Prioritisation and non-target screening

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NORMAN activities to identify the relevant emerging pollutants

Databases:
Monitoring
Toxicity
Properties data

Usage data/ Use index

Prioritisation

Target screening

Relevant pollutants

Non-target screening

NORMAN Validation protocol Measurement methods

Effect-Directed Analysis

NORMAN Massbank – identification of unknowns

LIST OF EMERGING SUBSTANCES (NORMAN list)

≥ 4 countries AND ≥ 100 sites with analysis ≥ 20 sites analysis > LOQ in the relevant matrix(ces) + Recent data (>last 6 years) ?

Insuff. (or never) monitored OR monitored in „wrong" matrix

Suff. monitored but low frequency of quantification

Suff. monitored. & quantif. in relevant matrix

LOQmax< PNEC (existing data in EMPODAT)?

Sufficient experimental data for hazard assesment?

yes

LOQmin (EMPODAT) OR LOQ expert labs < PNEC ?

no

Risk of exceedance of the Lowest PNEC ?

yes

no

yes

no

Sufficient experimental data for hazard assesment?

no

yes

no

yes

no

Cat. 2: Watch list

Cat. 5

Cat. 4: Action analytical

Cat. 6: Non-priority for regular monitoring

Cat. 1: Priority regular monitoring

Cat. 3: Action (eco)tox

Novel end points

NORMAN scheme for Prioritisation of Emerging Substances

1. Categorisation – to allocate substances to **action categories**

2. Prioritisation – to define priorities within each action category

NORMAN prioritisation criteria

- **Emission relevance**
  - N° of countries/sites with analyses, frequency of quantification
  - Use pattern
- **(Eco)toxicological relevance / Hazardous properties**
  - PBT, vPvB citeria
  - CMR properties
  - Endocrine disruption potential
  - Novel end points (behavioural effects)
- **Risk indicators**
  - Frequency of exceedence of the PNEC (spatial exposure)
  - Extent of exceedance of the PNEC (intensity of impact)

Risk indicators

- **INTENSITY OF IMPACT*:***

  – *Extent of Exceedance = MEC95 / Lowest PNEC*

Where,

  – *MEC95 is 95th percentile of the max conc. at each site*

  – *Lowest PNEC*
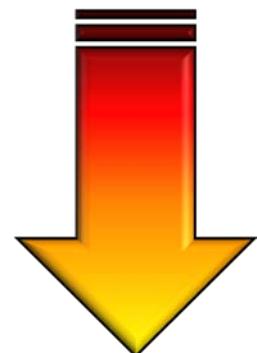
Score for „Exceedance of environmental treshold"
10> MEC95/lowest PNEC>1.... =0.1
100> MEC95/lowest PNEC>10... = 0.2
1000> MEC95/lowest PNEC>100.. =0.5
MEC95/lowest PNEC>1000........ = 1

- **SPATIAL EXPOSURE ASPECTS:**

– ***Frequency of Exceedance = n / N***

Where,

  – *n is the number of sites with MEC_{site} > Lowest PNEC*
  – *N is the total number of sites where the substance was measured*

Score: value between 0 and 1

- Cat. 1, 3, 6: calculated using RECENT DATA
- Cat. 2, 4, 5: calculated using ALL DATA (all YEARS)

NORMAN proposal for candidate substances for the 1st EU Watch List (Art 8 ter of 2013/39/EU Directive)
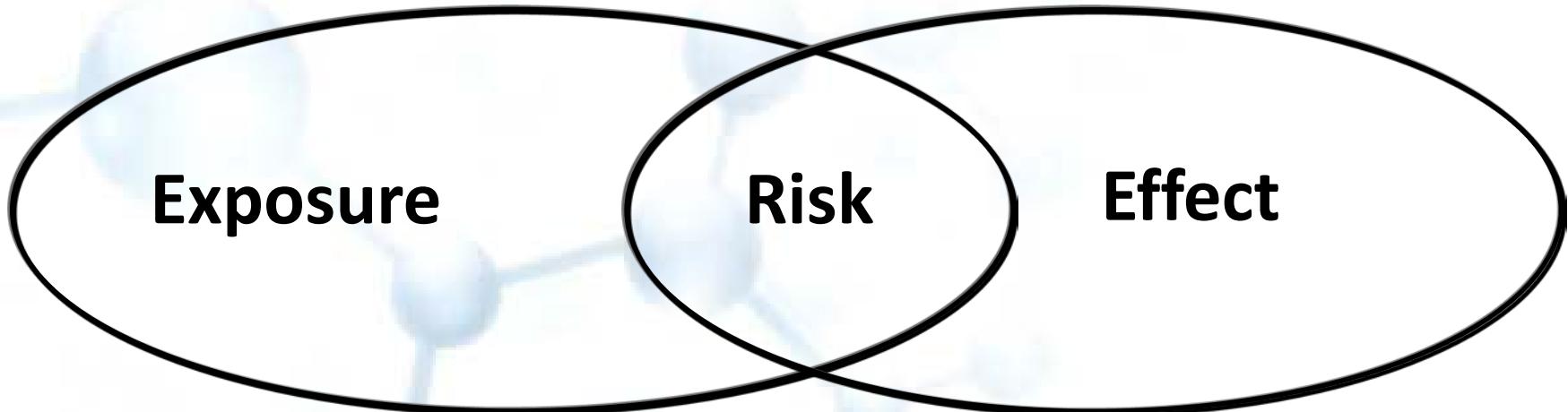
Category 2 – WATCH LIST

- Aminotriazole
- Azithromycin
- Ethylhexyl methoxycinnamate
- Diflufenican
- Ofloxacin
- Clarithromycin
- Erythromycin
- Triphenyl phosphate
- Ciprofloxacin
- Dimethenamid
- Methiocarb
- Oxadiazon

Category 1 - PS

- Bisphenol A
- Di-n-butylphthalate (DBP)
- Triclosan
- Diazinon
- Terbuthylazine
- Carbamazepine
- Estrone
- Diclofenac
- Ibuprofen
- Bentazone
- Metolachlor

Exposure Risk Effect

Tentatively identified

Predicted conc.

