

# 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)

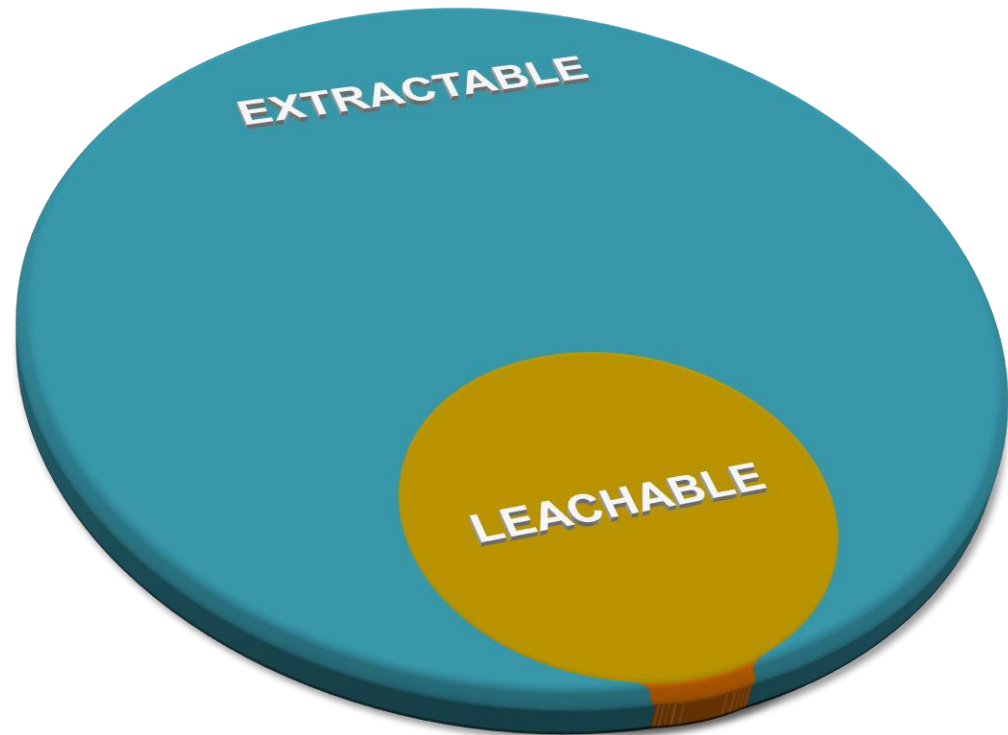
## EXTRACTABLE

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)

