

EXTRAHOVATELNÉ A LOUHOVATELNÉ LÁTKY

(E&L extractables/leachables)

Lukáš Plaček



pragolab

thermo
scientific

Extrahovatelné a louhovatelnné látky (E&L)



Extrahovatelné a louhovatelné látky (E&L)

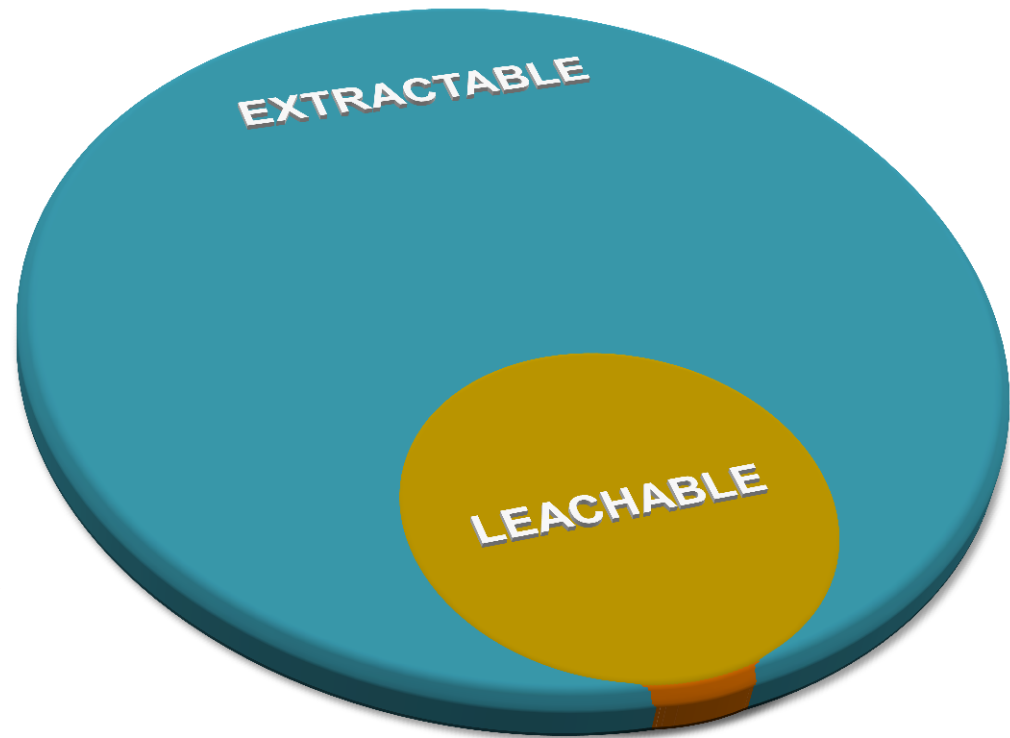
EXTRACTABLE

Chemické látky, které se **uvolňují** ze zařízení nebo obalu za **laboratorních podmínek extrakce**.

Proces nesmí degradovat ani deformovat materiál.

LEACHABLE

Chemické látky, které **migrují** z výrobního procesu, balení nebo transportu do lékové formy za **normálních podmínek užívání**.



L jsou většinou podmnožinou E

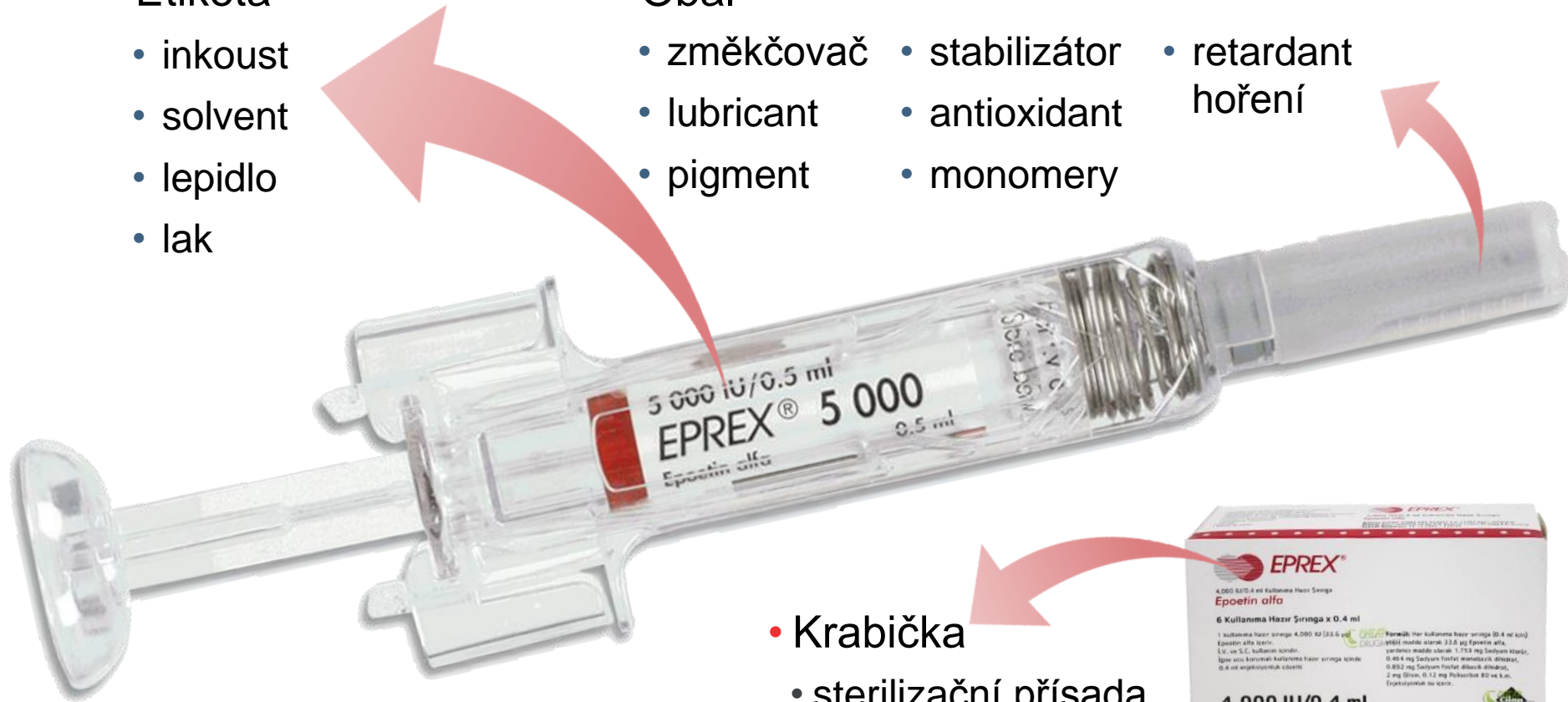
Extrahovatelné a louhovatelnné látky (E&L)

- Etiketa

- inkoust
- solvent
- lepidlo
- lak

- Obal

- změkčovač
- stabilizátor
- retardant hoření
- lubricant
- antioxidant
- pigment
- monomery

