NORMAN WG-1 Meeting

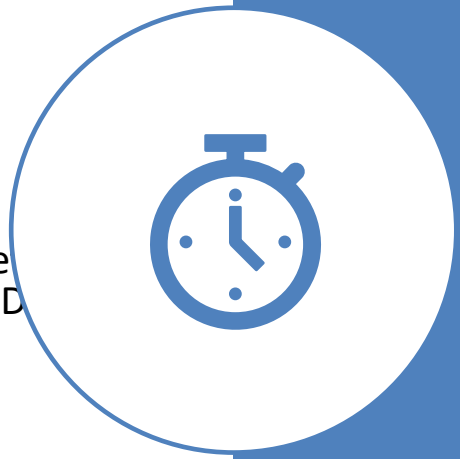
23 November 2023

Valeria Dulio, Peter von der Ohe, Nikiforos Alygizakis

Agenda 23 November
NORMAN WG-1 Prioritisation

- **Status of work done in 2023**
  - Watch List 5th WFD
  - Paper – Extended target /suspect screening prioritisation scheme
  - Mixture Risk Contribution (MRC): indicator for prioritisation of potential contributors to mixture risks
  - New models for prediction of toxicity data

- **Preparing new JPAs for 2024**
  - New development in the prioritisation tool:
    - Implementation of the online prioritisation tool linking targe monitoring data (EMPODAT), suspect screening data (EMPOD SUSPECT), PNEC values in ECOTOXICOLOGY database, etc.
    - Improving the interface of the target prioritisation tool
    - Visualisation features
    - Defining your own categories based on criteria and associated indicators (PARC)
  - Environmental status indicators
    - Number of chemicals exceeding (MRC, FoE)
    - Extent of exceedance (RQ_sum)
  - How to deal with multiple values (predicted/experimental) – creation of DCT and modules (important also for the Factsheets) *(if time available)*



Status JPA 2023

WG-1 Prioritisation

5th Watch List WFD – WG Chemicals – Member States consultation

NORMAN has contributed with comments on the candidate substances proposed by JRC – September 2023

Criteria for identification of candidate substances for WL update

The JRC proposes three criteria for the identification of new WL substances, in addition to the criterion that more (reliable) monitoring data are needed to determine the risk posed by them.

Respecting the requirements of the Environmental Quality Standards (EQS) Directive (Directive 2008/105/EC as amended by Directive 2013/39/EU), the JRC proposes the following **criteria** for identifying potential candidates for inclusion in the 5th WL:

1. Substances shortlisted, but not included in the 4th WL because of limitations in the monitoring methods available at the time or unreliable PNEC information, where for those substances an adequately sensitive analytical method and a reliable PNEC have become available.
2. Recommendations from MS and stakeholders as established in Article 8b of Directive 2008/105/EC, again where adequate methods and reliable PNECs are available.
3. Substances of emerging concern identified based on research projects and articles, in line with the article 8b of Directive 2008/105/EC (e.g. industrial products, pharmaceuticals, plant protection products and biocides), again where adequate methods and reliable PNECs are available.

NORMAN comments

Substance name / CAS number	NORMAN comments
Gemfibrozil CAS 25812-30-0	**In conclusion, significant FQ in fw but no evidence of exceedance of PNEC. Not a priority for inclusion on 5th WL**
Metazachlor CAS 67129-08-2	In line with the recommendation by JRC, **metazachlor should be designated as PS or at least as RBSP**
Propranolol CAS 525-66-6	**Propranolol is not a priority for inclusion on 5th WL as an individual compound. However, since several beta-blockers are frequently found in ww (e.g. bisoprolol metoprolol, sotalol, etc.) they could be considered as a group.**
Tetracycline CAS 60-54-8	**In consideration of the low FQ, Tetracycline and other compounds of this group are not recommended for inclusion in the 5th WL for freshwater. However, tetracycline and oxytetracycline are sorbing strongly. Therefore, water might not be the right matrix. Still, it could be a concern in soil or sediment. This could be checked.**
Oxytetracycline CAS 79-57-2	Data available for 11 countries, 63 sites, 64 analysis (2018 – 2023) and only 1 analysis > LOQ. MEC: 0.02 µg/L (LOQ < PNEC). Same conclusions as above for tetracycline. **Not recommended for inclusion in the 5th WL for freshwater. It could be further checked for sediment (see comment above).**
Norfloxacin CAS 70458-96-7	**In conclusion, low FQ. Data available can be considered sufficient. Norfloxacin is not recommended for inclusion in 5th WL**
Tylosin CAS 1401-69-0	**Current data show low FQ in freshwater. No risk of exceedance of PNEC. Tylosin is not recommended for inclusion in 5th WL.**
Climbazole CAS_38083-17-9	**Data available for a representative number of countries, but insufficient number of investigated sites. Due to high FQ and potential ED effects, Climbazole is recommended for inclusion in 5th WL.**