- Etiketeta

- inkoust
- solvent
- lepidlo
- lak

- Obal

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

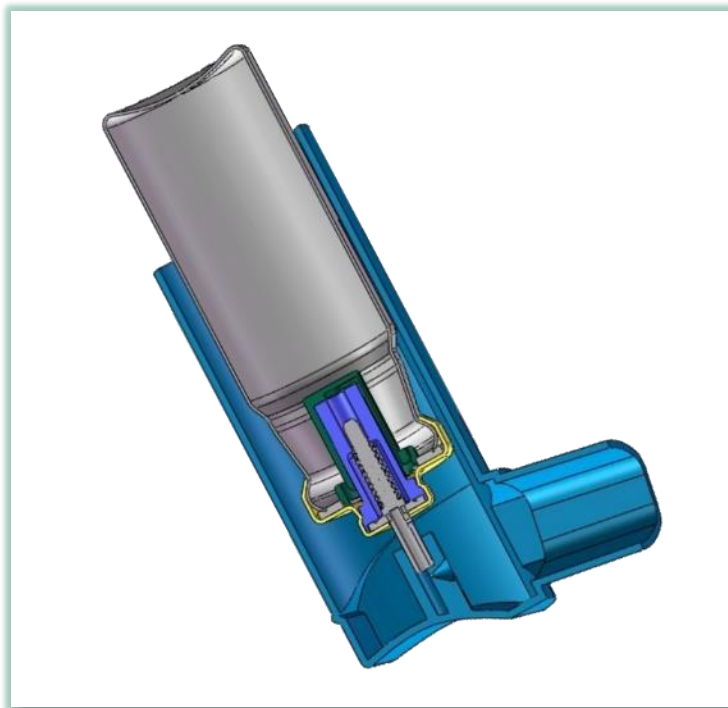


- Krabička

- sterilizační přísada
- konzervant
- potisk

# Extrahovatelné a louhovatelné látky (E&L)

## EXTRACTABLE



**Testuje se materiál**

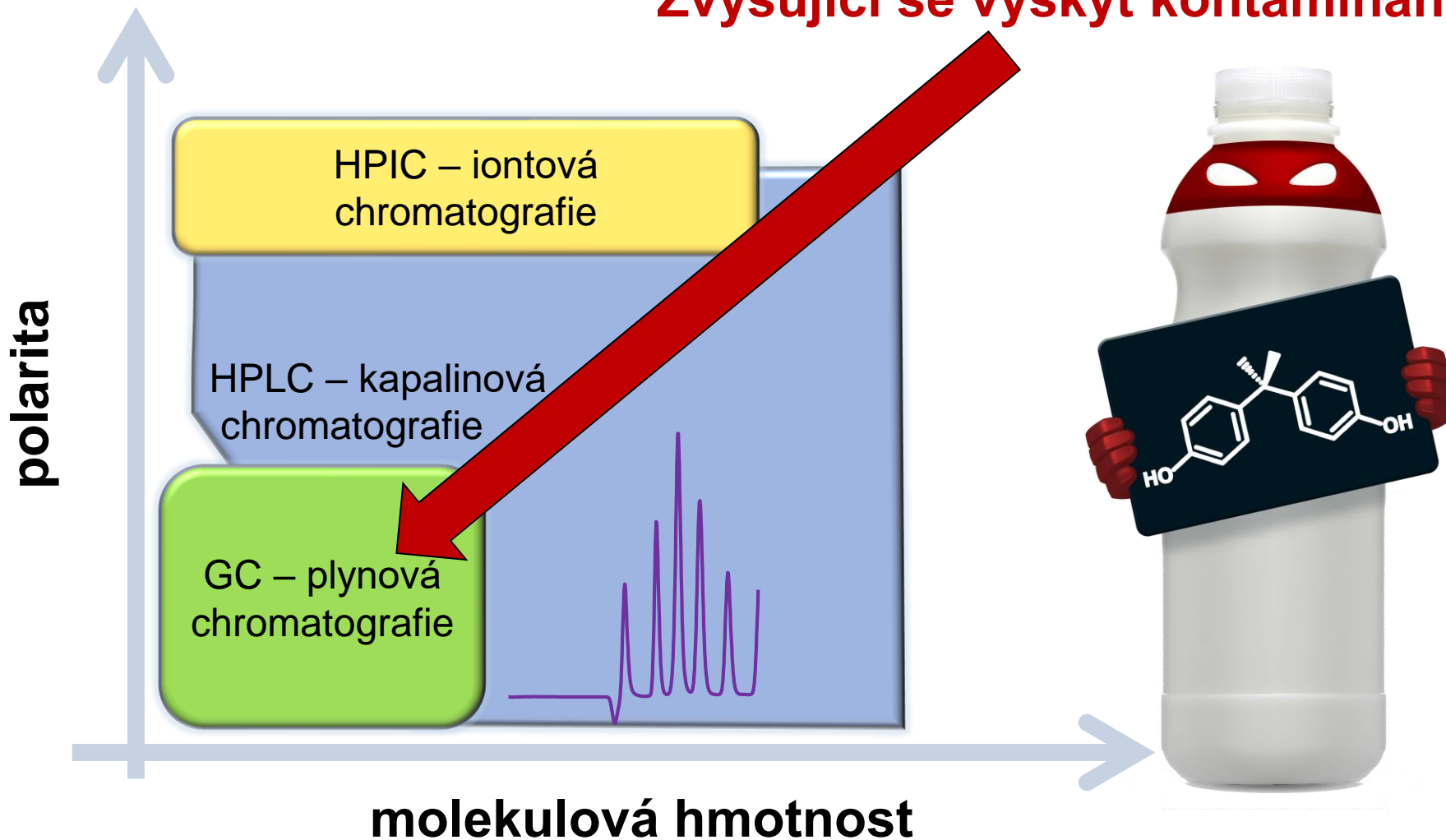
## LEACHABLE



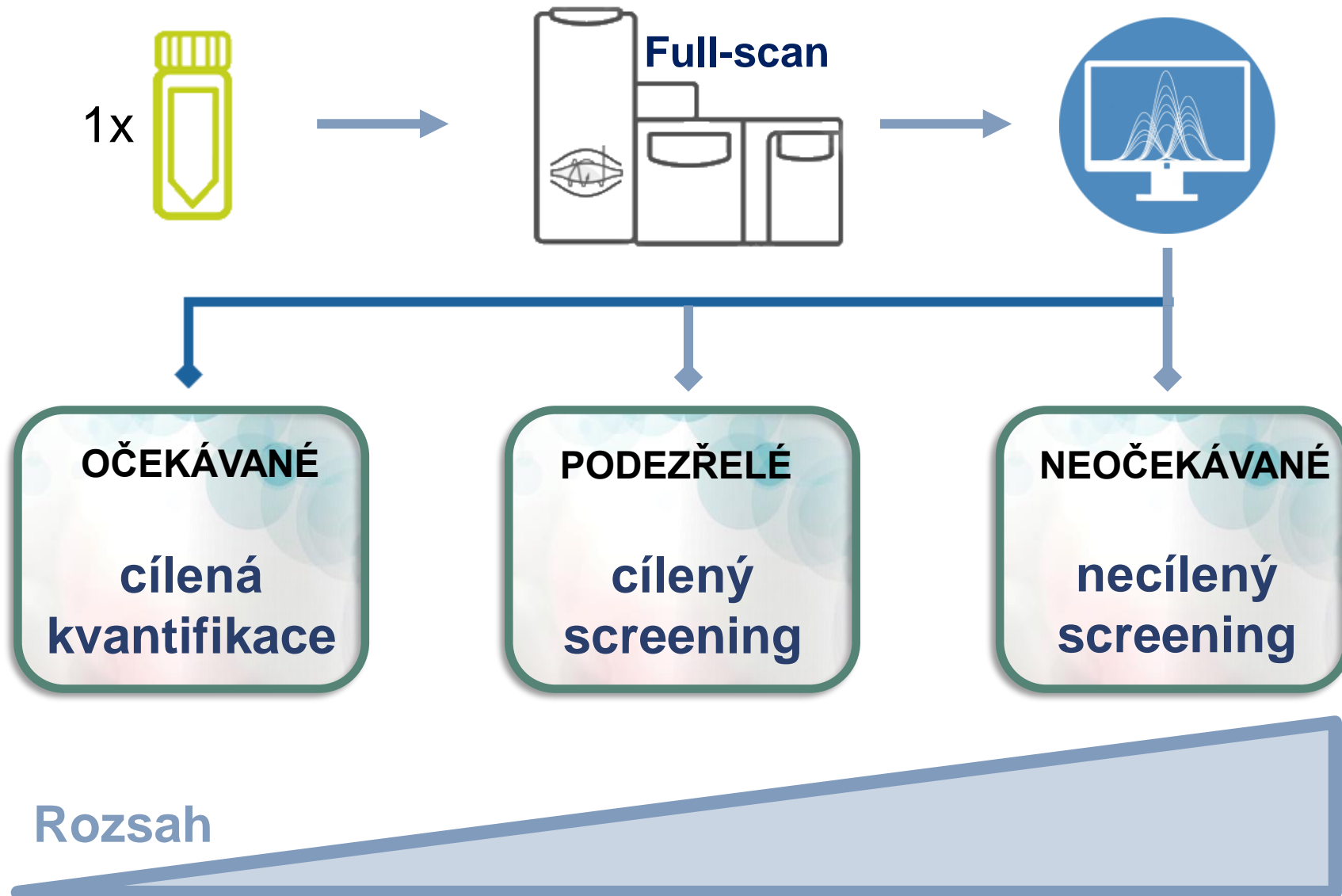
**Testuje se produkt**

# Analytická separace

Zvyšující se výskyt kontaminantů

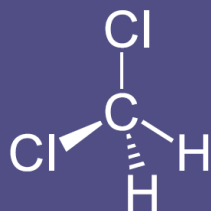


# Cílená a necílená analýza



# Analýza

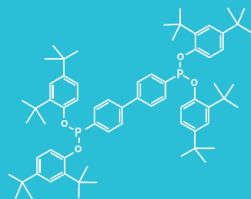
- GC-MS
- GC-HRMS
- Headspace
- EI & CI
- Library