➔ **MEC95**

MEC95
P-PNEC

Predicted toxicity
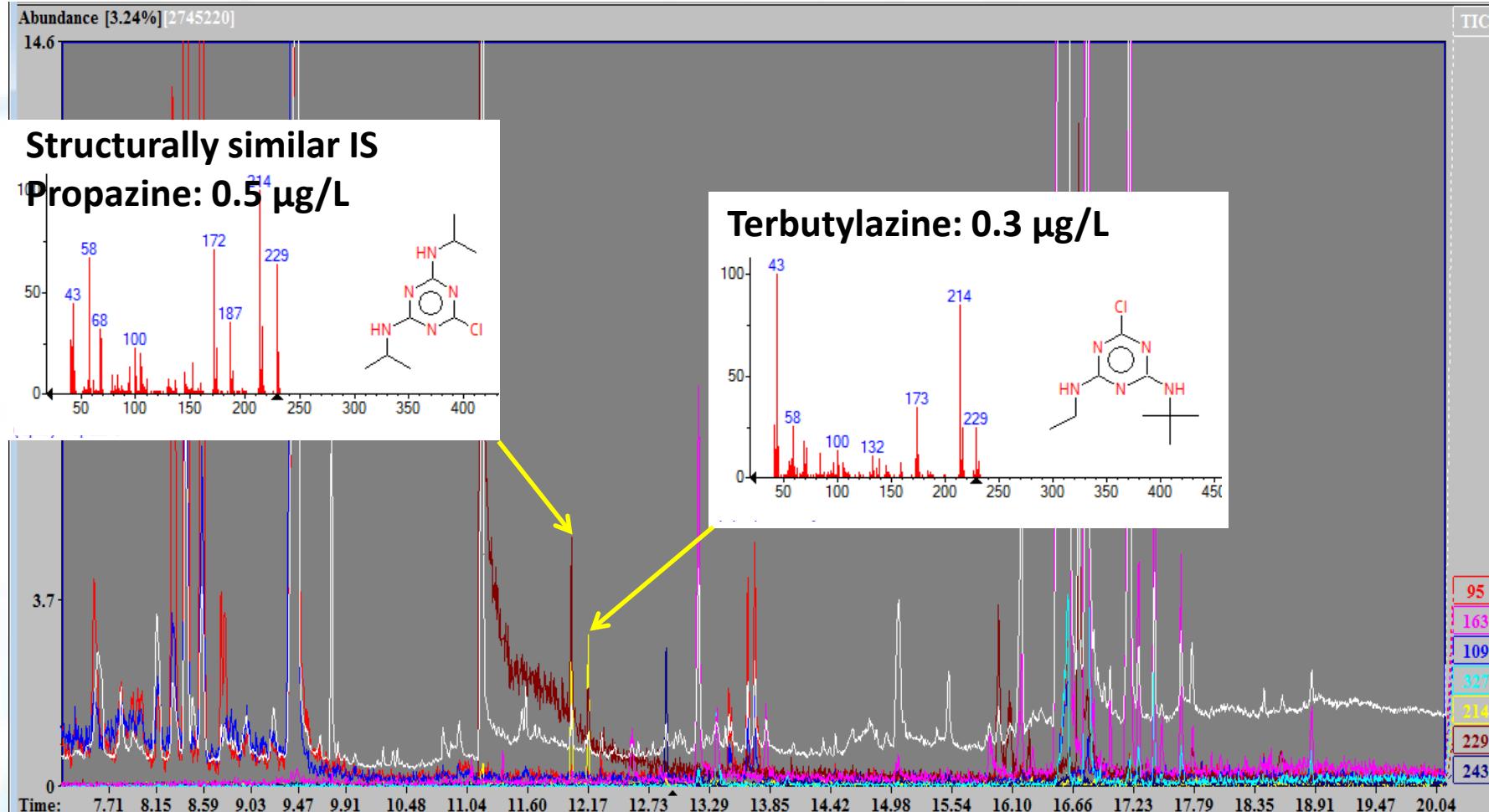
AF of 1000

➔ **P-PNEC**

Non-target screening – semiquantitative analysis

Structurally similar IS
Propazine: 0.5 µg/L

Terbutylazine: 0.3 µg/L

Non-target screening

<u>First application:</u>

Identification of river basin specific pollutants and derivation of environmental quality standards: A case study in the Slovak Republic

Jaroslav Slobodnik, Lea Mrafkova, Mario Carere, Fulvio Ferrara, Bruno Pennelli, Gerrit Schüürmann, Peter Carsten von der Ohe

Following the requirements of the European Water Framework Directive (WFD), a process of selecting relevant dangerous substances and developing related Pollution Reduction Programme (PRP) has started in the Slovak Republic in 2001. Based on the results of a three years investigative screening campaign, 59 chemical substances were identified as relevant dangerous substances in 2004 and included in the national PRP. This study describes two independent prioritization approaches that have been applied to revise the list of relevant dangerous substances in 2010. The first approach was using a classification system based on the occurrence monitoring data of these substances combined with self-monitoring data by industries on their emissions into wastewaters and data on production/usage of chemicals and agricultural pesticides. As an outcome, 41 of the 59 relevant substances were proposed to be retained in the updated PRP. The second approach was based on the evaluation of the Frequency of exceedance and the Extent of exceedance of environmental thresholds, referred to as predicted no effect concentrations (PNEC), for all organic compounds monitored in the river systems of the Slovak Republic from 2001 to 2010, with exclusion of WFD priority substances (PS). The results showed that 18 of 87 monitored compounds deserve closer attention in future revisions of the list, out of which 11 pollutants were

Non-target screening

Prioritisation based on GC-MS screening:

Table 7. Results of prioritisation based on the GC-MS screening data and (predicted) toxicity data

No.	CAS	Name	Max. conc.	MEC_{95}[a]	AA-EQS[b]	Source EQS	Lowest PNEC	Ref.[c]	TL[d]	Freq. PNEC[e]	Exceed. PNEC[f]	Priority[g]
1	629-62-9	Pentadecane	1.7	1.5			0.0015	B	A	0.20	1000	1.20
2	544-76-3	Hexadecane	3.6	2.4			0.0015	P	F	0.17	1600	1.17
3	95-16-9	Benzothiazole	30,958	4459	2	SK	2	E	D	0.12	2230	1.12
4	57-10-3	Hexadecanoic acid	15	3.7			0.021	B	F	0.53	176	1.03
5	629-50-5	Tridecane	8.0	4.3			0.023	B	F	0.50	187	1.00

Name	MEC_{95}	Lowest PNEC	Freq. PNEC	Exceed. PNEC	Priority
Benzylbutylphthalate (BBP)	2.7	0.27	0.22	10	0.42

17	92-52-4	Biphenyl		1.7	1	SK	0.36	E	D	0.22	5	0.32
18	2091-29-4	9-hexadeceno		1.8			0.032	B	P	0.12	56	0.32
19	120-72-9	1H-indo	84	34			1	E	D	0.08	34	0.28
20	128-37-0	Me	10	2.6	1.4	SK	1.4	E	D	0.15	1.86	0.25
21	615-22-5		14.0	3.8			0.31	P	D	0.05	12	0.25
22	1620-98	-4-ethyl-	9.3	5.4			0.59	B	D	0.08	9	0.18
23	33		9.8	0.86			0.26	P	A	0.07	3	0.17
24			9.0	6.8			1.2	B	D	0.04	6	0.14
			208	8	10	SK	4.7	E	F	0.02	2	0.12
			982	49	2.4	WFD	2.4	E	F	0.02	8	0.12
2		adecane	2.0				0.00024	P	F	0.11		0.11
28		Galaxolide	1.6				0.083	P	D	0.10		0.10
29		Cholesterol	4.1				0.0005	P	D	0.10		0.10
30	-21-4	Undecane	2.2				0.024	P	D	0.07		0.07

169 surface-water and samples!

Data File	MS_JDS_5...d
Sample Type	Sample
Instrument Name	QTOF1
Acq Method	MS_only_positive.m
IRM Calibration Status	Success
Comment	

Sample Name	MS_JDS_5a...
Position	P1-C4
User Name	
Acquired Time	9/30/2019 7:33:14 PM
DA Method	MFC_FINAL.m

Sample Group			
	Info.		
Funnel RF HP	150	Funnel RF LP	60
Acquisition SW	6200 series TOF/6500 series C-TOF B.05.01 (B5125)		
Version			