NORMAN comments

Substance name / CAS number	NORMAN comments
Ketoconazole CAS_65277-42-1	**In conclusion, the number and the quality of the available monitoring data are insufficient. Moreover, due to high FQ in ww with potential exceedance of PNEC, Ketoconazole is recommended for inclusion in the 5th WL.**
Itraconazole CAS_84625-61-6	**Final conclusion to be discussed in connection with the other compounds of the same group.**
Epoxiconazole CAS_133855-98-8	**In conclusion, the data currently available can be considered sufficient. However, due to high FQ and exceedance of PNEC at local level, epoxiconazole is proposed for inclusion in the 5th WL in order to check more systematically at EU level the potential risks**
Difenoconazole CAS_119446-68-3	**In conclusion, available monitoring data are insufficient. Available data show significant FQ in fw and ww, but no exceedance of PNEC. Difenoconazole is not a priority for inclusion in the 5th WL.**
Triticonazole CAS_131983-72-7	**Not found in ww (FQ=0%). All data show LOQ< PNEC.** **In conclusion, the data are sufficient to conclude no risk.**
Cyazofamid CAS_120116-88-3	FQ to be checked (recent data 2018 – 2023 show FQ_analysis: 0% while data 2013-2023 show FQ_analysis 4% and 1 site with conc > PNEC (MEC95: 0.002 µg/L; MEC99: 7,9 µg/L). Not found in ww (to be checked). Cat 4A in suspect screening. **Conclusion: ?**
Amisulbrom CAS_348635-87-0	Not data available in EMPODAT
Bromuconazole CAS_116255-48-2	Not data available in EMPODAT
Mefentrifluconazole CAS_1417782-03-6	Not data available in EMPODAT (to be checked)
Folpet (N-(trichloromethylthio)phthalimide) CAS 133-07-3	Data available in EMPODAT are from 3 countries (France, Netherlands and Ireland). **The monitoring data available are insufficient. The available data show low frequency of quantification and values below the PNEC.** **Folpet is not stable. If it is included as part of the WL, then the transformation products should also be monitored**.