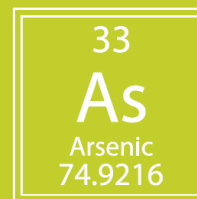
Volatile



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

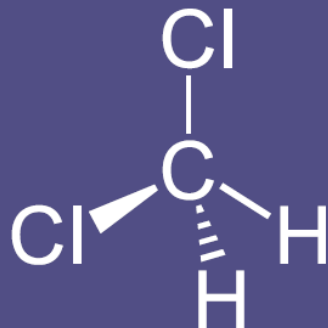
**ThermoFisher**  
S C I E N T I F I C



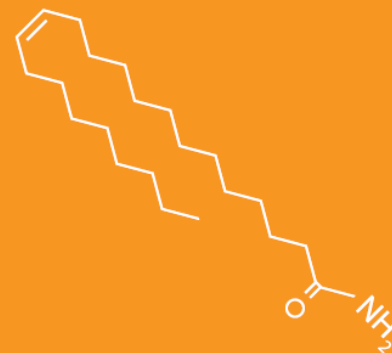


# Těkavé látky

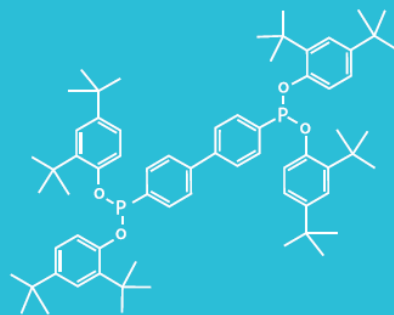
Těkavé



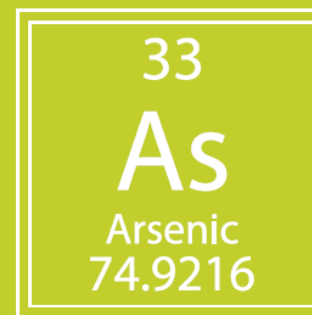
Volatile



Semi-volatile

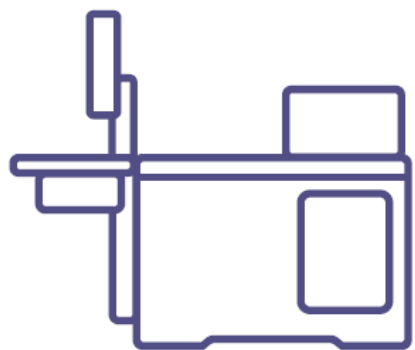


Non-volatile



Elemental

# Těkavé látky



Vzorek + valve & loop headspace



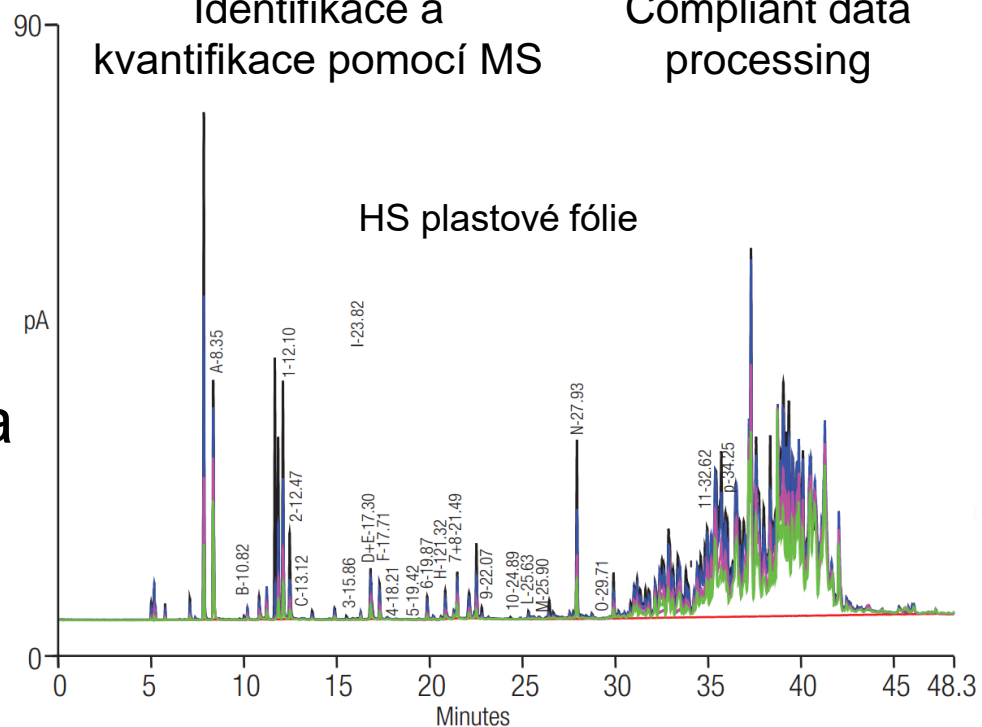
Robustní separace



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

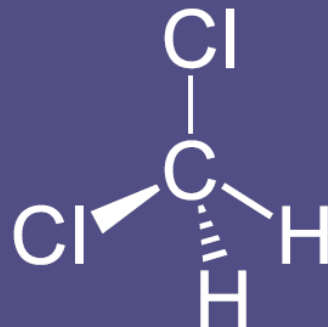


Thermo Scientific™ AppsLab Library™



# Netěkavé látky

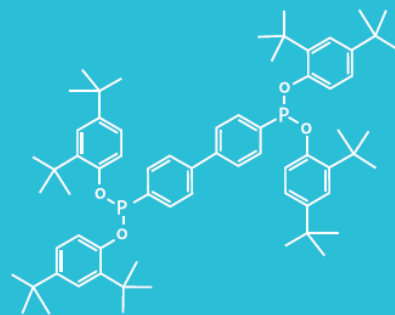
Netěkavé



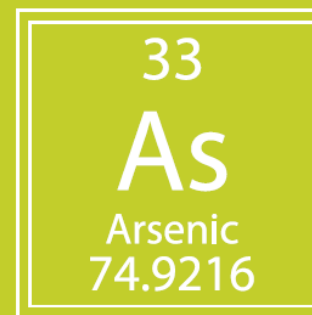
Volatile



Semi-volatile



Non-volatile



Elemental

# Netěkavé látky

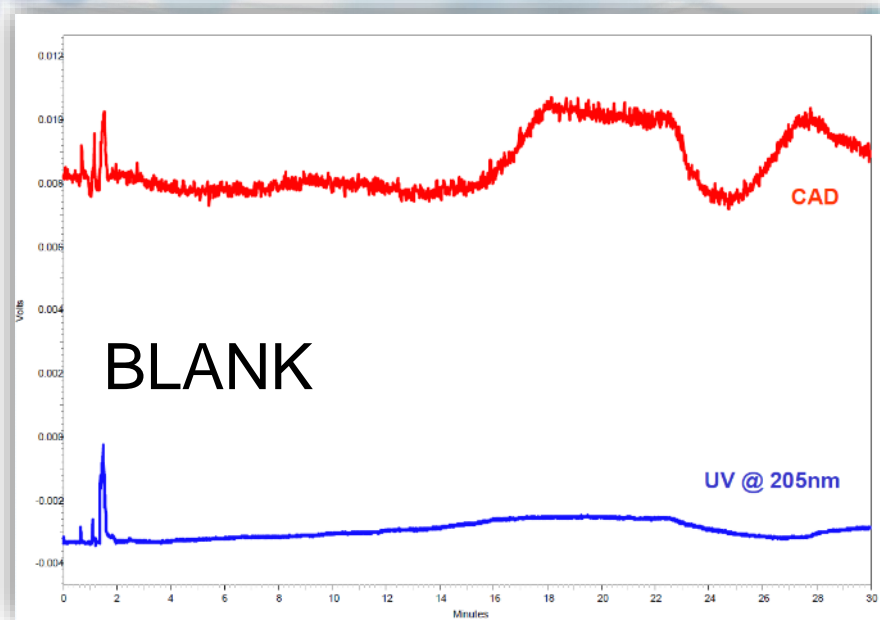


- Detekce v pozitivním i negativním módu
- **Elementární složení**
- Informace o struktuře (fragmentace)
- Zachytit vše – **kombinace s Corona CAD**