Suspect screening – ONE JDS sample phase I -MS only

Compound Table

Compound Label	RT	Mass	Abund	Name	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula	DB Diff (ppm)
Cpd 165: Fenchlorazole	1.065	372.87506	1016	Fenchlorazole	C10 H4 Cl5 N3 O2	372.87461	1.19	C10 H4 Cl5 N3 O2	C10 H4 Cl5 N3 O2	1.45
Cpd 141: Fluorodifen	1.09	328.03039	1320	Fluorodifen	C13 H7 F3 N2 O5	328.03071	0.59	C13 H7 F3 N2 O5	C13 H7 F3 N2 O5	2.44
Cpd 70: Cefazaflur	1.499	470.01153	3234	Cefazaflur	C13 H13 F3 N6 O4 S3	470.01125	0.59	C13 H13 F3 N6 O4 S3	C13 H13 F3 N6 O4 S3	-2.19
Cpd 95: 2,3-MDPEA / 2,3-Methylenedioxyphenethylamine	2.061	165.07883	3893	2,3-MDPEA / 2,3-Methylenedioxyphenethylamine	C9 H11 N O2	165.07898	-0.87	C9 H11 N O2	C9 H11 N O2	-0.21
Cpd 236: Merphos	2.078	298.10124	872	Merphos	C12 H27 P S3	298.10125	-0.04	C12 H27 P S3	C12 H27 P S3	1.89
Cpd 91: Vigabatrin	2.087	129.07889	7425	Vigabatrin	C6 H11 N O2	129.07898	-0.67	C6 H11 N O2	C6 H11 N O2	0.06
Cpd 78: o-Phenyleneurea (Benzimidazolone) (Droperidol-M)	3.381	134.048	8986	o-Phenyleneurea (Benzimidazolone) (Droperidol-M)	C7 H6 N2 O	134.04801	-0.01	C7 H6 N2 O	C7 H6 N2 O	-0.02
Cpd 151: Anatoxin a	3.782	165.11506	1043	Anatoxin a	C10 H15 N O	165.11536	-1.87	C10 H15 N O	C10 H15 N O	1.48
Cpd 255: (+)-cucurbic acid	3.799	212.14133	835	(+)-cucurbic acid	C12 H20 O3	212.14124	0.4	C12 H20 O3	C12 H20 O3	-0.14
Cpd 212: L-Adrenaline	3.884	183.0896	1378	L-Adrenaline	C9 H13 N O3	183.08954	0.31	C9 H13 N O3	C9 H13 N O3	-0.55
Cpd 54: 6-Hydroxynicotine (S)	4.31	178.11061	9978	6-Hydroxynicotine (S)	C10 H14 N2 O	178.11061	-0.01	C10 H14 N2 O	C10 H14 N2 O	-0.6
Cpd 51: Bufencarb	4.523	221.14166	15231	Bufencarb	C13 H19 N O2	221.14158	0.39	C13 H19 N O2	C13 H19 N O2	1.07
Cpd 265: Sotalol	4.676	272.11982	410	Sotalol	C12 H20 N2 O3 S	272.11946	1.33	C12 H20 N2 O3 S	C12 H20 N2 O3 S	-2.29
Cpd 129: Esculin (Polychrome)	4.702	340.07933	4476	Esculin (Polychrome)	C15 H16 O9	340.07943	-0.31	C15 H16 O9	C15 H16 O9	0.8
Cpd 254: 4-[2-(Propylamino)ethyl]-1,3-dihydro-2H-indol-2-one	4.795	218.14194	691	4-[2-(Propylamino)ethyl]-1,3-dihydro-2H-indol-2-one	C13 H18 N2 O	218.14191	0.13	C13 H18 N2 O	C13 H18 N2 O	-0.65
Cpd 1: Pramiracetam	4.864	269.21048	90695	Pramiracetam	C14 H27 N3 O2	269.21033	0.55	C14 H27 N3 O2	C14 H27 N3 O2	0.09
Cpd 248: Ciclacillin	4.957	341.14013	757	Ciclacillin	C15 H23 N3 O4 S	341.14093	-2.32	C15 H23 N3 O4 S	C15 H23 N3 O4 S	0.19
Cpd 121: Buformin	4.974	157.13254	3334	Buformin	C6 H15 N5	157.13275	-1.3	C6 H15 N5	C6 H15 N5	-0.25
Cpd 79: N-Hydroxymethylnorcotinine	4.983	192.08995	8963	N-Hydroxymethylnorcotinine	C10 H12 N2 O2	192.08988	0.38	C10 H12 N2 O2	C10 H12 N2 O2	-0.26
Cpd 62: Pribecaine	5.059	277.16761	9104	Pribecaine	C16 H23 N O3	277.16779	-0.65	C16 H23 N O3	C16 H23 N O3	-0.05
Cpd 231: Tecomine	5.085	179.12958	674	Tecomine	C11 H17 N O	179.13101	-8	C11 H17 N O	C11 H17 N O	6.81
Cpd 186: Diphacinone	5.179	340.11057	2460	Diphacinone	C23 H16 O3	340.10994	1.83	C23 H16 O3	C23 H16 O3	0.09
Cpd 259: Aramite	5.196	334.10086	806	Aramite	C15 H23 Cl O4 S	334.10056	0.89	C15 H23 Cl O4 S	C15 H23 Cl O4 S	0.43
Cpd 193: Triazamate	5.204	314.14124	1211	Triazamate	C13 H22 N4 O3 S	314.14126	-0.71	C13 H22 N4 O3 S	C13 H22 N4 O3 S	-0.76
Cpd 170: 1-(3-Pyridinyl)-1,4-butanediol	5.264	167.09458	2380	1-(3-Pyridinyl)-1,4-butanediol	C9 H13 N O2	167.09463	-0.29	C9 H13 N O2	C9 H13 N O2	0.12
Cpd 125: Homatropine	5.383	275.15169	2890	Homatropine	C16 H21 N O3	275.15214	-1.63	C16 H21 N O3	C16 H21 N O3	0.75
Cpd 117: Gabapentin	5.4	171.12593	3718	Gabapentin	C9 H17 N O2	171.12593	-0.05	C9 H17 N O2	C9 H17 N O2	-0.71
Cpd 190: Arecoline	5.485	155.09469	665	Arecoline	C8 H13 N O2	155.09463	0.39	C8 H13 N O2	C8 H13 N O2	-1.22
Cpd 39: Ambenoxan	5.553	267.14648	30587	Ambenoxan	C14 H21 N O4	267.14706	-0.97	C14 H21 N O4	C14 H21 N O4	1.87
Cpd 63: Oxprenolol	5.57	265.16778	14740	Oxprenolol	C15 H23 N O3	265.16779	-0.06	C15 H23 N O3	C15 H23 N O3	0.46
Cpd 178: Gly Trp	5.681	261.11121	2204	Gly Trp	C13 H15 N3 O3	261.11134	-0.49	C13 H15 N3 O3	C13 H15 N3 O3	-0.05
Cpd 106: Theophylline	5.69	180.06446	4737	Theophylline	C7 H8 N4 O2	180.06473	-1.49	C7 H8 N4 O2	C7 H8 N4 O2	1.35
Cpd 86: Dacarbazine	5.724	182.09149	8310	Dacarbazine	C6 H10 N6 O	182.09161	1.56	C6 H10 N6 O	C6 H10 N6 O	1.04
Cpd 42: Acetylhelenalin	5.826	304.13049	22757	Acetylhelenalin	C17 H20 O5	304.13107	-1.93	C17 H20 O5	C17 H20 O5	0.37
Cpd 80: Ephedrine	5.869	165.11524	7912	Ephedrine	C10 H15 N O	165.11536	-0.76	C10 H15 N O	C10 H15 N O	0.37
Cpd 75: O-Desmethyltramadol	5.979	249.17279	7869	O-Desmethyltramadol	C15 H23 N O2	249.17288	-0.34	C15 H23 N O2	C15 H23 N O2	0.42
Cpd 35: Arg Ser Ser	6.03	348.17585	37612	Arg Ser Ser	C12 H24 N6 O6	348.17573	0.33	C12 H24 N6 O6	C12 H24 N6 O6	-0.13
Cpd 163: 8-Hydroxychinolin (8-Hydroxyquinoline)	6.099	145.05283	2164	8-Hydroxychinolin (8-Hydroxyquinoline)	C9 H7 N O	145.05276	0.46	C9 H7 N O	C9 H7 N O	-0.9
Cpd 243: Nifenazone	6.124	308.12719	537	Nifenazone	C17 H16 N4 O2	308.12733	-0.45	C17 H16 N4 O2	C17 H16 N4 O2	-0.93
Cpd 161: Acetylpheneturide	6.133	248.11601	2037	Acetylpheneturide	C13 H16 N2 O3	248.11609	-0.35	C13 H16 N2 O3	C13 H16 N2 O3	-0.83
Cpd 37: Cotinine	6.252	176.09515	33290	Cotinine	C10 H12 N2 O	176.09496	1.07	C10 H12 N2 O	C10 H12 N2 O	-0.86
Cpd 245: Sudan 410	6.329	408.19579	789	Sudan 410	C26 H24 N4 O	408.19501	1.9	C26 H24 N4 O	C26 H24 N4 O	1.5
Cpd 49: Thr Gln Gln	6.576	375.17526	24305	Thr Gln Gln	C14 H25 N5 O7	375.1754	-0.36	C14 H25 N5 O7	C14 H25 N5 O7	0.1
Cpd 131: Fencamine	6.601	384.22733	2617	Fencamine	C20 H28 N6 O2	384.22737	-0.13	C20 H28 N6 O2	C20 H28 N6 O2	0.19
Cpd 237: Propacetamol	6.644	264.14756	973	Propacetamol	C14 H20 N2 O3	264.14739	0.63	C14 H20 N2 O3	C14 H20 N2 O3	-0.98
