Suspect and non-target screening approaches for GC-MS

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Hunts Needle in a Haystack

HOW LONG does it take to find a needle in a haystack? Jim Moran, Washington, D. C., publicity man, recently dropped a needle into a convenient pile of hay, hopped in after it, and began an intensive search for (a) some publicity and (b) the needle. Having found the former, Moran abandoned the needle hunt.

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Jim Moran
Publicity Stunts

...

...

February 1939: Searched for a needle in a haystack. The search took him 82.5 hours before he finally found it "near the bottom and slightly to the left of center."

He sent the found needle to the Smithsonian Institution.

...

...

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Target Screening

Suspect (clover)

Non-target (unexpected stuff)

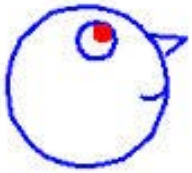
Suspect screening for river contaminants

- WFD compounds and candidates
- Lists of known river pollutants
- Use pattern based emission models
- Molecular level source-receptor emission models
- Top-down approach to identification

Non-target screening

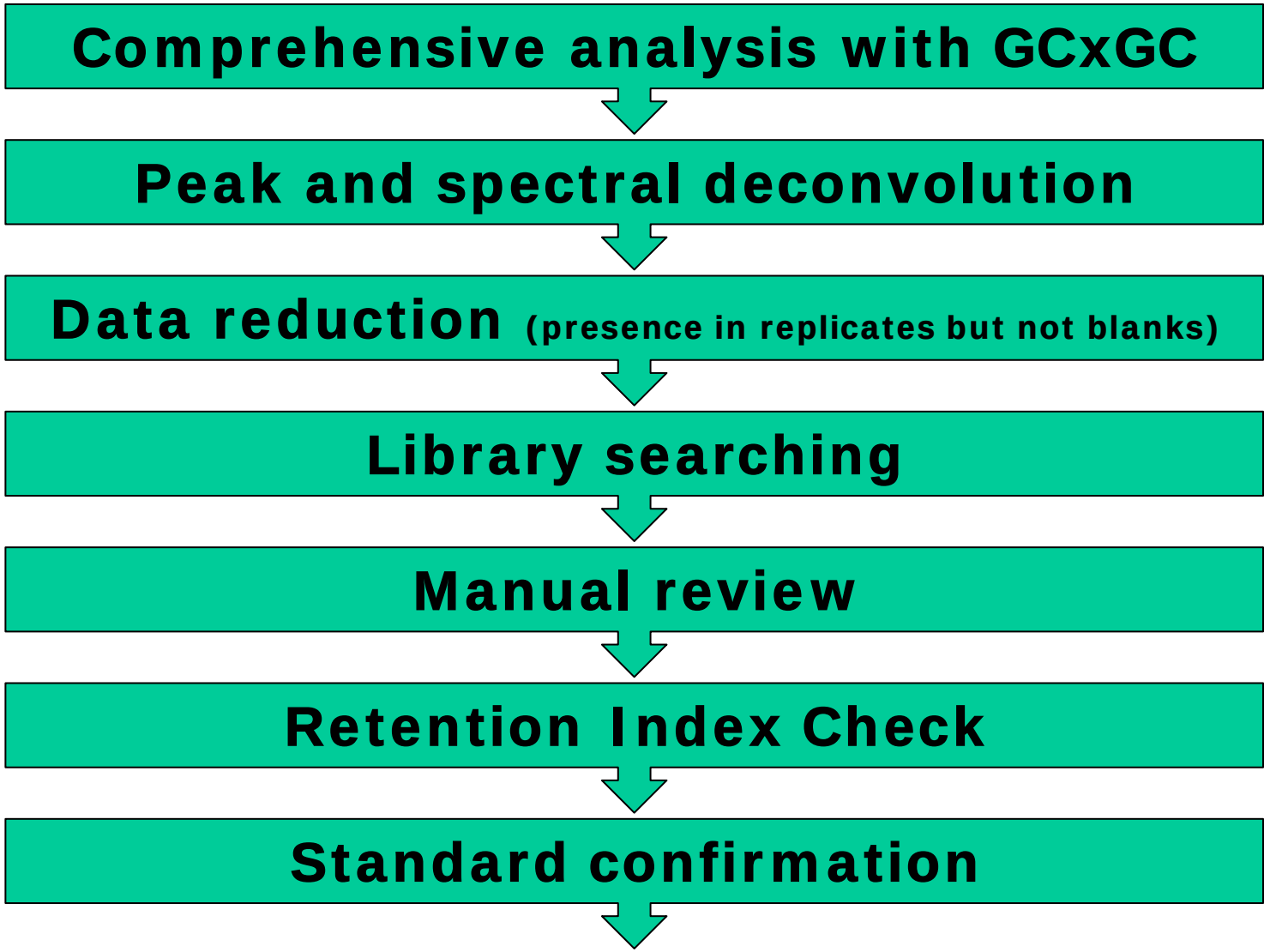
- Bottom-up approach to identification
- Unguided approach – Total characterization
- Guided approach – “omics”