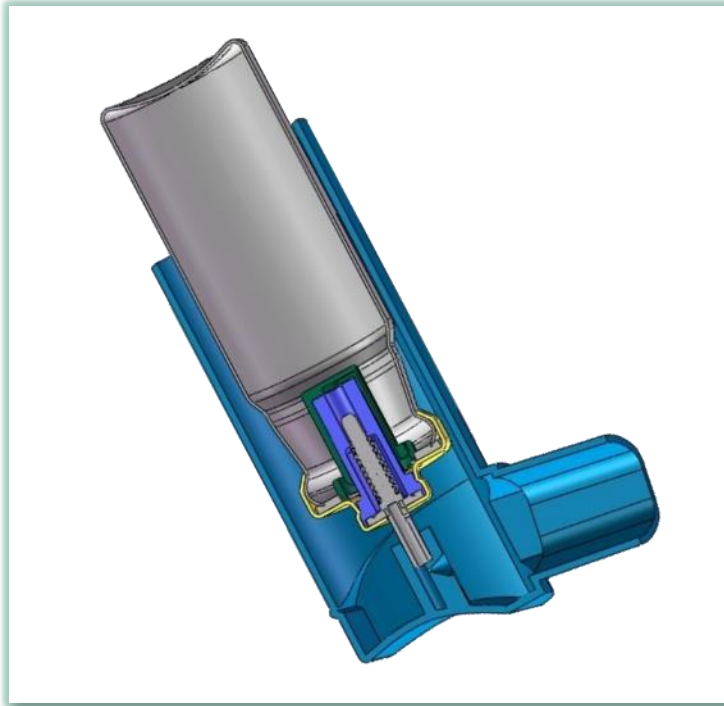


- Krabička

- sterilizační přísada
- konzervant
- potisk

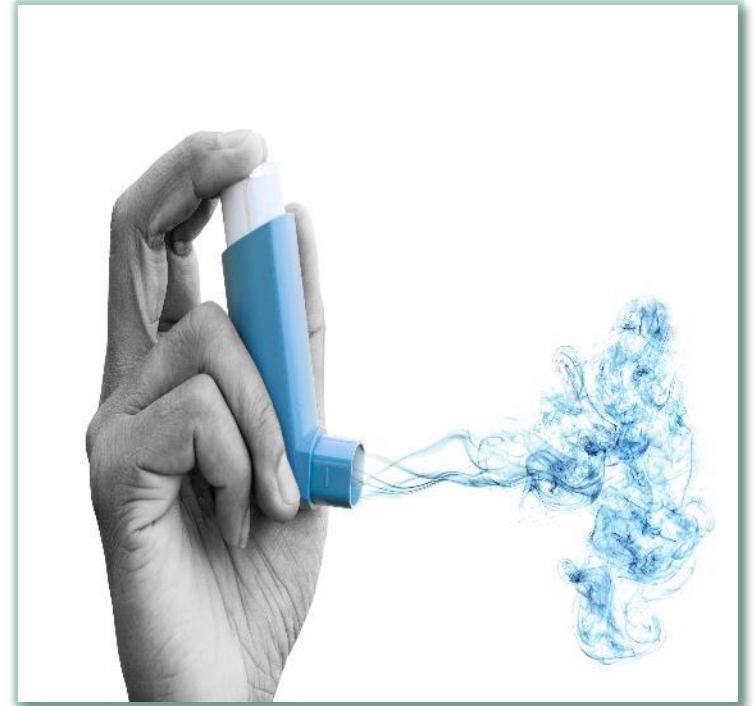
Extrahovatelné a louhovatelné látky (E&L)