Cpd 48: Etazolate	6.652	289.15384	22870	Etazolate	C14 H19 N5 O2	289.15387	-0.11	C14 H19 N5 O2	C14 H19 N5 O2	-0.14
Cpd 26: Octodrine	6.72	129.15117	21494	Octodrine	C8 H19 N	129.15175	-0.23	C8 H19 N	C8 H19 N	-0.15
Cpd 18: Thr Gln Asn	6.78	361.15968	50329	Thr Gln Asn	C13 H23 N5 O7	361.15975	-0.19	C13 H23 N5 O7	C13 H23 N5 O7	0.05
Cpd 195: Ampyrone	6.814	203.10596	12469	Ampyrone	C11 H13 N3 O	203.10586	0.47	C11 H13 N3 O	C11 H13 N3 O	0.21
Cpd 73: Aminoantipyrine	6.814	203.10596	12469	Aminoantipyrine	C11 H13 N3 O	203.10586	0.47	C11 H13 N3 O	C11 H13 N3 O	-0.28
Cpd 64: Dinaline	6.814	227.10595	13680	Dinaline	C13 H13 N3 O	227.10586	0.39	C13 H13 N3 O	C13 H13 N3 O	-0.22
Cpd 33: Caffeine	6.996	194.08052	39014	Caffeine	C8 H10 N4 O2	194.08038	0.72	C8 H10 N4 O2	C8 H10 N4 O2	-0.08
Cpd 188: 8-Oxodeoxycoformycin	6.993	266.10146	3801	8-Oxodeoxycoformycin	C11 H14 N4 O4	266.1015	-0.19	C11 H14 N4 O4	C11 H14 N4 O4	0.17
Cpd 114: Sulfadimidine	7.061	278.08372	4822	Sulfadimidine	C12 H14 N4 O2 S	278.08375	-0.09	C12 H14 N4 O2 S	C12 H14 N4 O2 S	-0.44
Cpd 99: Isoproturon	7.197	206.14213	2214	Isoproturon	C12 H18 N2 O	206.14191	1.07	C12 H18 N2 O	C12 H18 N2 O	-1.62
Cpd 46: Urapidil	7.248	387.22726	27154	Urapidil	C20 H29 N5 O3	387.22704	0.57	C20 H29 N5 O3	C20 H29 N5 O3	0.1
Cpd 269: Sulfamethoxazole	7.325	253.05192	632	Sulfamethoxazole	C10 H11 N3 O3 S	253.05211	-0.74	C10 H11 N3 O3 S	C10 H11 N3 O3 S	-0.89
Cpd 23: Clomiphene	7.359	405.18583	40060	Clomiphene	C26 H28 Cl N O	405.18594	-0.28	C26 H28 Cl N O	C26 H28 Cl N O	-0.31
Cpd 167: Arg Gln Arg	7.504	458.27174	2412	Arg Gln Arg	C17 H34 N10 O5	458.27136	0.82	C17 H34 N10 O5	C17 H34 N10 O5	0.35
Cpd 205: Aceclidine	7.657	169.11028	931	Aceclidine	C9 H15 N O2	169.11028	-0.01	C9 H15 N O2	C9 H15 N O2	0.13
Cpd 197: Gly Ser His	7.691	299.12272	984	Gly Ser His	C11 H17 N5 O5	299.12297	-0.83	C11 H17 N5 O5	C11 H17 N5 O5	-0.06
Cpd 105: Gly Gly Gly	7.87	288.1545	5239	Gly Gly Gly	C10 H20 N6 O4	288.1546	0.51	C10 H20 N6 O4	C10 H20 N6 O4	-0.18
Cpd 31: Vasicine	8.024	188.09511	43946	Vasicine	C11 H12 N2 O	188.09496	0.77	C11 H12 N2 O	C11 H12 N2 O	-0.04
Cpd 58: Terbucarb	8.143	277.20392	1014	Terbucarb	C17 H27 N O2	277.20418	-0.94	C17 H27 N O2	C17 H27 N O2	0.65
Cpd 136: Homosalate	8.151	262.15673	2600	Homosalate	C16 H22 O3	262.15689	-0.61	C16 H22 O3	C16 H22 O3	0.25
Cpd 68: N-Desmethylvenlafaxine	8.177	263.18848	10809	N-Desmethylvenlafaxine	C16 H25 N O2	263.18853	-0.19	C16 H25 N O2	C16 H25 N O2	0.08
Cpd 220: Congocidin (Netropsin)	8.296	430.2193	1313	Congocidin (Netropsin)	C18 H26 N10 O3	430.21893	0.86	C18 H26 N10 O3	C18 H26 N10 O3	-0.24
Cpd 41: 4-Nonynoic acid	8.509	154.09927	8665	4-Nonynoic acid	C9 H14 O2	154.09938	-0.73	C9 H14 O2	C9 H14 O2	0.21
Cpd 16: Metoprolol	8.662	267.18347	1369	Metoprolol	C15 H25 N O3	267.18344	0.1	C15 H25 N O3	C15 H25 N O3	0.11
Cpd 43: Esaprazole	8.705	225.18421	15221	Esaprazole	C12 H23 N3 O	225.18411	0.44	C12 H23 N3 O	C12 H23 N3 O	-0.05
Cpd 185: Anabasine	8.773	160.10001	1443	Anabasine	C10 H12 N2	160.10005	-0.24	C10 H12 N2	C10 H12 N2	-0.68
Cpd 150: His Gly Thr	8.799	313.13853	3858	His Gly Thr	C12 H19 N5 O5	313.13862	-0.3	C12 H19 N5 O5	C12 H19 N5 O5	0.35
Cpd 101: Lamotrigine	8.85	255.00785	2929	Lamotrigine	C9 H7 Cl2 N5	255.00785	-0.6	C9 H7 Cl2 N5	C9 H7 Cl2 N5	0.4
Cpd 137: PYCC / 1-(Pyrrolidin-1-yl)cyclohexanecarbonitrile	8.867	178.147	1436	PYCC / 1-(Pyrrolidin-1-yl)cyclohexanecarbonitrile	C11 H18 N2	178.147	0.03	C11 H18 N2	C11 H18 N2	-0.58
Cpd 210: Alprenolol	9.003	249.17255	1172	Alprenolol	C15 H23 N O2	249.17288	-1.33	C15 H23 N O2	C15 H23 N O2	1.01
Cpd 166: 2-Aminobenzimidazole	9.224	133.06415	3011	2-Aminobenzimidazole	C7 H7 N3	133.064	1.18	C7 H7 N3	C7 H7 N3	-2.66
Cpd 158: Lomifylline	9.267	278.13863	2969	Lomifylline	C13 H18 N4 O2	278.13789	2.67	C13 H18 N4 O2	C13 H18 N4 O2	-1.56
Cpd 108: Leptacline	9.293	181.18291	3262	Leptacline	C12 H23 N	181.18305	-0.77	C12 H23 N	C12 H23 N	0.5
Cpd 249: Crenatine A	9.446	568.30585	1015	Crenatine A	C34 H40 N4 O4	568.30496	1.57	C34 H40 N4 O4	C34 H40 N4 O4	0.22
Cpd 57: Gly Ala Arg	9.531	302.17014	15617	Gly Ala Arg	C11 H22 N6 O4	302.17025	-0.37	C11 H22 N6 O4	C11 H22 N6 O4	-0.14
Cpd 160: Quinprenaline	9.625	246.13637	1504	Quinprenaline	C14 H18 N2 O2	246.13683	-1.84	C14 H18 N2 O2	C14 H18 N2 O2	1.73
Cpd 196: Arg Ser Ala	9.77	332.1804	1600	Arg Ser Ala	C12 H24 N6 O5	332.18082	-1.26	C12 H24 N6 O5	C12 H24 N6 O5	0.31
Cpd 222: Acetryptin	9.778	202.11051	1261	Acetryptin	C12 H14 N2 O	202.11061	-0.53	C12 H14 N2 O	C12 H14 N2 O	-0.52
Cpd 184: Trepibutone	10.008	310.14128	1498	Trepibutone	C16 H22 O6	310.14164	-1.15	C16 H22 O6	C16 H22 O6	2.64
Cpd 204: Dihydrocoumarin	10.255	148.05227	874	Dihydrocoumarin	C9 H8 O2	148.05243	-1.09	C9 H8 O2	C9 H8 O2	0.21
Cpd 113: Ascaridole	10.315	168.11488	1730	Ascaridole	C10 H16 O2	168.11503	-0.86	C10 H16 O2	C10 H16 O2	0.1
Cpd 25: 2-hydroxy-10-undecenoic acid	10.323	200.14137	21616	2-hydroxy-10-undecenoic acid	C11 H20 O3	200.14124	0.61	C11 H20 O3	C11 H20 O3	0.17
Cpd 90: Cycluron	10.374	198.17321	3052	Cycluron	C11 H22 N2 O	198.17321	-0.05	C11 H22 N2 O	C11 H22 N2 O	-0.02
Cpd 66: Methfuroxam	10.749	229.11018	11426	Methfuroxam	C14 H15 N O2	229.11028	-0.42	C14 H15 N O2	C14 H15 N O2	1.39
Cpd 93: Albuterol	10.826	239.15218	6144	Albuterol	C13 H21 N O3	239.15214	0.16	C13 H21 N O3	C13 H21 N O3	0.08
Cpd 14: 9-Ribouranosyladenine	11.345	281.07622	58705	9-Ribouranosyladenine	C10 H11 N5 O5	281.07602	0.72	C10 H11 N5 O5	C10 H11 N5 O5	-0.43
Cpd 98: 2-tert-Butyl-4-methoxyphenol	11.882	180.1148	4148	2-tert-Butyl-4-methoxyphenol	C11 H16 O2	180.11503	-1.26	C11 H16 O2	C11 H16 O2	0.54
Cpd 110: Conhydrine	12.129	143.13091	4366	Conhydrine	C8 H17 N O	143.13101	-0.69	C8 H17 N O	C8 H17 N O	-0.1
