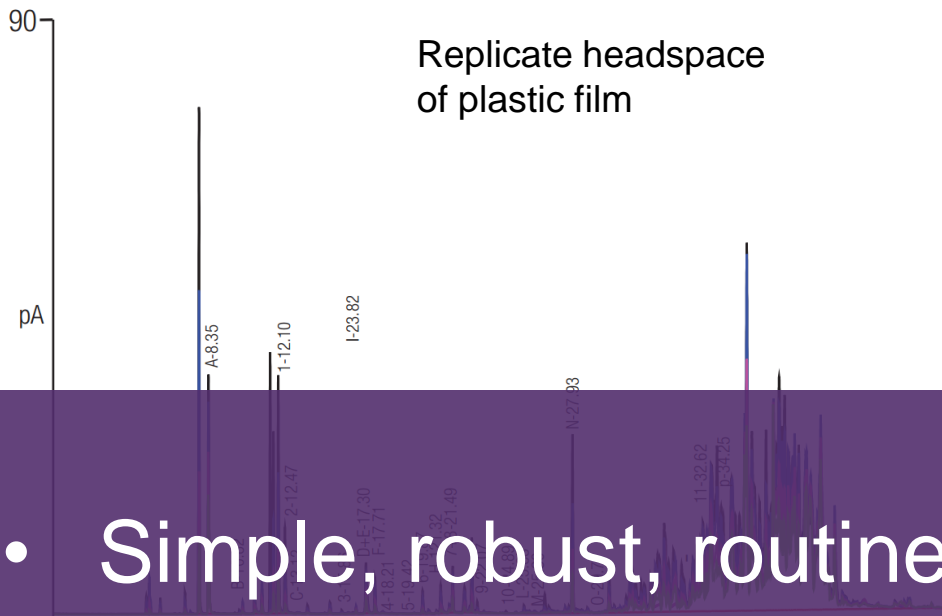
Components
Pentachloroethane
1,3-Dichlorobenzene
1,4-Dichlorobenzene-d4
1,4-Dichlorobenzene
1,2-Dichlorobenzene
Hexachloroethane
Nitrobenzene-d5
1,2,4-Trichlorobenzene
Naphthalene-d8
Hexachloropropene

Injection List
Instrument Method
Data Processing
Report Designer
Electronic Report
Spectral Library



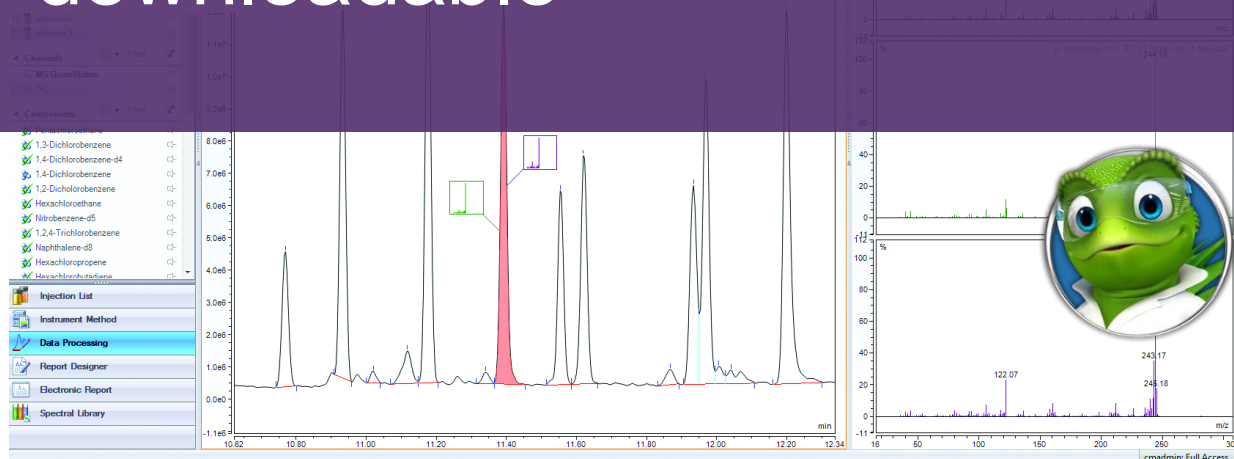
Volatiles headspace analysis

Replicate headspace
of plastic film

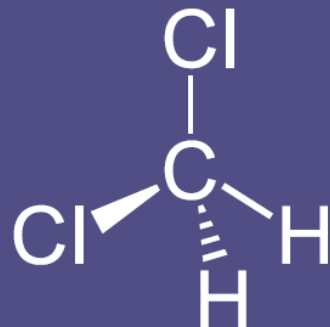


- Methods available on AppsLab
- One click Chromeleon eWorkflow
- Full **quantitative** and **qualitative** mass spectral analysis

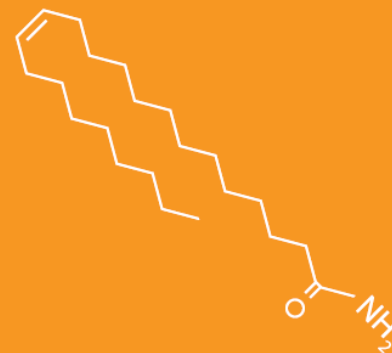
- Simple, robust, routine, compliant analysis
- Methods freely downloadable



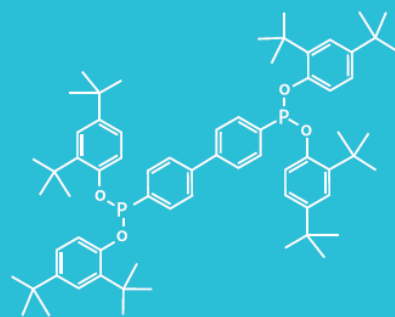
Non-Volatiles



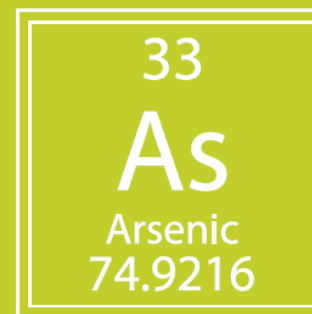
Volatile



Semi-volatile

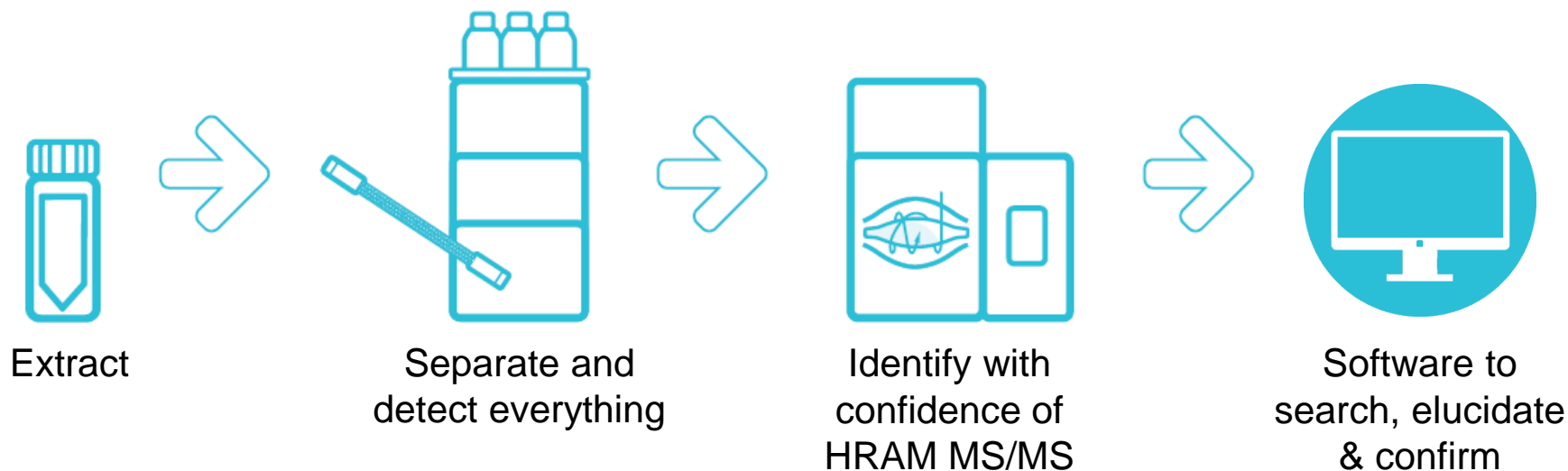


Non-volatile



Elemental

Non-volatiles unknown identification workflow

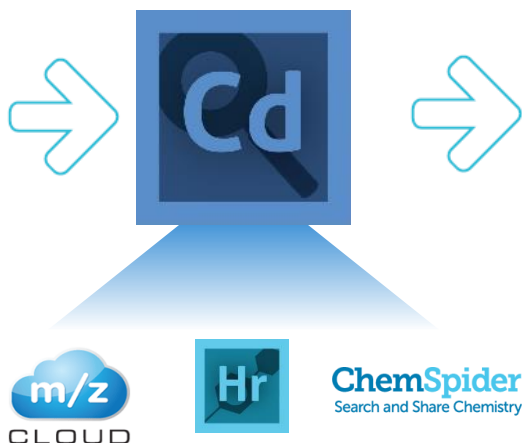
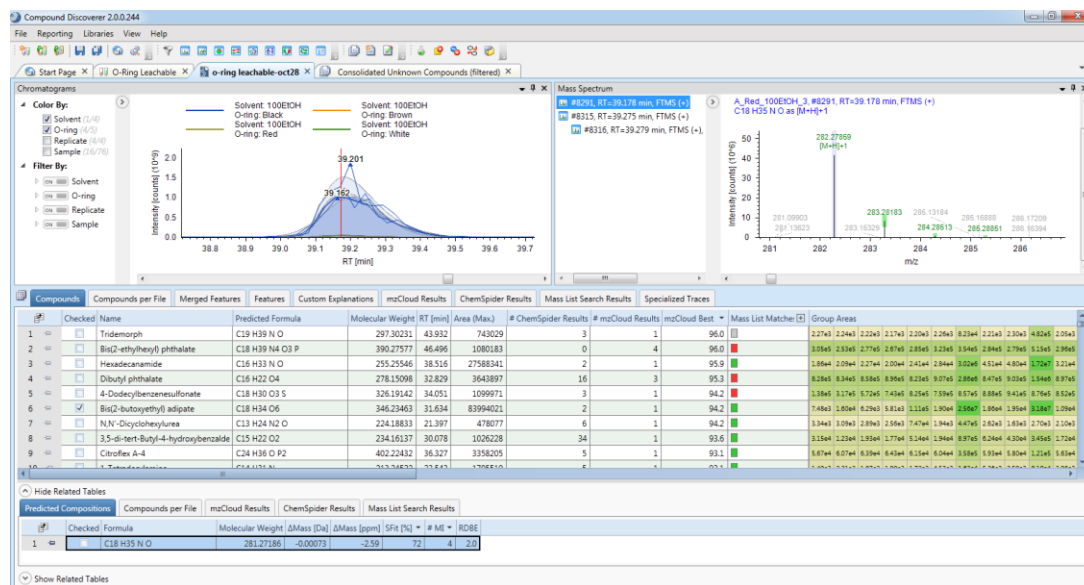
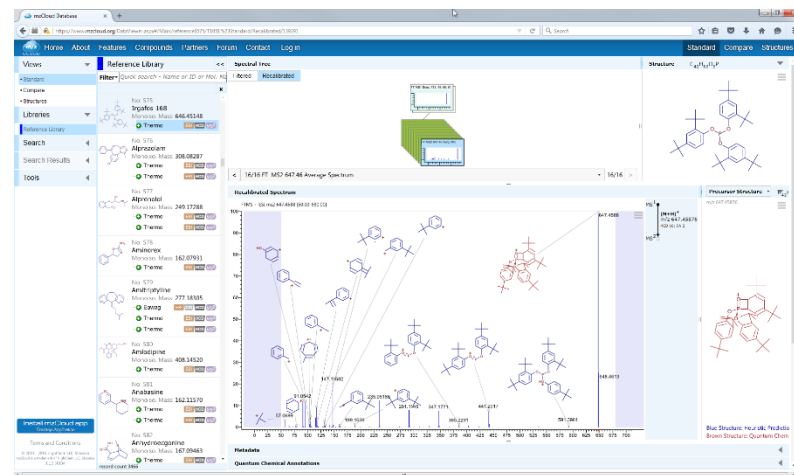


