The proposed PMT criteria: how many P, M and T compounds are registered under REACH and are in drinking water?

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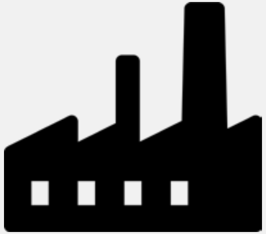
Workshop: PMT and vPvM substances under REACH
13. March 2018, Bundespresseamt, Berlin, Germany

Two goals



Chemical Industry

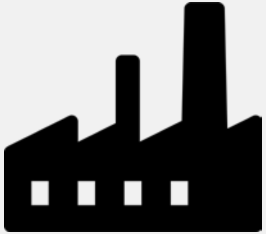
1. The European Chemical Industry continues to innovate, grow, and be internationally competitive.

2. Our drinking water is protected from undue levels of contamination.

Drinking water

Properties of a drinking water contaminant

Persistency and Mobility



Chemical Synthesis

Uses / Products

Transport through the environment or infrastructure

Water treatment and production

Consumption

Toxicity

Contents

Preliminary assessments of

- 1. How many P, PM and PMT substances are registered in REACH?
- 2.Can the PMT/vPvM criteria be used to predict drinking water contamination?
- 3. Are all REACH substances in drinking water PM or PMT substances?

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1. How many P, PM and PMT substances are registered in REACH?


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TECHNICAL NOTE

Preliminary assessment of substances registered under REACH that could fulfil the proposed PMT/vPvM criteria

BACKGROUND DOCUMENT TO THE WORKSHOP:
"PMT AND vPvM SUBSTANCES UNDER REACH"
MARCH 13'TH-14'TH. BUNDESPRESSEAMT, BERLIN, GERMANY

DOC.NO. 20160426-TN-01
2018-03-06

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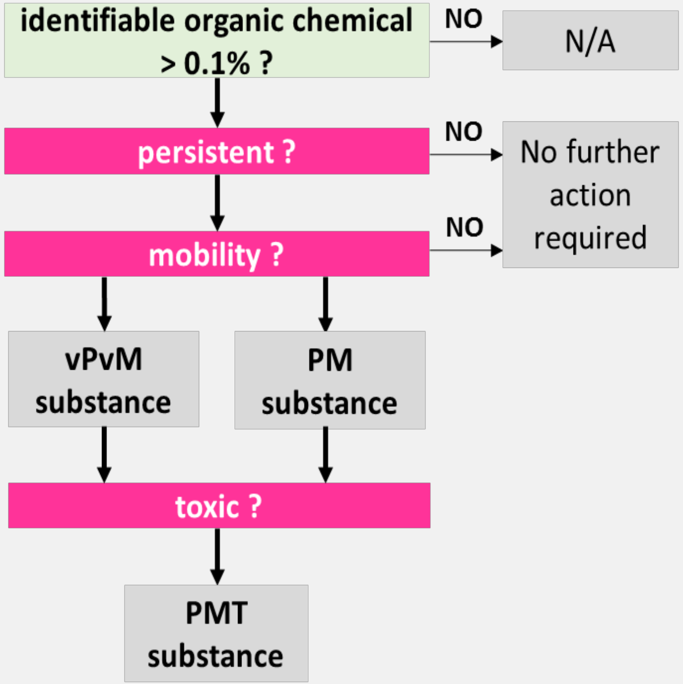
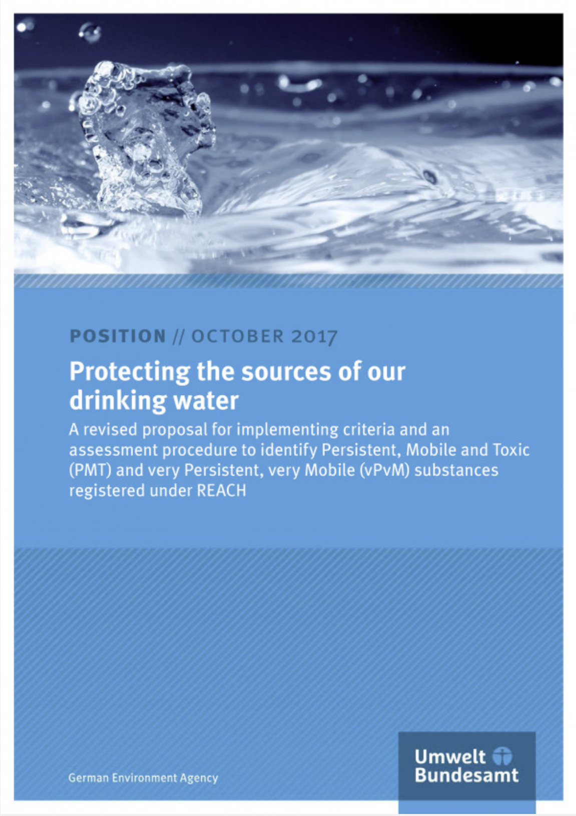
Defining PMT criteria based on substance properties





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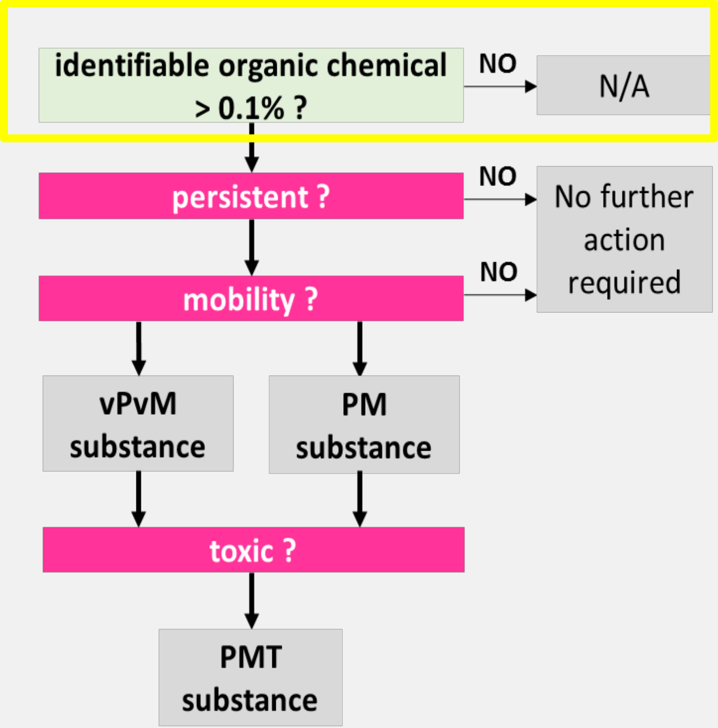
Identifying organic constitutents



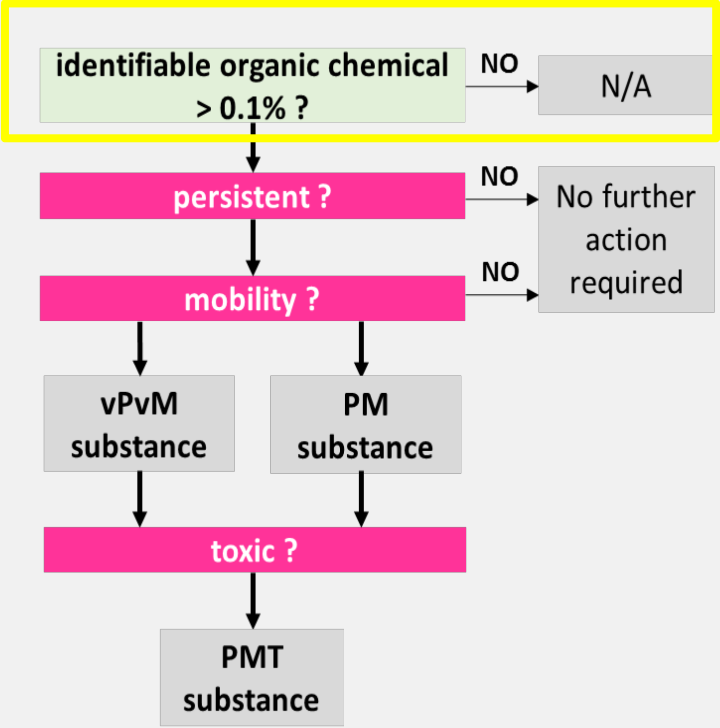
REACH Registered Substances, May 2017

Classification	Main organic constituent per substance
organic	9196
organoboranes	35
organosilanes	217
pseudo-organic	178
organometallic	115
Purely inorganic	653
no structural information	5075
Total	15469

9714 proceed

Sources: IUCLID 6 – SMILES and InChI data, CAS-SMILES libraries, last resort: Chemaxon name to structure converter.