Cpd 45: 13,14-dihydro-16,16-difluoro Prostaglandin D2	12.367	390.22216	42117	13,14-dihydro-16,16-difluoro Prostaglandin D2	C20 H32 F2 O5	390.22178	0.97	C20 H32 F2 O5	C20 H32 F2 O5	0.11
Cpd 132: 2E,4E,6E-Nonatrienal	12.41	136.08868	1298	2E,4E,6E-Nonatrienal	C9 H12 O	136.08882	-0.97	C9 H12 O	C9 H12 O	-0.61
Cpd 97: Cyclobutoic acid	12.419	186.12577	4749	Cyclobutoic acid	C10 H18 O3	186.12559	0.93	C10 H18 O3	C10 H18 O3	0.71
Cpd 118: 4-oxo-2E-Hexenal	12.47	112.05243	4669	4-oxo-2E-Hexenal	C6 H8 O2	112.05243	0.03	C6 H8 O2	C6 H8 O2	-0.3
Cpd 198: p-Methoxycinnamaldehyde	12.58	162.06787	1321	p-Methoxycinnamaldehyde	C10 H10 O2	162.06808	-1.3	C10 H10 O2	C10 H10 O2	-0.42
Cpd 252: Naphthalene	12.58	128.06252	1057	Naphthalene	C10 H8	128.0626	-0.63	C10 H8	C10 H8	-0.15
Cpd 47: DEET (Diethyltoluamide)	12.853	191.13106	27152	DEET (Diethyltoluamide)	C12 H17 N O	191.13101	0.25	C12 H17 N O	C12 H17 N O	0.01
Cpd 52: Aspirin (Acetylsalicylic acid)	12.853	180.0423	19243	Aspirin (Acetylsalicylic acid)	C9 H8 O4	180.04226	0.2	C9 H8 O4	C9 H8 O4	0.01
Cpd 20: Monoisobutyl phthalic acid	12.853	222.08938	20095	Monoisobutyl phthalic acid	C12 H14 O4	222.08921	0.79	C12 H14 O4	C12 H14 O4	0.97
Cpd 138: Picaridin (Bayrepel)	13.228	229.16744	2962	Picaridin (Bayrepel)	C12 H23 N O3	229.16779	-1.55	C12 H23 N O3	C12 H23 N O3	1.58
Cpd 232: NECA / 5'-(N-Ethylcarboxamido)adenosine	13.415	308.12343	337	NECA / 5'-(N-Ethylcarboxamido)adenosine	C12 H16 N6 O4	308.1233	0.43	C12 H16 N6 O4	C12 H16 N6 O4	-2.06
Cpd 147: Triphenylphosphine oxide	13.466	278.08607	7248	Triphenylphosphine oxide	C18 H15 O P	278.08605	0.05	C18 H15 O P	C18 H15 O P	-1.32
Cpd 214: Spectinomycin	13.594	332.15862	1023	Spectinomycin	C14 H24 N2 O7	332.15835	0.82	C14 H24 N2 O7	C14 H24 N2 O7	1.73
Cpd 175: Quercetin 3,3'-dimethyl ether 4'-(2-methylbutyrate)	13.671	414.13228	1348	Quercetin 3,3'-dimethyl ether 4'-(2-methylbutyrate)	C22 H22 O8	414.13147	1.95	C22 H22 O8	C22 H22 O8	0.3
Cpd 85: Cyclandelate	13.679	276.17244	6069	Cyclandelate	C17 H24 O3	276.17254	-0.37	C17 H24 O3	C17 H24 O3	-2.32
Cpd 262: Clebopride	13.684	373.15624	409	Clebopride	C20 H24 Cl N3 O2	373.1551	1.43	C20 H24 Cl N3 O2	C20 H24 Cl N3 O2	-1.44
Cpd 38: Embelin	13.764	294.18254	9051	Embelin	C17 H26 O4	294.18311	-1.93	C17 H26 O4	C17 H26 O4	0.54
Cpd 58: Torachrysone	13.973	246.08913	9027	Torachrysone	C14 H14 O4	246.08921	-0.32	C14 H14 O4	C14 H14 O4	0.05
Cpd 267: Procinonide	13.973	508.22726	620	Procinonide	C27 H34 F2 O7	508.22726	-0.17	C27 H34 F2 O7	C27 H34 F2 O7	-0.34
Cpd 127: Precocene II	14.667	220.11005	2686	Precocene II	C13 H16 O3	220.10994	0.5	C13 H16 O3	C13 H16 O3	-0.7
Cpd 28: His Lys Met	14.693	414.20389	19022	His Lys Met	C17 H30 N6 O4 S	414.20492	-2.5	C17 H30 N6 O4 S	C17 H30 N6 O4 S	0.03
Cpd 211: Benzylhydroxybenzoate	14.786	228.07865	1012	Benzylhydroxybenzoate	C14 H12 O3	228.07864	0.02	C14 H12 O3	C14 H12 O3	0.01
Cpd 36: Xanthinol Nicotinate	14.795	434.19119	37453	Xanthinol Nicotinate	C19 H26 N6 O6	434.19138	-0.44	C19 H26 N6 O6	C19 H26 N6 O6	-0.04
Cpd 227: Nifedipine	15.136	346.11705	1046	Nifedipine	C17 H18 N2 O6	346.11649	1.64	C17 H18 N2 O6	C17 H18 N2 O6	1.87
Cpd 111: Cyclandelate	15.221	276.1727	6588	Cyclandelate	C17 H24 O3	276.17254	0.56	C17 H24 O3	C17 H24 O3	-2.53
Cpd 153: Triphenyl phosphate	15.408	326.07035	2806	Triphenyl phosphate	C18 H15 O4 P	326.0708	-1.36	C18 H15 O4 P	C18 H15 O4 P	-0.47
Cpd 207: Dinocton	15.885	354.1427	1624	Dinocton	C16 H22 N2 O7	354.1427	1.61	C16 H22 N2 O7	C16 H22 N2 O7	-5
Cpd 77: Tributylphosphate	16.013	266.16479	43448	Tributylphosphate	C12 H27 O4 P	266.1647	0.37	C12 H27 O4 P	C12 H27 O4 P	-0.36
Cpd 12: Caffeic acid	16.021	180.04231	56429	Caffeic acid	C9 H8 O4	180.04226	0.26	C9 H8 O4	C9 H8 O4	-0.59
Cpd 72: Aspidodasycarpine	16.047	370.18858	11098	Aspidodasycarpine	C21 H26 N2 O4	370.18926	-1.84	C21 H26 N2 O4	C21 H26 N2 O4	-0.33
Cpd 200: 6β-Hydroxyprednisolone	16.107	376.18804	1195	6β-Hydroxyprednisolone	C21 H28 O6	376.18859	-1.46	C21 H28 O6	C21 H28 O6	1.49
Cpd 69: 3,5-Diprenyl-4-Hydroxyacetophenone	16.294	272.17721	7359	3,5-Diprenyl-4-Hydroxyacetophenone	C18 H24 O2	272.17712	-1.55	C18 H24 O2	C18 H24 O2	0.34
Cpd 246: Simmondsin-2'-ferulate	16.354	551.19947	771	Simmondsin-2'-ferulate	C26 H33 N O12	551.20028	-1.47	C26 H33 N O12	C26 H33 N O12	-0.22
Cpd 155: Butibufen	16.354	220.14626	16588	Butibufen	C14 H20 O2	220.14633	-0.33	C14 H20 O2	C14 H20 O2	-0.26
Cpd 209: Met-Asn-OH	16.413	371.07672	1437	Met-Asn-OH	C14 H17 N3 O7 S	371.07872	-5.4	C14 H17 N3 O7 S	C14 H17 N3 O7 S	1.04
Cpd 171: Amicetin	16.524	618.30149	1473	Amicetin	C29 H42 N6 O9	618.30133	0.27	C29 H42 N6 O9	C29 H42 N6 O9	0.11
Cpd 174: Dipyridamole	17.342	504.31802	884	Dipyridamole	C24 H40 N8 O4	504.31921	1.53	C24 H40 N8 O4	C24 H40 N8 O4	2.73
Cpd 225: Milbemectin A3	17.35	528.30815	653	Milbemectin A3	C31 H44 O7	528.3087	-1.05	C31 H44 O7	C31 H44 O7	0.04
Cpd 208: Thr Trp Met	17.469	436.17847	989	Thr Trp Met	C20 H28 N4 O5 S	436.17804	0.98	C20 H28 N4 O5 S	C20 H28 N4 O5 S	-0.84
Cpd 164: Xiboml	17.502	258.19813	2462	Xiboml	C18 H26 O	258.19837	-0.89	C18 H26 O	C18 H26 O	-0.45
Cpd 82: Palmitic amide	17.555	255.25634	8212	Palmitic amide	C16 H33 N O	255.25621	0.5	C16 H33 N O	C16 H33 N O	-0.56
Cpd 270: 2-Formyl-1-indanone	17.66	160.05243	717	2-Formyl-1-indanone	C10 H8 O2	160.05243	-1.24	C10 H8 O2	C10 H8 O2	-0.3
Cpd 256: Aspoxicillin	17.963	493.16354	772	Aspoxicillin	C21 H27 N5 O7 S	493.16312	0.85	C21 H27 N5 O7 S	C21 H27 N5 O7 S	2.56
Cpd 100: Gentamicin A	18.279	468.24328	4372	Gentamicin A	C18 H36 N4 O10	468.24314	0.3	C18 H36 N4 O10	C18 H36 N4 O10	0.25
Cpd 172: 3'-Deoxystreptomycin 6,3"-bis-phosphate	18.474	725.2024	1633	3'-Deoxystreptomycin 6,3"-bis-phosphate	C21 H41 N7 O17 P2	725.20342	-1.41	C21 H41 N7 O17 P2	C21 H41 N7 O17 P2	3.04