EXTRACTABLE



Testuje se materiál

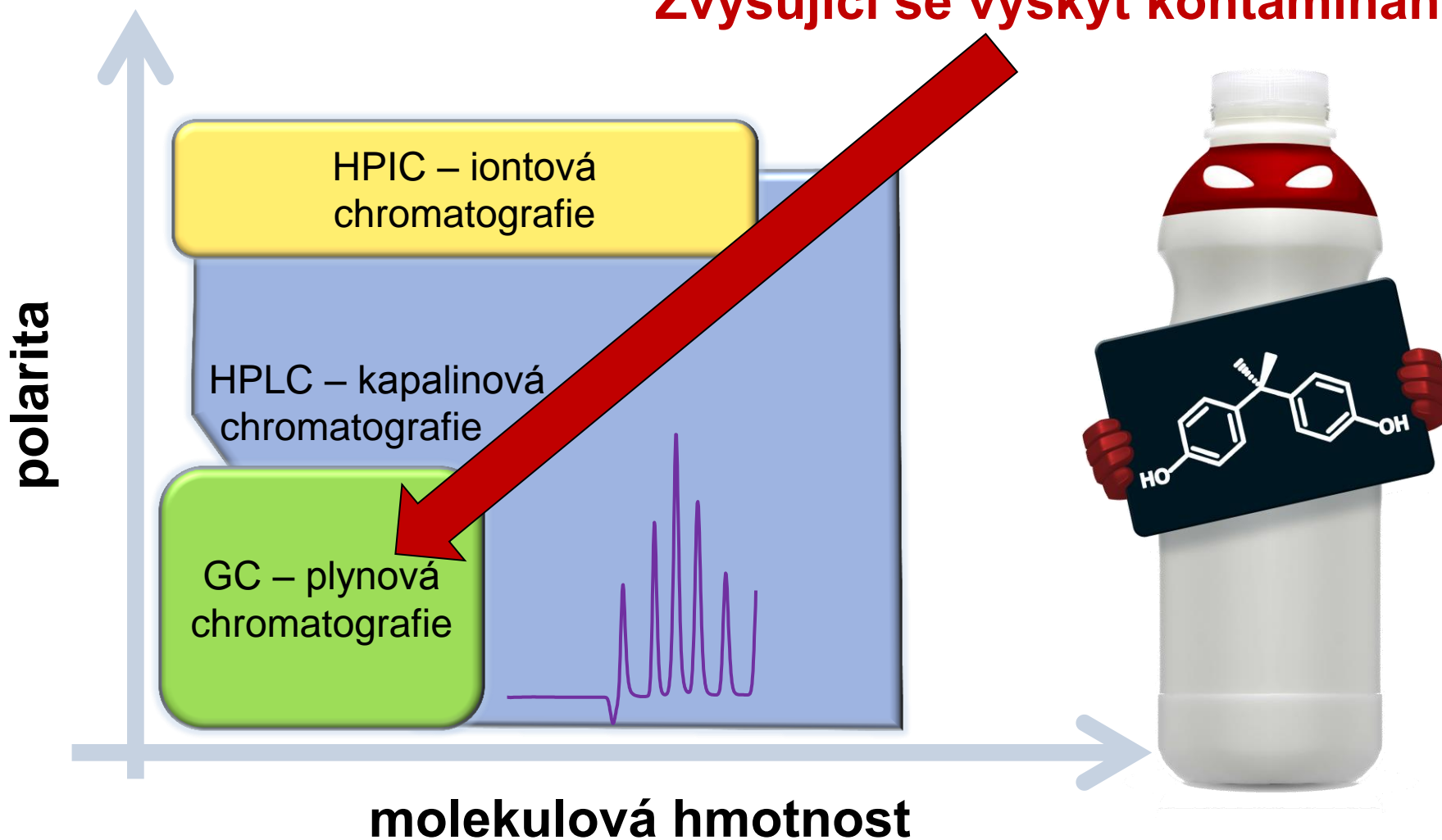
LEACHABLE



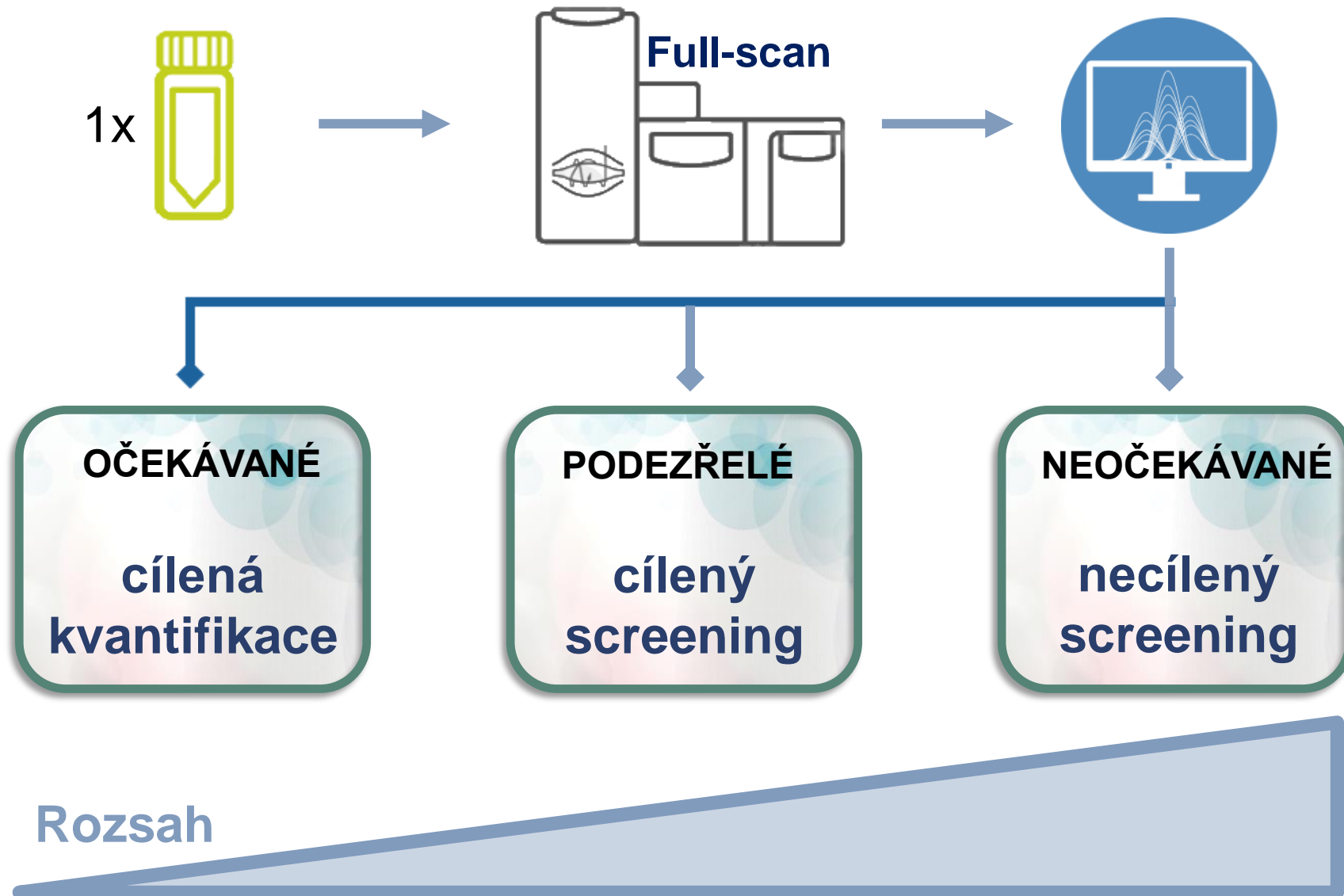
Testuje se produkt

Analytická separace

Zvyšující se výskyt kontaminantů

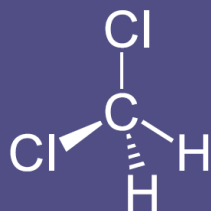


Cílená a necílená analýza



Analýza

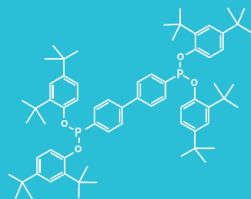
- GC-MS
- GC-HRMS
- Headspace
- EI & CI
- Library