Suspect



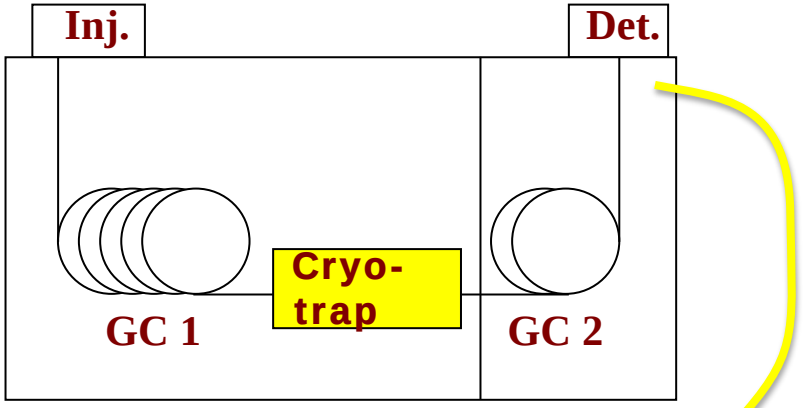
Non-target

Unguided: e.g. Norman NTS

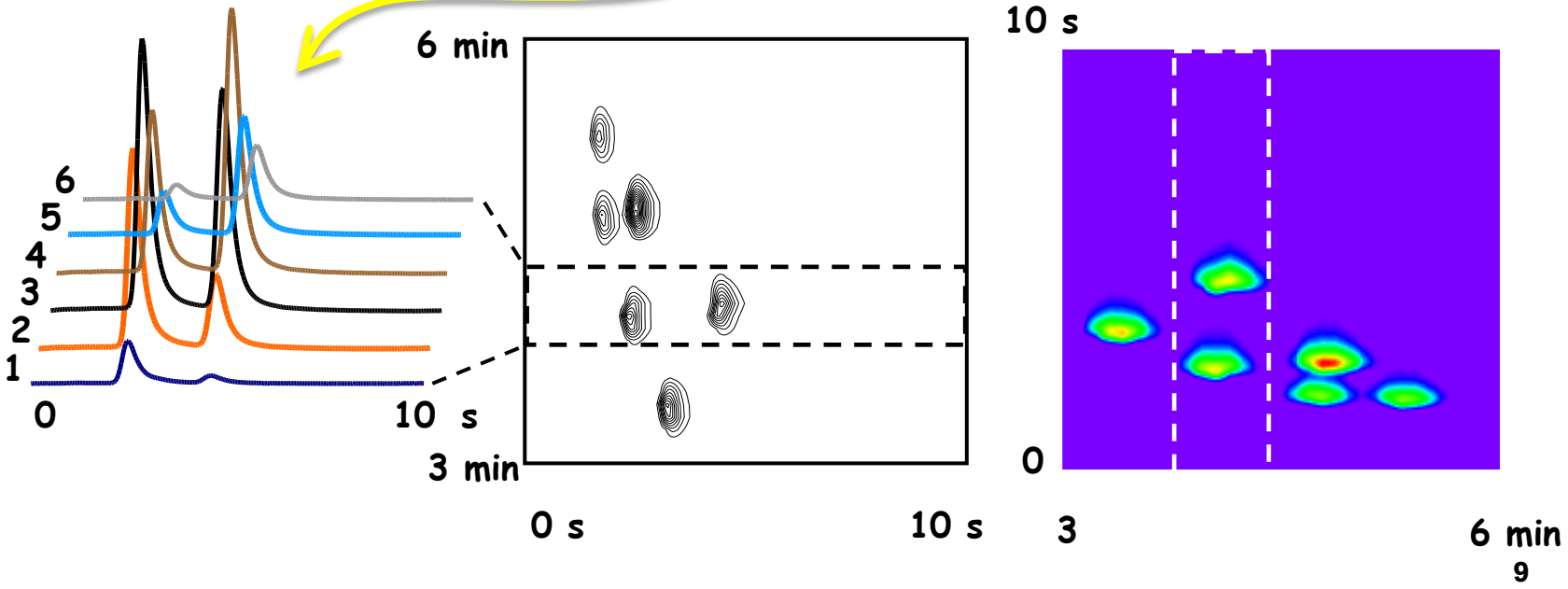


Guided: e.g. C-omics

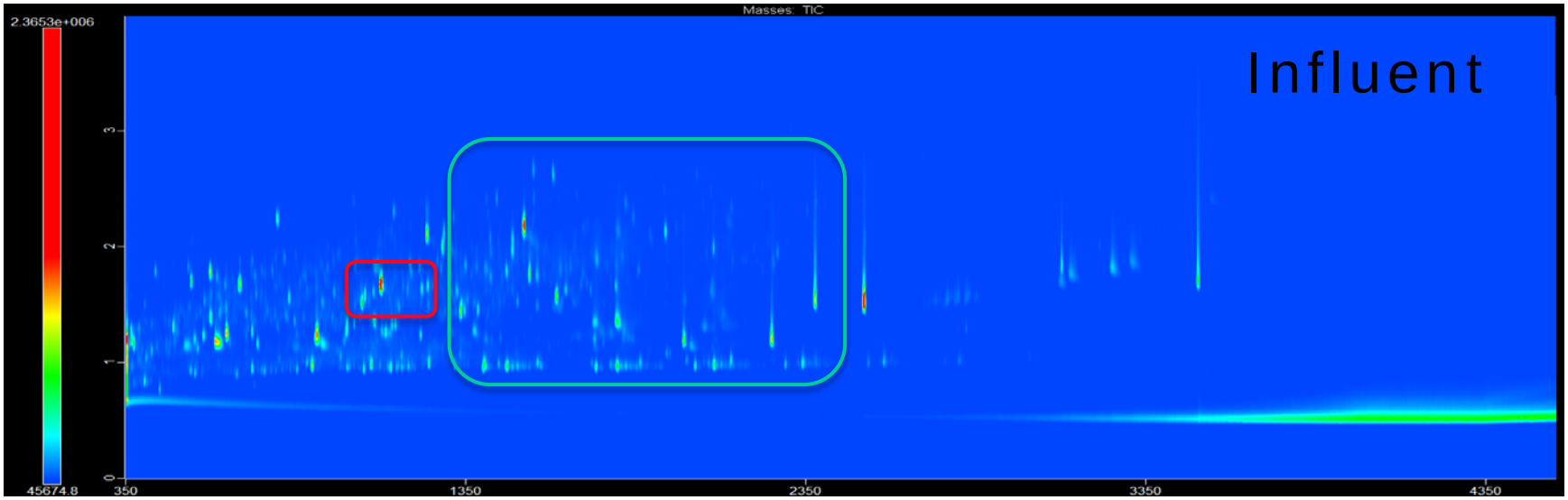
More separation space: GCxGC

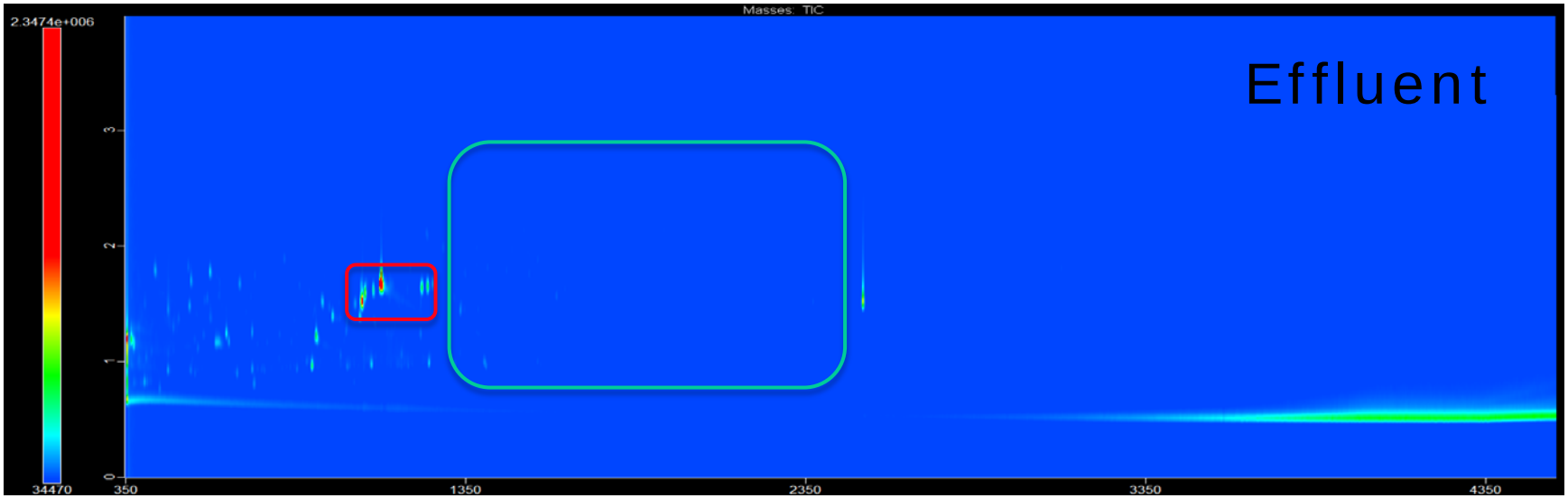


10 seconds modulation period



Example: Sewage treatment plant water



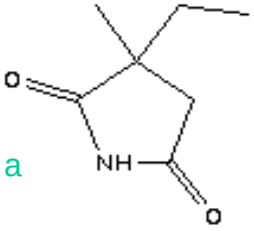


STP efficiency evaluation

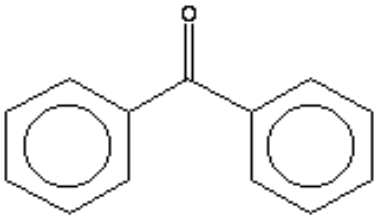
- All peaks (compounds) are detected and integrated