- Catch everything with orthogonal detection
- Detect in both positive and negative ion mode
- Have absolute confidence in elemental composition
- Get full sub-structural information
- Search wide variety of data sources in parallel



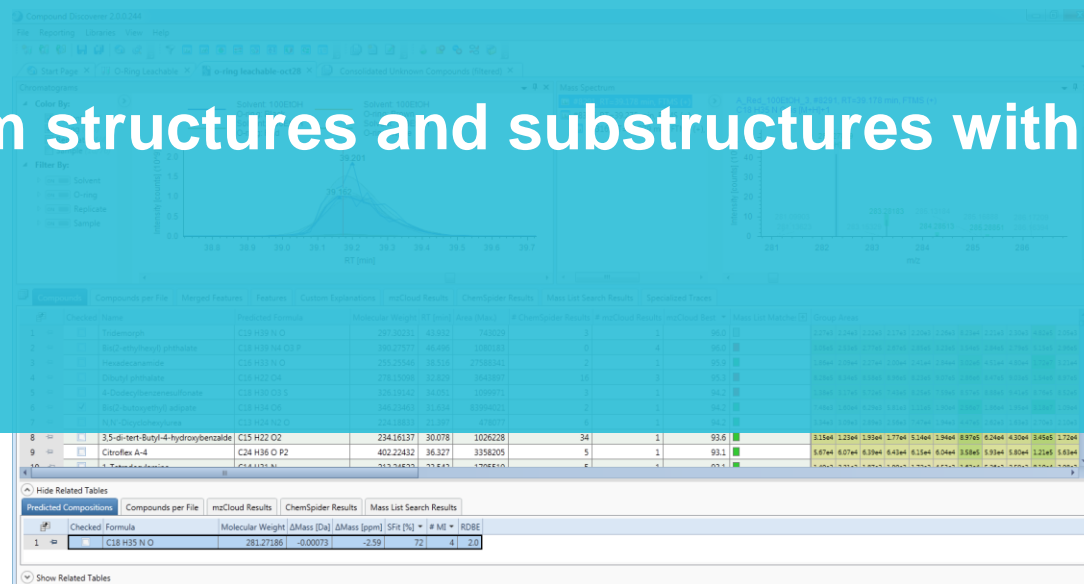
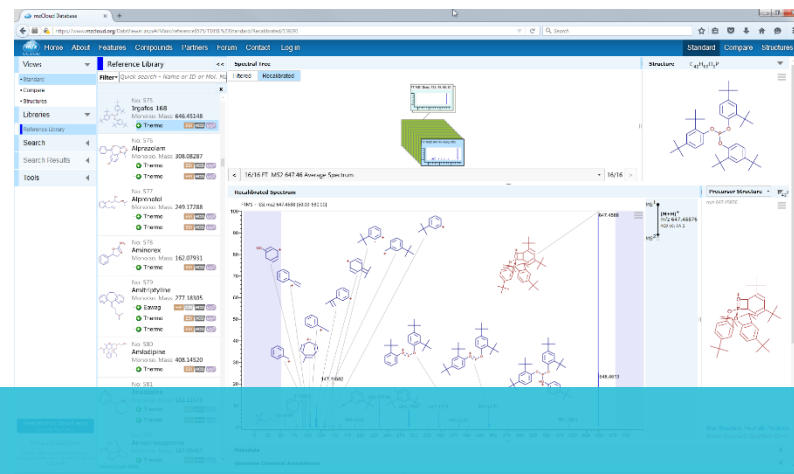
Confidently go from spectra to structure

- Thermo Scientific™ Compound Discoverer™ Software
 - HRAM MS/MS spectra
 - Compare batches and replicates
 - Search multiple databases in parallel including mzCloud.org
 - Deliver one unified report



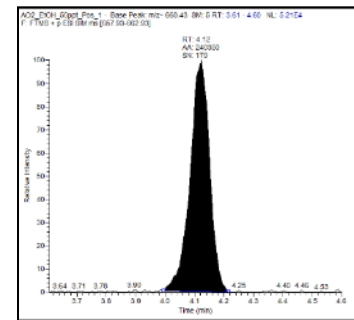
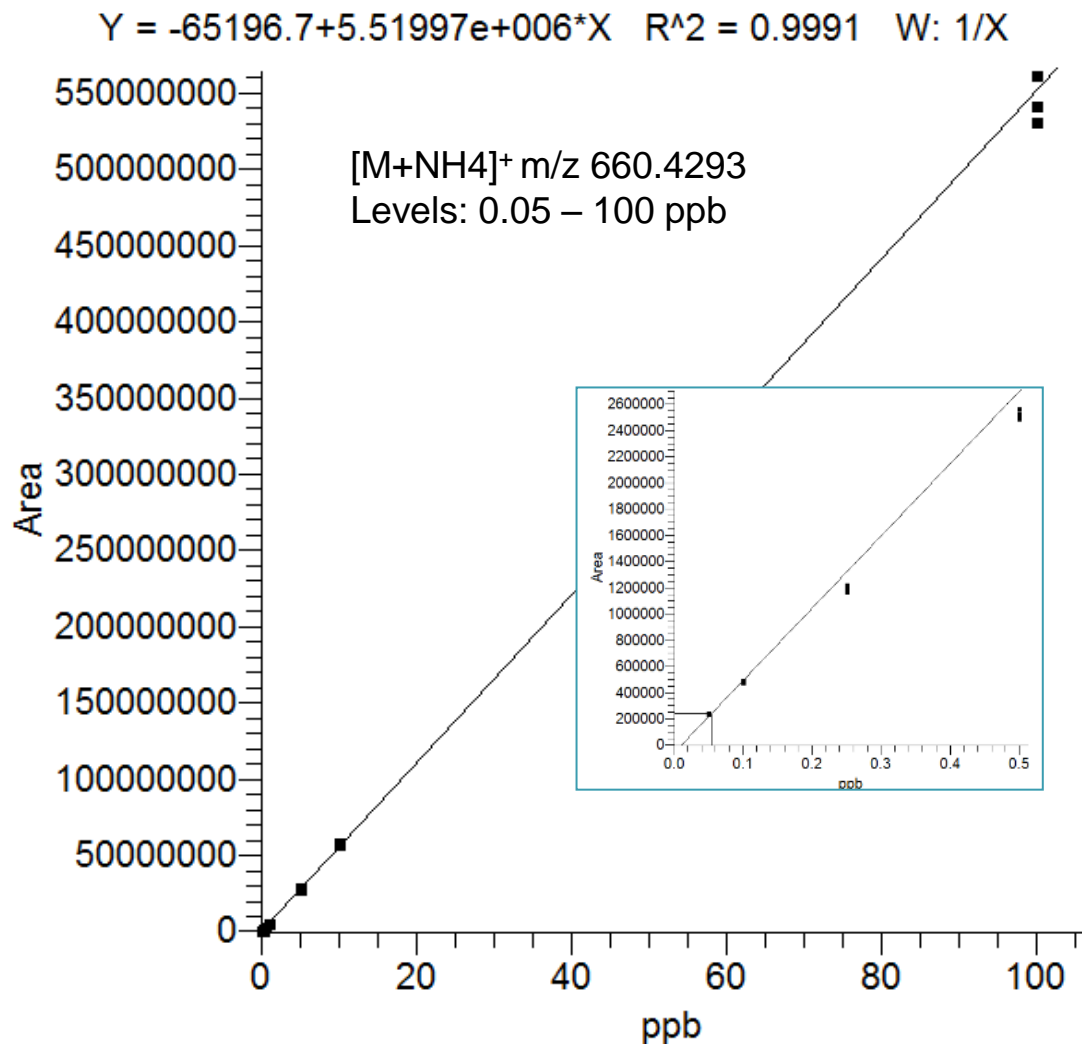
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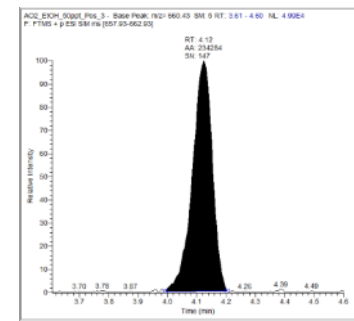
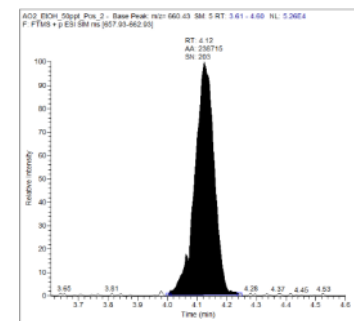


ChemSpider
Search and Share Chemistry

Quantify non-volatile extractables – Irganox1035



+VE



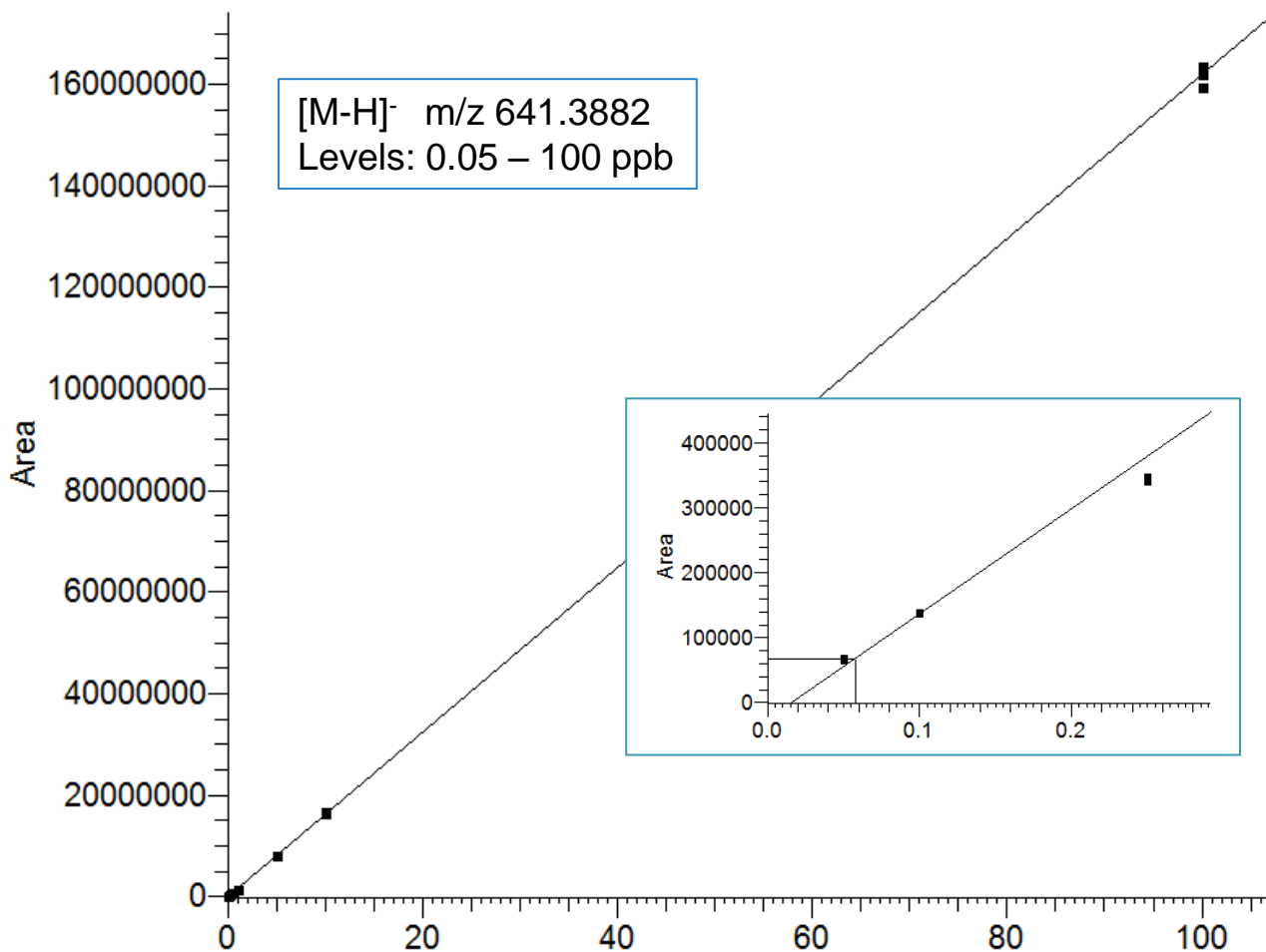
50 ppt
(Triple Injections)