New candidates – proposals NORMAN

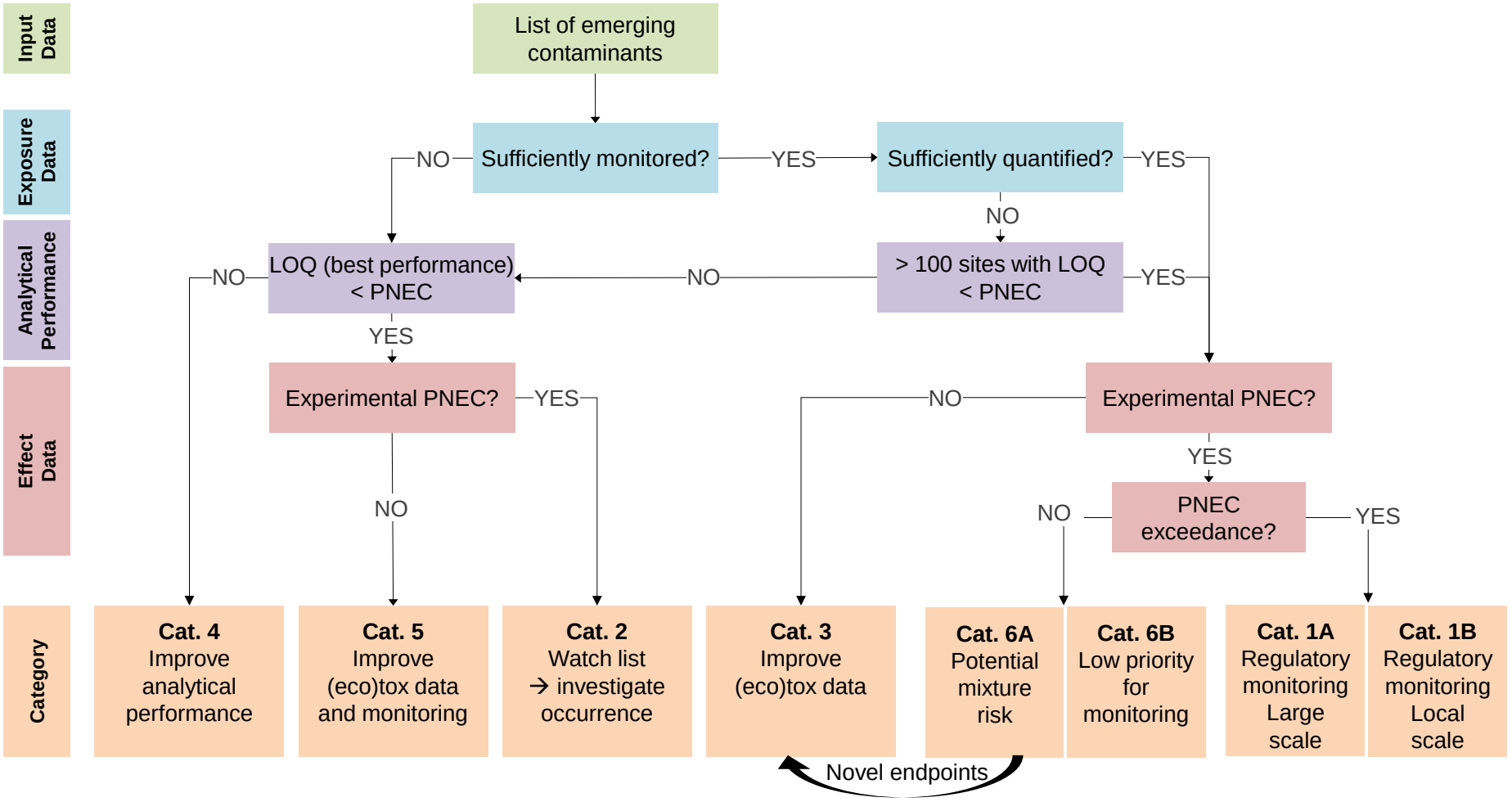
Substance name / CAS number	Approved use	NORMAN comments
Terbutylazine CAS 5915-41-3	Herbicide	Data available for 16 countries and 2564 sites (2013-2023); of which 12 countries with 185 sites with recent data from 2018-2023. For 2018-2023: FQ_sites: 85%; FQ_analysis: 75%; Evidence of risk at 13% of the sites (MEC95: 0.5; MEC99: 2.87). The substance is classified Cat 1A! Moreover, additional data from Switzerland and Germany show that local exceedances are observed in small stream monitoring campaigns, and it is RBSP in some countries (e.g. Germany and Switzerland). **In conclusion, significant FQ in fw and evidence of exceedances of PNEC justifies inclusion on 5th WL**
Terbutylazin-2-hydroxy CAS 66753-07-9	TP of Terbutylazine	Data available for 13 countries and 333 sites (2013-2023); of which 133 with recent data from 2018-2023. FQ_sites: 70%; FQ_analysis: 62%; Evidence of risk (MEC95: 0.06; MEC99: 0.2) at 52% of the investigated sites. The substance is classified Cat 1A (exceedance of large scale), however, due to a rather low PNEC. **Conclusion: Terbutylazin-2-hydroxy has significant FQ in fw and potential exceedances of PNEC. Hence, the TP might be considered for inclusion in the 5th WL, together with parent compound.**
S-Metolachlor CAS 87392-12-9 **(Metolachlor CAS 51218-45-2)**	Herbicide approved as PPP. However, the renewal may not be granted due to GW risks	Data available for the legacy pollutant Metolachlor (51218-45-2) for 16 countries and 2284 sites (2013-2023); of which 169 with recent data from 2018-2023. Very high FQ (FQ_sites: 86%; FQ_analysis: 63%) and