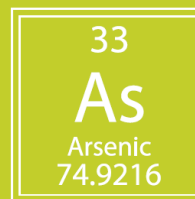
Volatile



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

Komplexní řešení pro E&L

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

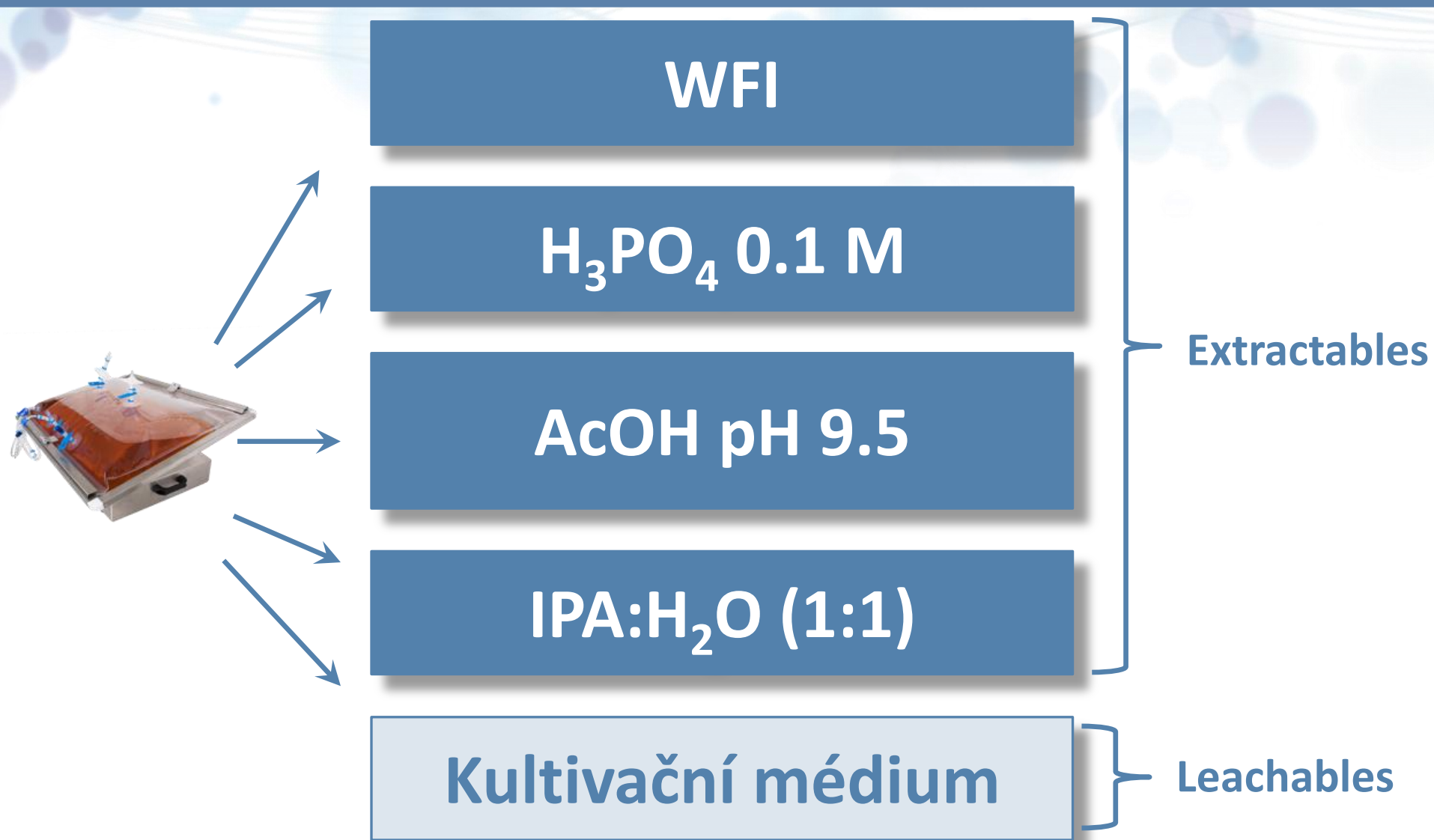
EXTRAKCE

ANALÝZA A REPORTOVÁNÍ

Komplexní řešení pro E&L

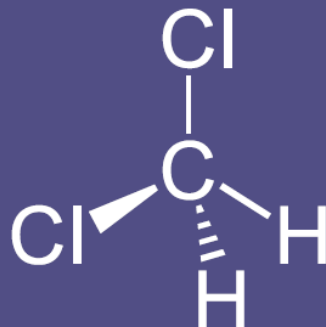
ThermoFisher
S C I E N T I F I C



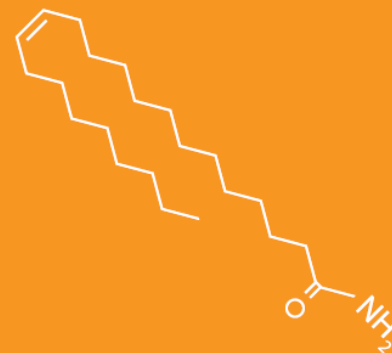


Těkavé látky

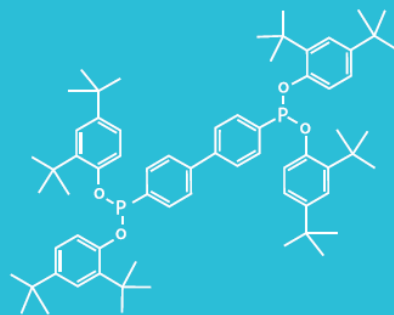
Těkavé



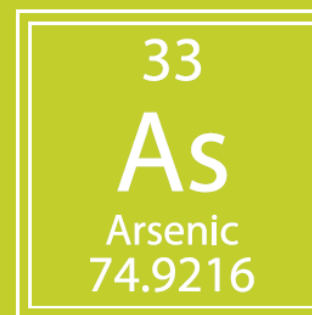
Volatile



Semi-volatile

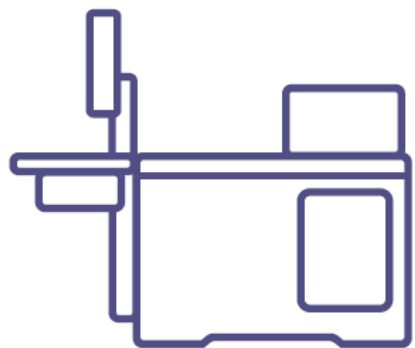


Non-volatile



Elemental

Těkavé látky



Vzorek + valve & loop headspace



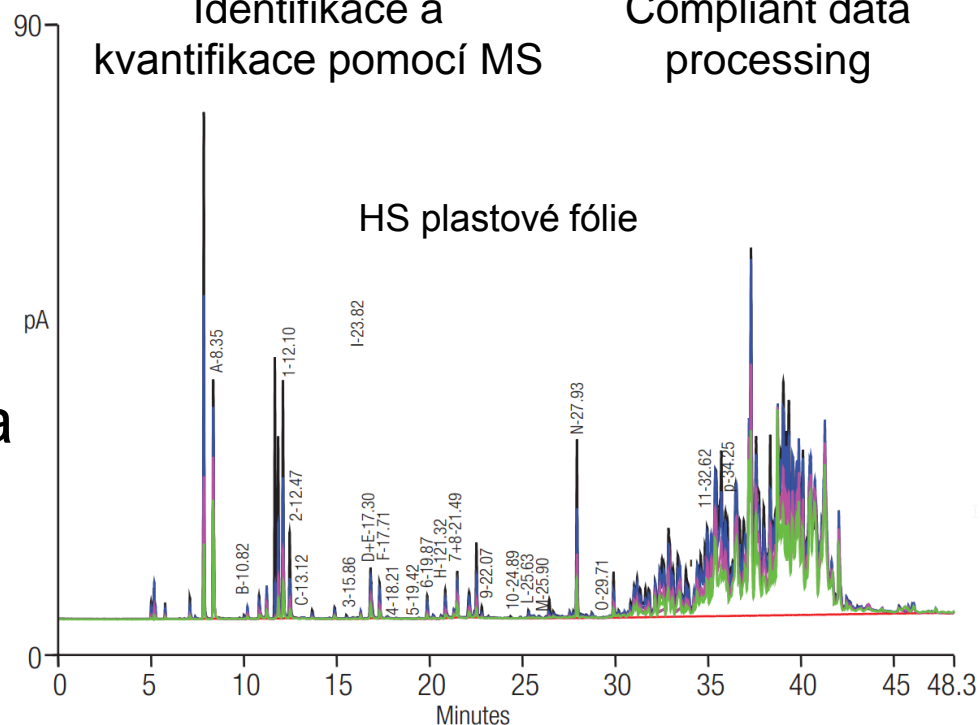
Robustní separace



Identifikace a kvantifikace pomocí MS



Compliant data processing



- Analogické k **USP 467**
- Molekuly jsou obecně známé a **jednoduše kvantifikovatelné**

Těkavé látky



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

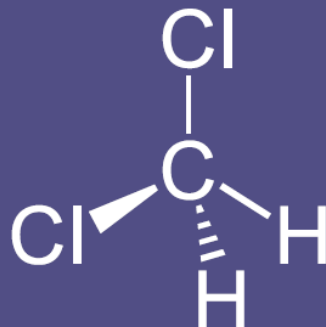


Thermo Scientific™ AppsLab Library™



Netěkavé látky

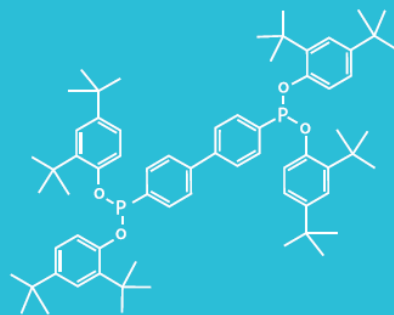
Netěkavé



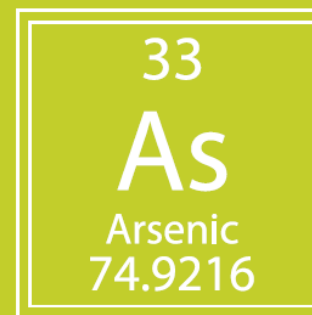
Volatile



Semi-volatile



Non-volatile



Elemental

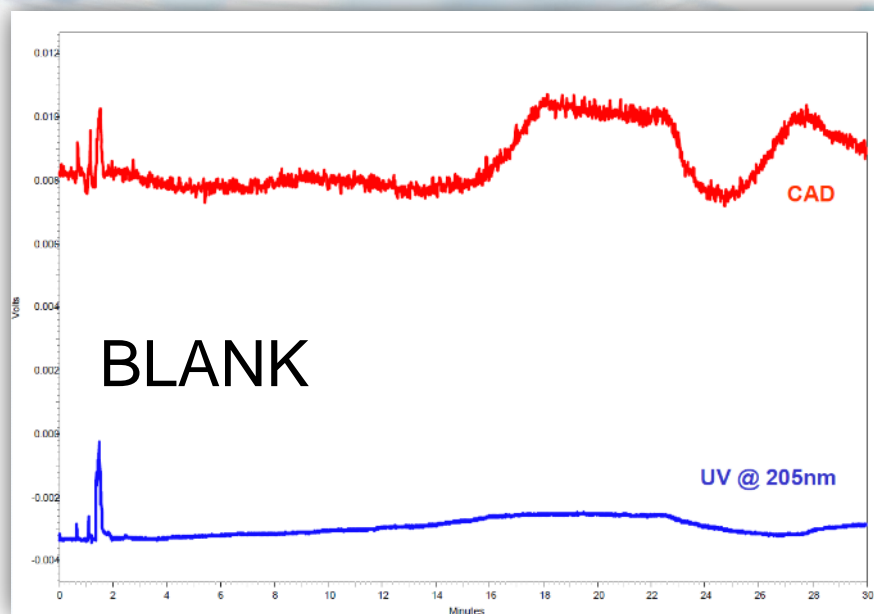
Netěkavé látky



- Detekce v pozitivním i negativním módu
- **Elementární složení**
- Informace o struktuře (fragmentace)
- Zachytit vše – **kombinace s Corona CAD**