Detect in positive and negative ion mode in the same run

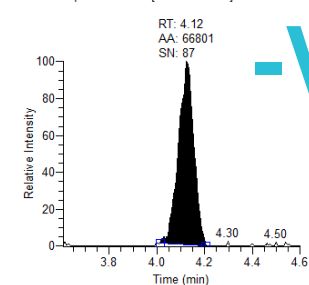
Quantify non-volatile extractables – example Irganox1035

cas 41484-35-9

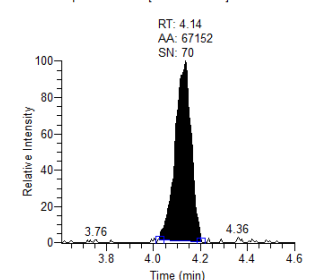
$$Y = -27525.8 + 1.61911e+006 * X \quad R^2 = 0.9998 \quad W: 1/X$$



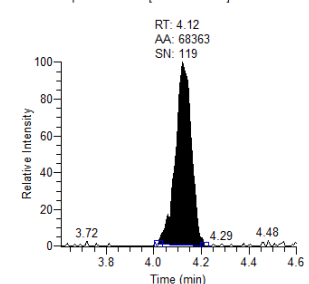
AO2_EtOH_50ppt_Neg_1 - Base Peak: m/z= 641.39 ...
F: FTMS - p ESI SIM ms [638.89-643.89]



AO2_EtOH_50ppt_Neg_2 - Base Peak: m/z= 641.39 ...
F: FTMS - p ESI SIM ms [638.89-643.89]



AO2_EtOH_50ppt_Neg_3 - Base Peak: m/z= 641.39 ...
F: FTMS - p ESI SIM ms [638.89-643.89]



50 ppt
(Triple Injections)

Full sensitivity in negative ion mode

See what you're missing with Charged Aerosol Detection

- Detection without chromophore
- Quantify without exact standards
 - Relative quantification due to consistent response
 - Use virtually any standard for simplified AET calculations
- Consistent analyte response
- Four orders dynamic range



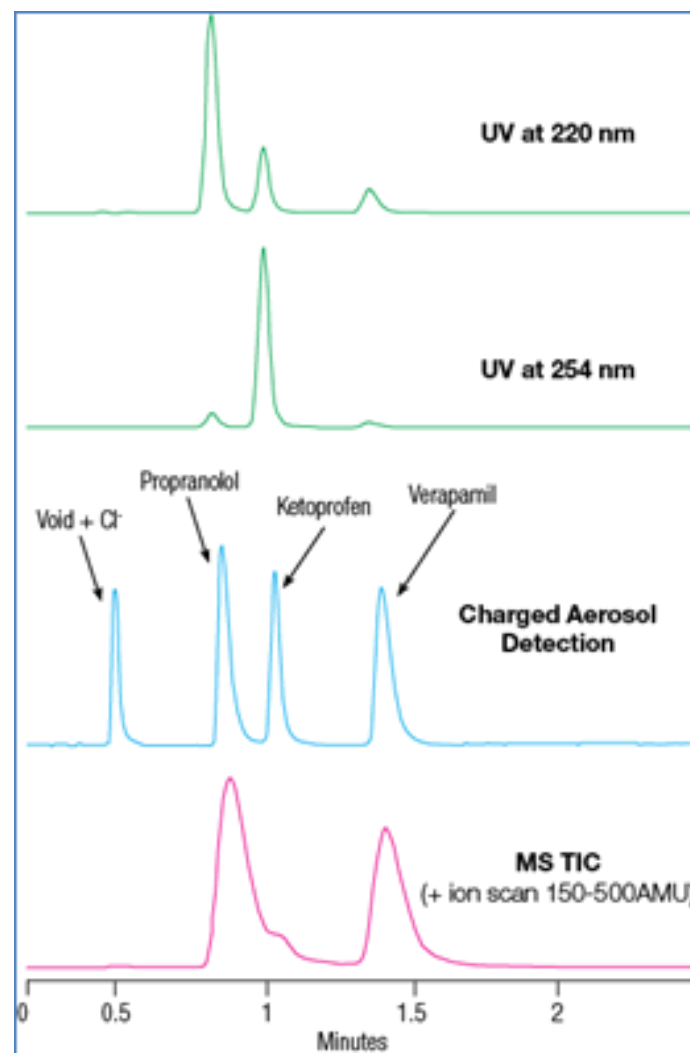
Released 2015

**Thermo Scientific™
Vanquish™ Charged
Aerosol Detector**

Full integration with Thermo Scientific™ Vanquish™ UHPLC platform, slide-in module design, reduced flow path for optimum operation

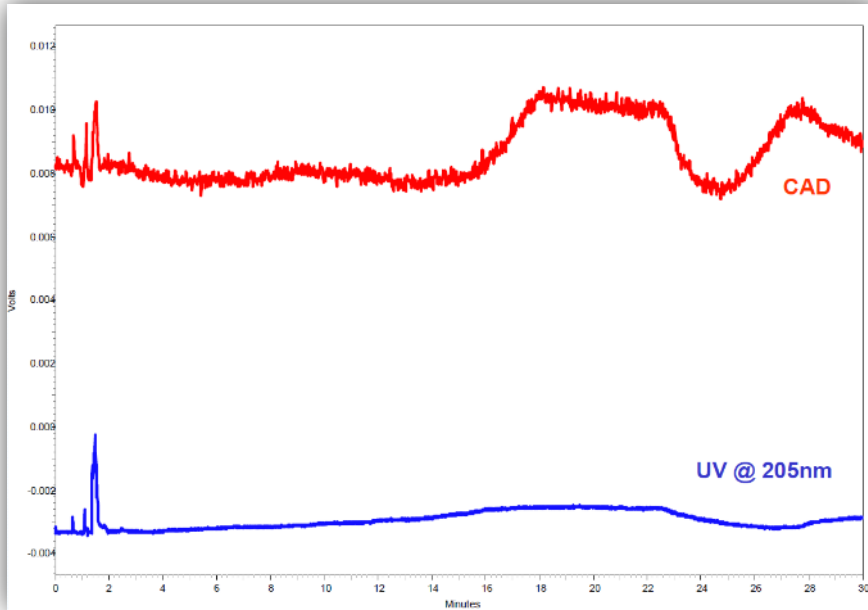


Comparison of Charged Aerosol Detection to UV and MS



CAD for extractables and leachables

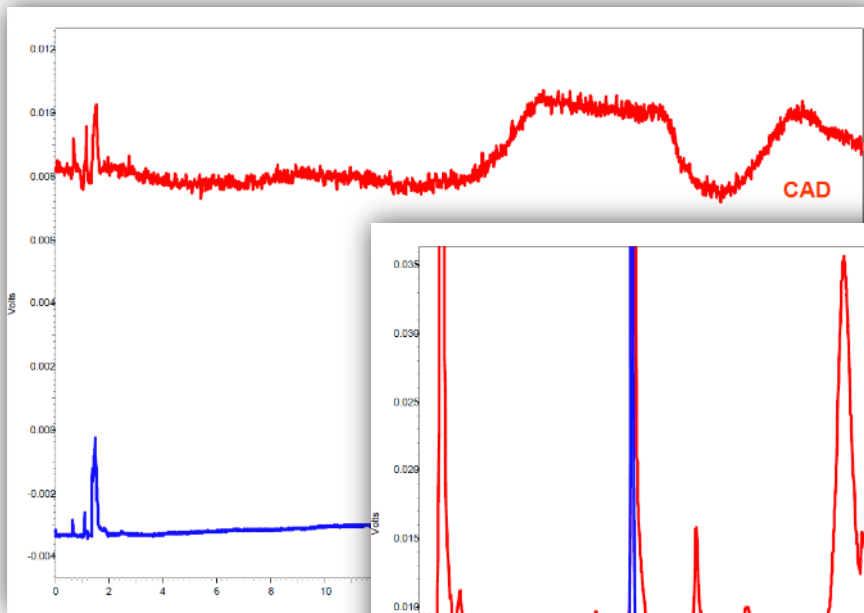
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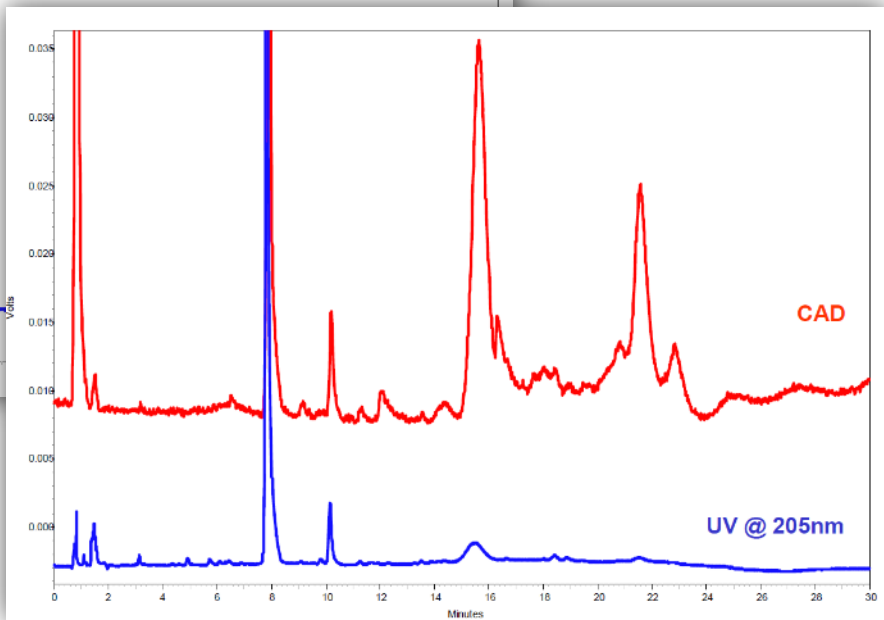
Data from ESA Biosciences, Inc., Chelmsford, MA

CAD for extractables and leachables

IPA blank



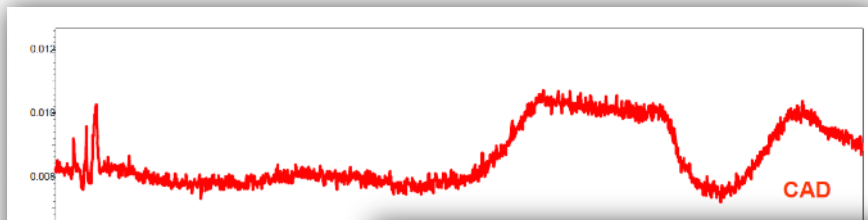
Rubber



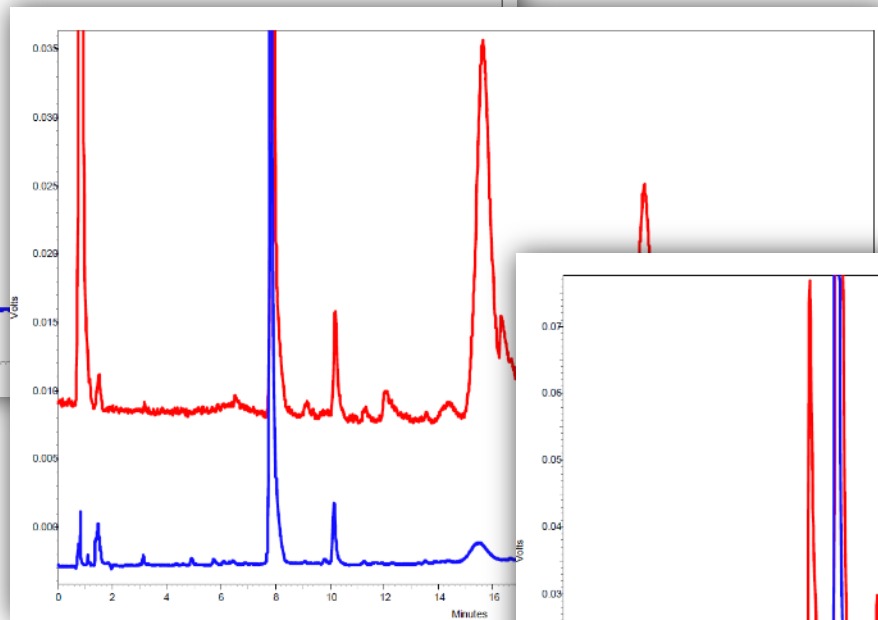
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CAD for extractables and leachables