Assessing persistency (P and vP)



P and vP criteria identical to Annex XIII to the REACH Regulation

	Persistence (P) in any of the following situations	Very persistent (vP) in any of the following situtations
Marine water	half-life > 60 days	half-life > 60 days
Fresh water	half-life > 40 days	half-life > 60 days
Marine sediment	half-life > 180 days	half-life > 180 days
Fresh water sediment	half-life > 120 days	half-life > 180 days
Soil	half-life > 120 days	half-life > 180 days

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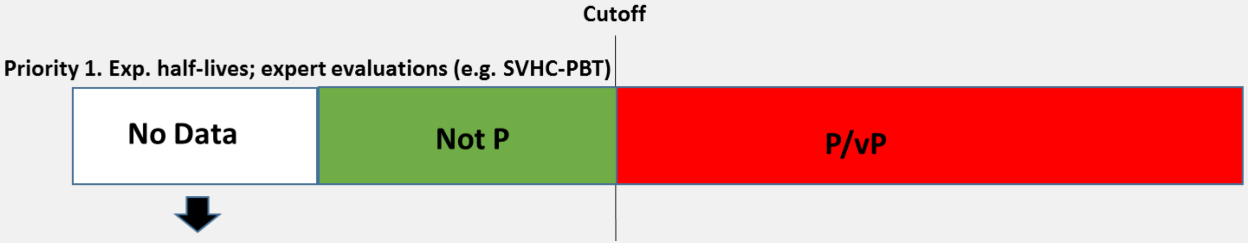
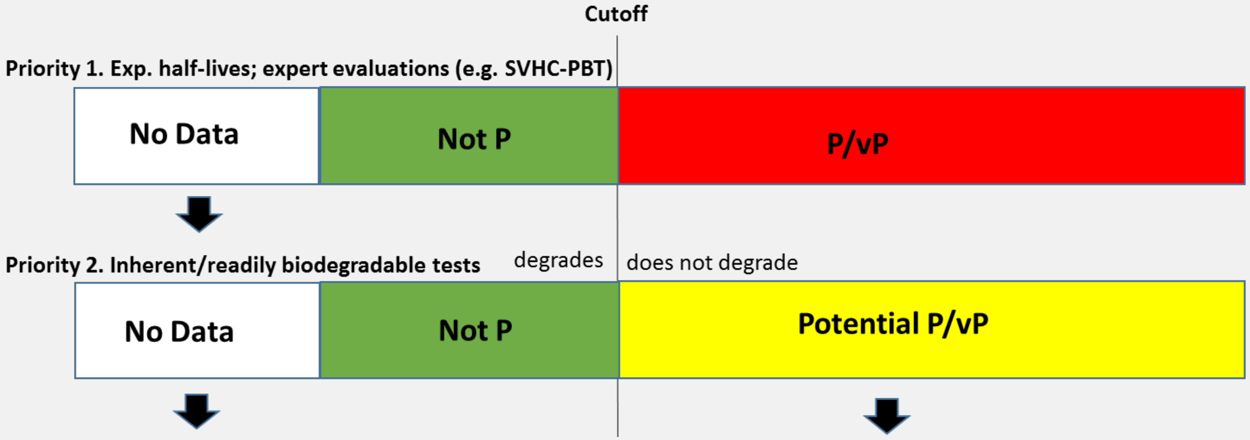
ECHA Chapter R.11. Version 3.0 (June 2017)

Assessing Persistency based on weight-of-evidence



Good quality half-life data is rare (e.g. following OECD TG 307, 308, 309). Expensive and time consuming.

Assessing Persistency based on weight-of-evidence



Good quality half-life data is rare (e.g. following OECD TG 307, 308, 309). Expensive and time consuming.

ECHA recommends inherent/ready/enhanced biodegredation tests can be used to conclude «not persistent»

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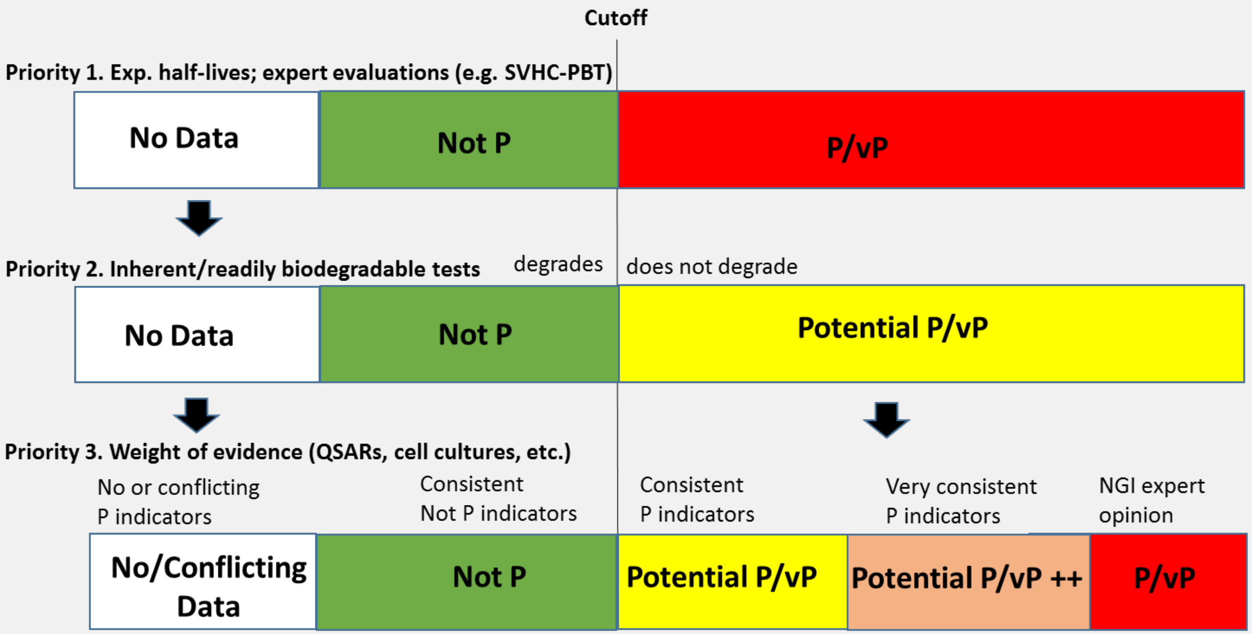
Assessing Persistency based on weight-of-evidence



Good quality half-life data is rare (e.g. following OECD TG 307, 308, 309). Expensive and time consuming.

ECHA recommends inherent/ready/enhanced biodegredation tests can be used to conclude «not persistent»

NGI conducted its own weight-of-evidence assessment experimental half-lives biodegrdation tests known.

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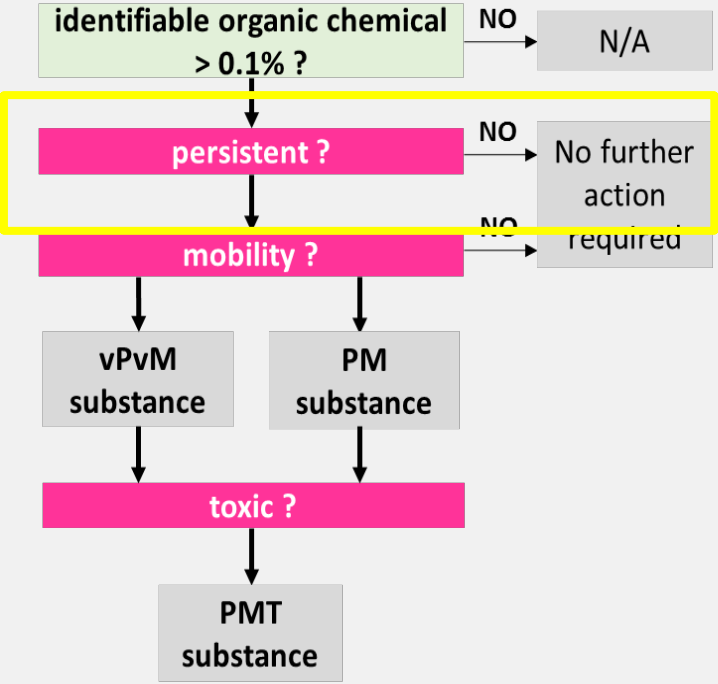
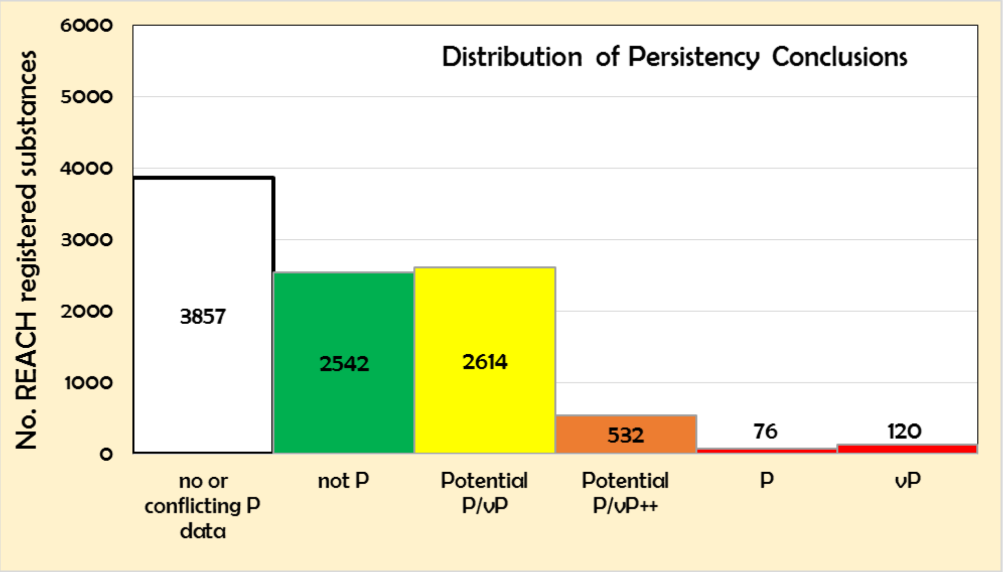
Persistency, results





1) Very few definitive conclusions on P/vP due to limited half-life data
2) If soil/sediment half-lives not considered, then even fewer.