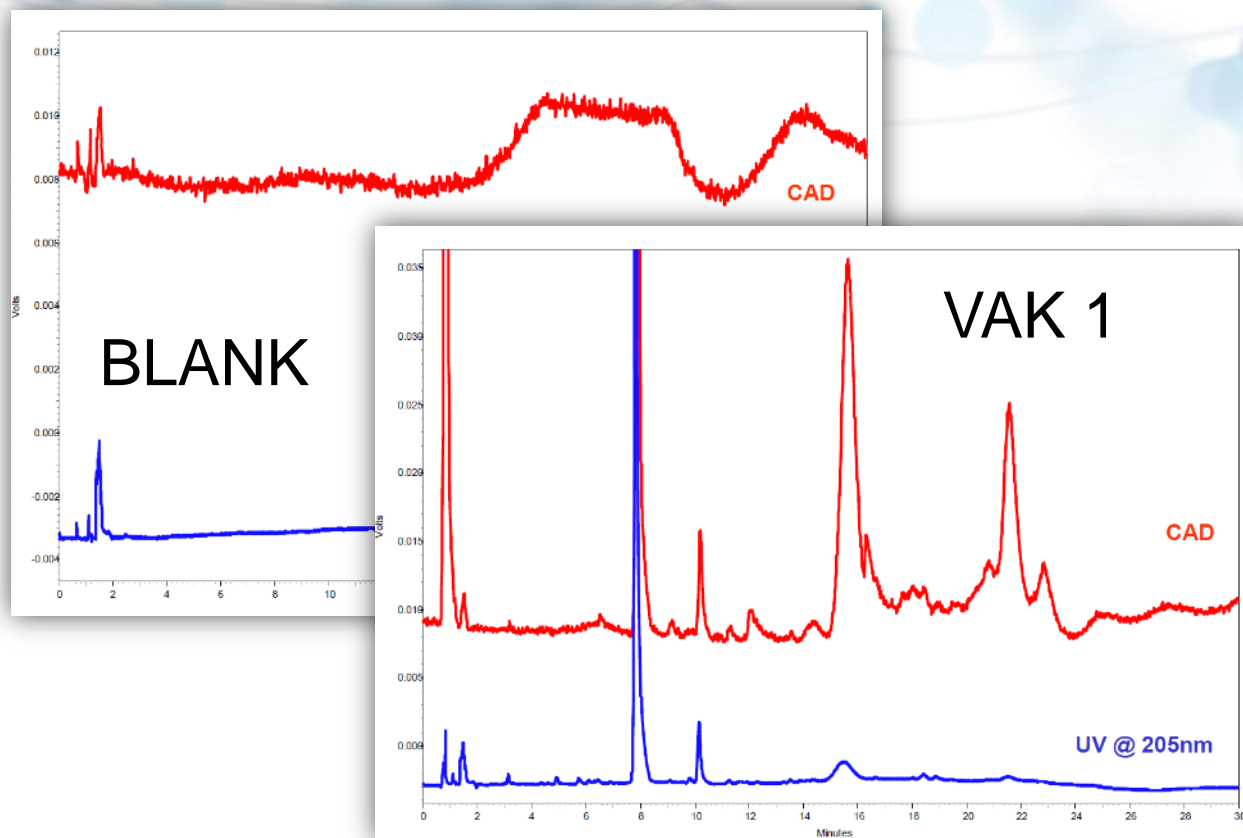


Netěkavé látky



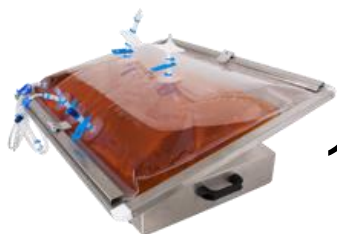
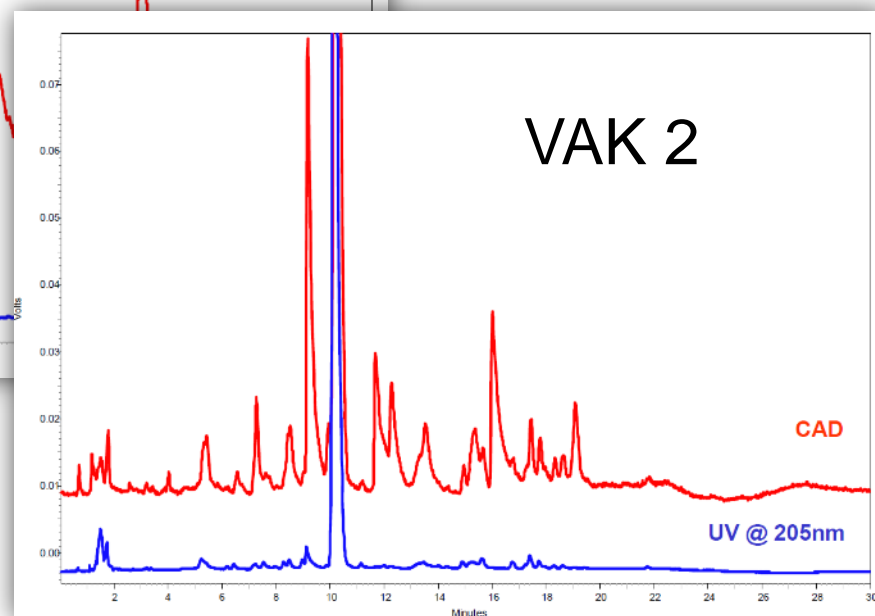
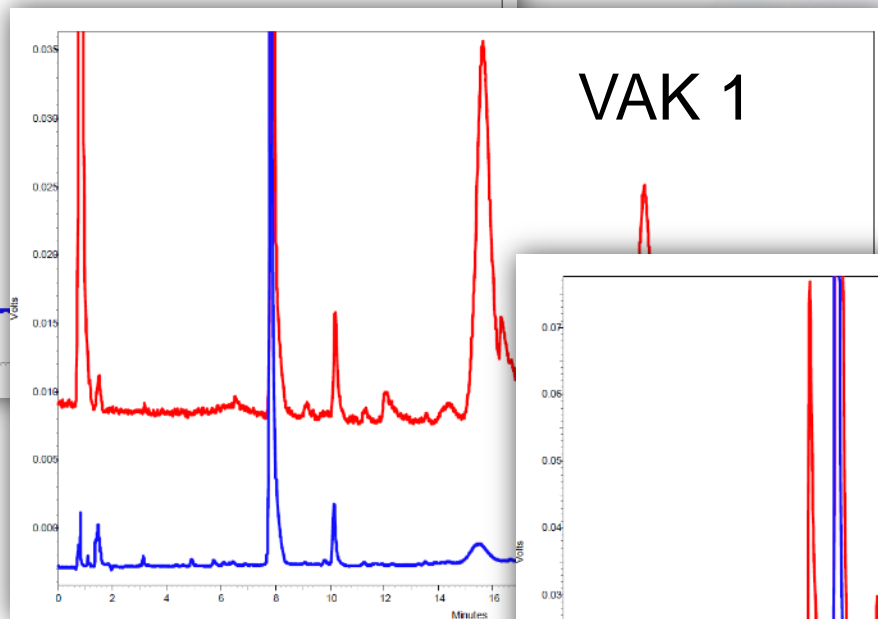
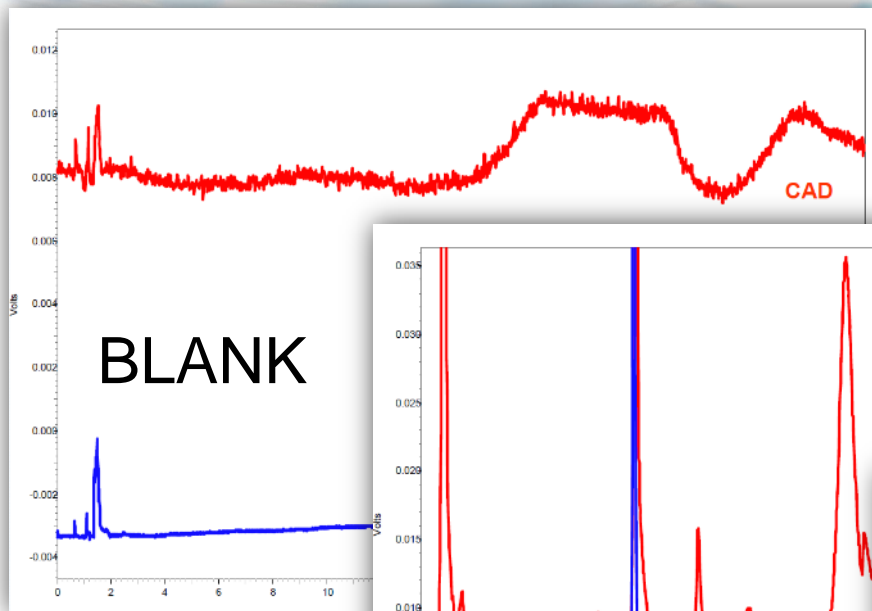
Data from ESA Biosciences, Inc., Chelmsford, MA

Netěkavé látky



Data from ESA Biosciences, Inc., Chelmsford, MA

Netěkavé látky

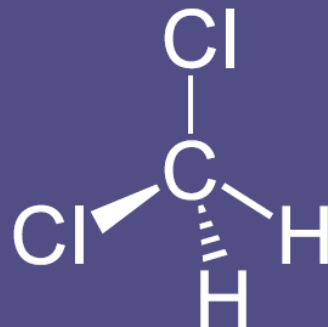


120 nalezených látek

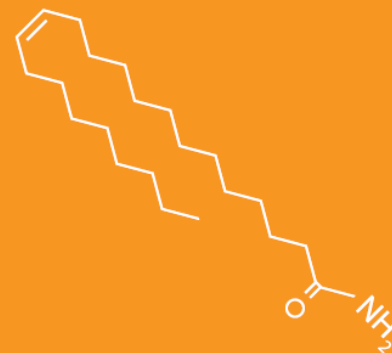
Data from ESA Biosciences, Inc., Chelmsford, MA