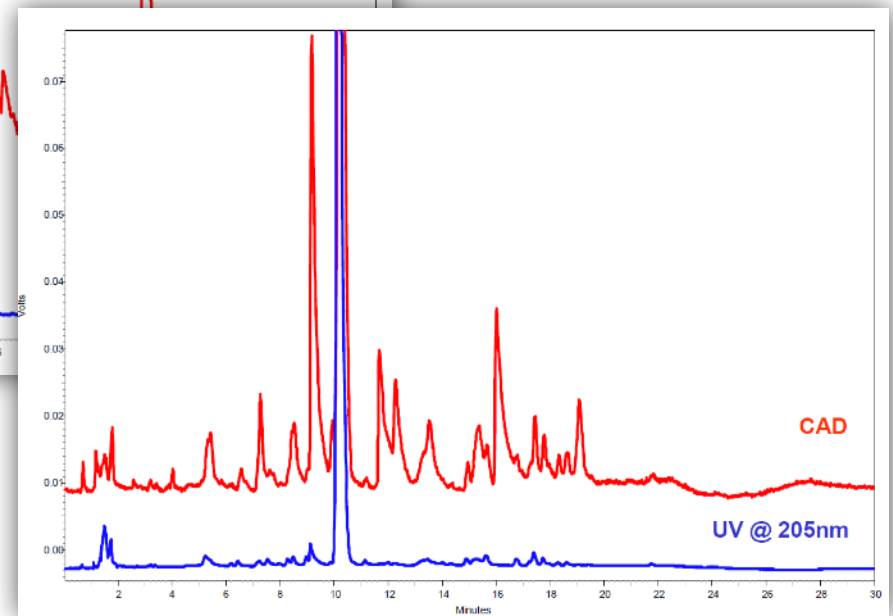
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Rubber



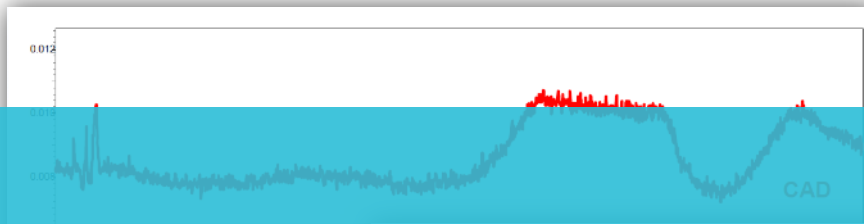
Butyl Rubber



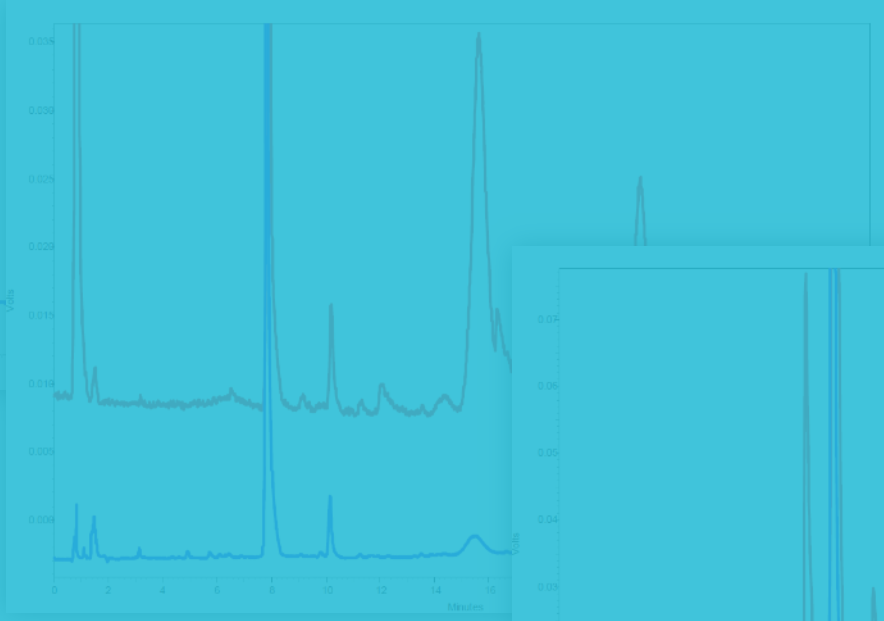
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CAD for extractables and leachables

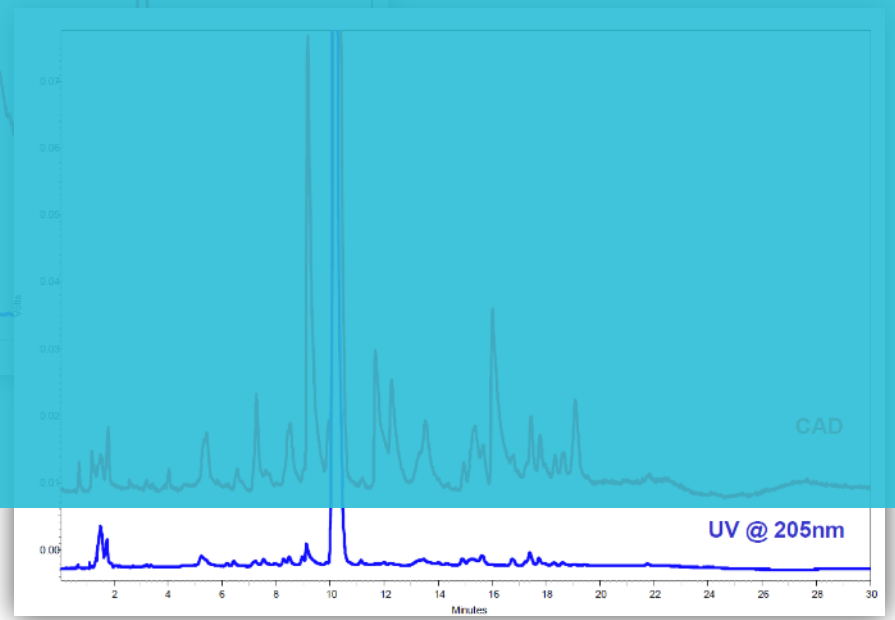
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Rubber



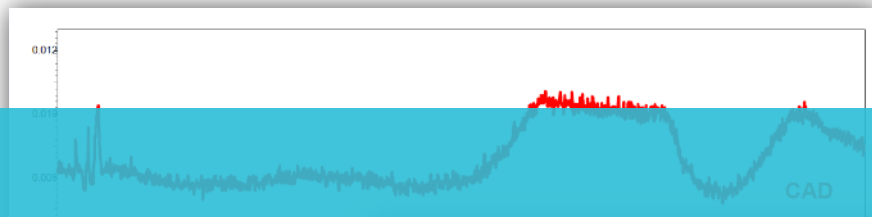
Butyl Rubber



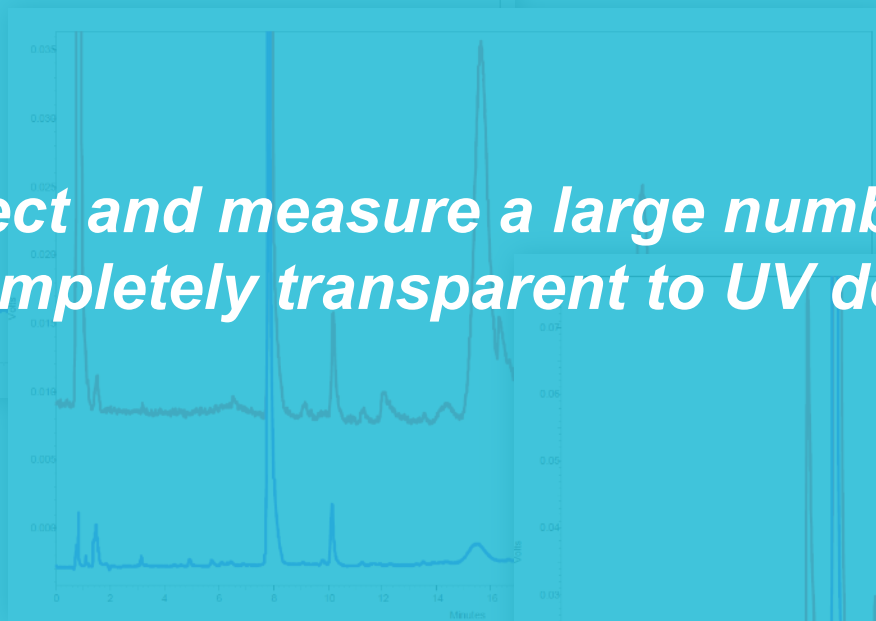
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CAD for extractables and leachables

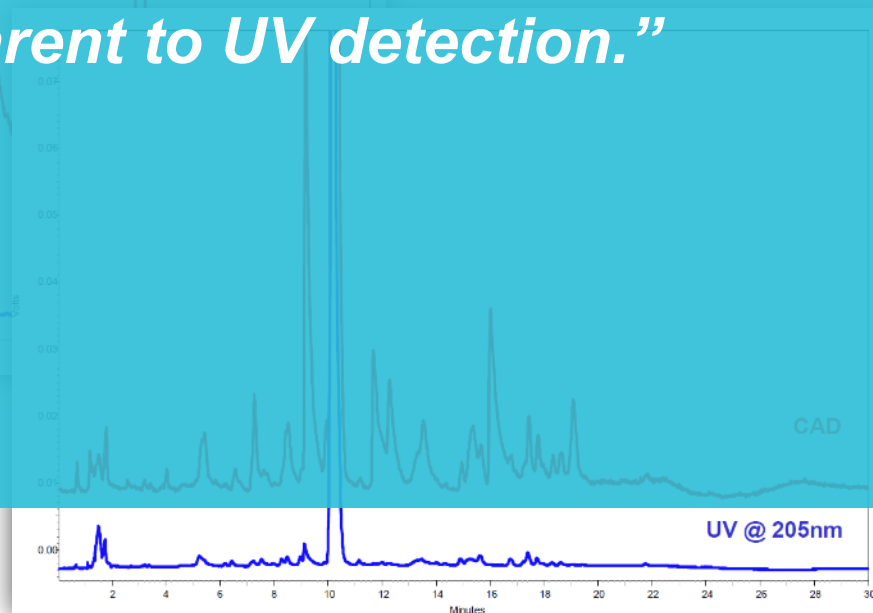
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Rubber



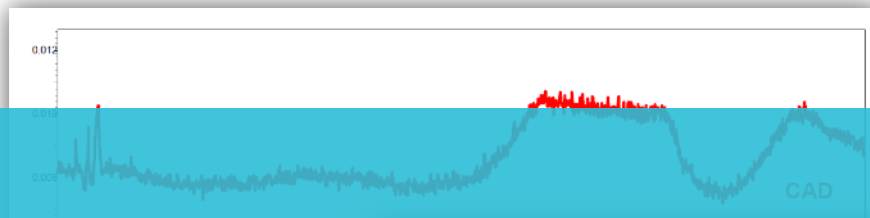
• ***“able to detect and measure a large number of compounds that were completely transparent to UV detection.”***