- A composite influent water used as template to which all samples (effluent and influent) were compared.
  - Effluent/influent << 1, **treatment successful**
  - Effluent/influent ratio = 1, **treatment failed**
  - Effluent/influent > 1, **transformation product**

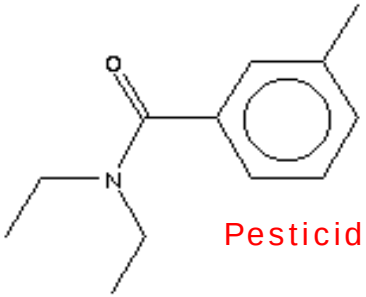
Some (expected) Stuff...

PPCP,
Anti-
eptileptica

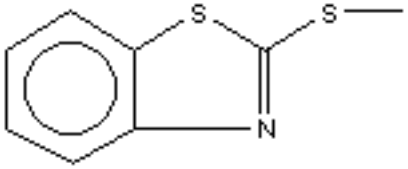


PPCP,
UV-blocker



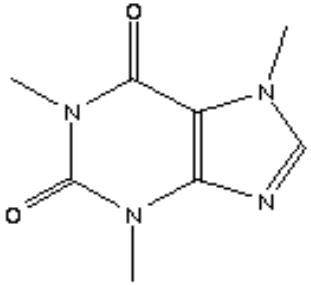


Pesticide

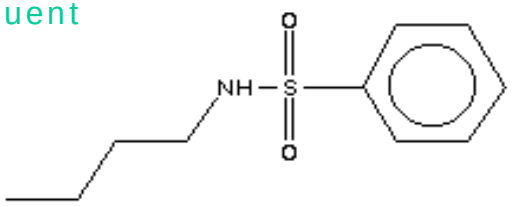


Traffic, tyres,
rubber accelerator (MBT)