evidence of risk (MEC95: 0.44; MEC99: 2.2 at 19% of the investigated sites (from recent data 2018-2023) The substance is classified Cat 1A (risk exceedance at large scale). **Conclusion: significant FQ in fw and evidence of exceedance of PNEC justify inclusion on 5th WL**
Metolachlor OXA CAS 152019-73-3	TP metolachlor	Data available for fw from 13 countries, >100 sites and 1000 analysis (2013-2023), among which 12 countries, 119 sites and 513 analysis with recent data from 2018-2023. No exceedance of PNEC but high FQ: FQ_sites: 78%: FQ_analysis: 56% **Metolachlor OA is a relevant TP of S-Metolachlor and might be considered for inclusion in the 5th WL, together with the parent compound**
Metolachlor ESA CAS: 171118-09-5	TP metolachlor	**Similar as above**
Lithium CAS: 7439-93-2 (lithium carbonate; lithium chloride; lithium hydroxide)	Emerging risk due to increasing EU lithium mining projects in addition to energy transition which will heavily rely on the use of lithium batteries	Data available for fw from France >890 sites and 15,000 analysis (recent data). Very high: FQ_sites > 90%. Average concentration (with less than LOQ values = LOQ): 3.8 µg/L; MEC95: 23µg/L. According to KWR Report, all lithium concentrations in the Rhine river in the Netherlands exceeded the derived background concentration of 3.5 µg/L of lithium in surface waters in the Netherlands, derived by Osté et al. in 2013 (Osté, 2013). **Due to hazard properties of lithium, current lack of data (insufficient number of countries with data) and increasing mining activities in Europe, plus potential local risks already identified, Lithium should be considered for inclusion in the WL.**