728 of substances proceed to the «mobility» step

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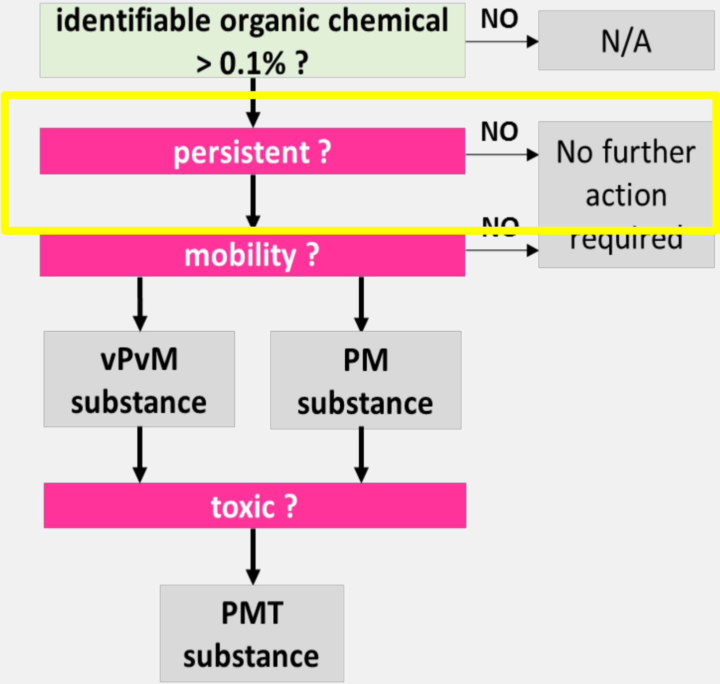
Assessing Mobility



No existing REACH definition of mobility.
UBA's proposal:

	Mobile (M) if it fulfills P or vP and any of the following situations	very Mobile (M) if it fulfills P or vP and any of the following situations
lowest experimental log K_{OC} (pH 4-9)	≤ 4.0	≤ 3.0
log D_{ow} (pH 4-9)	≤ 4.0 and no exp log K_{OC} data available	≤ 3.0 and no log K_{OC} data available

728 of substances proceed to the «mobility» step

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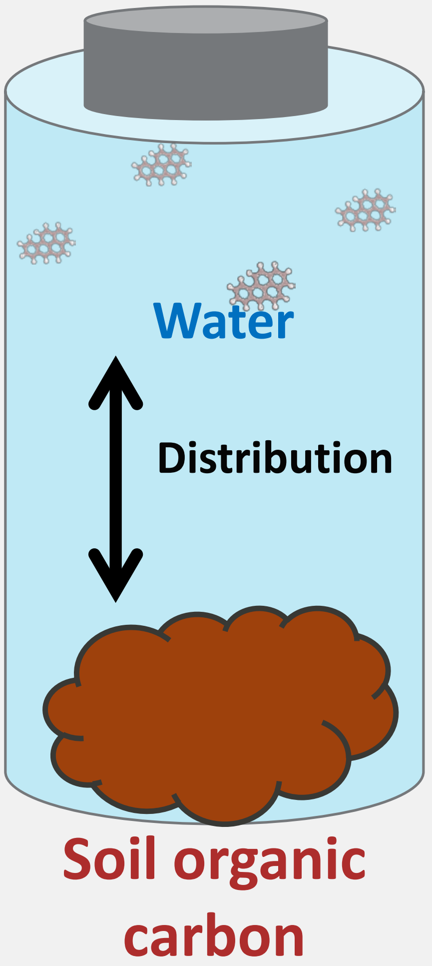
What is log Koc?

- K_{OC} = equilibrium distribution of a chemical between organic carbon (in soil, sediment or sludge) and water

$$K_{OC} = \frac{C_{soil\ OC}}{C_{water}}$$



What is log Dow?

- **K_{ow}** = equilibrium distribution of a chemical between n-octanol and water for non-ionizable substances

- **D_{ow}** = pH dependant K_{OW} for ionizable substances

  $D_{ow} = K_{ow} /(1+10^{pH - pKa})$ - monoprotic acids

- **pH 4-9** = typical environmental range (e.g. OECD 111)

- **K_{ow} / D_{ow}** – more commonly available than K_{oc}, also QSARs work better because of this (more data available, n-octanol is homogenous)

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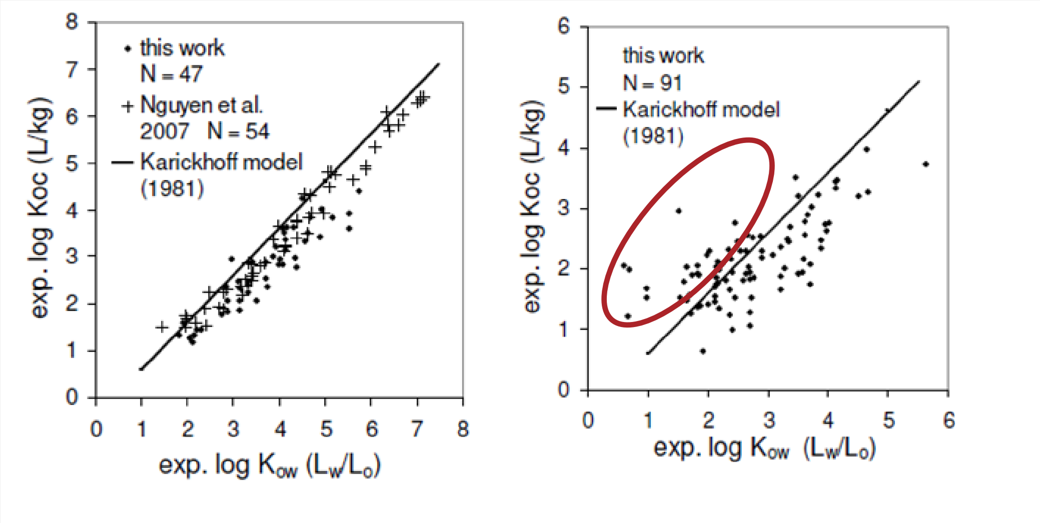
log Dow as a proxy for log Koc

- **$D_{ow} \approx K_{oc}$**
  - K_{ow} can be greater than K_{oc} for mobile substances (by 1 order of magnitude), but in general is usually less.
  - Overall, slightly conservative and simplifying assumption that accounts for uncertainty between the two parameteres

Non-polar substances

Polar substances



Bronner & Goss, ES&T, 2011

Mobility weight-of-evidence and ionic charge

When no experimental data exists, QSARs for D_{OW} can be used, but should be interpreted correctly.

Charge type	Number of substances (largest organic constituent) REACH registered May 2017)
neutral	5095
ionizable	3218
anionic	1086
cationic	300
zwitterionic	60

Neutral compounds

- Best QSARs work within 1 order of magnitude for K_{OW} (Arp et al. 2017)

Ionizable compounds,

- QSARs needed for both K_{OW} and pK_a. Accuracy considered within 2 orders of magnitude for D_{OW}