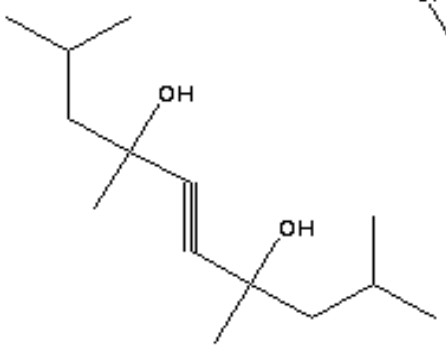
Traffic,
exhaust



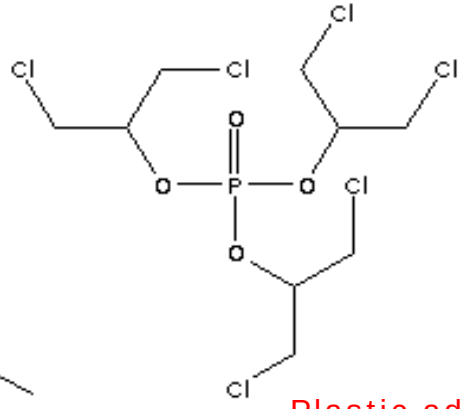
Food
Additive/
Constituent



Plastic additive,
plasticizer

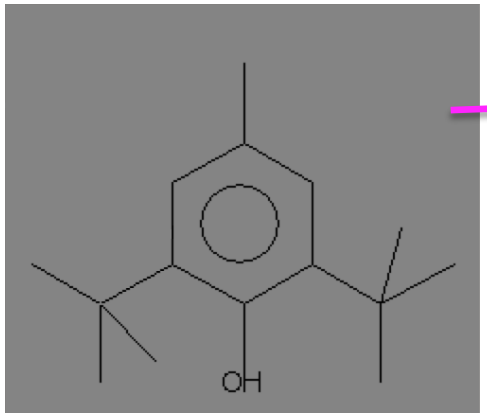


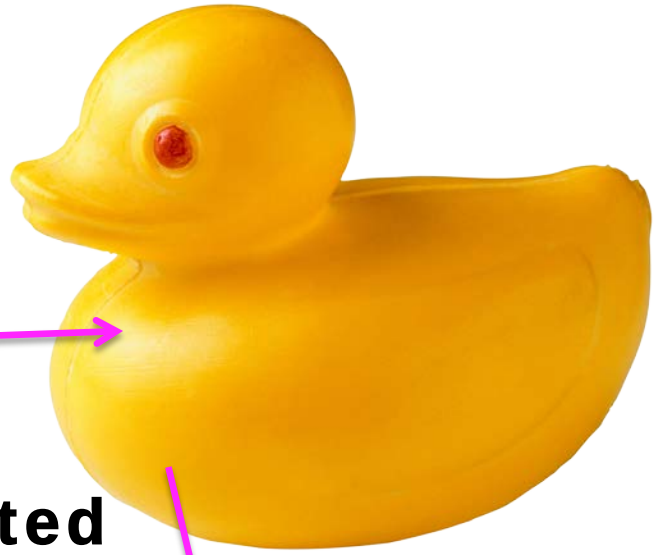
Defoamer, paint etc.



Plastic additive,
Flame retardant

Stuff put into Stuff...

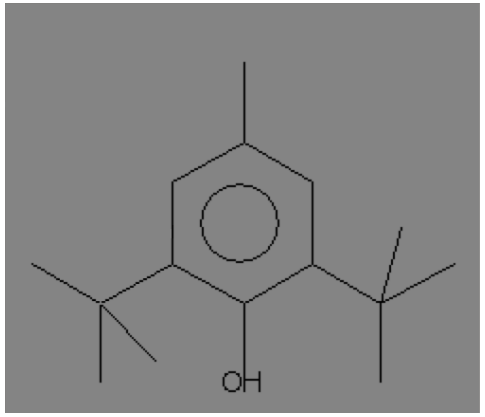




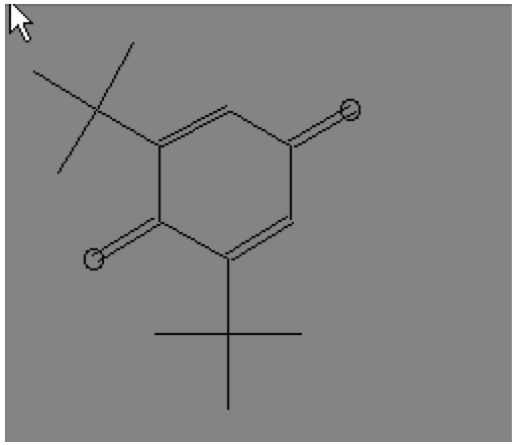
Expected

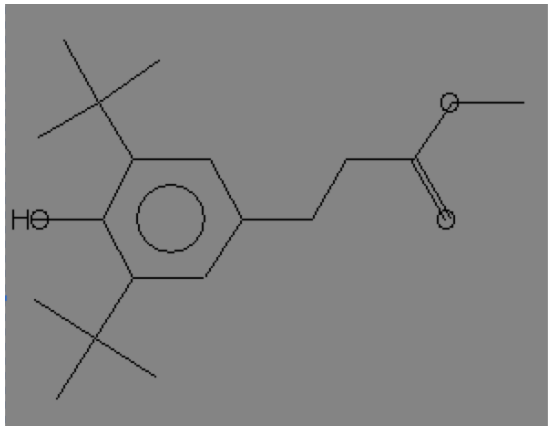
STP

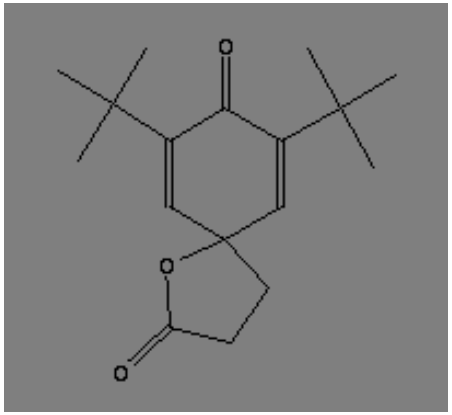
Stuff from Stuff...