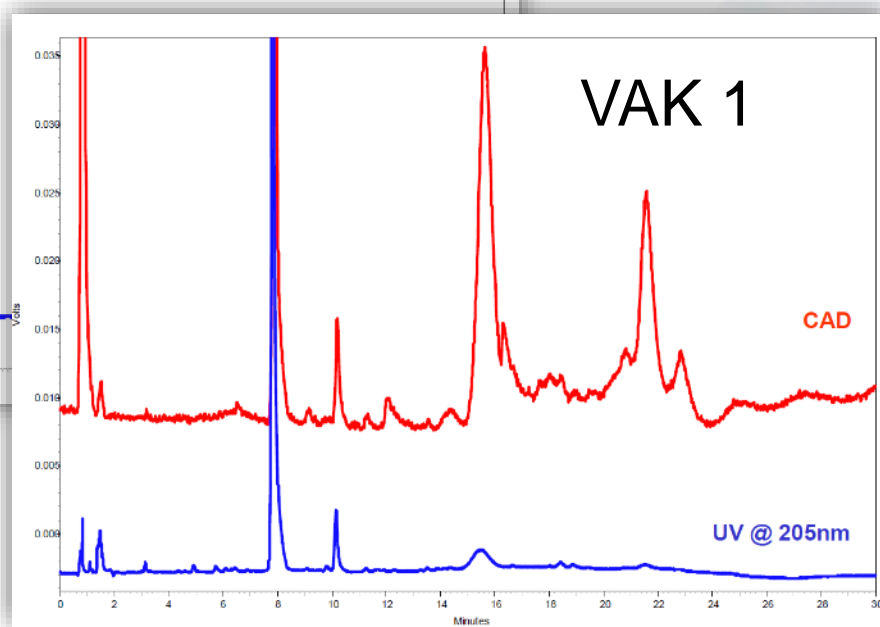
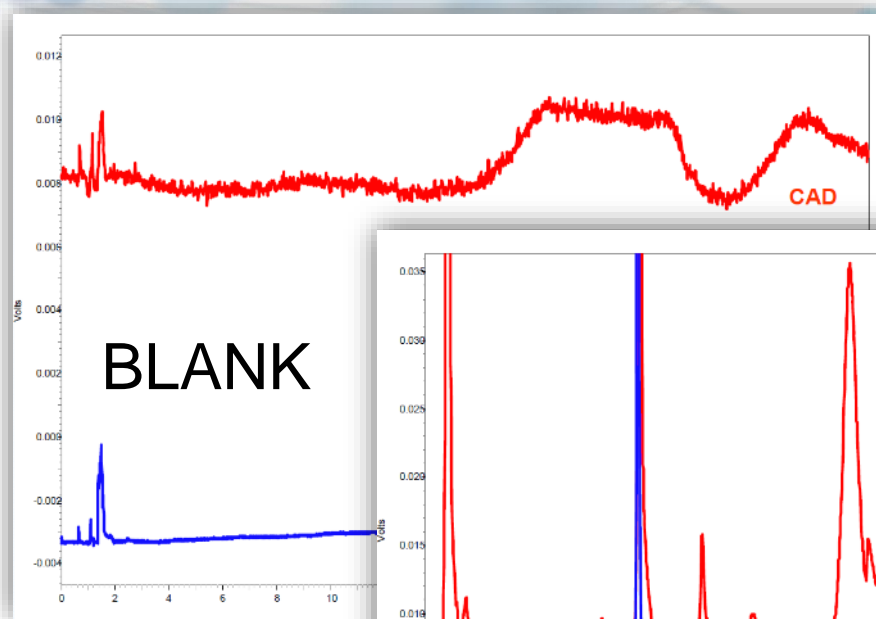


# Netěkavé látky



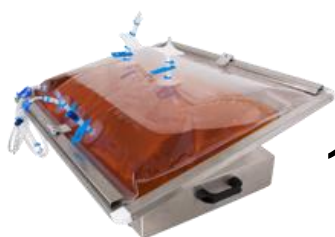
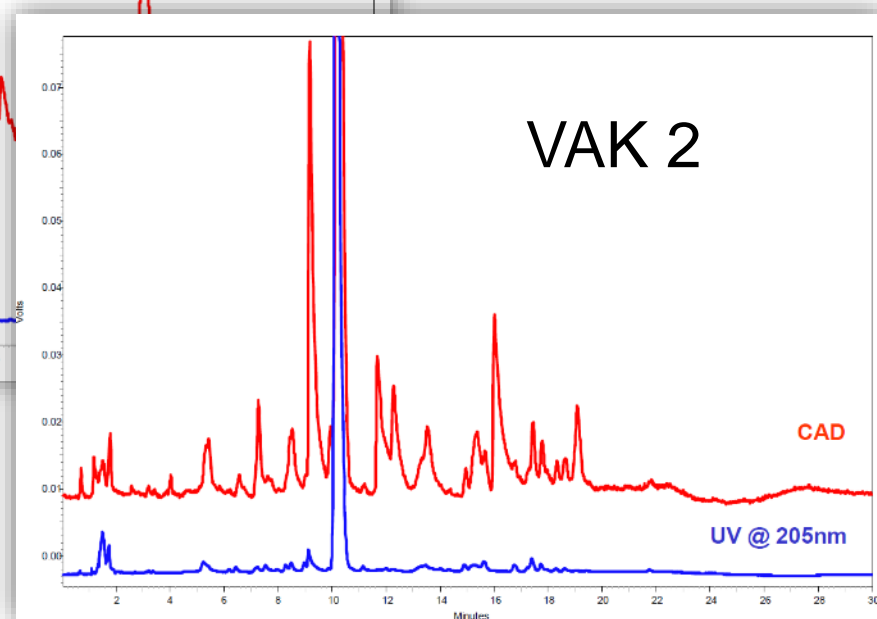
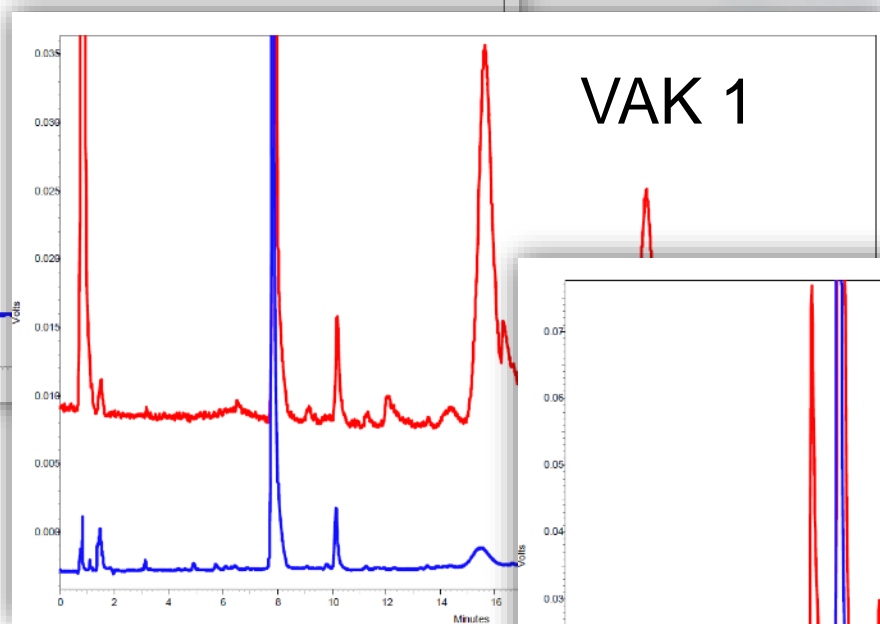
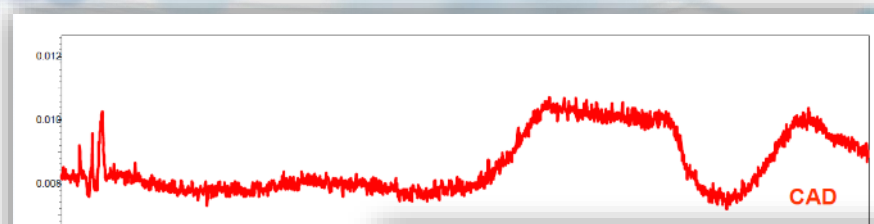
Data from ESA Biosciences, Inc., Chelmsford, MA