Anions

- $K_{OC}<D_{OW}$, as *soil surface is anionic*

Cations

- $K_{OC}>D_{OW}$ as opposites attract

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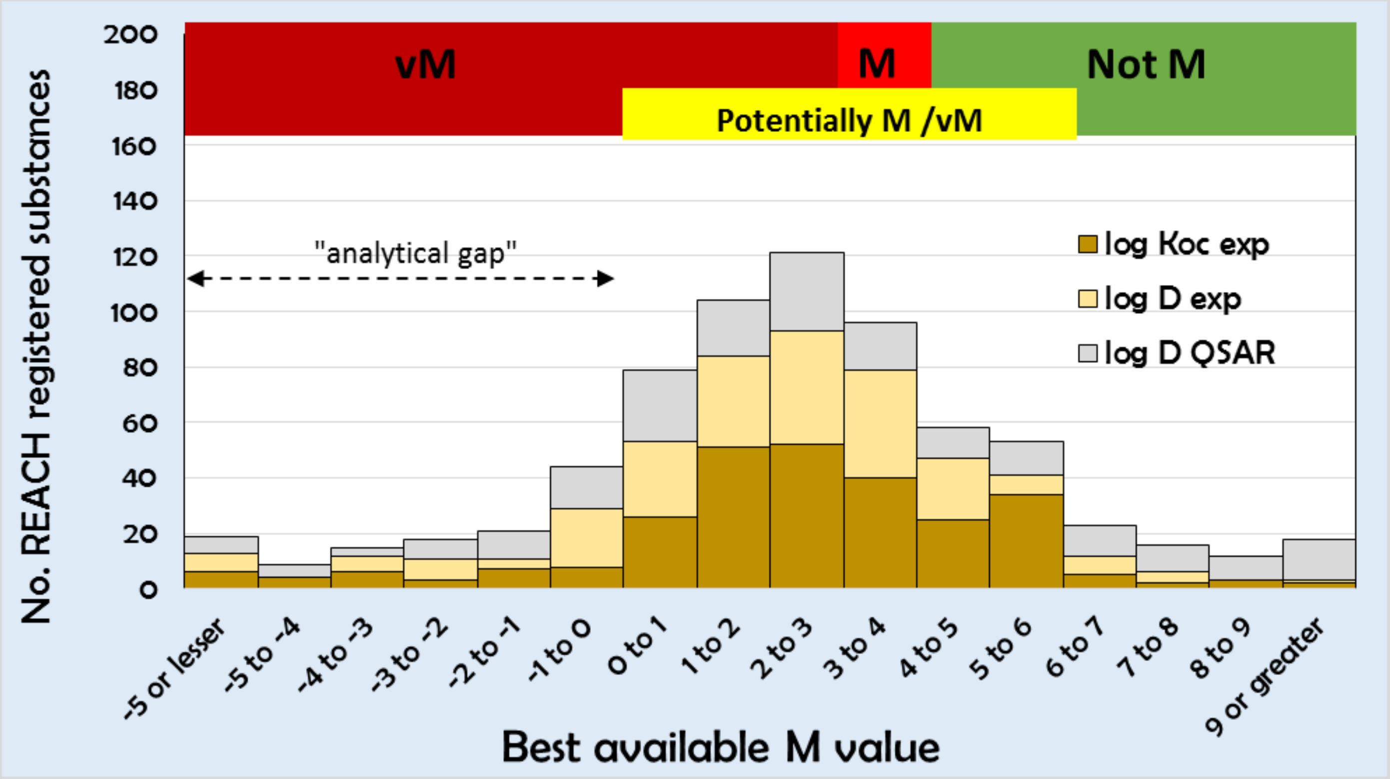
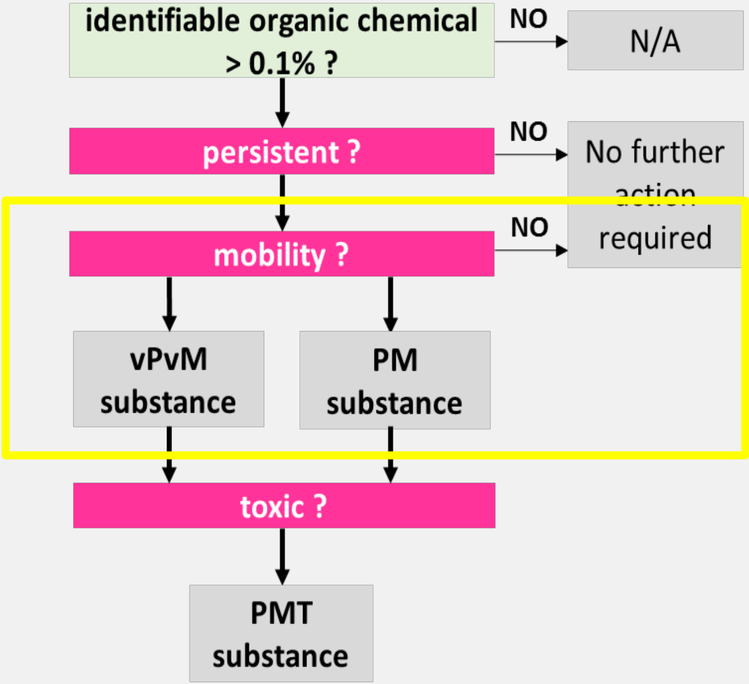
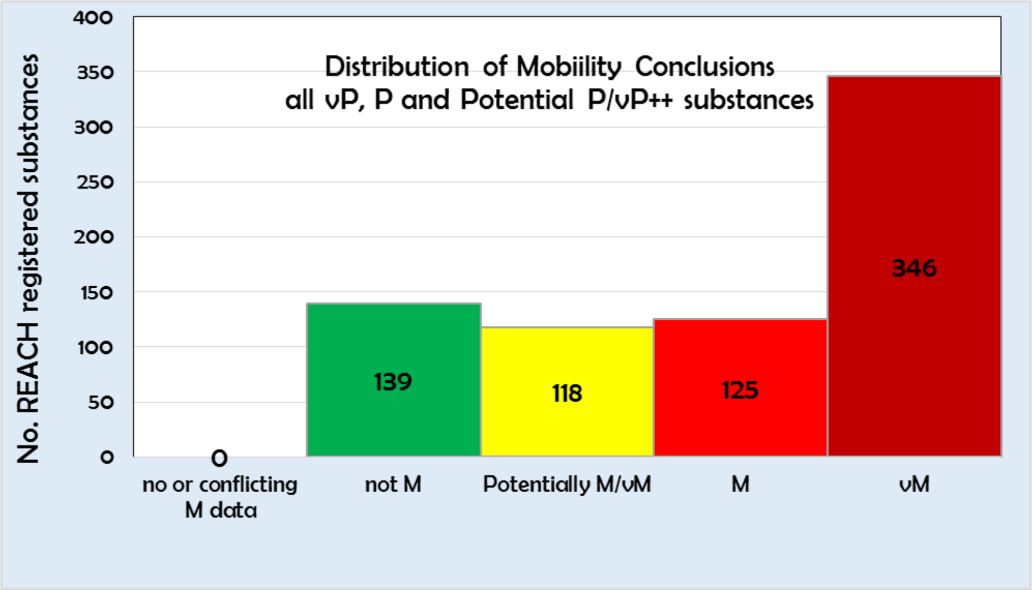
Distribution of log Koc and log DOW



Potentially M/vM: QSAR log D results within uncertainty range. Varies for neutral, ionizable, anions, cations and zwitterions.

Mobility, results





471 substances meet the M or vM criteria

- **vPvM** (53 substances)
- **PM** (but not vPvM, 79 substances)
- **potential PM/vPvM** (339 substances, no experimental half-life data but likely P)

471 of substances proceed to the «toxicity» step

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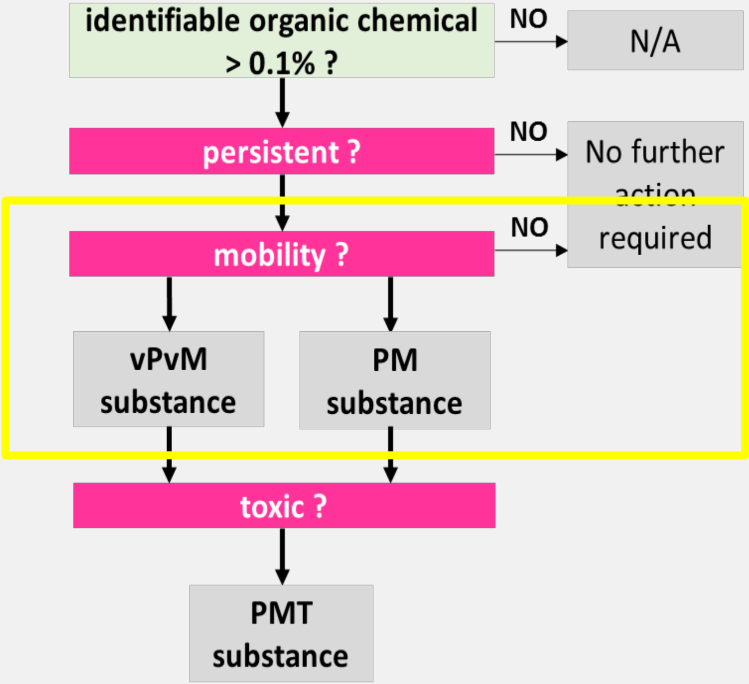
Assessing Toxicity



T criterion criteria identical to Annex XIII to the REACH Regulation, though with additions

A substance fulfils the toxicity criterion (T) in any of the following situations:

a) Long term NOEC/EC10 for marine/freshwater organisms < 0.01 mg/L

b) Carcinogenic (category 1A, 1B **or 2**); germ cell mutagenic (category 1A, 1B **or 2**); toxic for reproduction (category 1A, 1B **or 2**).