Data from ESA Biosciences, Inc., Chelmsford, MA

CAD for extractables and leachables

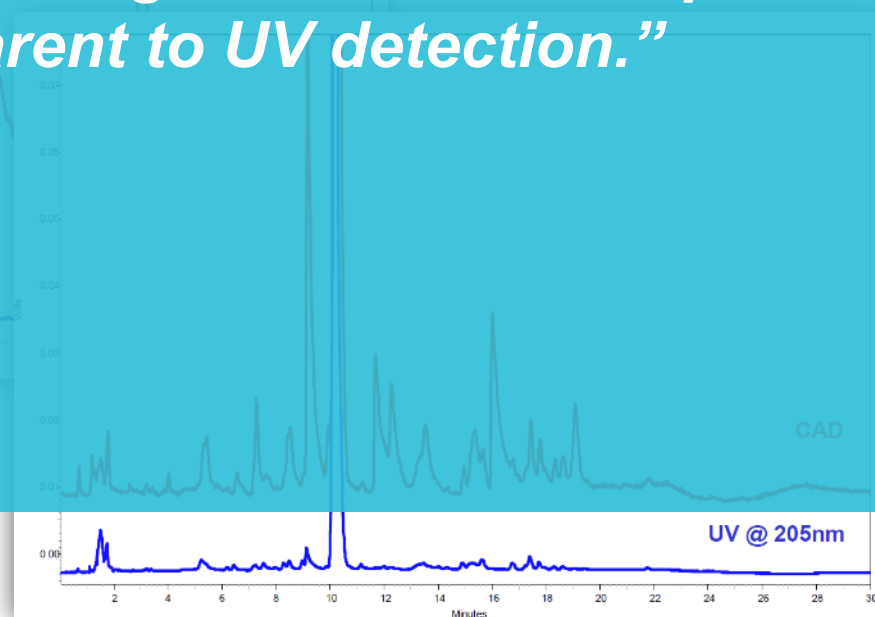
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Rubber

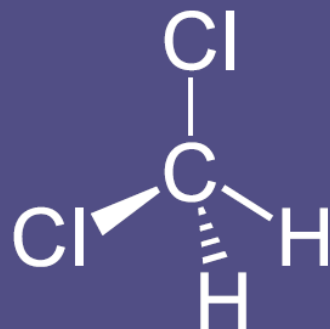


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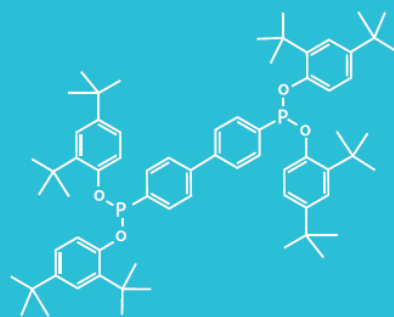
Elemental impurities



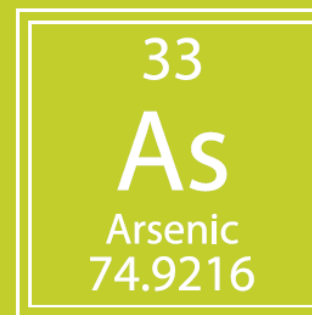
Volatile



Semi-volatile

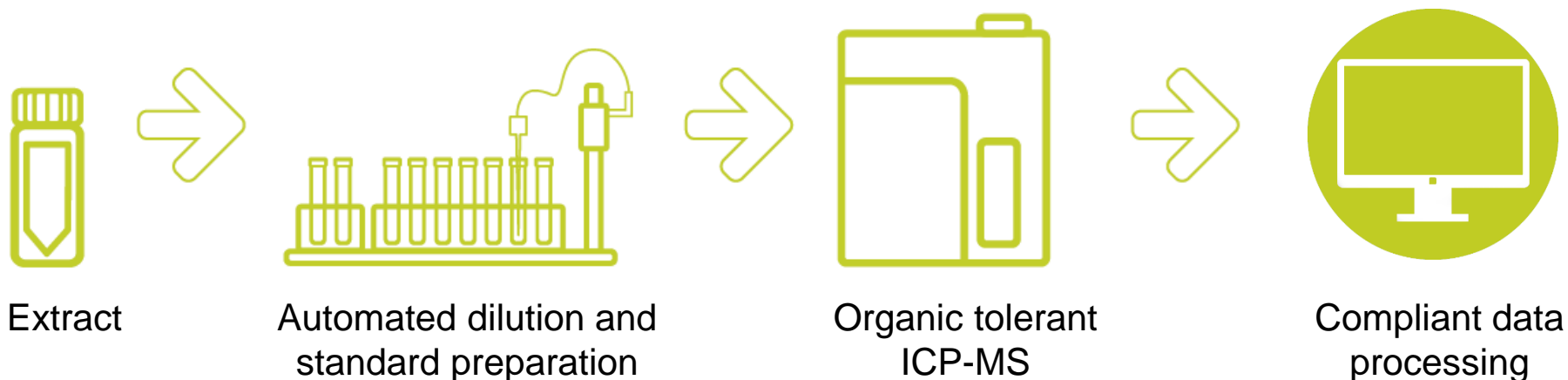


Non-volatile



Elemental

Elemental impurity workflow

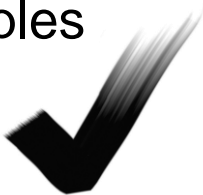


- Workflow analogous to ICH Q3D and USP 232 & 233
- Demands organic tolerance and robust trace analysis
 - Polymer, extraction solvent and cell media
- Thermo Scientific™ iCAP™ RQ ICP-MS with prepFAST
- Thermo Scientific™ Qtegra™ ISDS software



Analysis of pharmaceutical valve o-rings to USP 232/233

- Calibration Range: between 1000-fold and 10-fold dilution of lower limit
 - **R^2 better than 0.99**
- Sensitivity Verification: Analysis @ 0.5x lower limit
 - **$\pm 30\%$ of prepared concentration**
- Accuracy Check: Spike recovery of a 0.2 mg/L solution after complete sample acidification routine
 - **$\pm 20\%$ of expected concentration**
- Drift Check: Standard 2 (500x dilution) was analyzed every 10 samples
 - **$\pm 30\%$ of prepared concentration**



Analysis of pharmaceutical valve o-rings to USP 232/233

Qtegra - [Example Reporting Labbook]

Home Page | Example Reporting Labbook

Content

- Summary
- iCAP Q
 - Method Parameters
 - Analytes
 - Acquisition parameters
 - Monitor Analytes
 - Survey scan settings
 - Interference correction
 - Standards
 - Quantification
 - Ratios
 - Quality Control
 - Evaluation Results
 - Concentrations**
 - Concentration Ratios
 - Intensities
 - Intensity Ratios
 - Survey Intensities
 - Survey Concentrations
 - Spectra View
 - Instrument State
 - Cetac ASX-520
 - Sample List
 - Log Messages
 - Signing
 - Query
 - Query
 - Reports

No	Time	Sample Type	Label	45Sc (KED)	72Ge (KED)	75As (KED) [ppb]	89Y (KED)	111Cd (KED) [pp]	159Tb (KED)	208Pb (KED) [pp]	232Th (KED)
21	6/17/2013 6:02:16 PM	UNKNOWN	CCB	110.3%	105.1%	0.014	103.5%	0.016	91.4%	0.017	88.0%
22	6/17/2013 6:06:04 PM	UNKNOWN	6020S MDL BLANK	86.9%	93.0%	0.017	94.7%	0.014	97.3%	0.036	99.1%
23	6/17/2013 6:09:53 PM	UNKNOWN	6020S MDL 1	86.9%	92.7%	0.532	94.8%	0.100	97.9%	0.153	101.0%
24	6/17/2013 6:13:41 PM	UNKNOWN	6020S MDL 2	87.9%	94.1%	0.517	94.8%	0.084	97.2%	0.132	99.2%
25	6/17/2013 6:17:30 PM	UNKNOWN	6020S MDL 3	88.0%	94.8%	0.561	97.0%	0.102	96.7%	0.143	100.4%
26	6/17/2013 6:21:18 PM	UNKNOWN	6020S MDL 4	86.9%	93.7%	0.508	94.7%	0.079	97.3%	0.155	98.6%
27	6/17/2013 6:25:08 PM	UNKNOWN	6020S MDL 5	87.8%	93.8%	0.502	94.6%	0.087	98.1%	0.134	99.4%
28	6/17/2013 6:28:57 PM	UNKNOWN	6020S MDL 6	85.5%	92.8%	0.511	93.5%	0.081	97.2%	0.123	100.5%
29	6/17/2013 6:32:45 PM	UNKNOWN	6020S MDL 7	86.7%	91.8%	0.554	94.0%	0.105	99.1%	0.144	100.1%
30	6/17/2013 6:36:34 PM	UNKNOWN	6020S MDL 8	84.8%	90.7%	0.509	94.8%	0.081	96.9%	0.132	100.2%
31	6/17/2013 6:40:23 PM	QC - CCV	CCV	91.0%	96.8%	204.956 (102.5%)	96.8%	206.580 (103.3%)	98.0%	201.981 (101.0%)	99.8%
32	6/17/2013 6:44:12 PM	UNKNOWN	CCB	94.5%	97.4%	0.058	96.0%	0.045	95.8%	0.046	95.4%
33	6/17/2013 6:48:00 PM	UNKNOWN	CCB	96.2%	98.6%	0.052	98.6%	0.053	94.5%	0.059	93.7%
34	6/17/2013 6:51:39 PM	UNKNOWN	6020S halfMDL BLAN	84.6%	90.1%	-0.004	92.2%	0.005	96.6%	0.022	100.3%
35	6/17/2013 6:55:28 PM	UNKNOWN	6020S halfMDL 1	82.6%	89.2%	0.267	91.9%	0.039	96.0%	0.068	99.3%
36	6/17/2013 6:59:16 PM	UNKNOWN	6020S halfMDL 2	82.7%	89.2%	0.258	92.3%	0.039	97.5%	0.065	99.3%
37	6/17/2013 7:03:05 PM	UNKNOWN	6020S halfMDL 3	82.3%	88.8%	0.254	92.2%	0.045	96.1%	0.070	98.6%
38	6/17/2013 7:06:53 PM	UNKNOWN	6020S halfMDL 4	82.4%	88.0%	0.280	90.0%	0.037	95.8%	0.063	98.0%
39	6/17/2013 7:10:42 PM	UNKNOWN	6020S halfMDL 5	82.0%	89.1%	0.267	89.4%	0.036	95.5%	0.064	98.7%
40	6/17/2013 7:14:31 PM	UNKNOWN	6020S halfMDL 6	82.5%	87.8%	0.253	90.4%	0.044	94.4%	0.068	99.5%
41	6/17/2013 7:18:19 PM	UNKNOWN	6020S halfMDL 7	82.6%	88.0%	0.251	92.2%	0.036	95.0%	0.062	98.9%
42	6/17/2013 7:22:08 PM	UNKNOWN	6020S halfMDL 8	82.5%	88.0%	0.256	92.7%	0.034	95.9%	0.062	98.6%
43	6/17/2013 7:25:57 PM	QC - CCV	CCV	89.1%	92.0%	207.303 (103.7%)	95.4%	203.082 (101.5%)	96.5%	203.752 (101.9%)	97.6%
44	6/17/2013 7:29:45 PM	UNKNOWN	CCB	92.5%	94.3%	0.078	93.9%	0.072	93.8%	0.085	93.9%
45	6/17/2013 7:33:33 PM	UNKNOWN	CCB	97.2%	96.4%	0.054	96.0%	0.054	95.6%	0.056	93.8%

Details

Sample list line 43: 75As (KED) 111Cd (KED) 208Pb (KED)

Recovery [%]

Sample Number

Sample list line 43:

Add Comment

Status: Success
 Creation: Added during runtime
 Description:
 Comment:
 Start time: 6/17/2013 7:25:57 PM
 Stop time: 6/17/2013 7:29:45 PM
 User name: iCAPQ-PCVCAPQ

Quality control

CCV test passed.