# Netěkavé látky



Data from ESA Biosciences, Inc., Chelmsford, MA

# Netěkavé látky

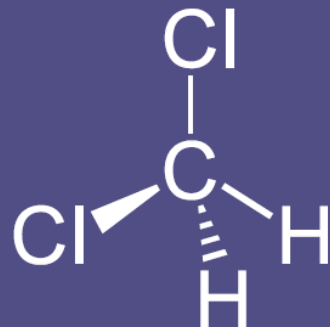


120 nalezených látek

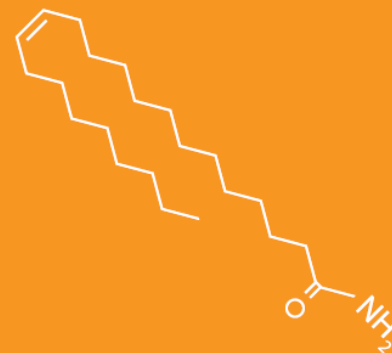
Data from ESA Biosciences, Inc., Chelmsford, MA

# Prvková analýza

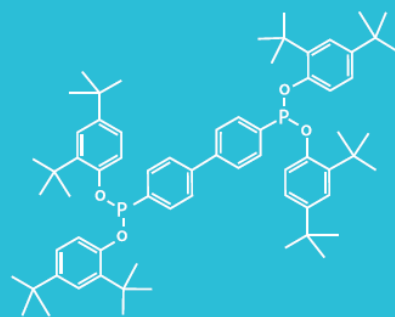
Kovy



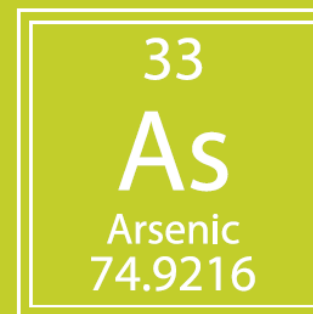
Volatile



Semi-volatile

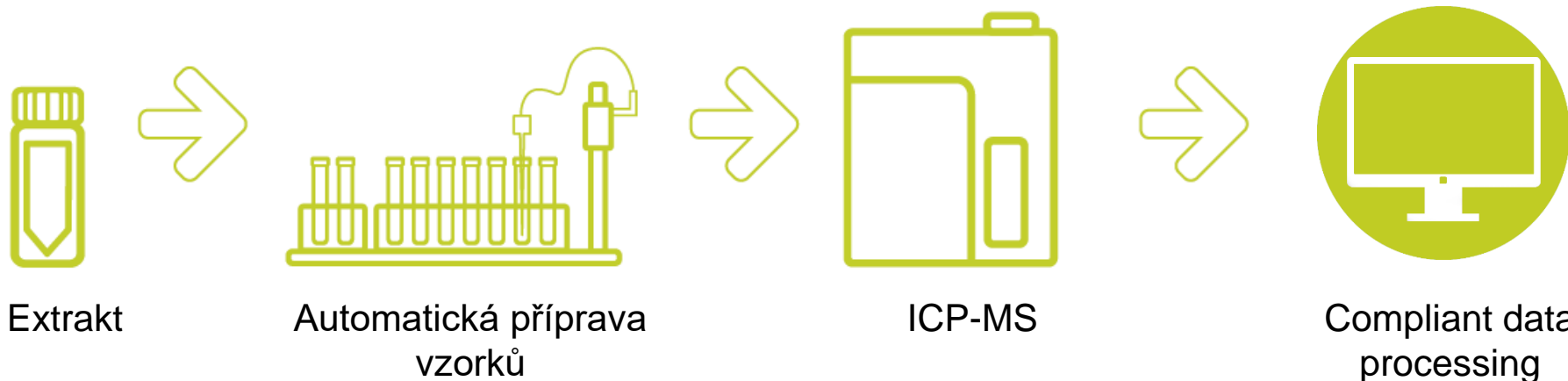


Non-volatile



Elemental

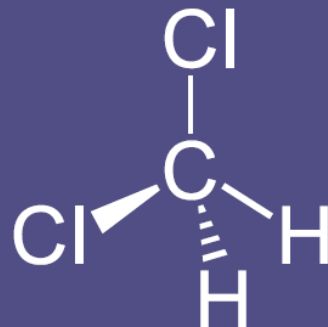
# Prvková analýza



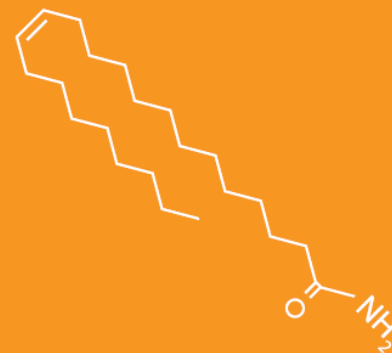
- Analogické k **ICH Q3D a USP 232 & 233**
- Stopová analýza kovů, tolerance k org. matrici
- Thermo Scientific™ iCAP™ RQ ICP-MS
  - Stříbro (Ag) se uvolnilo ze 4 vaků
  - Olovo (Pb) se uvolnilo z 28 vaků