c) Specific target organ toxicity after repeated exposure (STOT RE category 1 or 2)

d) additional category for effects on or via lactation

e) Derived-No-Adverse-Effect-Level (DNEL) is ≤ 9 µg/kg/d (oral, long term, general population

f) Suspected endocrine disruption

471 of substances proceed to the «toxicity» step

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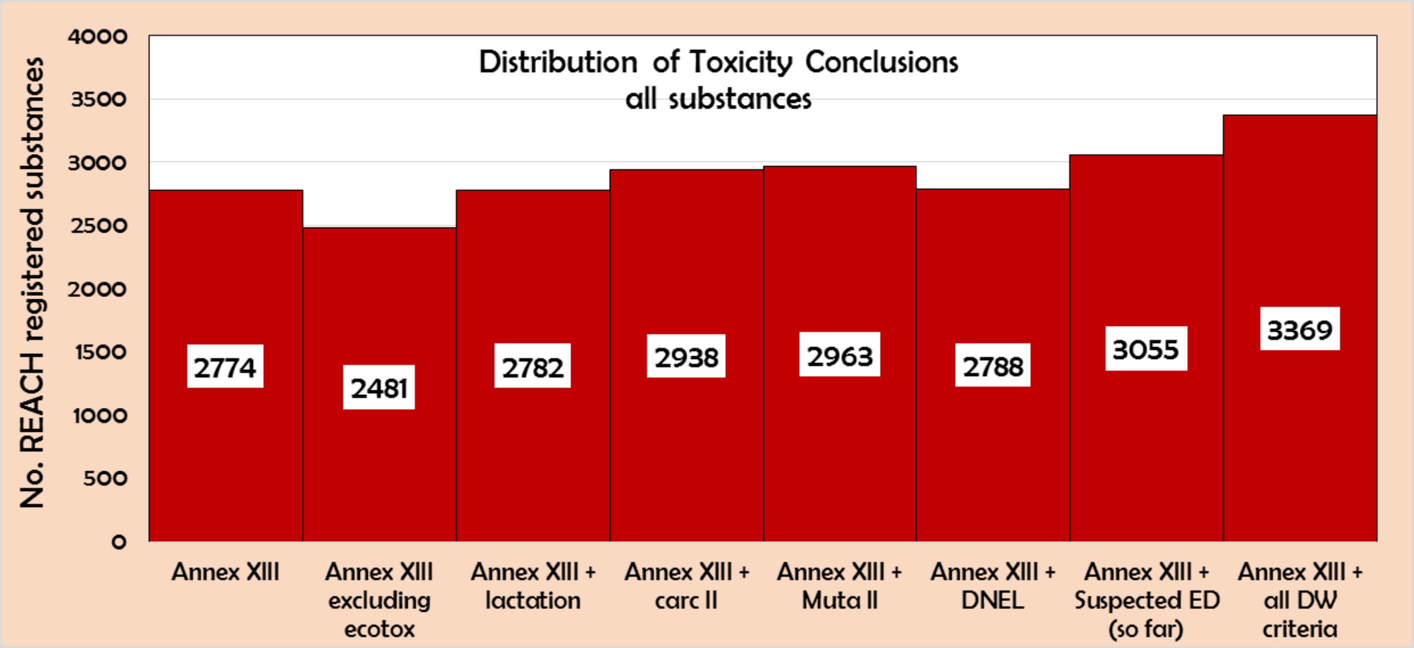
Frequency of toxicity criteria amongst 15469 REACH registered substances (May 2017)



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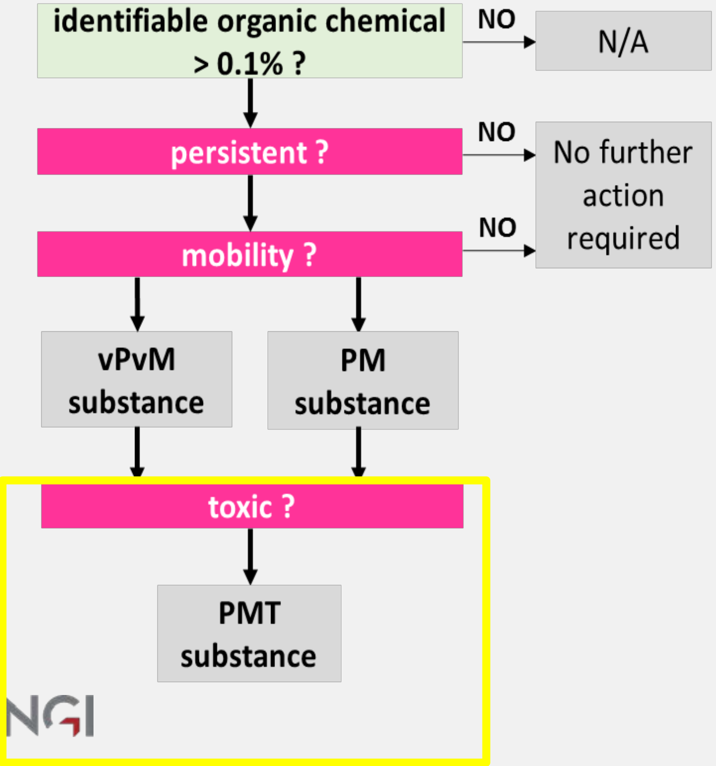
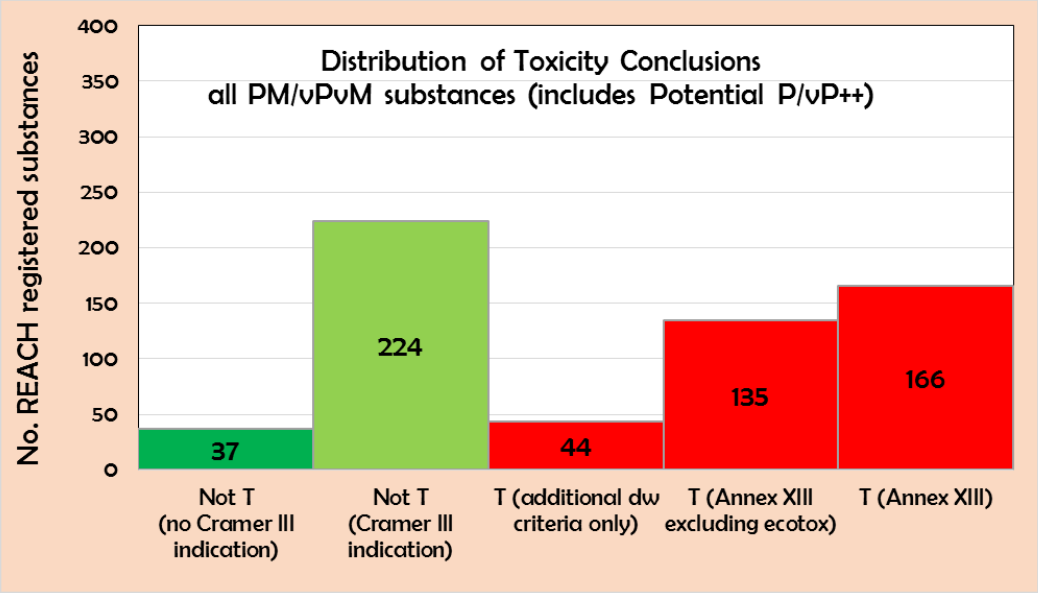
Toxicity, results





210 substances meet the PMT criteria

vPvMT (23 substances)

PMT (but not vPvMT, 35 substances)

high potential PMT (152 substances)

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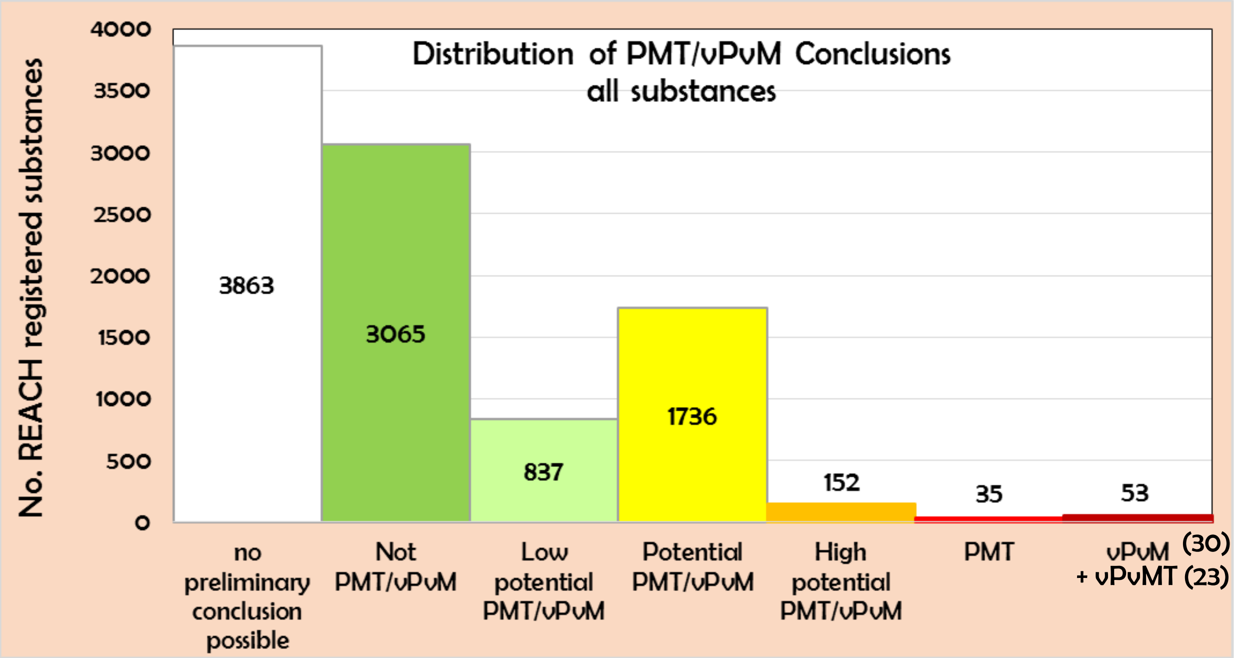
Conclusion to part 1:
How many PMT substances are there in REACH?