Prvková analýza

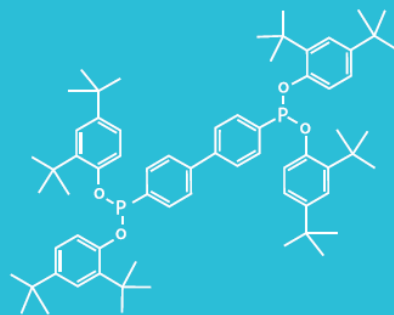
Kovy



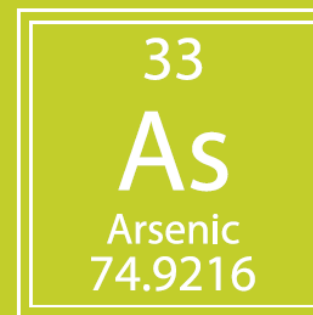
Volatile



Semi-volatile

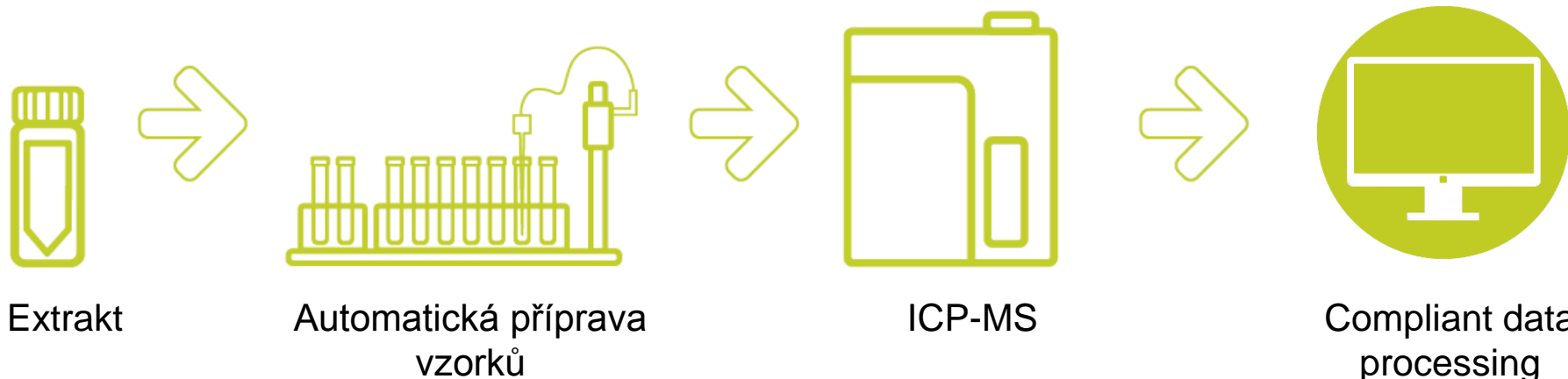


Non-volatile



Elemental

Prvková analýza

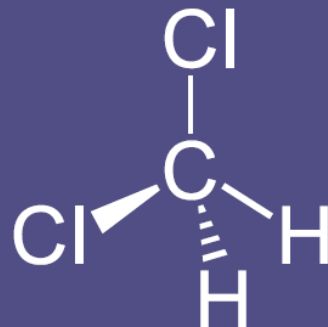


- Analogické k **ICH Q3D a USP 232 & 233**
- Stopová analýza kovů, tolerance k org. matrici
- Thermo Scientific™ iCAP™ RQ ICP-MS
 - Stříbro (Ag) se uvolnilo ze 4 vaků
 - Olovo (Pb) se uvolnilo z 28 vaků



Odpařitelné, semi-volatilní

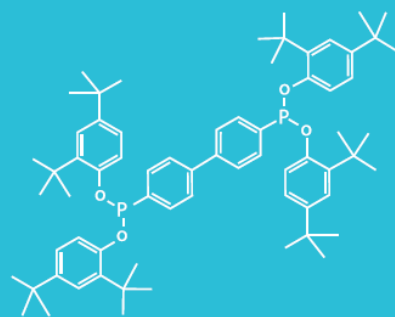
Semi-volatiles



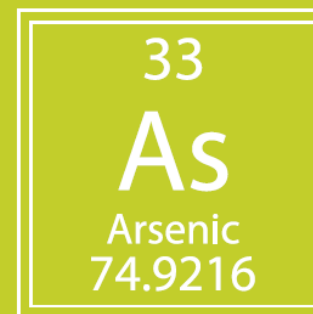
Volatile



Semi-volatile



Non-volatile



Elemental

Odpařitelné, semi-volatilní



- EI/CI ionizace, full scan **HRMS 120k**
- Možnost MS/MS
- Excelentní SW podpora
- Thermo Scientific™ Q Exactive™ GC system



Identifikace



Q Exactive GC Hybrid Quadrupole-Orbitrap GC-MS/MS system

Trace 1310 GC system

TraceFinder software

TRACE 1310 GC Parameters

Injection Volume (uL):	1
Liner	Single gooseneck
Inlet (°C):	280
Carrier Gas, (mL/min):	He, 1.3

Oven Temperature Program:

Temperature 1 (°C):	40
Hold Time (min):	1
Temperature 2 (°C):	320
Rate (°C/min)	5.5
Hold Time (min):	12

Q Exactive GC MS Parameters

Transfer line (°C):	280
Ionization type:	EI
Ion source(°C):	230
Electron energy (eV):	70
Acquisition mode:	Full scan
Mass range (Da):	50-700
Mass resolution (FWHM):	120k
Lockmass (m/z):	207.03235

Identifikace

Vzorky těsnění

- **A** červené
- **B** hnědé
- **C** bílé
- **D** černé
- **Blank**



Plechovka

- **300 ml hexanu**
- **16 hod/lab. teplota**
- **Zakoncentrování na 1 ml**

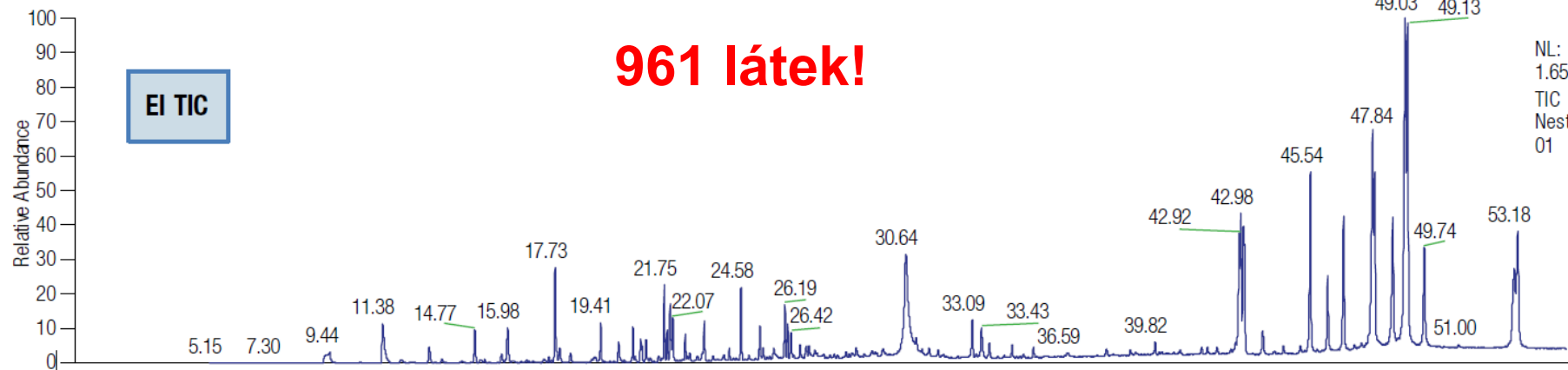


Identifikace

RT: 0.00 - 55.01

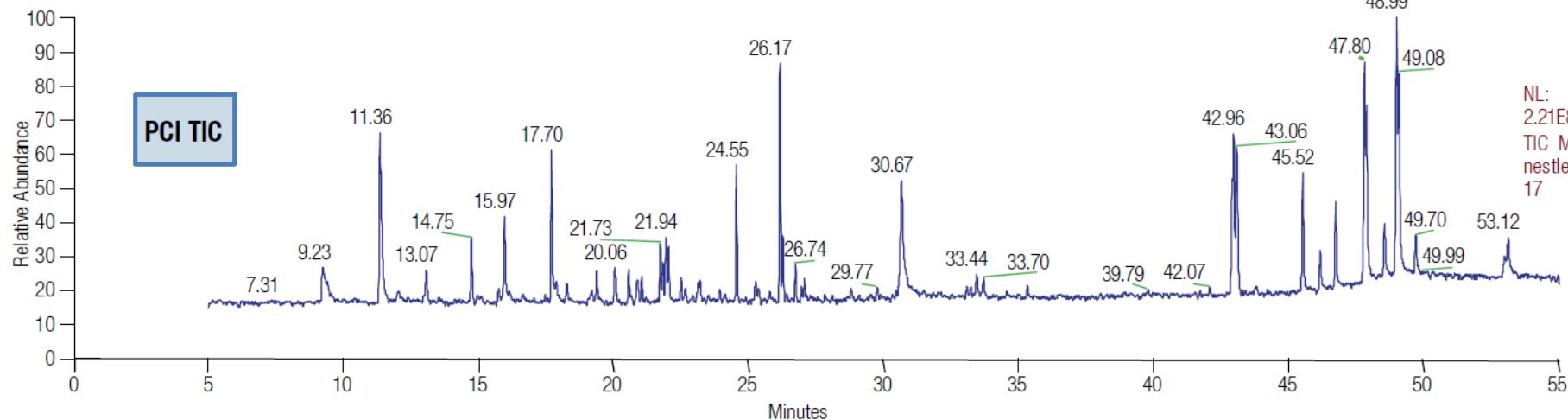
961 látek!