# Odpařitelné, semi-volatilní

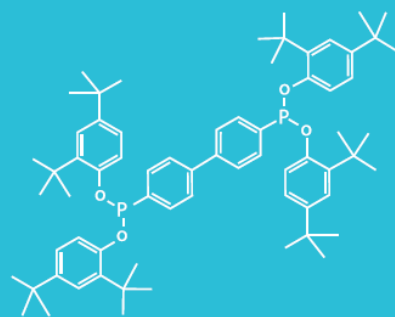
## Semi-volatiles



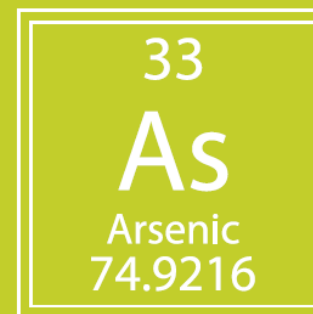
Volatile



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**

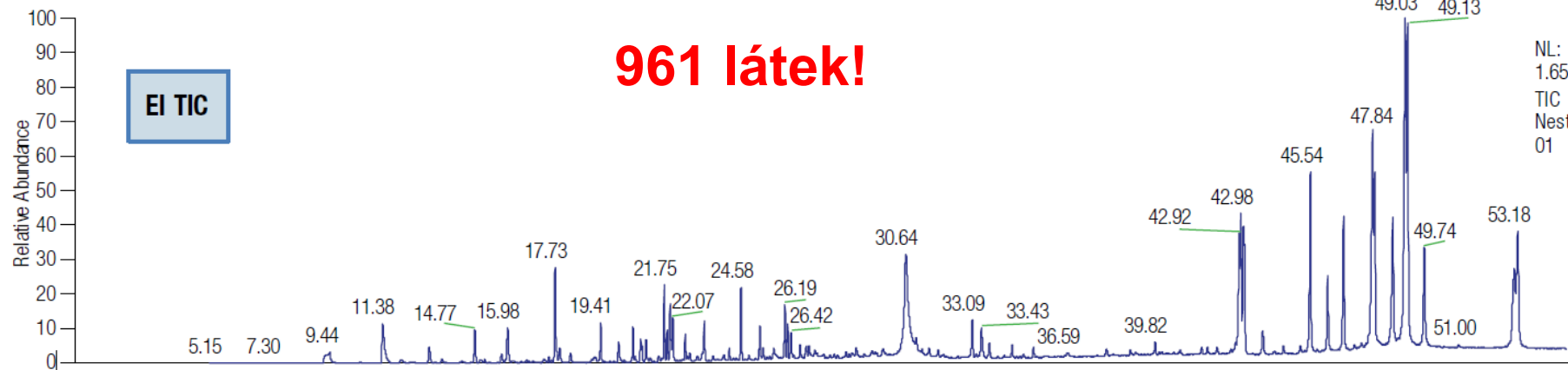


# Identifikace

RT: 0.00 - 55.01

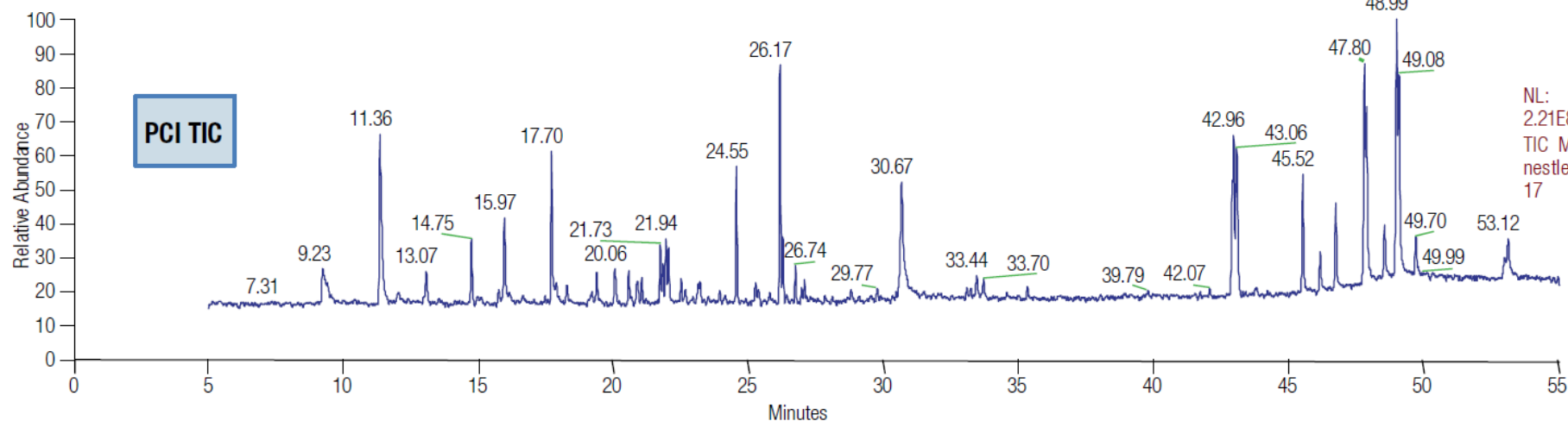
## 961 látek!

EI TIC



NL:  
1.65E10  
TIC MS  
Nestle\_pk\_0  
01

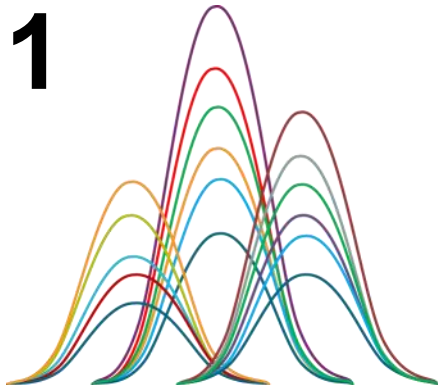
PCI TIC



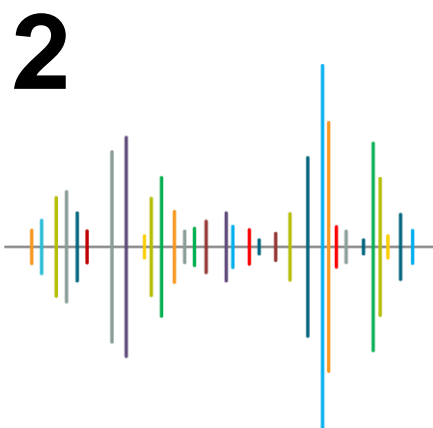
NL:  
2.21E8  
TIC MS  
nestle\_pk\_0  
17

# Identifikace

## Detekce/dekonvoluce Generování kandidátů

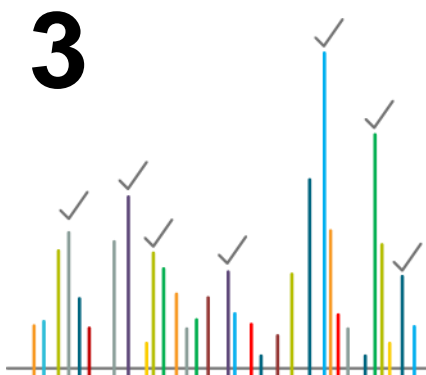


- detekcí píků
- HR dekonvoluce
- „čištění“ spektra



- 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 (%)