Joint Programme of Activities 2013 - 2014

- **NORMAN MassBank**
- **NORMAN Collaborative Trial on non-target screening**
- **Prioritisation of non-target screening data**
- ChemProp
  - Automated collection of physico-chemical and ecotox properties of large number of emerging substances
- **Joint Danube Survey 3**
- **Digital Sample Banking** – European archive for storage of raw mass spectral data; **retrospective analysis**
- Development of minimal requirements for storage of MS data in libraries
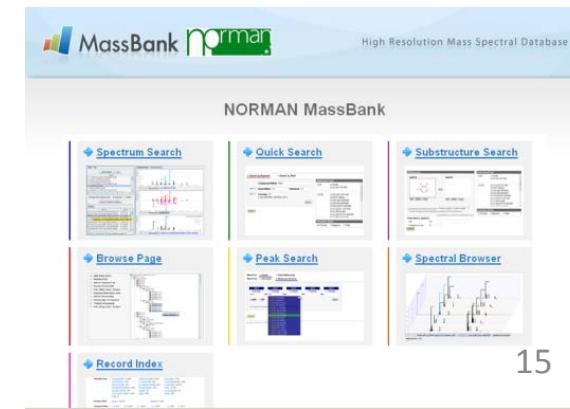
NORMAN MassBank – "let's share the knowns and focus on the unknowns"

- **VISION** =>> bringing together community of environmental chemists and set up of **a common and open access mass spectral database for identification purposes**

- Upgrade of the former NORMAN EMPOMASS database =>> hosted and maintained by UFZ, Leipzig
- NORMAN joined MassBank consortium (existing global platform *) in 2012
- Members of the NORMAN network committed to provide mass spectra to fill up the database

*MassBank Horai et al., 2010; www.massbank.jp
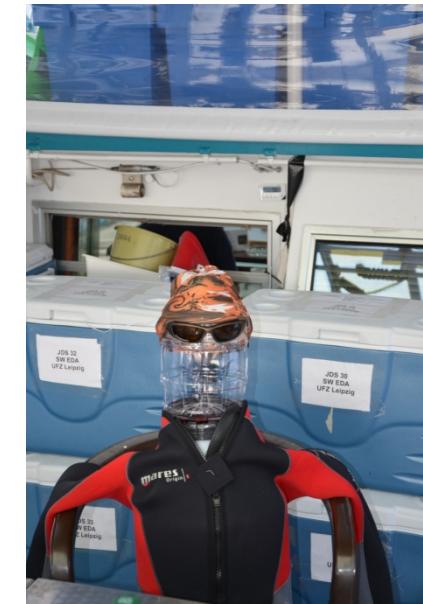
http://massbank.normandata.eu/MassBank/

NORMAN Collaborative Trial

Non-target screening of organic substances in river water samples
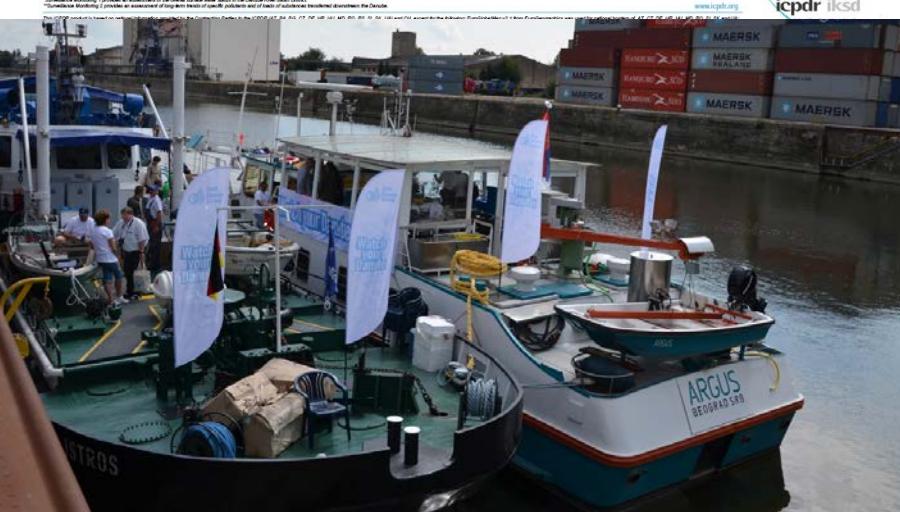
Joint Danube Survey 3
ICPDR, the biggest river expedition in the world
11 August – 26 September 2013

Expected outcomes
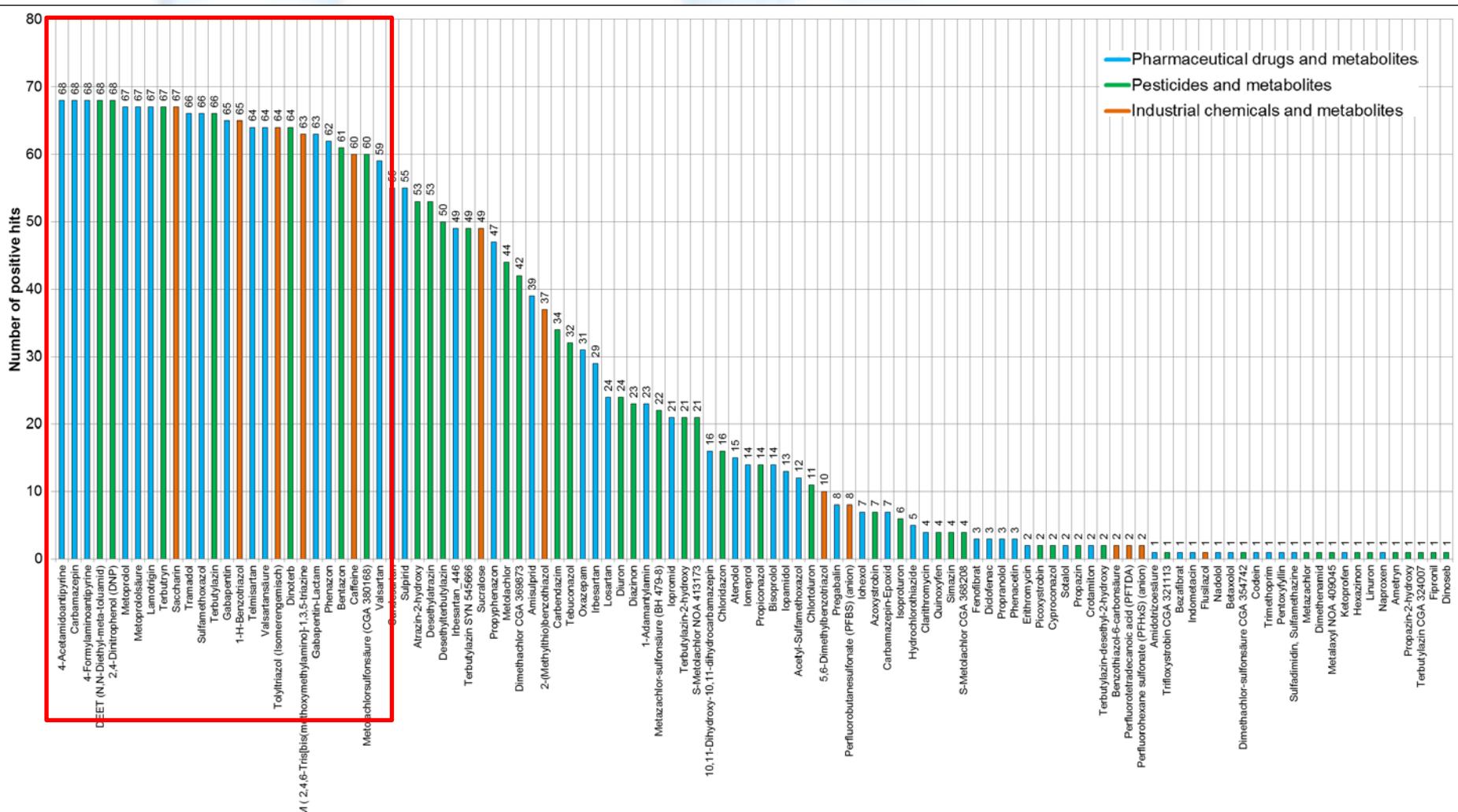
- Generation of a dataset for **development and testing of the methodology for prioritisation of pollutants identified with non-target screening** methods at the river basin scale.;

- Follow up:
  - PNEC values for each of the identified compounds;
  - Chemometry studies on the large datasets of MS data (SOLUTIONS).