Reason: Concentration in range for 7Li (STD): 210.8299 ppb (105.41%),
 Concentration in range for 9Be (STD): 210.5639 ppb (105.28%),
 Concentration in range for 10B (STD): 203.7010 ppb (101.85%),
 Concentration in range for 23Na (KED): 2629.1815 ppb (105.17%),
 Concentration in range for 25Mg (KED): 2528.8460 ppb (101.15%),
 Concentration in range for 27Al (STD): 199.7484 ppb (99.87%),
 Concentration in range for 28Si (KED): 2629.8458 ppb (105.19%),
 Concentration in range for 39K (KED): 2405.5280 ppb (96.22%),
 Concentration in range for 43Ca (STD): 2507.4377 ppb (100.30%),
 Internal standard recovery in range for 45Sc (KED) (89.10%),
 Internal standard recovery in range for 45Sc (STD) (90.46%)

Scheduler | Completed LabBooks | Log View

Installer with ASX 520 | Idle | Empty queue

Analysis of pharmaceutical valve o-rings to USP 232/233

The screenshot displays the Qtegra software interface for an 'Example Reporting Labbook'. The main window shows a table of concentrations for various samples. The table includes columns for sample number, time, sample type, label, and concentrations for 14 different elements: 45Sc (KED), 72Ge (KED), 75As (KED) [ppb], 89Y (KED), 111Cd (KED) [pp], 159Tb (KED), 208Pb (KED) [pp], and 232Th (KED). The data shows recovery percentages for each element across multiple samples, with some samples showing significantly lower recovery (e.g., sample 29 at 88.1% for 75As).

Overlaid on the screenshot are three bullet points:

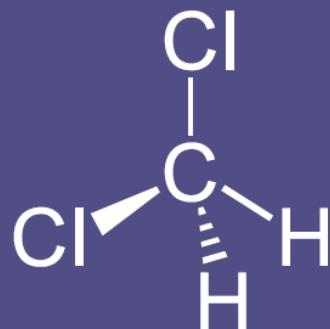
- All QC parameters automatically reported
- High concentration samples automatically diluted
- Full compliance and automatic reporting

Below the table, a 'Recovery (%)' plot is shown. The x-axis is 'Sample Number' (10 to 40) and the y-axis is 'Recovery (%)' (0 to 200). A horizontal red line is drawn at approximately 90% recovery. Data points for 75As (KED), 111Cd (KED), and 208Pb (KED) are plotted, showing most points above the 90% line, with a few points for 75As (KED) falling below it.

To the right of the plot, a 'Reason:' section lists the following concentrations and recovery percentages:

- Concentration in range for ⁷Li (STD): 210.8299 ppb (105.41%)
- Concentration in range for ⁹Be (STD): 210.5639 ppb (105.28%)
- Concentration in range for ¹⁰B (STD): 203.7010 ppb (101.85%)
- Concentration in range for ²³Na (KED): 2629.1815 ppb (105.17%)
- Concentration in range for ²⁵Mg (KED): 2528.8460 ppb (101.15%)
- Concentration in range for ²⁷Al (STD): 199.7484 ppb (99.87%)
- Concentration in range for ²⁸Si (KED): 2629.8458 ppb (105.19%)
- Concentration in range for ³⁹K (KED): 2405.5280 ppb (96.22%)
- Concentration in range for ⁴³Ca (STD): 2507.4377 ppb (100.30%)
- Internal standard recovery in range for 45Sc (KED) (89.10%)
- Internal standard recovery in range for 45Sc (STD) (90.46%)

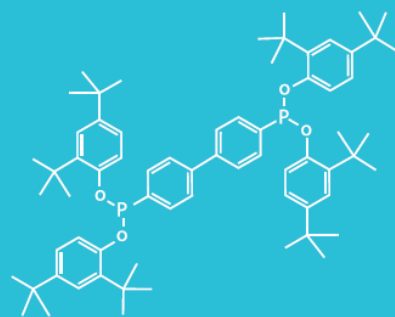
Semi-volatiles



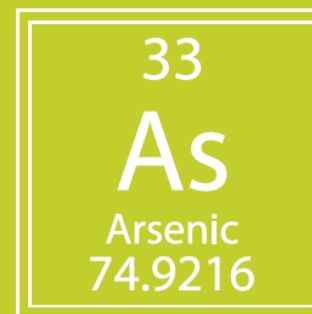
Volatile



Semi-volatile

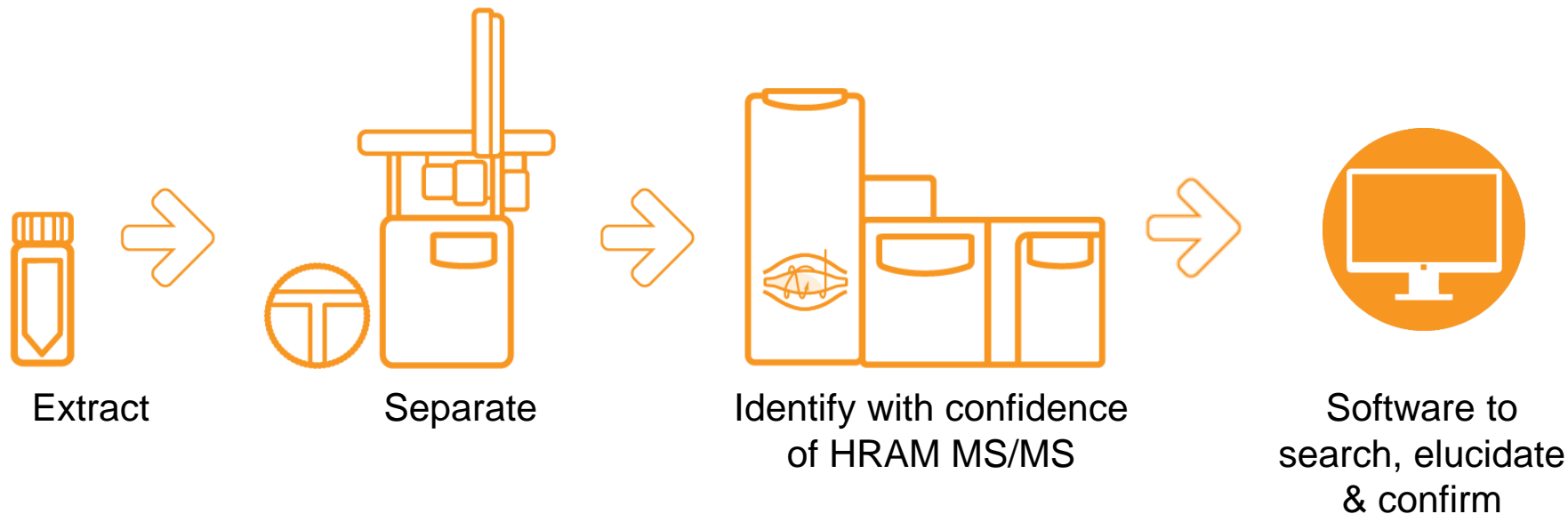


Non-volatile



Elemental

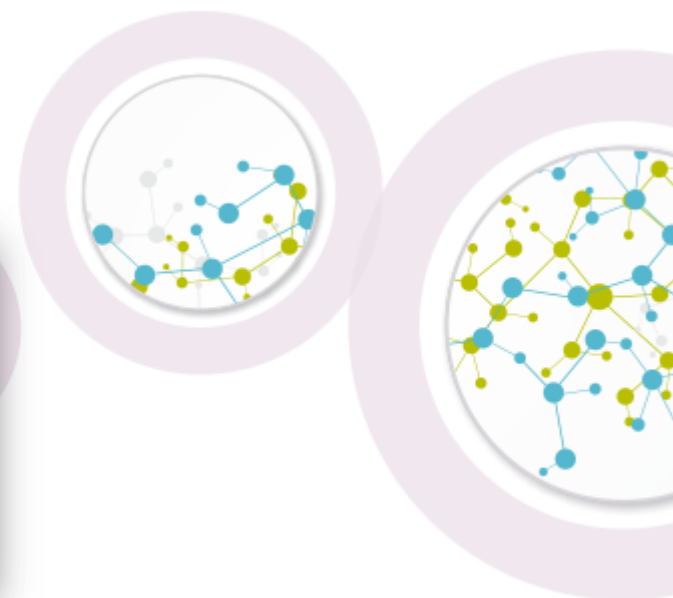
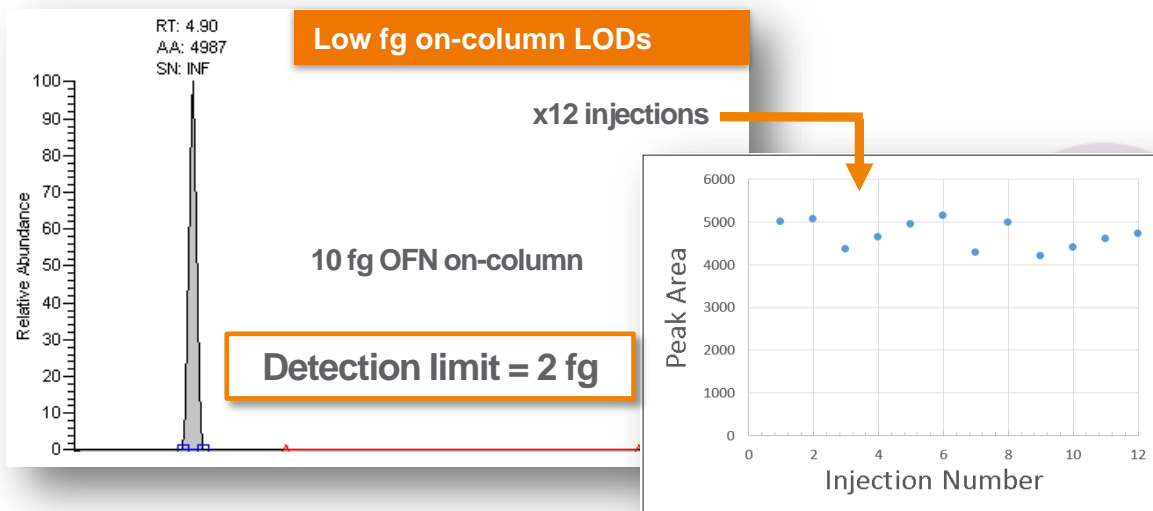
Semi-volatile impurity identification and quantification workflow



- Deconvolve, identify and quantify even the narrowest GC peaks
- Unambiguously calculate empirical formulae without needing to average scans
- Simplify data review and report
- Thermo Scientific™ Q Exactive™ GC system
- Thermo Scientific™ TraceFinder™ software



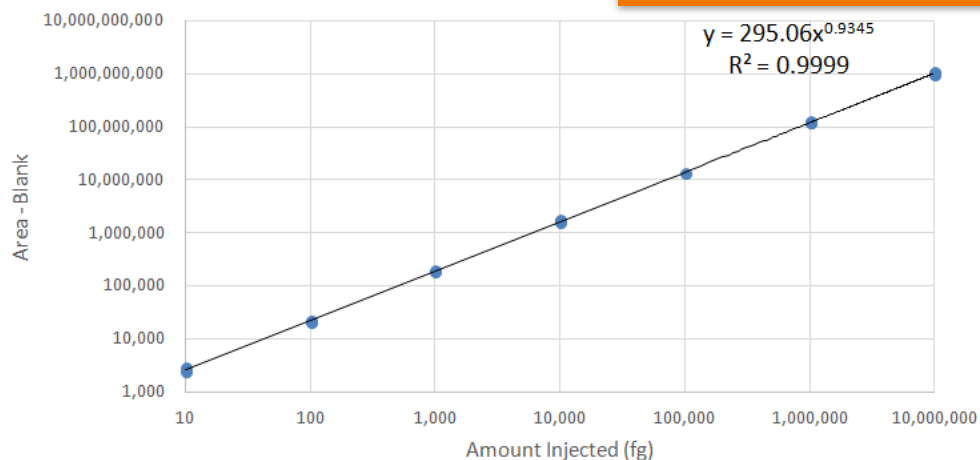
Detect, quantify and identify at any concentration