EI TIC



NL:
1.65E10
TIC MS
Nestle_pk_0
01

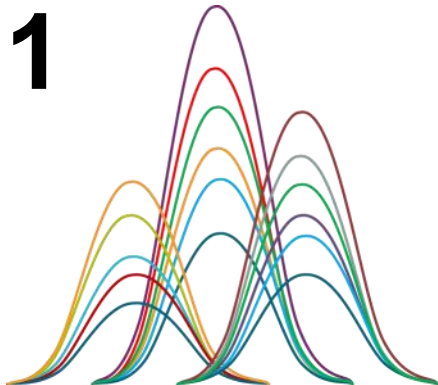
PCI TIC



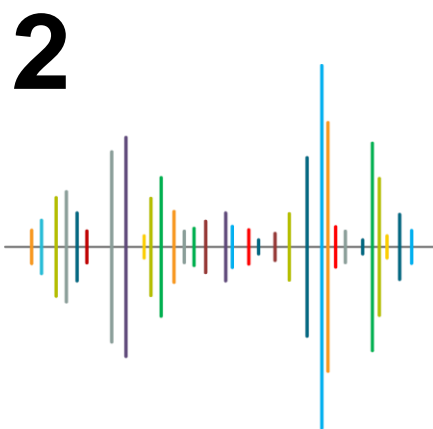
NL:
2.21E8
TIC MS
nestle_pk_0
17

Identifikace

Detekce/dekonvoluce Generování kandidátů

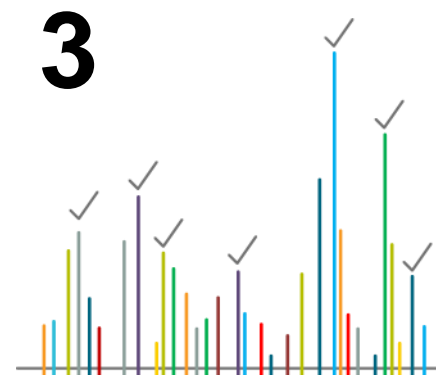


- detekcí píků
- HR dekonvoluce
- „čištění“ spektra



- hledání v knihovnách
- generování kandidátů

Filtrování, identifikace



- HR filtrování kandidátů
- hypotéza, identifikace

preferován (semi)automatizovaný proces

Identifikace

Kombinace SI (search index) a HRF (high resolution filtering) = hodnota skóre (%)

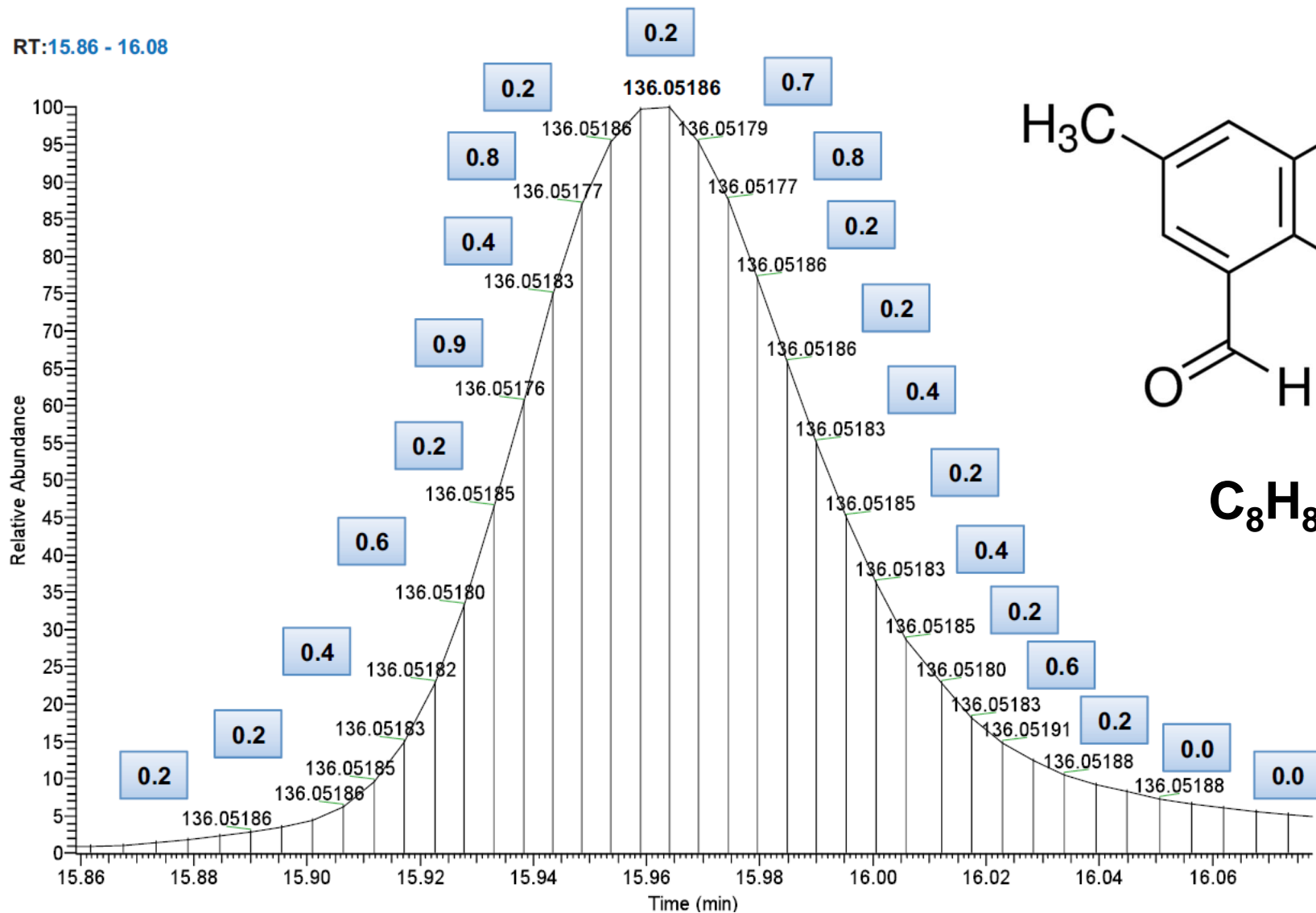
Peak Identification

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

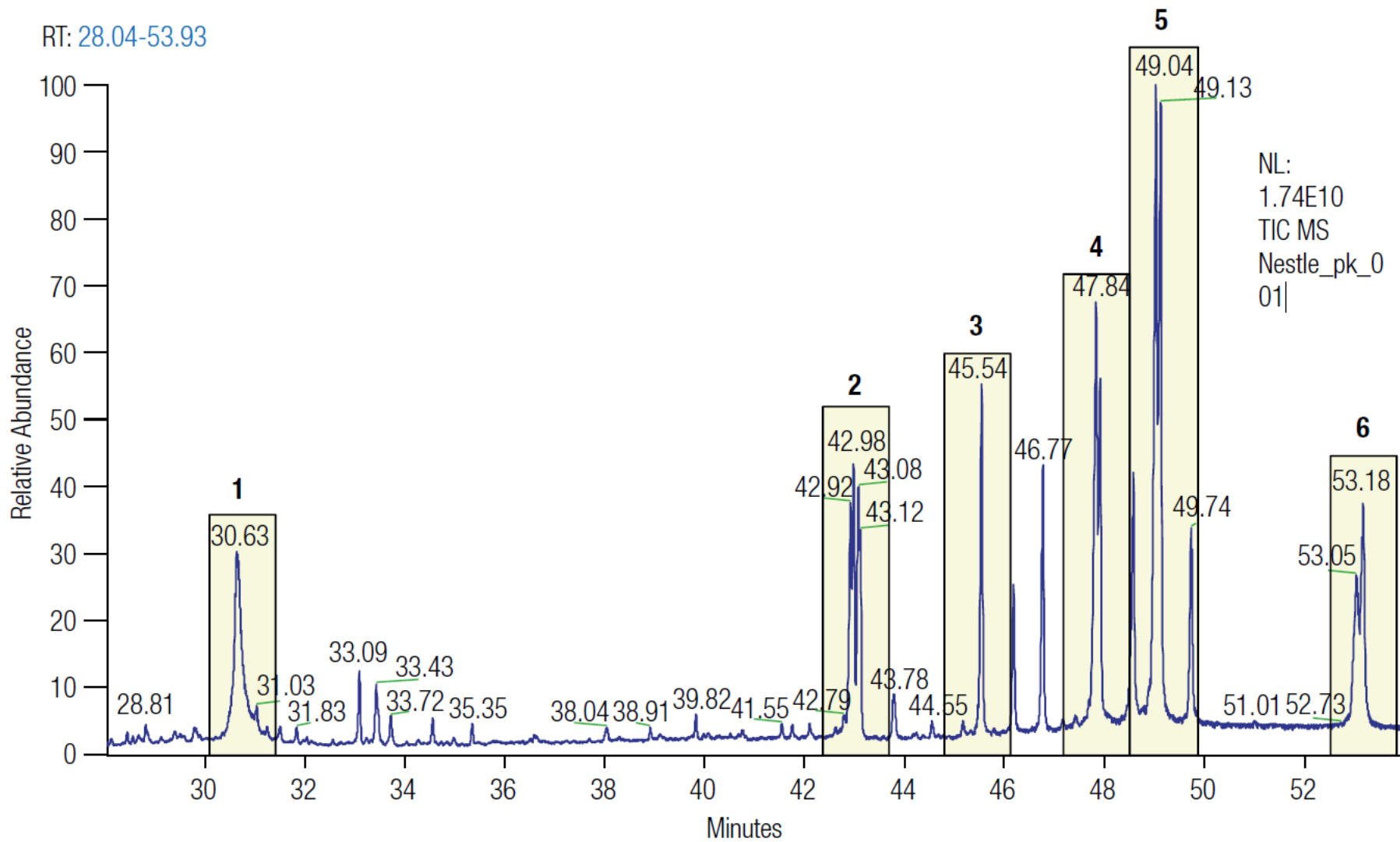
$$\text{HRF skóre} = \frac{\sum (m/z * \text{Intenzita})_{\text{vysvětlené}}}{\sum (m/z * \text{Intenzita})_{\text{nalezené}}} \times 100\%$$