Also found in sample







Transformation products ?!

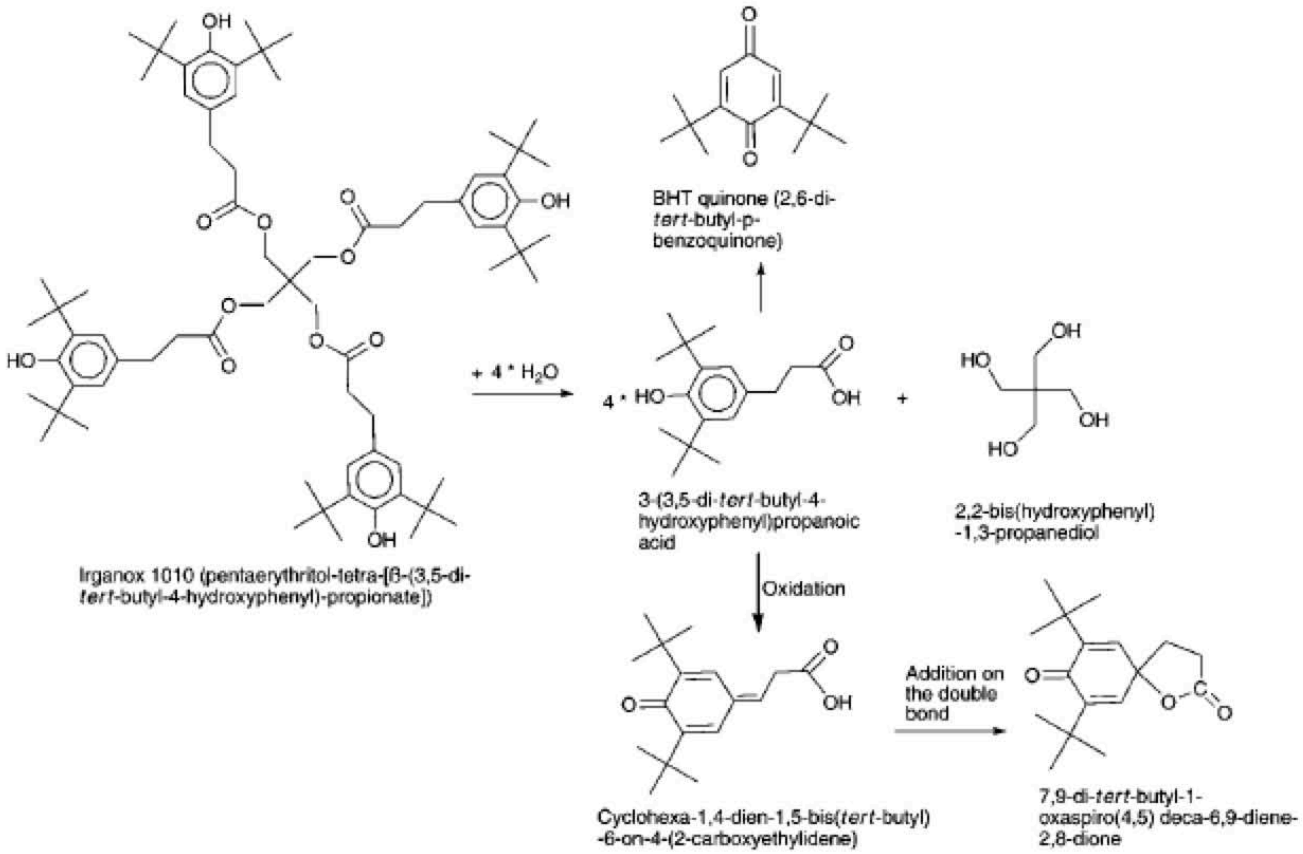


Fig. 7 Proposed degradation of antioxidant type 1010.

Transformation products ?!