Detect, quantify and identify at any concentration

OFN 10 fg - 10 ng

>6 Orders Linearity

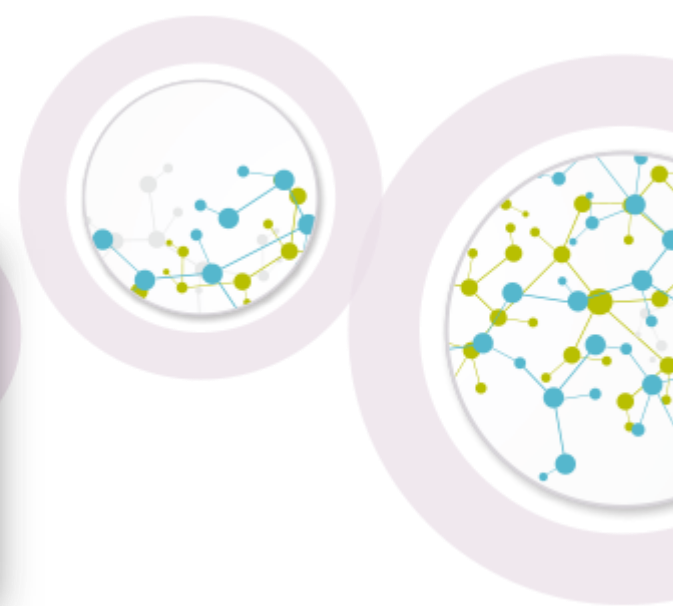
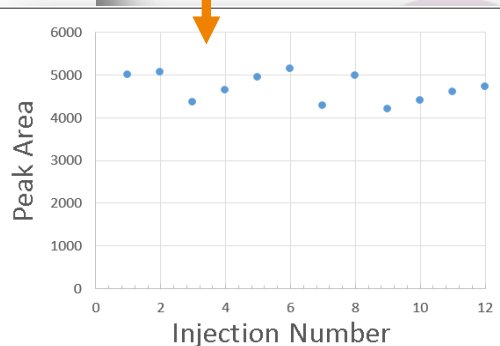
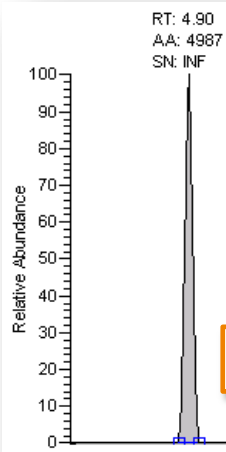


Low fg on-column LODs

x12 injections

10 fg OFN on-column

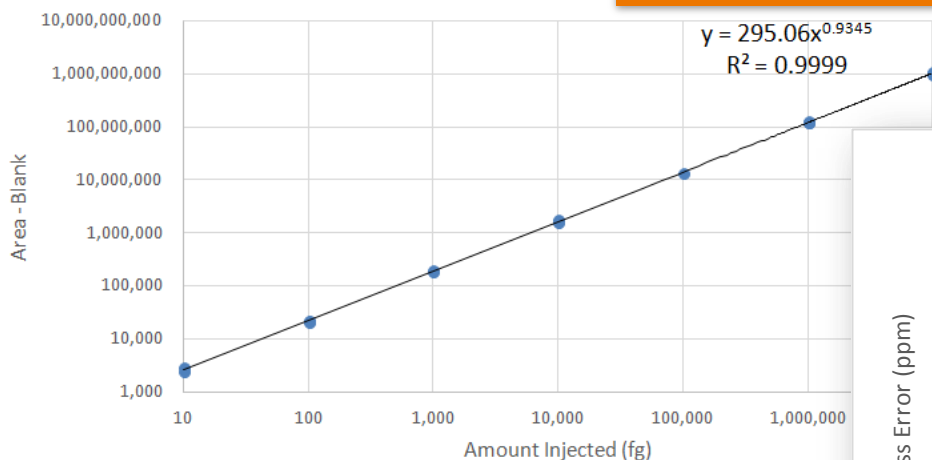
Detection limit = 2 fg



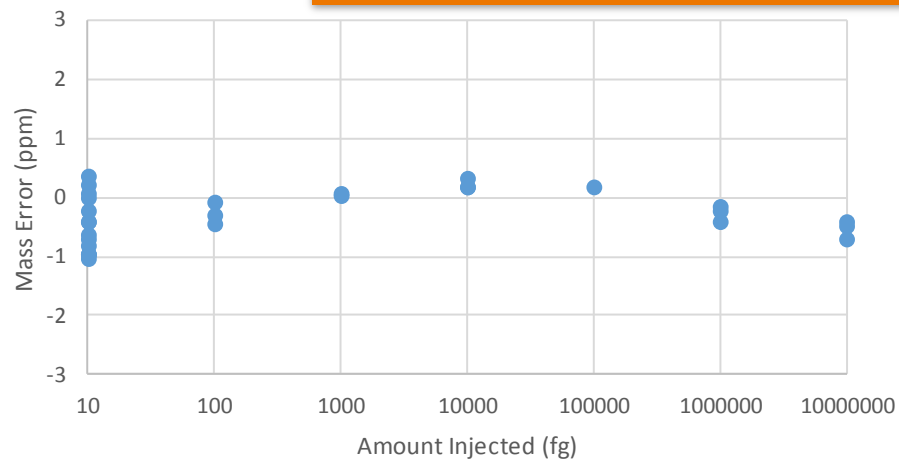
Detect, quantify and identify at any concentration