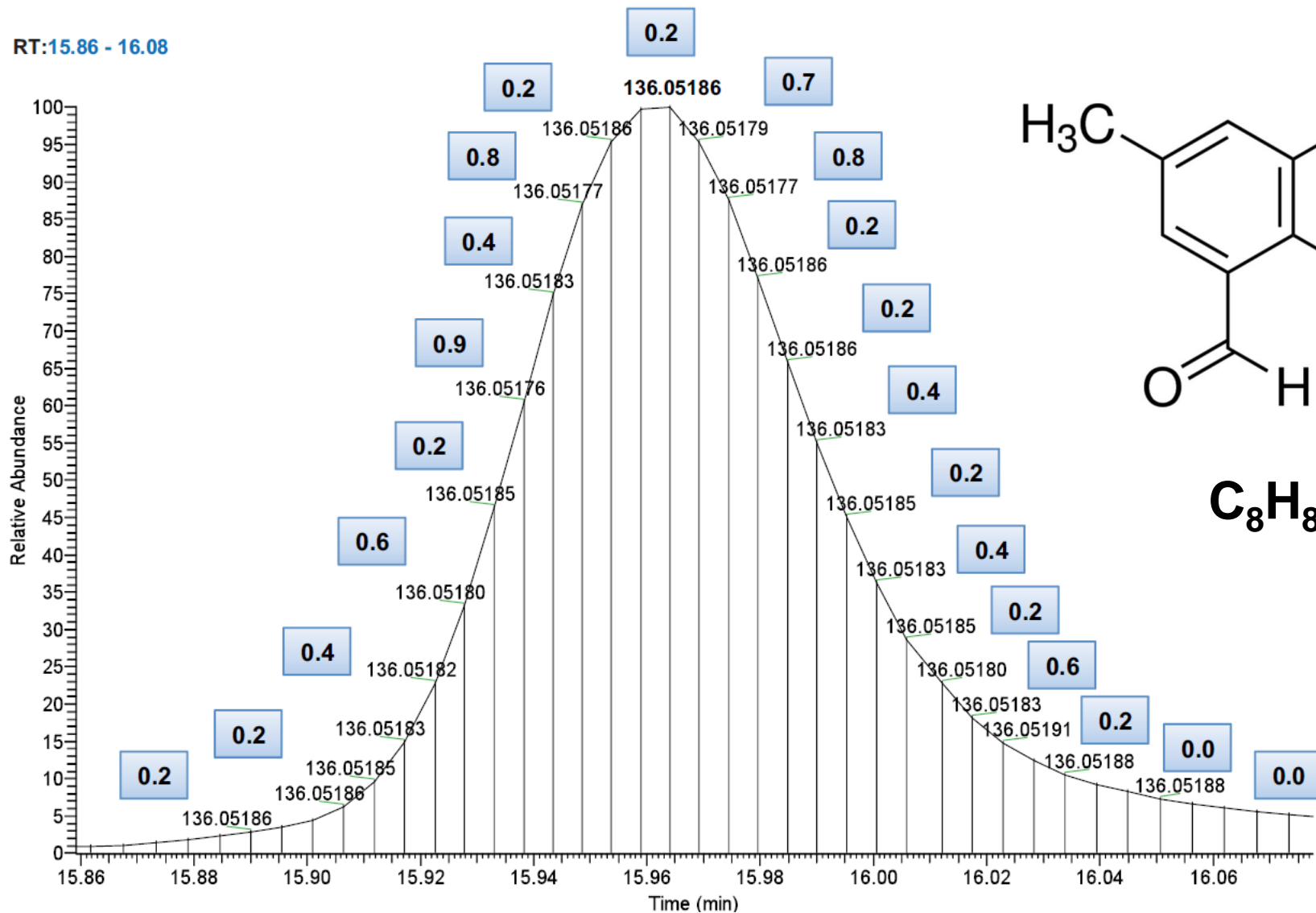
Peak Identification

Score	Matched Compound	Formula	CAS	SI	HRF Score	M+ m/z	M+	M+ Lib	% Elements
<b>94.4</b>	<b>1,4-Dihydrophenacetic acid,...</b>	<b>C18H30O2</b>		<b>728</b>	<b>99.4959</b>	<b>278.22403</b>	<b>Yes</b>	<b>Yes</b>	<b>100</b>
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

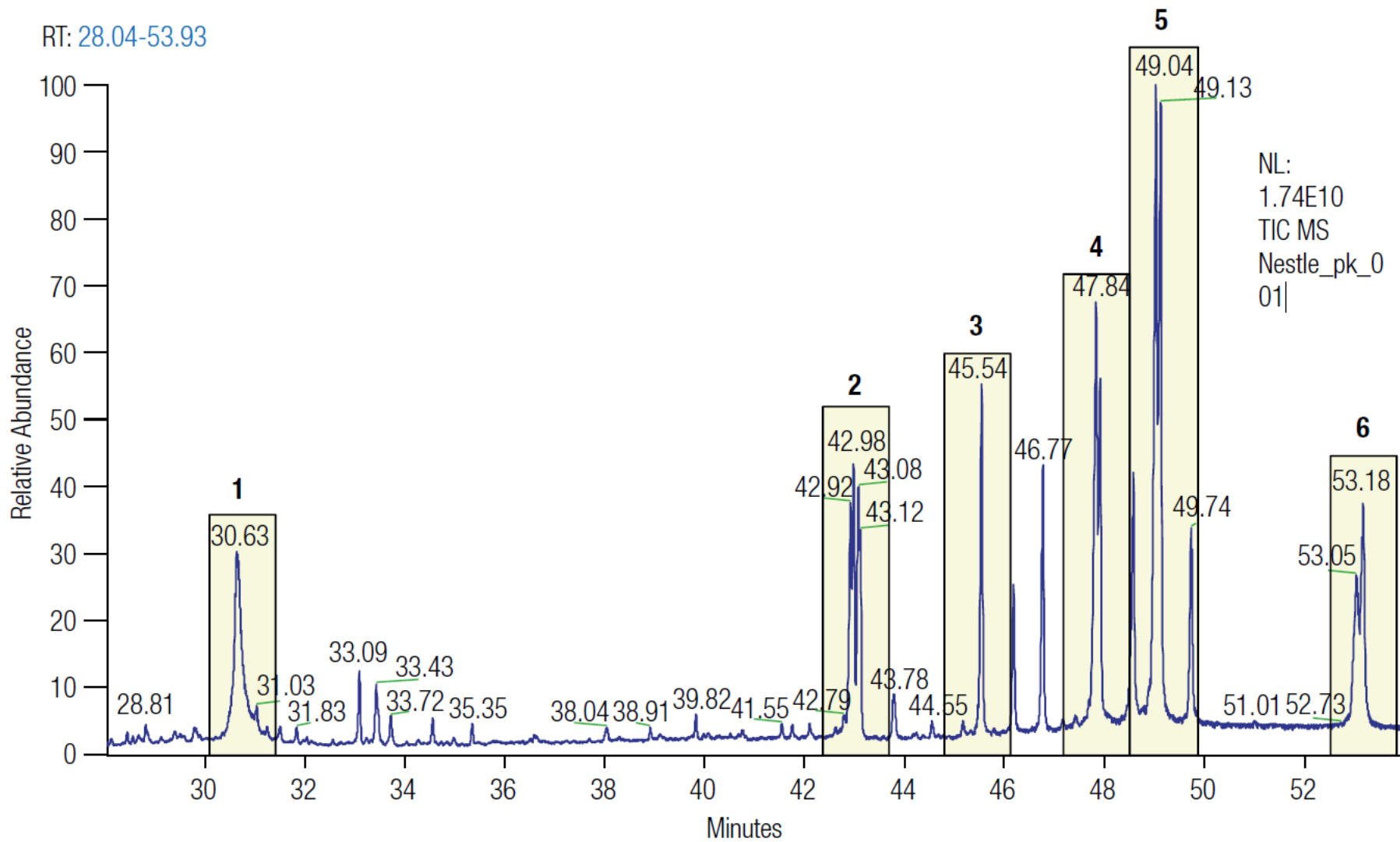
$$\text{HRF skóre} = \frac{\sum (m/z * \text{Intenzita})_{\text{vysvětlené}}}{\sum (m/z * \text{Intenzita})_{\text{nalezené}}} \times 100\%$$