Unknown unknowns

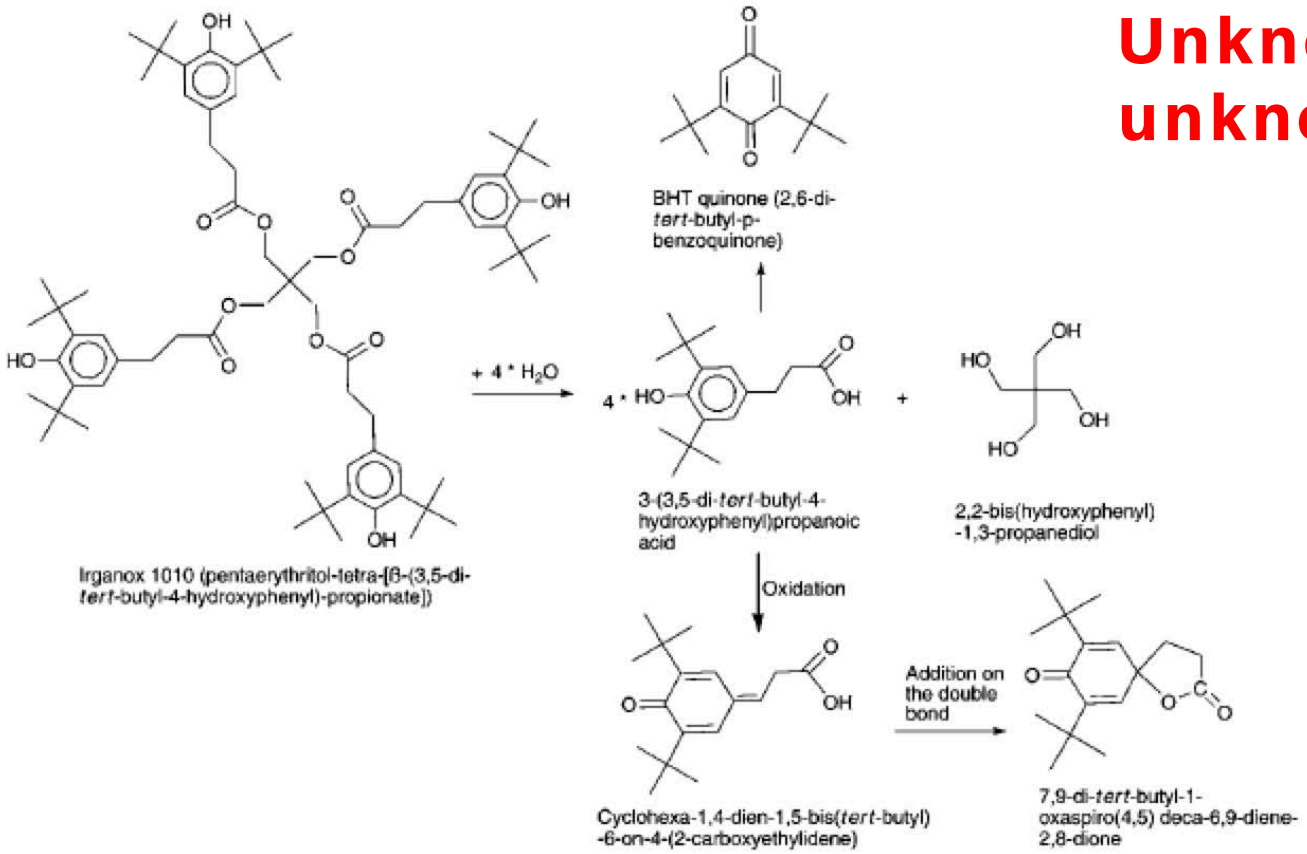
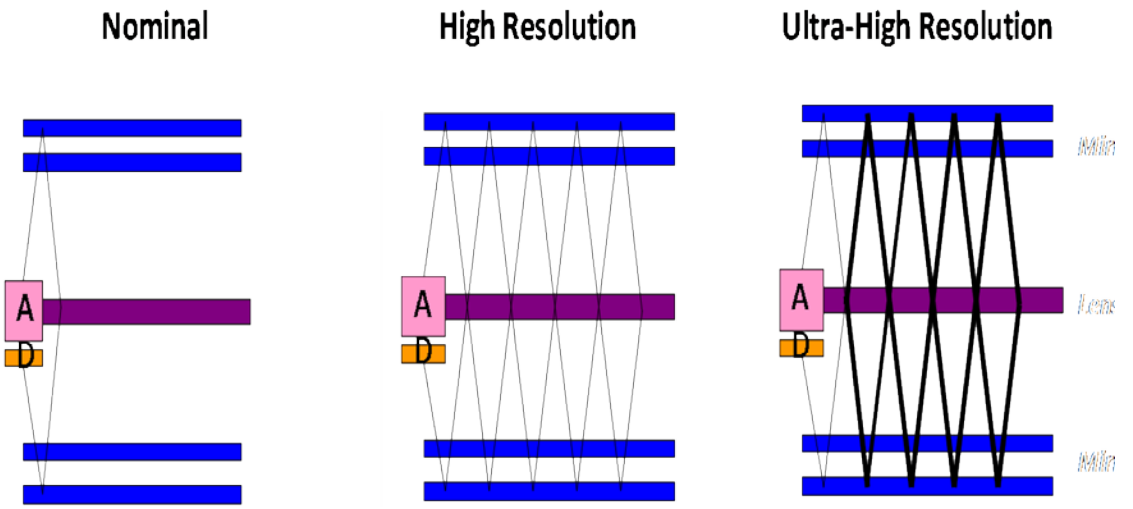


Fig. 7 Proposed degradation of antioxidant type 1010.