Paper – NORMAN prioritisation scheme

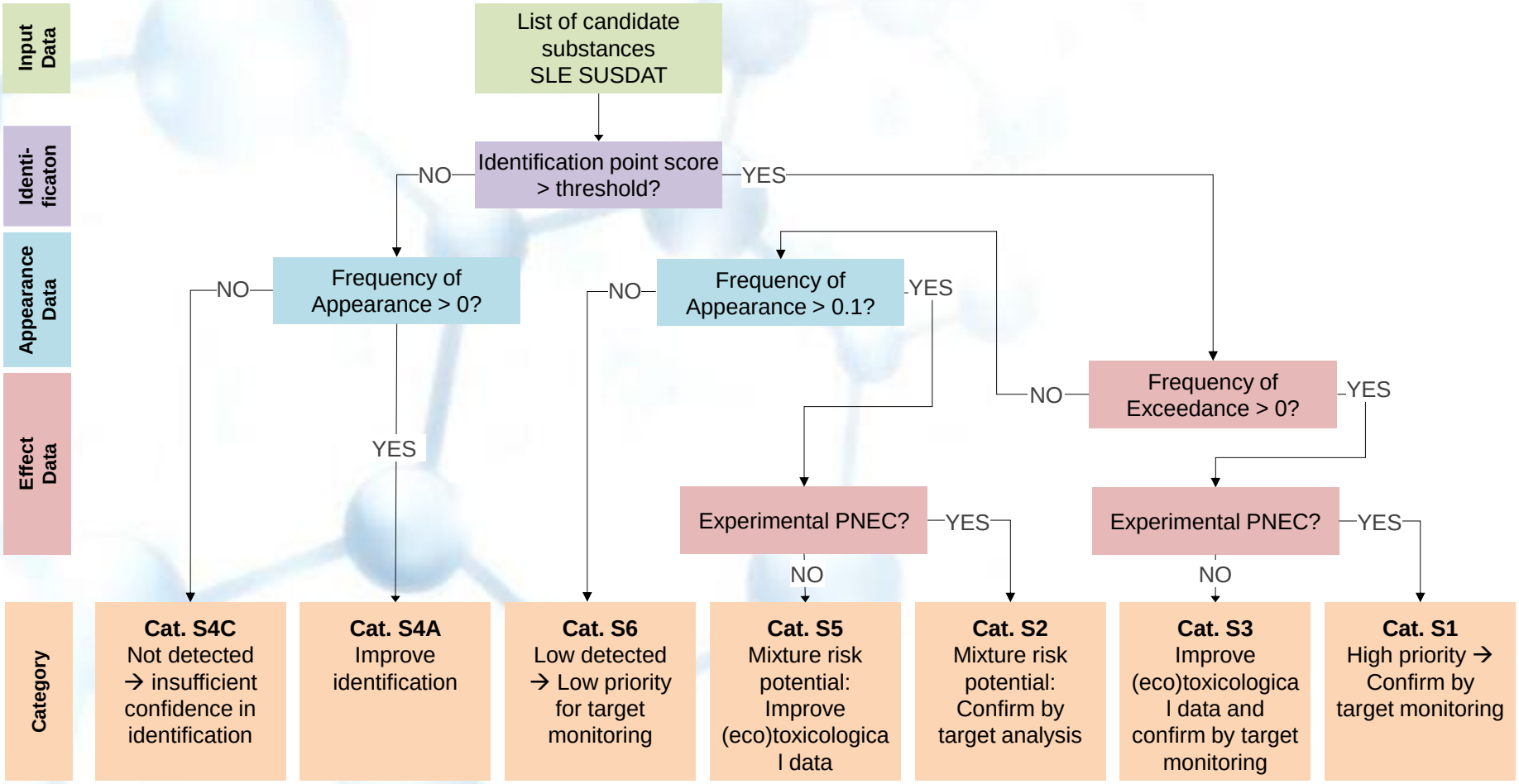
- Almost ready for submission
- Contains the new extended prioritisation scheme, including
  - Target
  - Suspect screening
  - Cross-table to use combination of the two lines of evidence for final priority actions

- Highlights:
  - More emphasis of the combination of the 2 lines of evidence
  - Revised schemes to make it easier for the users to understand the categorisation process
  - Integration of a Mixture Risk Contribution (MRC) indicator i) for categorisation (Category 6) and ii) for ranking the compounds

Target monitoring prioritisation scheme



Suspect screening prioritisation scheme



Cross-table

Combining lines of evidence

Cat target	Cat suspect							
	Cat S1	Cat S3	Cat S2	Cat S5	Cat S4A	Cat S4C	Cat S6	Total substances
Cat 1	3	n.a.	16	n.a.	12			31
Cat 3	n.a.	1	n.a.	44	81	17	2	145
Cat 2	8	n.a.	49	n.a.	197	91	2	347
Cat 5	n.a.	12	n.a.	277	979	486	17	1771
Cat 4	4			1	72	68		145
Cat 6A (0.1≤RQ<1)	1	n.a.	10	n.a.	9	1		21
Cat 6B (RQ<0.1)	1	n.a.	28	n.a.	63	17		109
No data	3	472	26	5744	37907	18672	289	63113
Total substances	**20**	**485**	**129**	**6066**	**39320**	**19352**	**310**	**65682**

Legend:

High priority	Medium priority	Low priority	Uncertainty

Scoring system

Indicators			Application to categories	Value	Sub-score	Final score
Exposure	$Expo_{\_target}$	FoQ	All categories	0.00 - 1.00	$Expo_{\_target}$ = FoQ + EI (optional)	Expo score = $Expo_{\_target}$ + $Expo_{\_suspect}$
		EI (Exposure Index)	Optional for Cat 2,4,5 (target monitoring)	0.00 - 1.00		
	$Expo_{\_suspect}$	FoA	All categories	0.00 - 1.00	$Expo_{\_suspect}$ = FoA	
Hazard	$Haz_{\_Human\ Health}$	CMR	All categories	0.00 - 1.00	Haz score is counted only once in the final score	Haz score[1] = CMR + ED + PBT/vPvB + PMT/vPvM
		ED		0.00 - 1.00		
	$Haz_{\_Other\ properties\ of\ concern}$	PBT /vPvB		0.00 - 1.00		
		PMT/vPvM		0.00 - 1.00		
Risk	$Risk_{\_target}$	$FoE_{\_target}$	All categories	0.00 - 1.00	$Risk_{\_target}^{2}$ = $FoE_{\_target}$ + $MRC_{\_target}$ + $EoE_{\_target}$	Risk score = $Risk_{\_target}$ + $Risk_{\_suspect}$
		$MRC_{\_target}$				
		$EoE_{\_target}$	Only Cat 1, 3 and 6	0.00 - 1.00		
	$Risk_{\_suspect}$	$FoE_{\_suspect}$	All categories	0.00 - 1.00	$Risk_{\_suspect}^{2}$ = $FoE_{\_suspect}$ + $MRC_{\_suspect}$ + $EoE_{\_suspect}$	
		$MRC_{\_suspect}$				
		$EoE_{\_suspect}$		0.00 - 1.00		
Final score (target + suspect screening)						= Expo + Haz + Risk

Final score = Expo_score ($Expo_{\_target}$ + $Expo_{\_suspect}$) + Haz_score + Risk_score ($Risk_{\_target}$ + $Risk_{\_suspect}$)

Case study on WW effluents to test the new workflow

- Prioritisation based on Suspect screening – **DSFP / SUSPECT DB**:
  - 65,690 substances from SusDat
  - From 2017 to 2021
  - 13 countries
  - 57 sites
  - 84 (24h composite) Wastewater effluents samples
  - Analytical technique employed for NTS data acquisition: LC-HRMS bbCID and AutoMS

- Prioritisation based on **Target monitoring - EMPODAT**:
  - 2,557 substances
  - From 2009 to 2021
  - 19 countries
  - 248,542 analysis

Results of the case study on CECs in wastewater

- Combined results from suspect screening and target workflows ➔ 577 high priority compounds for actions (red zone)
- For many substances ➔ insufficient data from target monitoring and uncertainty in identification from suspect screening
- Most of the compounds in the candidate list (64,825 chemicals) had only predicted PNECs ➔ Cat S3 / S5

Cat target	Cat suspect							
	Cat S1	Cat S3	Cat S2	Cat S5	Cat S4A	Cat S4C	Cat S6	Total substances
Cat 1	3	n.a.	16	n.a.	12			31
Cat 3	n.a.	1	n.a.	44	81	17	2	145
Cat 2	8	n.a.	49	n.a.	197	91	2	347
Cat 5	n.a.	12	n.a.	277	979	486	17	1771
Cat 4	4			1	72	68		145
Cat 6A (0.1≤RQ<1)	1	n.a.	10	n.a.	9	1		21
Cat 6B (RQ<0.1)	1	n.a.	28	n.a.	63	17		109
No data	3	472	26	5744	37907	18672	289	63113
Total substances	**20**	**485**	**129**	**6066**	**39320**	**19352**	**310**	**65682**

Legend:
High priority | Medium priority | Low priority | Uncertainty

Mixture Risk Contribution (MRC)

Indicator for prioritisation of substances ➔ identification of potential contributors to mixture risks