Identifikace

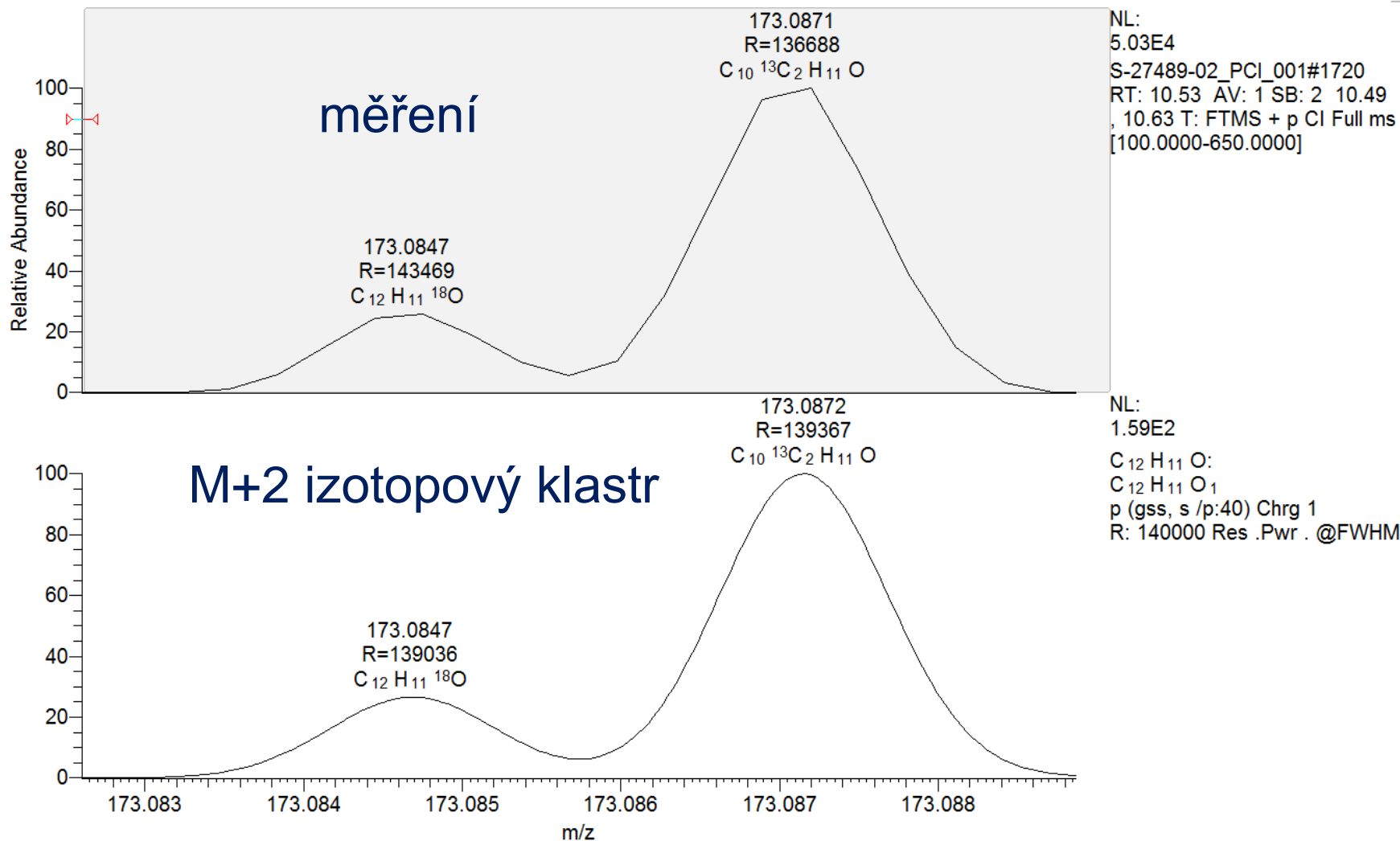
RT: 15.86 - 16.08



Identifikace



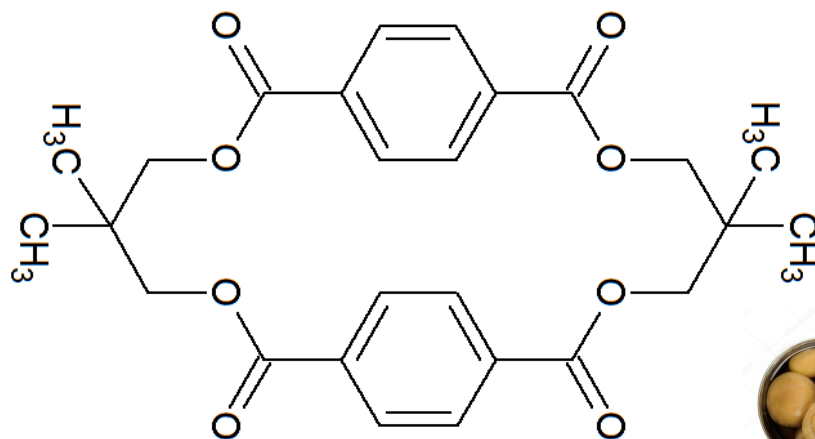
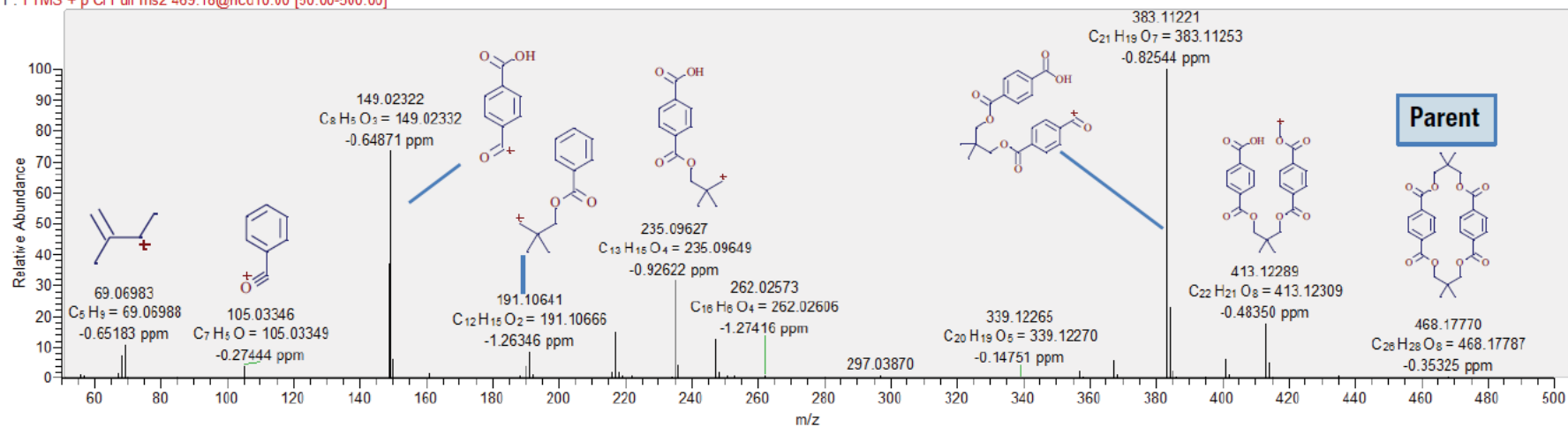
Identifikace



NUM

Identifikace – přehled

Packaging_MSMS_001 #7300 RT: 23.47 AV: 1 NL: 2.80E5
 F: FTMS + p Cl Full ms2 469.18@hcd10.00 [50.00-500.00]



Compound Discoverer 2.0

Děkuji za pozornost!