# Identifikace

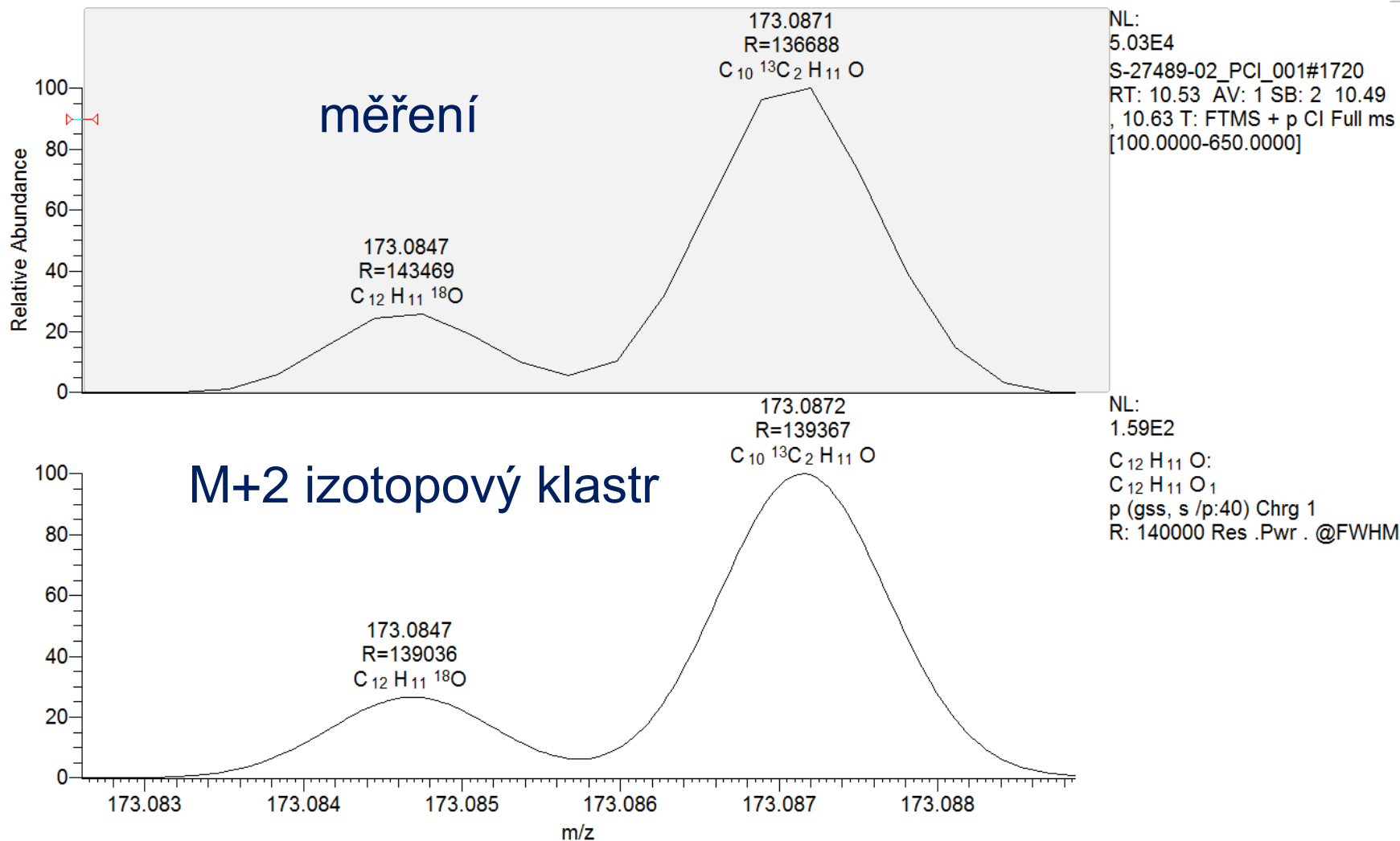
RT: 15.86 - 16.08



# Identifikace



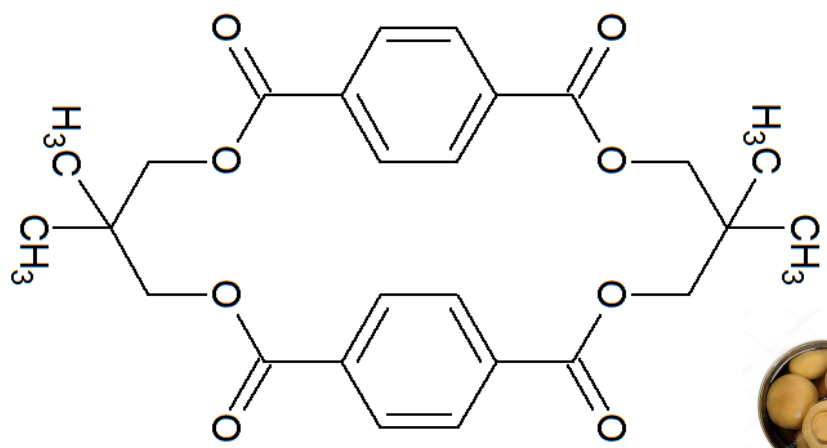
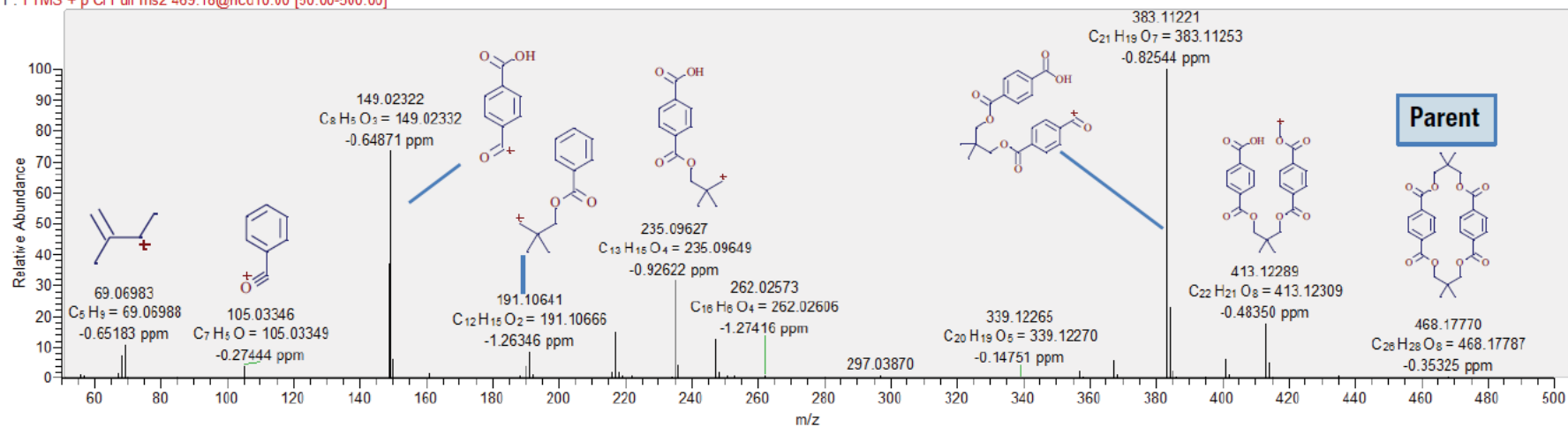
# Identifikace



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!