Mixture Risk Contribution (MRC) Indicator for NORMAN prioritisation scheme

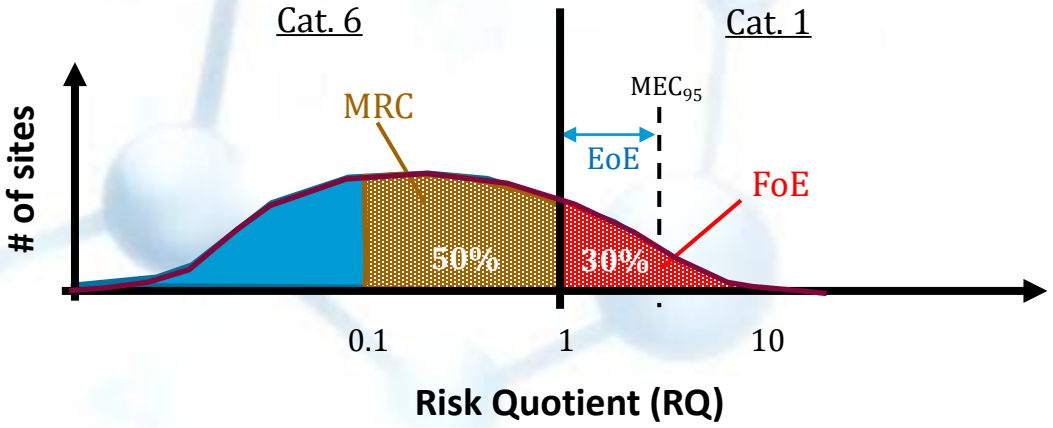
So far: two risk-based indicators for the prioritisation of individual substances

Extent of Exceedance = MEC_{95} / *PNEC*

➔ How high is the PNEC exceeded?

Frequency of Exceedance = *# sites* (MEC_{site} > *PNEC*) / *# all sites*

➔ How wide-spread are the exceedances?



➔ **Mixture risks now integrated**

Priority Candidates based on single Exceedance and Contributions to Mixture Risk

$$FoE_i = \frac{Nb\ sites\ where\ substance\ i\ shows\ RQi > 1}{Nb\ sites\ where\ substance\ i\ was\ monitored}$$

$$MRC\_i = \frac{Nb\ sites\ where\ substance\ i\ shows\ 0.1 \leq RQi < 1}{Nb\ sites\ where\ substance\ was\ monitored}$$

Prioritisation of risk drivers

FoE + MRC = Risk Score

➔ **Complementary** indicators for ranking of substances

Name	FoE	MRC	FoQ
Benzo(a)pyrene	0,56	0,00	0,32
Pyrene	0,47	0,08	0,17
Chrysene	0,41	0,15	0,23
Perfluorooctanesulfonic acid (PFOS)	0,37	0,00	0,19
Diflufenican	0,28	0,25	0,40
Formaldehyde	0,27	0,00	0,08
Nicosulfuron	0,22	0,02	0,08
Dibenz(a,h)anthracene	0,21	0,25	0,26
Benzo(g,h,i)perylene	0,20	0,50	0,39
Propyzamide	0,20	0,26	0,18
Metolachlor	0,18	0,34	0,37
Flufenacet	0,18	0,18	0,10
Diclofenac	0,18	0,27	0,26
1,3,5-Triazin-2(1H)-one, 4-((1,1-dimethylethyl)amino)-6-(ethylamino)-	0,16	0,02	0,09
Benzo(b)fluoranthene	0,15	0,50	0,40
Benz(a)anthracene	0,14	0,44	0,21
Metazachlor	0,13	0,21	0,14
Carbamazepine	0,13	0,39	0,40
Dimethenamid	0,11	0,28	0,21
Butylated hydroxytoluene	0,09	0,00	0,01
Imazamox	0,08	0,04	0,03
Chlorate	0,08	0,36	0,22
Iobitridol	0,07	0,01	0,06
2-Ethylhexyl-2-cyano-3,3-diphenylacrylate	0,07	0,00	0,02
Iopromide	0,06	0,04	0,06
Imidacloprid	0,06	0,04	0,03
Benzo(k)fluoranthene	0,05	0,39	0,26
Bisphenol A	0,05	0,33	0,15