Tentative (Library) Identification

Tentative name	Effluent conc. (ng/L)	Functional group(s)										Retention time		Break-through (%)	% in water		Origin
		Acid	Amine/amide	Aromatic	Halogenated	Ketone/ester	Nitro	OH	Phosphate	S/O-ether	S,N,O-heterocyclic	Other	^{1}D (s)	^{2}D (s)		Influent	Effluent	
2,4,7,9-Tetramethyl-5-decyn-4,7-diol	12000							X				X	1042	0.46	73	85	97	Defoamer in paint
Benzenesulfonamide, N-butyl-	5500		X	X									1770	1.53	100	38	89	Plasticizer
Tris(butoxyethyl) phosphate	3600					X			X				2586	0.75	100	94	98	Floor polish
Benzothiazole, 2-(methylthio)-	2200			X						S	NS		1454	1.70	100	88	99	Rubber industry
Tricyclo[5.2.1.0(2,6)]dec-3-en-10-one	1500					X							842	1.17	77	100	100	Natural
Tris(3-chloropropyl) phosphate (TCPP 1)	1500				X				X				1758	1.04	67	85	98	Flame retardant
Benzophenone	930			X		X							1494	1.53	100	87	94	UV initiator
Benzothiazole, 2-(methylthio) derivative?	650			X						S	NS		1820	0.23	56	100	100	Rubber industry
Ethyl citrate	520					X		X					1506	0.97	71	100	100	Plasticizer, food additive
Caffeine	460					X					N		1916	1.82	100	87	100	Coffee, soft drinks
Tris(3-chloropropyl) phosphate (TCPP 2)	390				X				X				1780	1.05	63	81	98	Flame retardant
Tris(2-chloroethyl) phosphate	360				X				X				1726	1.44	100	97	98	Flame retardant
2,2,2-Trichloro-1-phenylethanol	320			X	X			X					1268	1.34	100	100	100	Flavor and fragrance
Oxybenzone	230			X		X					O		2144	1.54	100	68	97	Cosmetics, sunscreen
4-*tert*-butyl-cyclohexanone	220					X							750	0.71	100	100	100	Cosmetics, fragrance
Ethosuximide	150					X					N		812	1.08	98	79	98	Pharmaceutical
Tris(1,3-dichloroisopropyl) phosphate (TCDPP)	150				X	X			X				2534	1.39	72	76	98	Flame retardant
Isoquinoline	140			X							N		770	1.18	100	97	100	Traffic
4-*tert*-octyl-phenol	140			X				X					1410	0.96	69	37	86	Surfactants; resins
Hexadecenoic acid, Z-11-*	120	X											1944	0.53	37	0	40	Natural
Diethyltoluamide (DEET)	110		X	X									1386	1.20	100	100	100	Insect repellent
Benzenesulfonamide, N-ethyl-2-methyl-	100		X	X									1554	1.70	100	99	100	Plasticizer
2,3,6,7-Tetramethylquinoxaline	100			X							N		1586	1.16	56	73	100	Traffic