OFN 10 fg - 10 ng

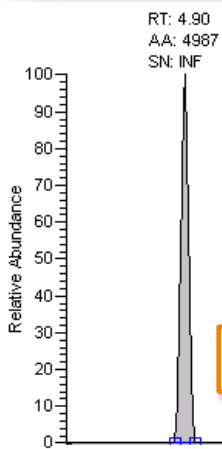
>6 Orders Linearity



Always low mass error



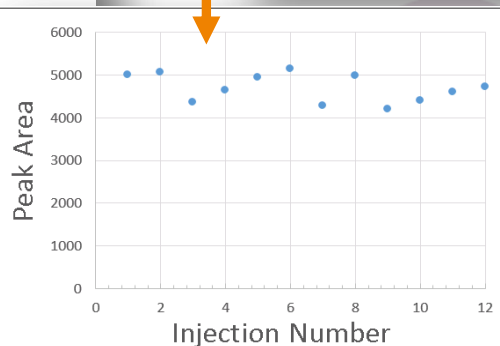
Low fg on-column LODs



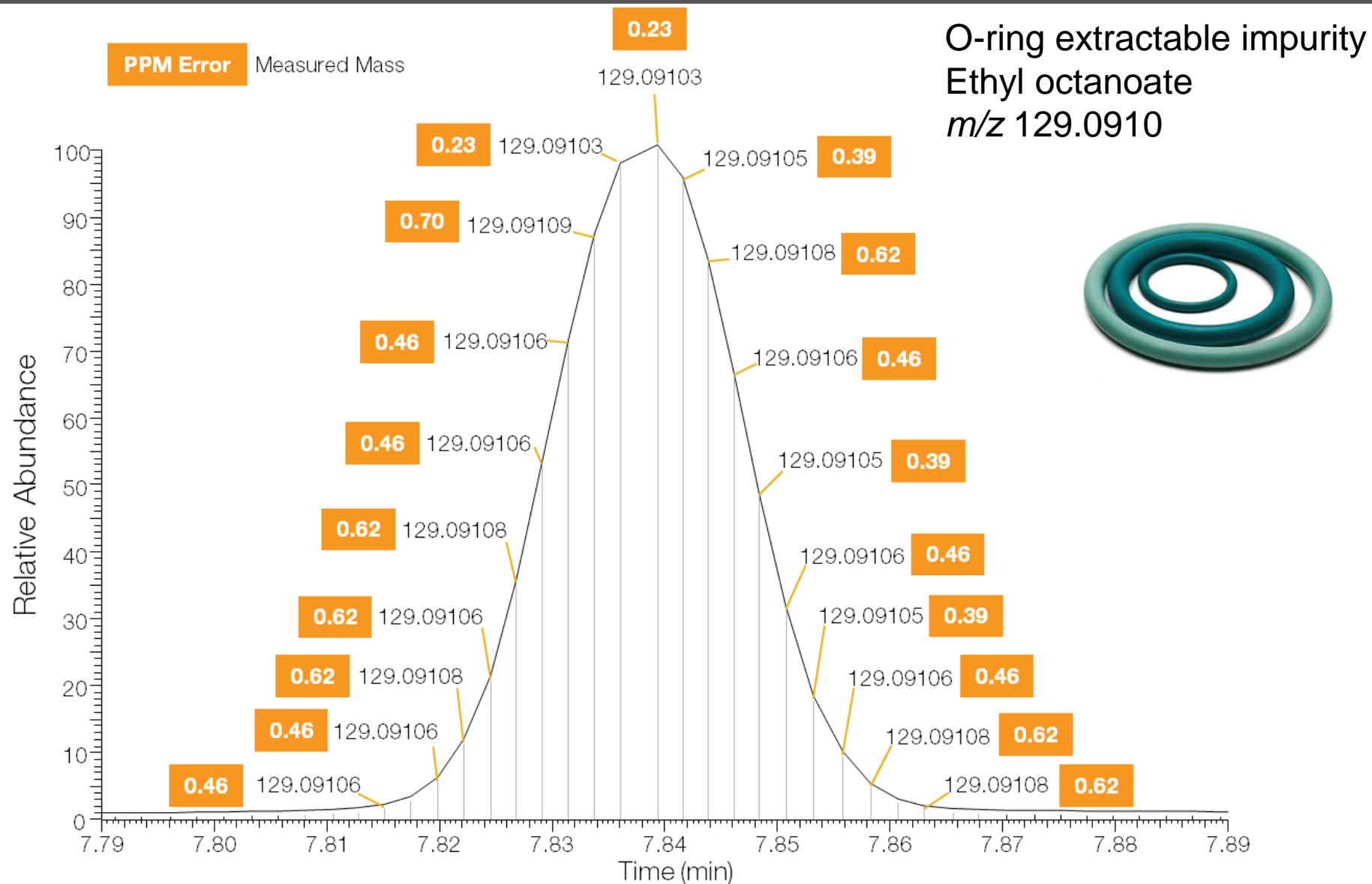
10 fg OFN on-column

Detection limit = 2 fg

x12 injections



Scan speed and accurate mass error across a peak



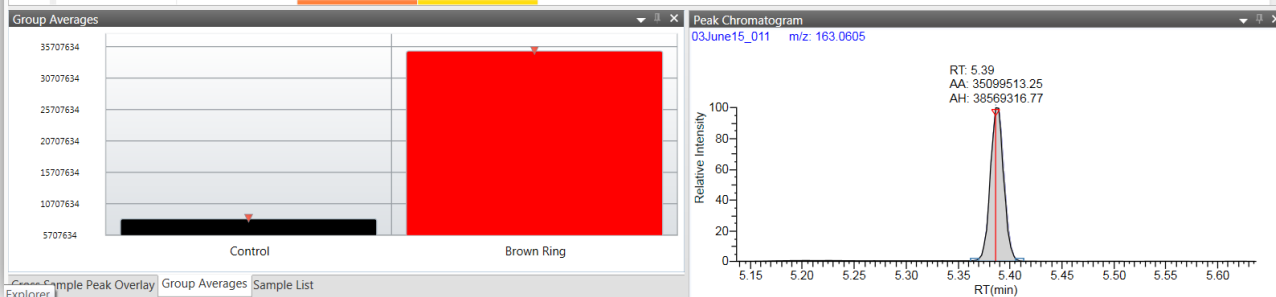
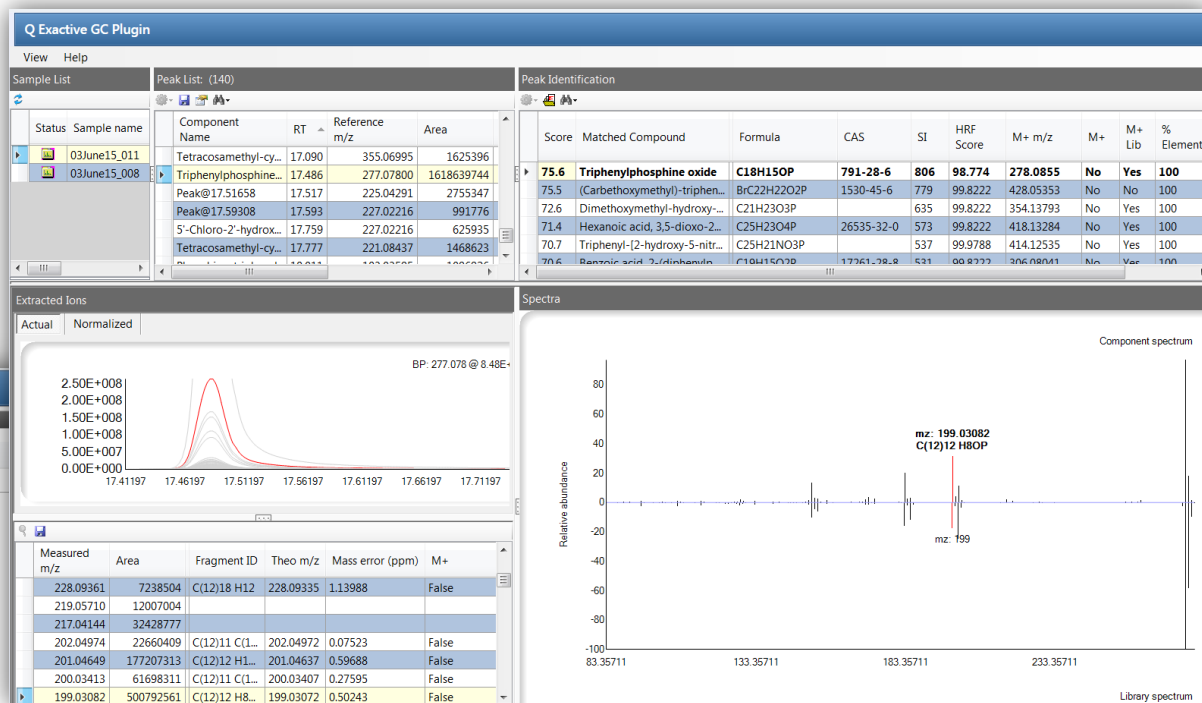
Isolate peaks of interest, identify with confidence

- Heat map shows peaks elevated in sample versus control

Data Review - Smithers Brown Ring 100% Ethanol [Unknown]

Heat Map

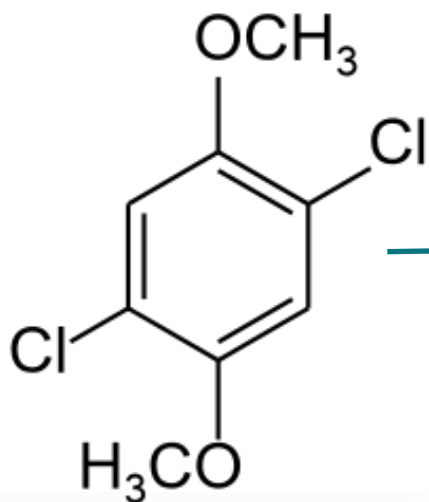
	Retention Time	M/Z	03June15_011 MS Area	03June15_008 MS Area
1	17.49	277.078	1,613,614,467	79,771
2	4.16	225.043	250,124,178	59,318,952
3	4.14	225.043	245,796,796	59,403,820
4	15.42	183.036	146,937,559	8,822
5	5.10	116.024	116,931,439	64,836,840
6	4.86	151.024	115,515,172	65,874,174
7	11.10	219.174	79,016,292	25,917
8	5.66	149.063	74,423,683	119,322,246
9	5.67	149.063	74,423,573	119,322,246
10	5.52	139.042	44,584,675	53,088,222
11	4.69	91.021	41,165,401	54,566,843
12	4.78	119.052	37,843,751	48,065,445
13	7.65	105.034	37,276,135	58,720,844
14	5.39	163.060	35,099,513	8,379,623
15	5.70	265.020	34,532,011	4,799,743



- Simple intuitive data interpretation
- Easily quantify

High Resolution Filtering

Candidate Compounds



Subset formulae

Acq m/z	Fragment ID	Theo m/z	Mass Error (ppm)
147.9477	C ₅ Cl ₂ H ₂ O	147.9477	0.20277
148.9369	C ₅ Cl[37]ClHO	148.9369	0.2679
149.9448	C ₅ Cl[37]ClH ₂ O	149.9448	0.06602
151.9419	C ₅ [37]Cl ₂ H ₂ O	151.9418	0.72528
154.9895	C ₇ ClH ₄ O ₂	154.9894	0.38712
155.9974	C ₇ ClH ₅ O ₂	155.9973	0.89745
157.9943	C ₇ [37]ClH ₅ O ₂	157.9943	0.25381
159.9479	C ₆ Cl ₂ H ₂ O	159.9477	0.87529
161.9446	C ₆ Cl[37]ClH ₂ O	161.9448	0.80213
162.9711	C ₆ Cl ₂ H ₅ O	162.9712	0.36816
163.9745	C ₅ [13]CCl ₂ H ₅ O	163.9745	0.3342
164.9682	C ₆ Cl[37]ClH ₅ O	164.9682	0.24186
165.9716	C ₅ CCl[37]ClH ₅ O	165.9716	0.02832

$$\text{HRF Score} = \frac{\sum (m/z * \text{Intensity})_{\text{explained}}}{\sum (m/z * \text{Intensity})_{\text{observed}}} \times 100\%$$

Confidently identify

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 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		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

Confidently identify

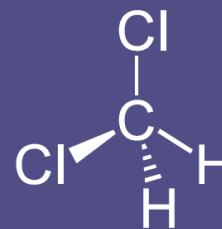
Combined SI and HRF values give an overall score (%) to quickly and confidently identify the compound. Eliminates other hits that would be valid if only SI used.

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
77.1	1,5-Dihydrophenacetic acid,...	C18H30O2		524	99.4959	278.22403	Yes	Yes	100
57.0	2,6-Bis(tert-butyl)phenol, TMS...	C17H30OSi		506	99.4959	278.22403	Yes	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-Cyclonex-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

• Simple unambiguous identification

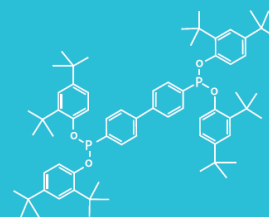
Complete capabilities for Extractables & Leachables



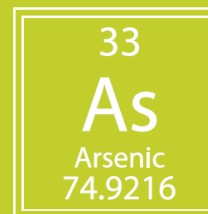
Volatile



Semi-volatile



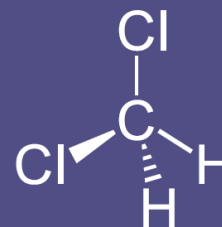
Non-volatile



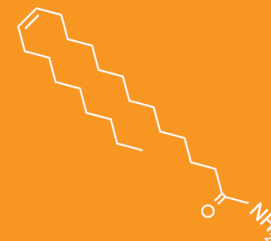
Elemental

Complete capabilities for Extractables & Leachables

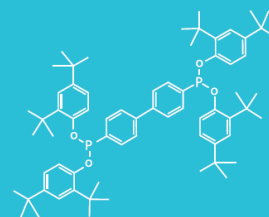
- **Confidently quantify**



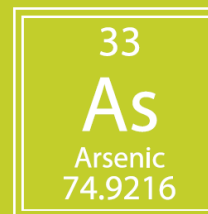
Volatile



Semi-volatile



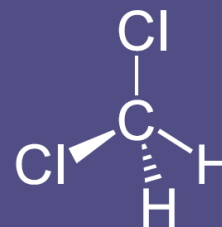
Non-volatile



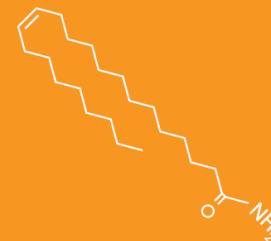
Elemental

Complete capabilities for Extractables & Leachables

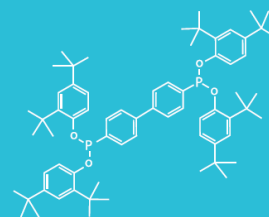
- **Confidently quantify**
- **Unambiguously identify**



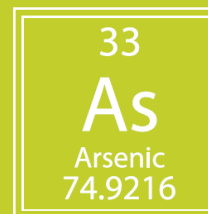
Volatile



Semi-volatile



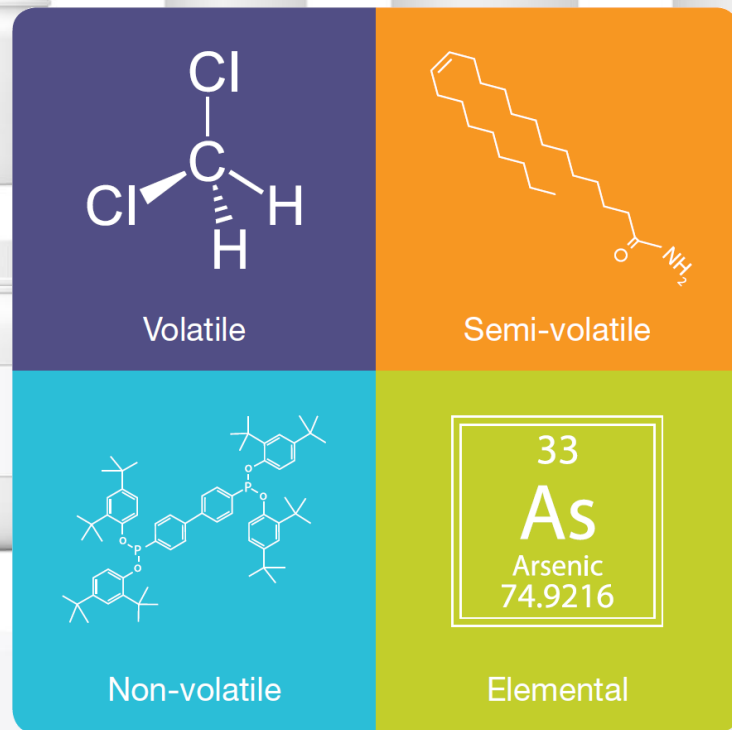
Non-volatile



Elemental

Complete capabilities for Extractables & Leachables

- **Confidently quantify**
- **Unambiguously identify**
- **Easily report**



- Webinars
- Applications
- Blogs
- Regulatory updates
- White papers
- And more...

The screenshot shows the Thermo Scientific website's 'Extractables and Leachables' community page. The page features a navigation bar with 'Products', 'Communities', 'Services', 'Support', and 'About Us'. The main content area is titled 'Extractables and Leachables' and includes a large banner with the text 'No more unknowns' and 'Identify all extractables and leachables contaminants with HRAM workflows and advanced compound identification'. Below the banner, there is a section titled 'Pharmaceutical Quality Assurance and Control' with a sidebar menu listing various topics such as 'Pharma and Biopharma', 'Bioprocessing and Drug Manufacturing', 'Drug Discovery', 'Drug Development', 'Pre-Clinical and Clinical Drug Testing', 'Pharmaceutical Quality Assurance and Control', 'Residual Solvent Analysis', 'Elemental Impurities', 'Extractables and Leachables', 'Impurity Analysis', 'Counter Ion Analysis', and 'Pharmaceutical Data Management'. The main text discusses the use of polymeric materials in pharmaceutical production and packaging, and the importance of identifying contaminants. It also mentions Thermo Fisher Scientific's comprehensive analytical workflows for extractables and leachables testing. There are several call-to-action buttons, including 'Join the Community', 'Subscribe Now', 'Join us at E&L Europe', 'Register today if you are in', 'Free cloud-based mass spectral database', and 'A history of GC-MS'. The page also features a 'Give Feedback' button on the right side.

www.thermoscientific.com/Leachables

Thank you