210 PMT

30 vPvM (not PMT)

More half-life data needed...

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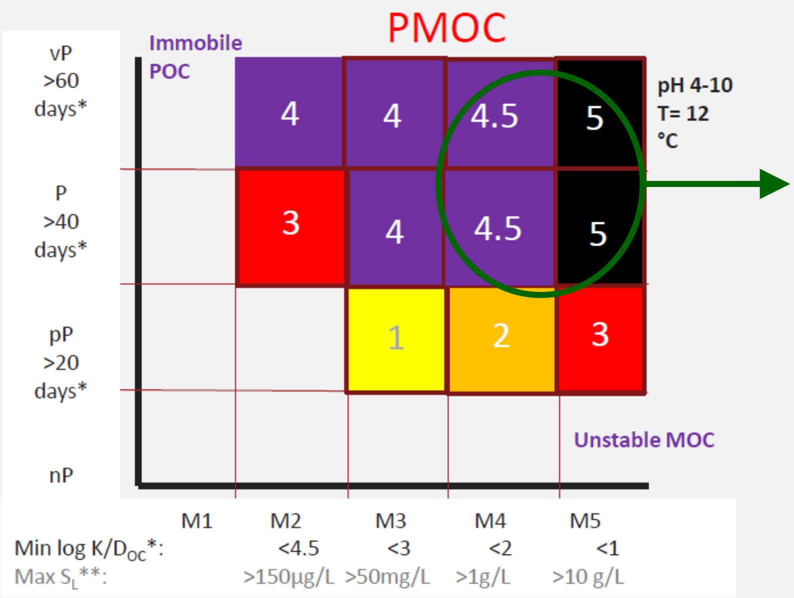
2. Can the PMT criteria be used to predict drinking water contamination?

http://www.ufz.de/promote/

PMOC selection for monitoring



Use descriptors

- High release to environment
- Wide dispersive use
- Closed system use
- Intermediate use
- Consumer use
- Professional use
- Substance in article

Marketing volumes

Estimating P and vM

Arp et al. (2017) Environ. Sci. Process Impacts, 19, 939-955

Ranking emission potential

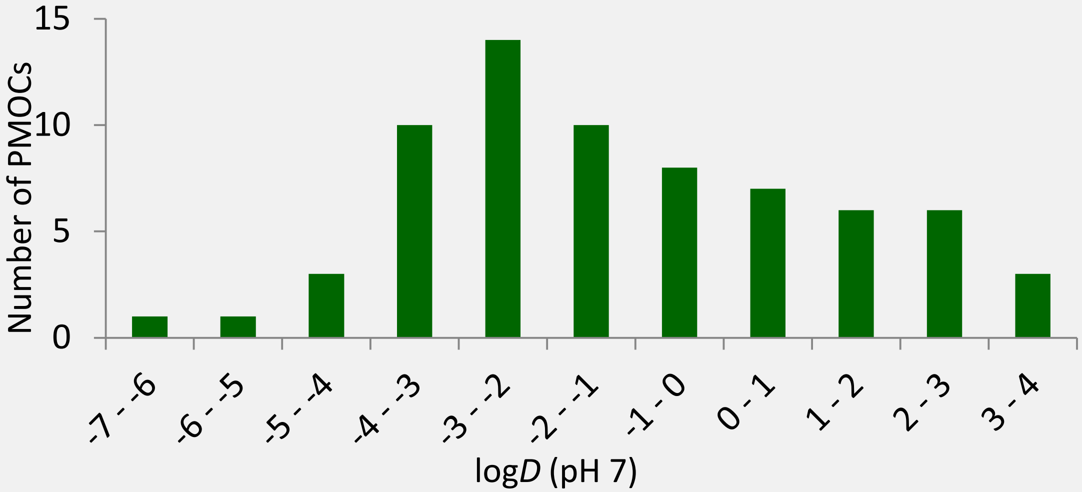
Schulze et al. Science of The Total Environment 625, 1122-1128

→ Ranked list of 1100 suspected PMOCs

→ 70 compounds chosen

Selected 70 PM substances

- 70 PM substances with high tonnages and uses that indicate emissions
- Mixture of neutral, ionizable (acids, bases) and permanently charged (cations, anions, amphoteric) substances
- Log*D* range (pH 7, Chemaxon)



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Water JPI PROMOTE

European water samples

Approx. 50 samples from 5 countries

- Surface water
- Groundwater
- Bank filtrate
- Different stages of drinking water treatment incl. reverse osmosis permeate and concentrate

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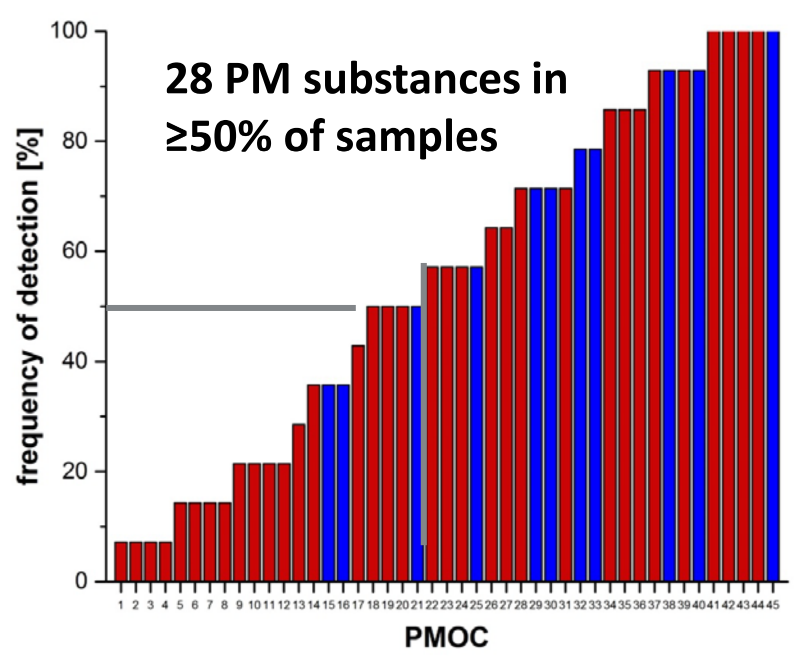
Water JPI PROMOTE

Results from qualitative monitoring

Number and frequency of detected PMs



28 PM substances

A total of 45 (of 70 analyzed) PMs detected in 14 water samples

- Some PMs frequently detected, others in single samples
- Detection of „**known**“ as well as „**novel**“ PMOCs

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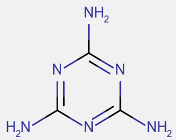
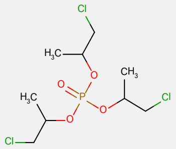
Water JPI PROMOTE

Results from qualitative monitoring

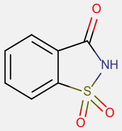
Examples I – „Known“ PMOCs



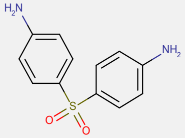
Melamine



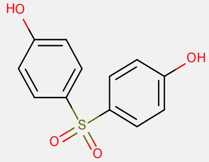
TCPP



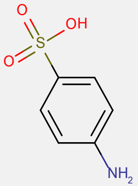
Saccharine



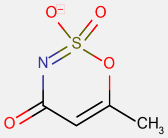
Dapsone



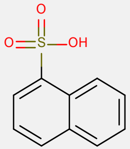
Bisphenol S



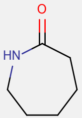
Sulfanilic acid



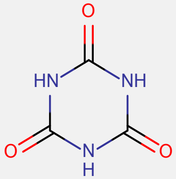
Acesulfame



Naphthalene sulfonic acid



Ɛ-Caprolactam

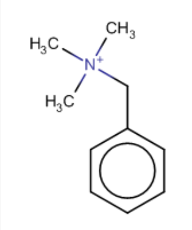


Cyanuric acid

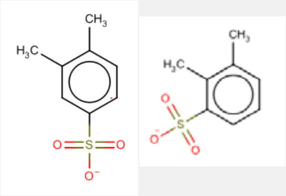
Results from qualitative monitoring

Examples II – „Novel“ PMOCs

Benzyltrimethyl ammonium

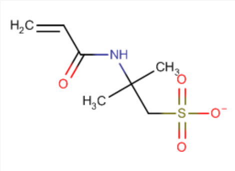


Dimethylbenzene sulfonic acid

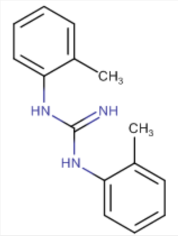


Trifluoro and Cl/Br methanesulfonic acids

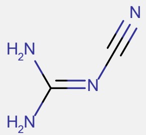
2-Acrylamido-2-methylpropane sulfonic acid



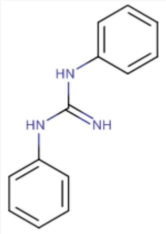
1,3-Di-*o*-tolylguanidine



Cyanoguanidine



1,3-Diphenylguanidine



Can the PMT criteria be used to predict drinking water contamination?