- Development of **a harmonised methodology for identification of WFD river basin specific pollutants at the large international river basin scale using non-target screening data.**

JDS3 – preliminary prioritisation
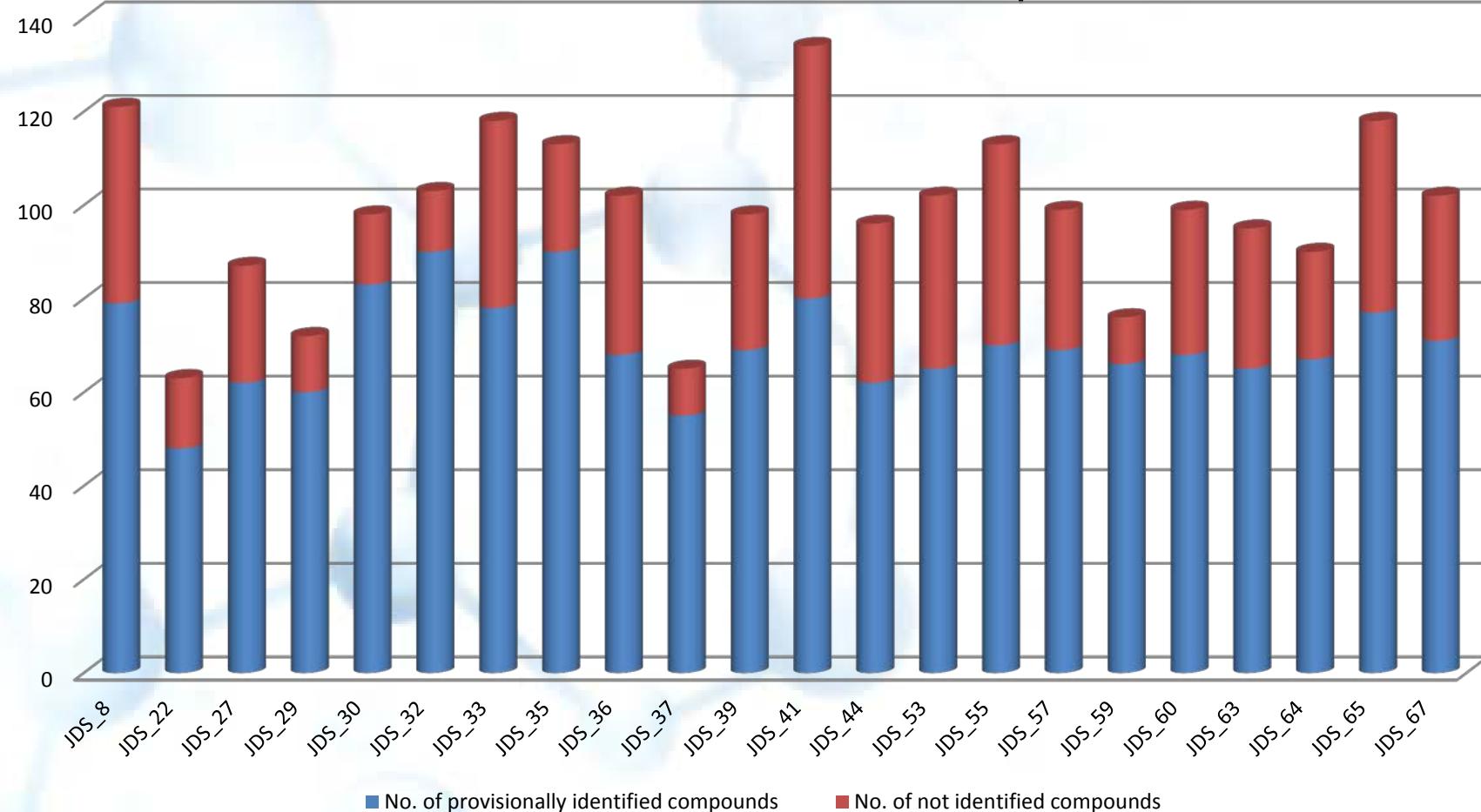
No.	Substance	No. of sites substance detected	C_{max}[1]	MEC_{95}[2]	Lowest PNEC/EQS	Type	EoE[3]	EoE score	FoE[4]	Final score
1	2,4-Dinitrophenol (DNP)	68	0.06	0.04	0.001	EQS chronic water[5]	40	0.2	1.00	1.20
2	PFOS (Perfluorooctansulfonate)	63	0.026	0.02	0.00065	EQS chronic water[5]	31	0.2	0.93	1.13
3	Chloroxuron	65	0.04	0.02	0.0024	PNEC acute	8.3	0.1	0.93	1.03
4	PFOA (Perfluorooctanoate)	66	0.036	0.02	0.0029	P-PNEC[6]	6.9	0.1	0.90	1.00
5	Desethylterbutylazine	54	0.028	0.01	0.0024	EQS chronic water[5]	4.2	0.1	0.79	0.89
6	2-hydroxy atrazine	53	0.06	0.02	0.002	EQS chronic water[5]	10	0.1	0.76	0.86
7	PFNA (Perfluorononanoate)	52	0.003	0.003	0.00039	P-PNEC[6]	7.7	0.1	0.76	0.86
8	Bromacil	31	0.19	0.14	0.01	EQS chronic water[5]	14	0.2	0.46	0.66
9	Dimefuron	58	0.041	0.04	0.008	EQS chronic water[5]	5.0	0.1	0.56	0.66
10	Bisphenol A	30	1.94	1.03	0.1	EQS chronic water[5]	10	0.2	0.16	0.36

JDS3 - Frequency of appearance

of 110 'identified' suspect pollutants (315 tested) in JDS3 surface water samples; results obtained from non-target screening workflow by HPLC-ESI-Q-TOF-MS operated in ESI⁺ and ESI⁻ modes

JDS3 - Number of compounds detected with LVI-GC-MS in the 22 JDS3 surface water samples obtained with the LVSPE sampling technique

■ No. of provisionally identified compounds   ■ No. of not identified compounds
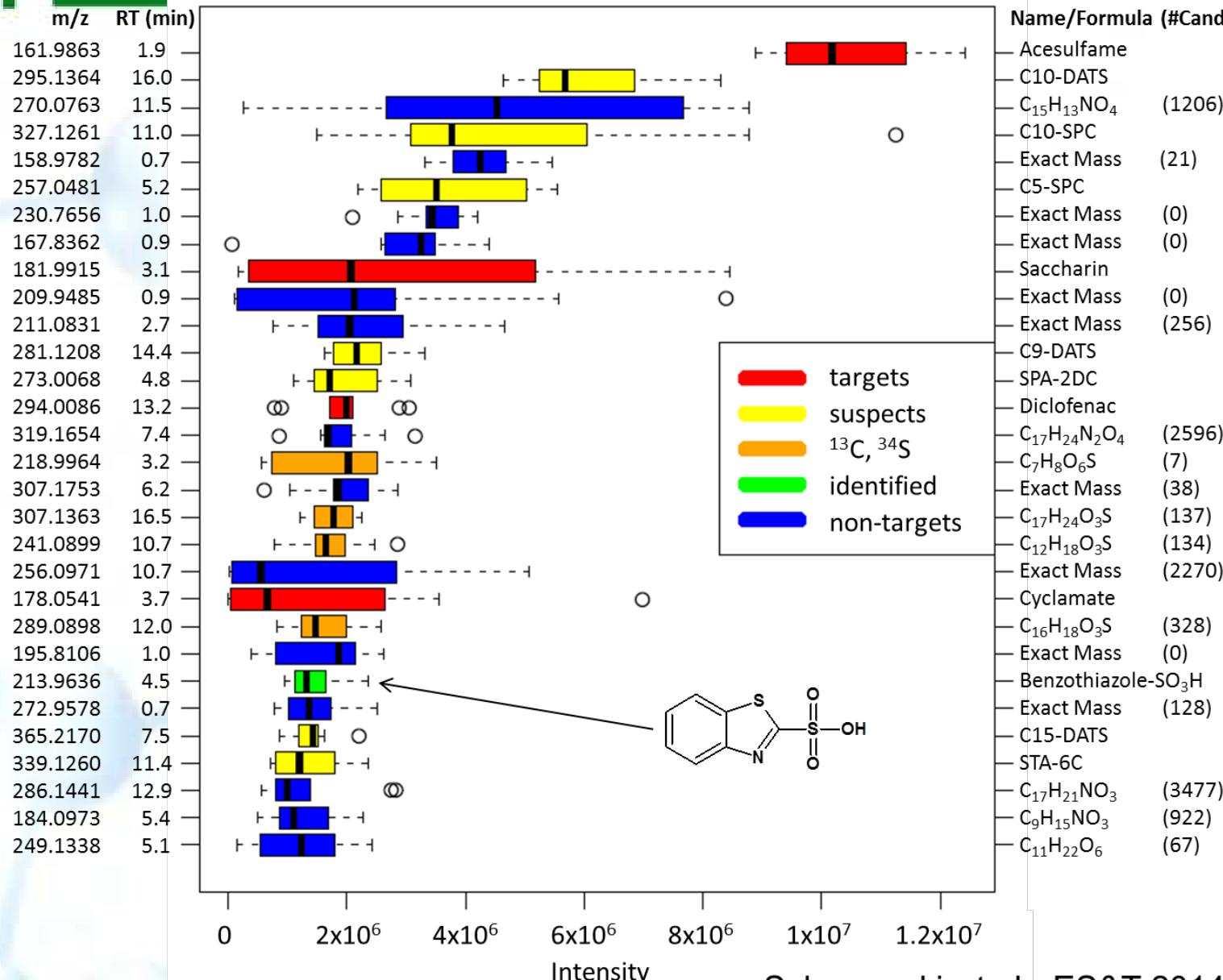
Example Switzerland: Sampling of 10 typical wastewater treatment plants