Validation by GC-HRMS

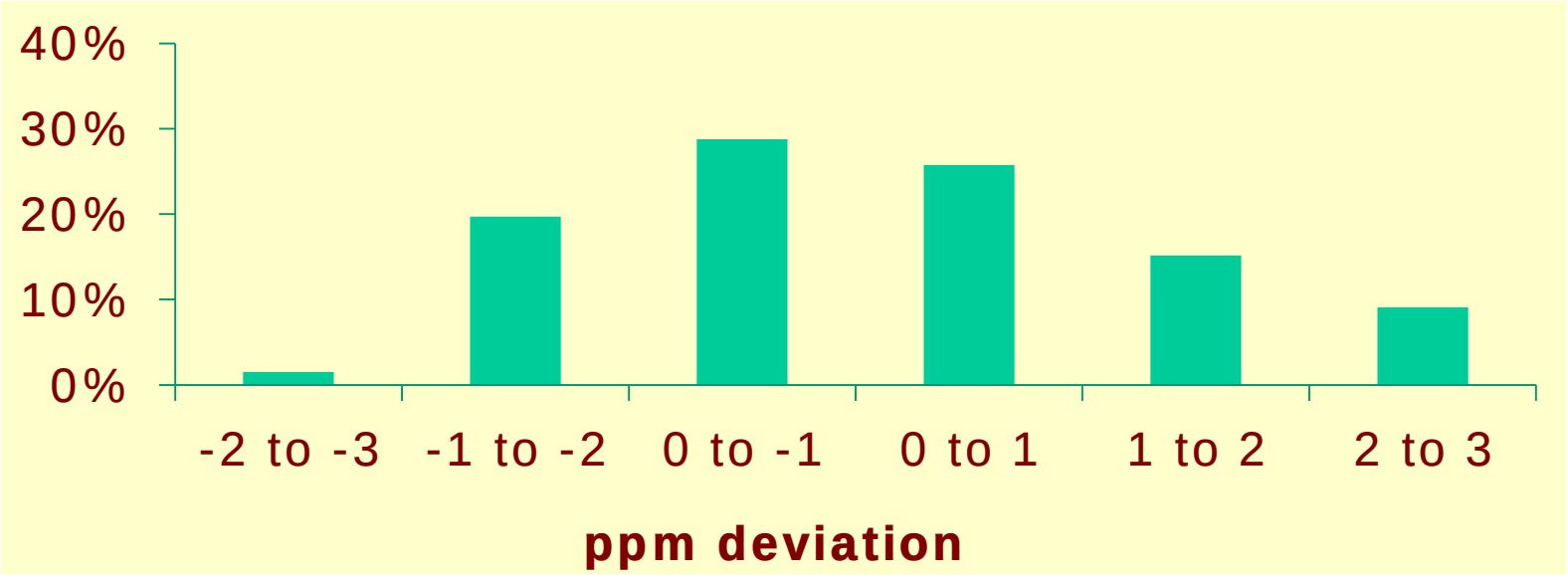


L = 2m
R = 1,800

L = 20m
R = 25,000

L = 40m
R = 50,000

GCxGC-HRMS validation



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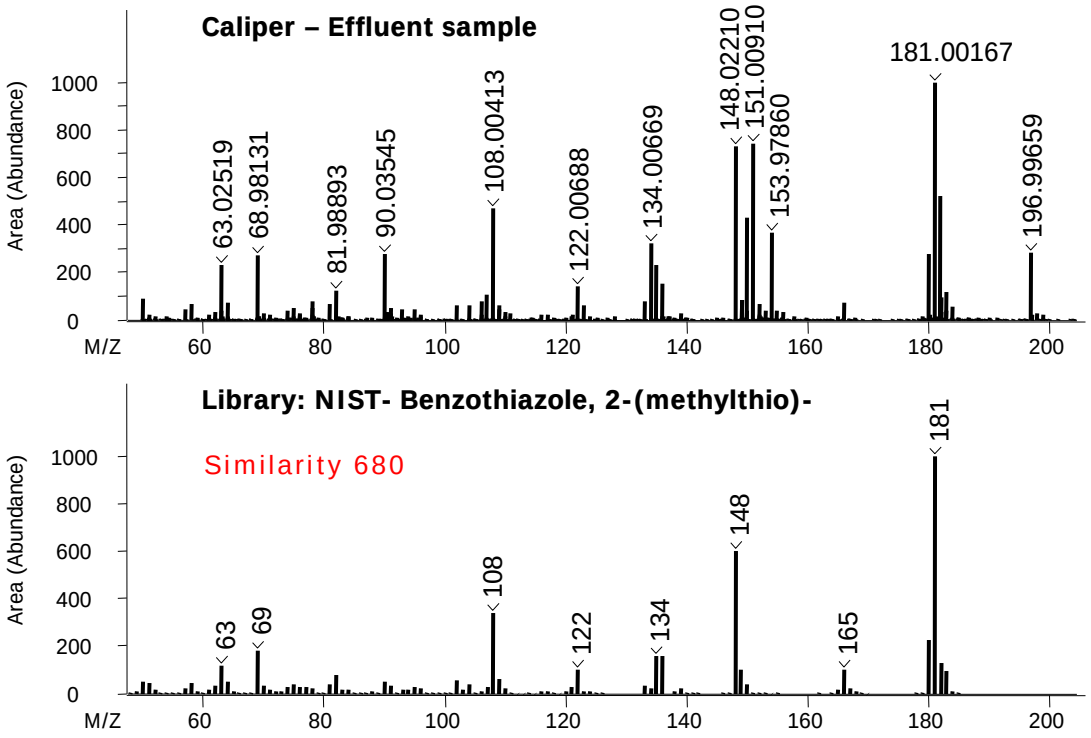

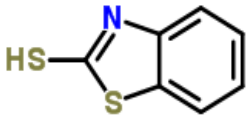

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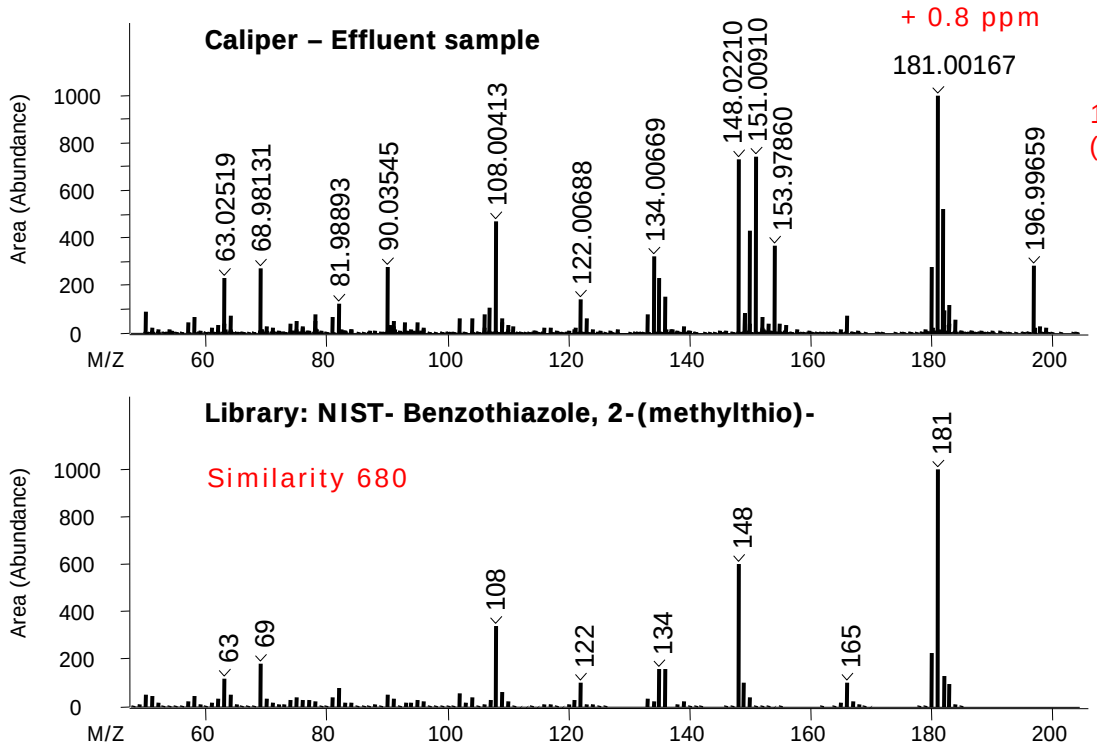
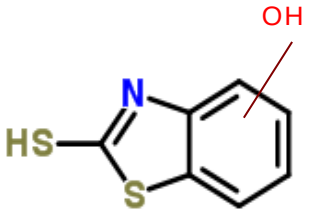


15.99492 amu
(oxygen 15.99491 amu)



What to do when it is not easy?

Go the LC-MS way!

What to do when it is not easy?

- Generate:
  - HRMS data
  - Molecular ion information
  - Formula
- Search databases
- Evaluate:
  - Retention times of candidates
  - Fragmentation of candidates
- (Manual) spectral interpretation
- Full *in-silico* structure generation and ranking

Needs

- Accurate mass GCxGC-HRMS
- HRMS libraries
- Soft ionization (CI, soft-EI, SP-PI)

  (SW for matching with EI data)
- Better software
  - Automation!
  - Peak picking / deconvolution
  - Fragmentation prediction
  - Retention time prediction
  - ...