Answer: YES!
But, use, production volume or emission information also needed

3. Are all REACH substances in drinking water PM or PMT substances?

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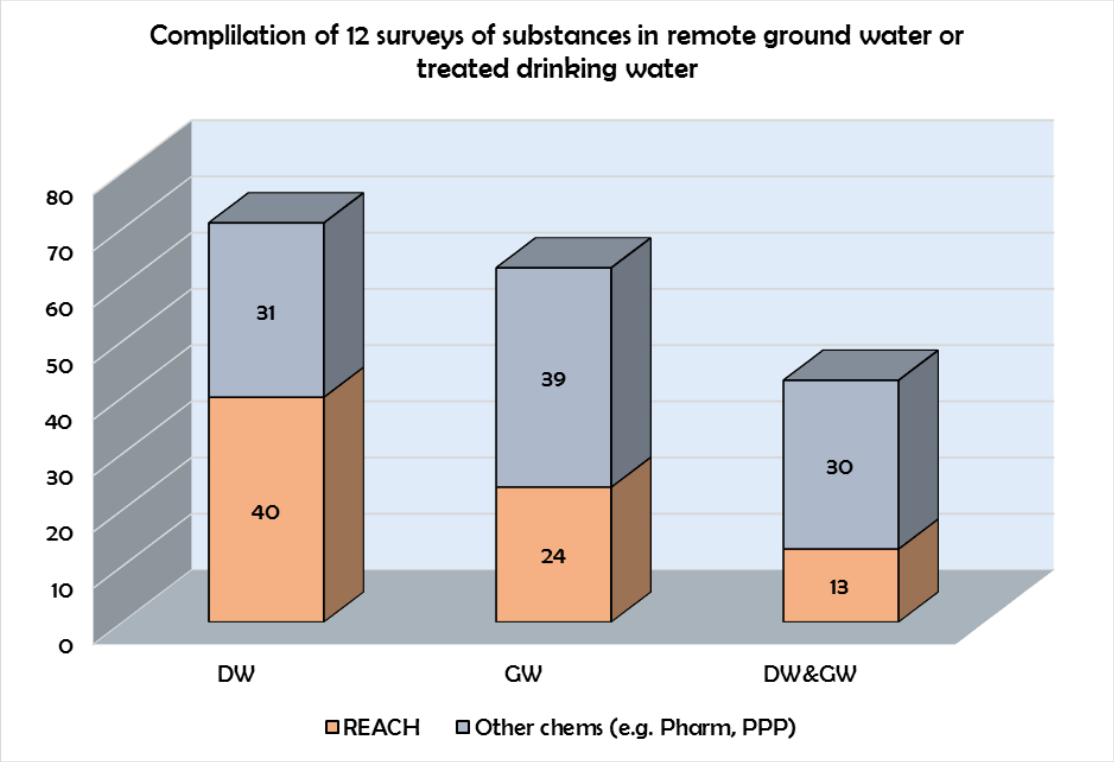
Literature survey: remote GW and treated DW

Treated DW/ Remote GW	Chemical types	Area	Reference
GW	various	Europe	Loos et al. Water Res. 2010- 44, 4115-4126.
GW	pharm.	Europe	Wolter (2016)
GW	pharm.	USA	Barnes et al. STOTEN 2008. 402, 192- 200.
GW	various	International	Lapworth et al. Environ. Pollut. 2012. 163, 287-303.
DW	various	Europe	EurEau (2017)
DW	various	Europe	**PROMOTE project (2018) – «published chems only/partial list»**
DW	solvents	Europe	DWD Regulation 98/73/EC
DW&GW	various	Europe	Kuhlman et al. (2010) Research project FKZ No 363 01 241
DW	PFAS	International	Kaboré et al. STOTEN 2018. 616, 1089-1100.
DW	various	USA	Stackleberg et al. STOTEN 2007. 377(2-3), 255-272.
DW	various	USA	Benotti et al. ES&T 2008. 43(3), 597-603

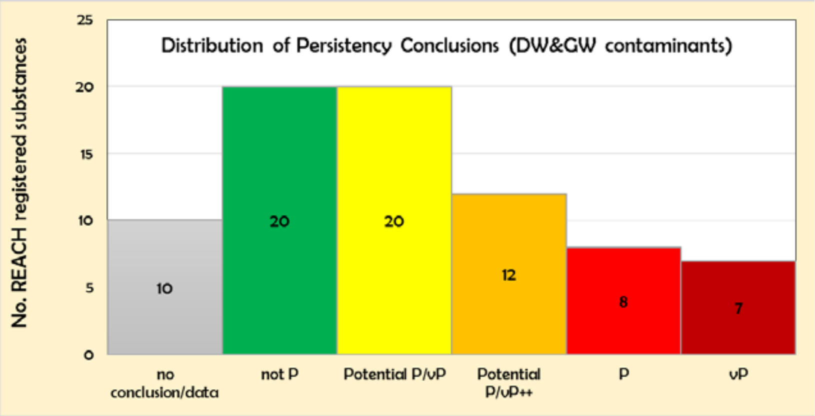
REACH vs Non-REACH sbubstances in DW&GW



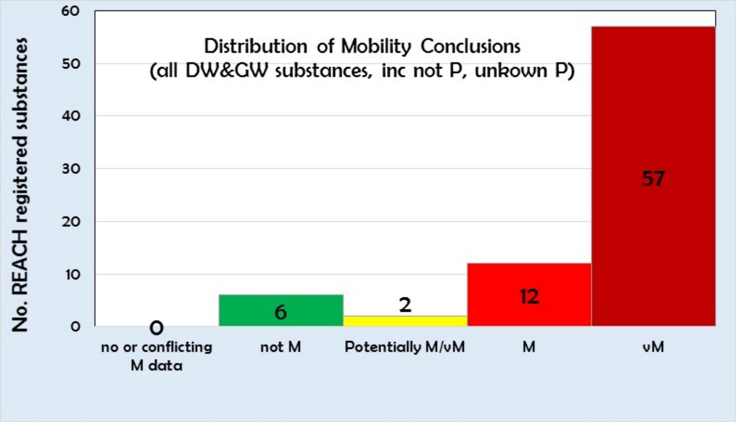
Total number of REACH substances = 77

How many of these are PMT/vPvM?

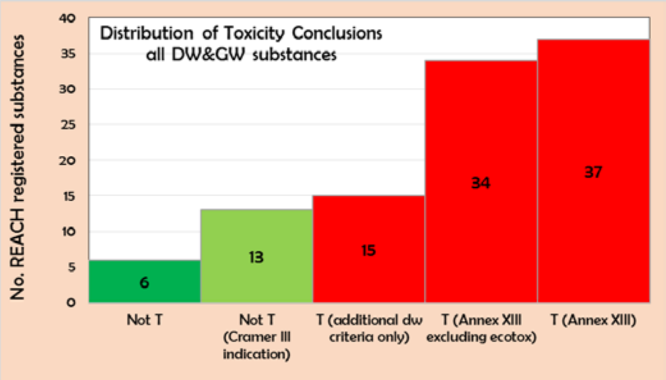
Distribution of P, M and T in 77 REACH registered DW&GW contaminants



P: 27 to 47



M: 69 to 71



T: 52

Including potential PM:
PM = 42
PMT = 37
vPvM = 5 (all also PMT)

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How can «not P» substances be in DW/GW?

- Reason # 1. They are vM and have large production volumes

Not P substances	M	Public REACH registered volume
Trifluoroacetic acid	vM	1000 - 10000;
Triacetin	vM	10000 - 100000
ε-caprolactam	vM	1000000 - 10000000
Naphthalene-2-sulphonic acid	vM	1000 - 10000
Tributyl phosphate	vM	1000 - 10000;
1,2-benzisothiazol-3(2H)-one 1,1-dioxide, sodium salt	vM	1000 - 10000
Pentasodium (carboxylatomethyl)iminobis(ethylenenitrilo)tetraacetate	vM	10000 - 100000
Xylenesulphonic acid	vM	1000 - 10000

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How can not P substances be in DW/GW?

- Reason # 2. vM + widespread use outside REACH

Not P substances	M	REACH exempt use	Production volume (Public/REACH)
Estradiol	Mscreen	Pharmaceutical	Intermediate Use Only
O-acetylsalicylic acid	vM	Pharmaceutical	100 - 1000
Estrone	M	Pharmaceutical	0 - 10;0 - 10
Caffeine	vM	Pharmaceutical	100 - 1000
Salicylic acid	vM	Pharmaceutical	10000 - 100000
Triethyl citrate	vM	Pharmaceutical	1000 - 10000;100 - 1000
Pyrazole	vM	Pharmaceutical/PPP	Intermediate Use Only
Mecoprop	vM	PPP	Intermediate Use Only
N-carboxymethyliminobis(ethylenenitrilo)tetra(acetic acid)	vM	Pharmaceutical	100 - 1000;Intermediate Use Only
Edetic acid	vM	Pharmaceutical	1000 - 10000;Intermediate Use Only
Camphor	vM	PPP	100 - 1000
Nitrilotriacetic acid	vM	Pharmaceutical	100 - 1000;0 - 10

How can «Not M» substances be in DW/GW?