Characterisation of wastewater effluent (10 plants)
Ranking by presence and intensity – Negative
Ionisation

m/z	RT (min)		Name/Formula (#Cand)
161.9863	1.9		Acesulfame
295.1364	16.0		C10-DATS
270.0763	11.5		$C_{15}H_{13}NO_4$ (1206)
327.1261	11.0		C10-SPC
158.9782	0.7		Exact Mass (21)
257.0481	5.2		C5-SPC
230.7656	1.0		Exact Mass (0)
167.8362	0.9		Exact Mass (0)
181.9915	3.1		Saccharin
209.9485	0.9		Exact Mass (0)
211.0831	2.7		Exact Mass (256)
281.1208	14.4		C9-DATS
273.0068	4.8		SPA-2DC
294.0086	13.2		Diclofenac
319.1654	7.4		$C_{17}H_{24}N_2O_4$ (2596)
218.9964	3.2		$C_7H_8O_6S$ (7)
307.1753	6.2		Exact Mass (38)
307.1363	16.5		$C_{17}H_{24}O_3S$ (137)
241.0899	10.7		$C_{12}H_{18}O_3S$ (134)
256.0971	10.7		Exact Mass (2270)
178.0541	3.7		Cyclamate
289.0898	12.0		$C_{16}H_{18}O_3S$ (328)
195.8106	1.0		Exact Mass (0)
213.9636	4.5		Benzothiazole-SO_3H
272.9578	0.7		Exact Mass (128)
365.2170	7.5		C15-DATS
339.1260	11.4		STA-6C
286.1441	12.9		$C_{17}H_{21}NO_3$ (3477)
184.0973	5.4		$C_9H_{15}NO_3$ (922)
249.1338	5.1		$C_{11}H_{22}O_6$ (67)

Legend:
- targets
- suspects
- $^{13}C, ^{34}S$
- identified
- non-targets

Intensity: 0, $2x10^6$, $4x10^6$, $6x10^6$, $8x10^6$, $1x10^7$, $1.2x10^7$

Schymanski et al., ES&T 2014, 48:1811-1818

Science for Peace and Security (SPS)
North Atlantic Treaty Organisation

Development of a Decision Support System for Reducing Risk from Environmental Pollution in the Bosna River

Bosna River Survey 2012

Aims:

- To provide screening of urban and industrial waste water streams for identification of major polluters and discharged substances

➔ **Prioritisation of most relevant "Bosna RBSPs" and establishment of emission limit values for major polluters**

Priority rank of the 11 polluters based on non-target analysis

SITE	CAS No.	Compound Name	Est. conc (ug/l)	Lowest PNEC (ug/l)	Exc.
I-3 Prevent Leather	59-48-3	2H-Indol-2-one, 1,3-dihydro-	50	0.50	100
I-3 Prevent Leather	620-92-8	Phenol, 4,4'-methylenebis-	33	1.69	20
I-3 Prevent Leather	106-44-5	p-Cresol	28	1.4	20
I-3 Prevent Leather	57-11-4	Octadecanoic acid	0.03	0.0013	20
I-3 Prevent Leather	141-02-6	2-Butenedioic acid (E)-, bis(2-ethylhexyl) ester	0.14	0.0094	14
I-3 Prevent Leather	3735-92-0	Carbamodithioic acid, dimethyl-, methyl ester	0.26	0.049	5
I-3 Prevent Leather	80-05-7	Bisphenol A	0.27	0.2	1
I-3 Prevent Leather	78-51-3	Tri(butoxyethyl)phosphate	8.9	6.8	1
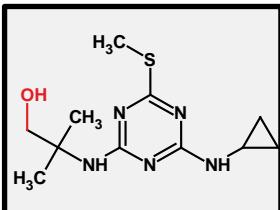
Non-target screening – categorisation and prioritisation

IIentifying Small Molecules via High Resolution Mass
Spectrometry: Communicating Confidence

Example	Identification confidence	Minimum data requirements
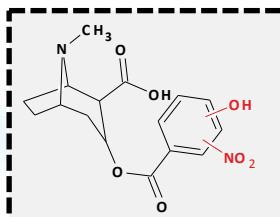
Level 1: Confirmed structure
    by reference standard
MS, MS^2, RT, Reference Std.

Level 2: Probable structure
    a) by library spectrum match
    b) by diagnostic evidence
MS, MS^2, Library MS^2
MS, MS^2, Exp. data
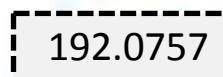
Level 3: Tentative candidate(s)
structure, substituent, class
MS, MS^2, Exp. data

$C_6H_5N_3O_4$ — **Level 4: Unequivocal molecular formula** — MS isotope/adduct

192.0757 — **Level 5: Exact mass** of interest — MS

Non-target screening

- **Category 1 - CONFIRMED STRUCTURE**
  - **Action:** Derive PNECs, physico-chemical properties, exposure index??; RANKING; **move top ranking substances to the NORMAN list of substances**; prioritise retrospectively using available semi-quantitative data

- **Category 2 – PROBABLE STRUCTURE**
  - **Action:** Derive PNECs, physico-chemical properties, exposure index??; RANKING; confirm structures; semi-quantify retrospectively; **move to Category 1**
  - **Problem: mix of data with estimated concentrations and no information on concentration**
  - **Use a set of internal standards, use the one with closest structural similarity**

Non-target screening

- **Category 3 – TENTATIVE CANDIDATES**
  - **Action:** Derive PNECs, physico-chemical properties, exposure index??; RANKING; confirm structures; semi-quantify retrospectively; **move to Category 2/1**

- **Category 4 – UNEQUIVOCAL MOLECULAR FORMULA**
  - **Action:** Ranking based on **Frequency of appearance (FoA)/ Retention time characteristic**; Improve/use state-of-the-art mass spectral elucidation tools; **move to Category 2/1**

- **Category 5 – EXACT MASS OF INTEREST/ MASS SPECTRUM (GC-MS)**
  - **Action:** Ranking based on **Frequency of appearance/ Retention time characteristic**; Improve/use state-of-the-art mass spectral elucidation tools; **move to Category 2/1**

  - **FoA: At how many places we see the substance**

Non-target screening

1. Samples of water/sediment/biota/soil/air **screened** with **GC-MS and/or LC-accurate mass-MS**
2. **Provisional identification and semi-quantification** of substances present in samples
3. Mass spectral **data stored** in NORMAN MassBank
4. Collection of existing/derivation of **provisional PNECs** for each substance using ChemProp (QSAR)…
5. **Prioritisation** based on occurrence, toxicity…

- **Top listed non-target substances ➡ target monitoring**

Proposal: NORMAN network Early Warning System (**NEWS**)

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Norwegian Institute for Water Research

An opportunity to collaborate!

- A network of laboratories within NORMAN that are active in non-target analysis

- **Concept:** when one group identifies a new contaminant, MS and other I.D. criteria are sent to other members of the group

- Other members use **retrospective** techniques to check their own samples

Concept for 2015

- Invite labs to join NEWS
  - Ideally labs with active non-target projects studing env. samples and/or transformation
  - Help if they had archived data for retrospective analysis

- Workshop to establish how the network will function
  - To discuss the details of how the group will operate, what kind of samples, IPR, publication etc.

- Run a pilot activity

Conclusions

- The need to **look beyond the traditional target pollutants** is now generally

It is not possible to develop the necessary knowledge and methodologies solely at the national scale

- **RI/Retention prediction information, internal standards for semi-quantification**

International cooperation – NORMAN EG on prioritisation of non-target substances established; interested to join?

Common views of the scientific community on research needs and **priorities for future legislation**