- Reason: P, high production volume or uses outside REACH

Not Mobile chemicals	P evaluation	REACH exempt uses	Production (as of May 2017)
Cholesterol	Potential P/vP	Pharmaceutical/Natural	100 - 1000
p-nonylphenol	no conclusion/data		0 – 10* previously higher production volume
2,6-di-tert-butyl-p-cresol	Potential P/vP++	Food additive	10000 - 100000
Pyrene	Potential P/vP	Natural/combustion by product	Intermediate Use Only
4-(1,1,3,3-tetramethylbutyl)phenol	P		10000 - 100000
galaxolide	vP		1000 – 10000* previously higher production volume

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Conclusions

Preliminary assessments of

- 1. How many P, PM and PMT substances are there in REACH?

  Answer: 728, 471 and 240. But if more persistency data was available, this would increase.

- 2. Can we use REACH to identify potential drinking water chems?

  Yes! The PM and PMT criteria work to identify new contaminants in drinking water, if use and production info are also considered.

- 3. Are all REACH substances in drinking water PM or PMT substances?

  Approximately half are; the remaining are all either just P or just M, with large production volumes and emission likelyhood (via uses within or outside of REACH)

Implications

- 1. From the preliminary assessment of 240 substances fulfilling this PMT/vPvM criteria, follow up is recommended:
  - a) quality assurance of the PMT assessment
  - b) emission characterization assessment (as with PBT/vPvB)
  - c) if needed risk mamangement measures (as with PBT/vPvB)

Section 6.5 of Annex I to to the REACH Regulation further requires that:
"For substances satisfying the PBT and vPvB criteria the manufacturer or importer shall use the information as obtained in Section 5, Step 2 when implementing on its site, and recommending for downstream users, RMM which minimise exposures and emissions to humans and the environment, throughout the life-cycle of the substance that results from manufacture or identified uses."

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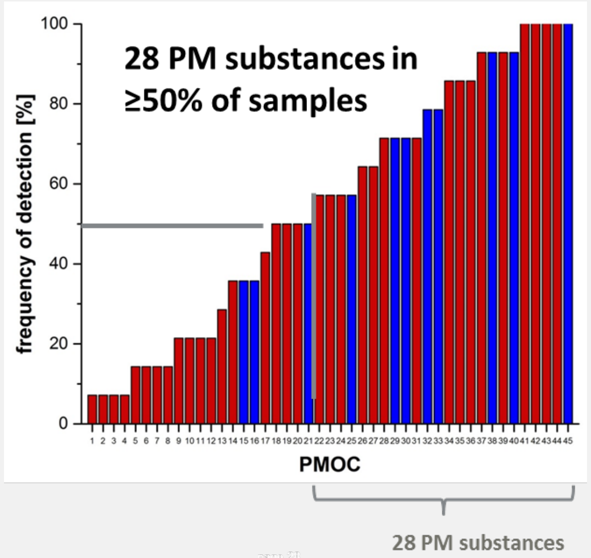
Implications

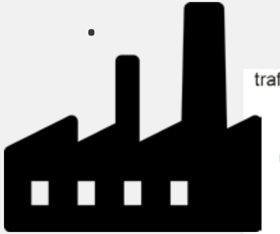
- 2. Knowledge of which PMT substances are out there are very usefull for monitoring by water authorities/researchers, both before and after water treatment.

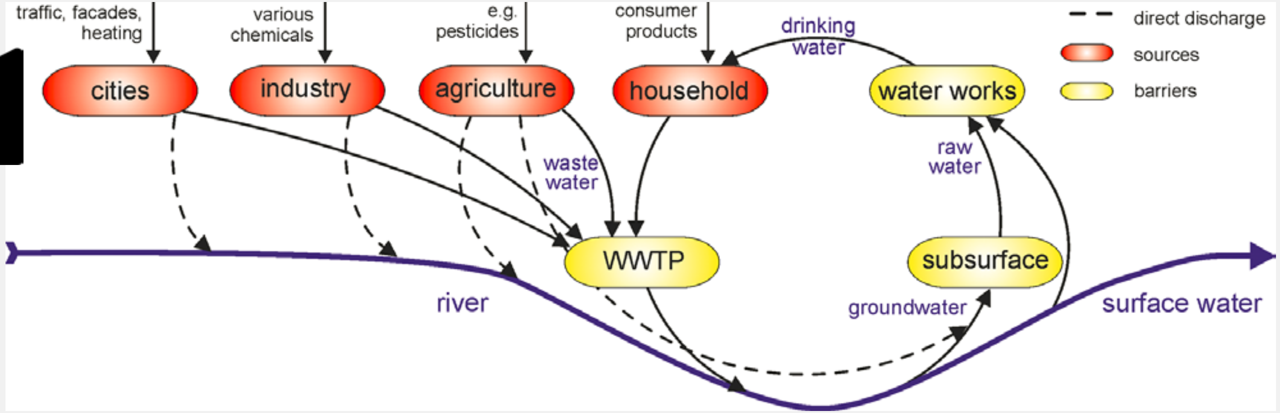


Emperical proof PMT criteria in addition to emission assessement can be used to predict DW contamination via monitoring

Implications

- 3. Drinking water contaminants can be PM or not PM, but PM substances more persistent in the drinking water cycle.





Reemtsma et al. 2016

Acknowledgment: Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety of Germany. Research project FKZ 3716 67 416 0: "REACH: Weiterentwinklung des Leitfadens zur Identifizierung und Bewertung Rohwasserrelevanter Stoffe

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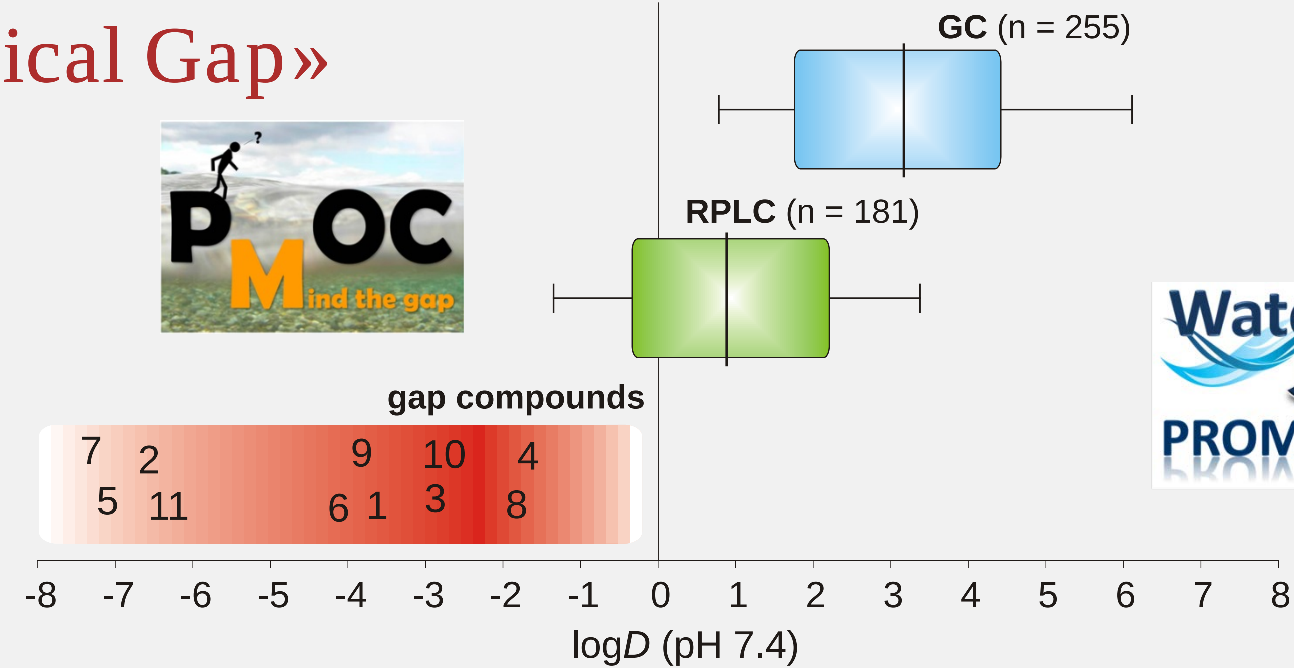
«Analytical Gap»



GC-MS: EPA methods 8270 D and 8290 A

RPLC-MS: Schymanski et al. (2014) Environ. Sci. Technol. 48, 1811-1818.

1: AMPA, 2: Paraquat, 3: Cyanuric acid, 4: DMS, 5: Diquat, 6: 5-Fluorouracil, 7: Glyphosate, 8: Melamine, 9: Metformin, 10: Perfluoroacetic acid, 11: EDTA

Reemtsma et al. (2016) Environ. Sci Technol. 50, 10308-10315