Prediction models

New models for prediction of toxicity endpoints / toxicity data

Application domain for the prediction models that we use in NORMAN

Compilation of data and model predictions for hazard assessment

JPA 2023

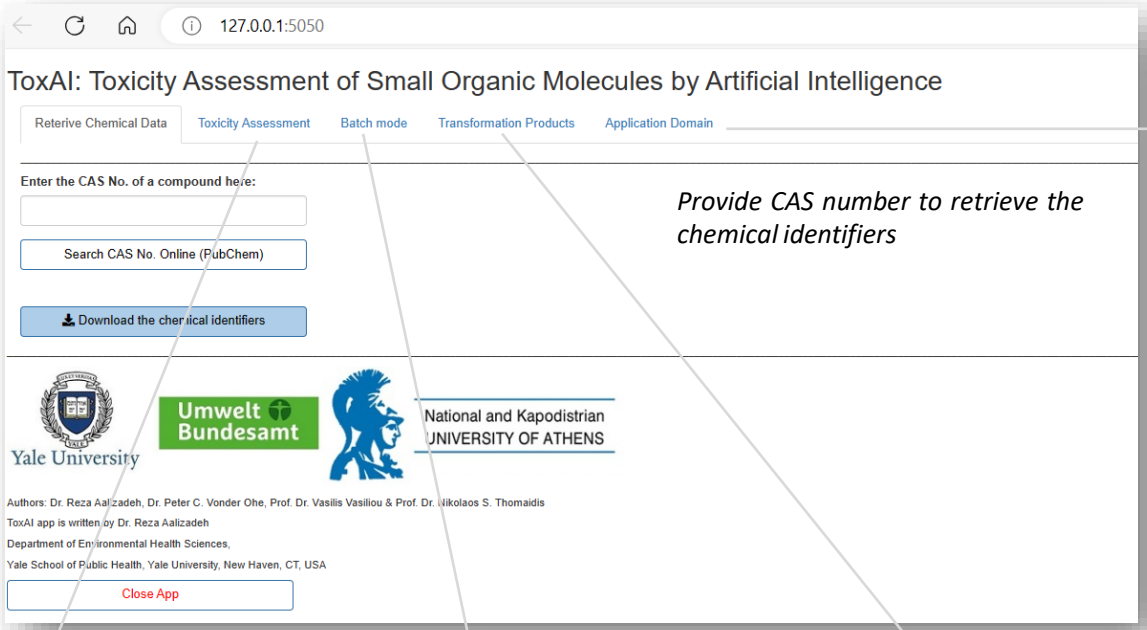
- So far, NORMAN used acute predictions in *Daphnia magna, Pimephales promelas* and *Selenastrum capricornutum* (i.e. three trophic levels) ➔ extended to additional species (3 additional fish species and 1 insect and 1 crustacean)
- Compilation of ca. **15,000 experimental rat toxicity endpoints**, available from HH risk assessments, to derive a **new ecotox thresholds** for protection of **birds and mammals** ➔ creation of a **deep learning model** for rat toxicity prediction
- Compilation of exp. data for BCF and Koc and other hazardous properties (ED, CMR, PBT, PMT)

JPA 2024

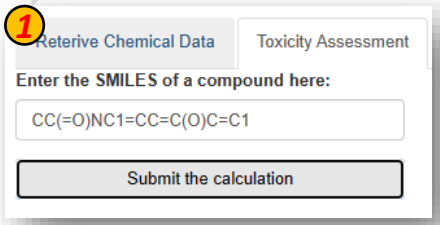
- With ToxAI, we propose to add predictions for:
  - the **acute toxicity** of up to 5 crustaceans (including 3 marine species), 8 fish species (incl. 1 marinefish), 2algae and 2 aquatic plants.
  - the **chronic toxicity** in up to 3 fish species, Daphnia and algae, allowing for derivation of chronic-based P-PNEC, using a lower AF.
- IMPORTANT: Definition of model‘s applicability domain ➔ development of a harmonised procedure

ToxAI; Open source R and Python-based app to perform in silico risk assessment and environmental fate analysis towards more than **105** end points

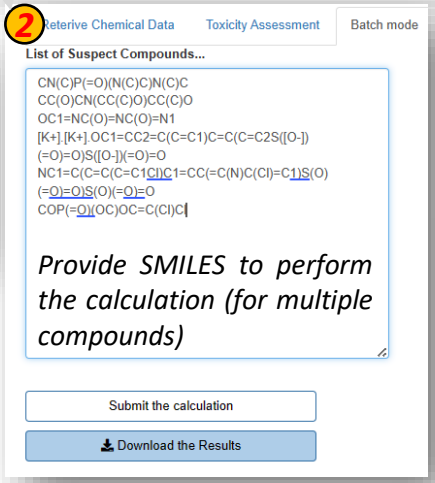
Graphical User Interface:

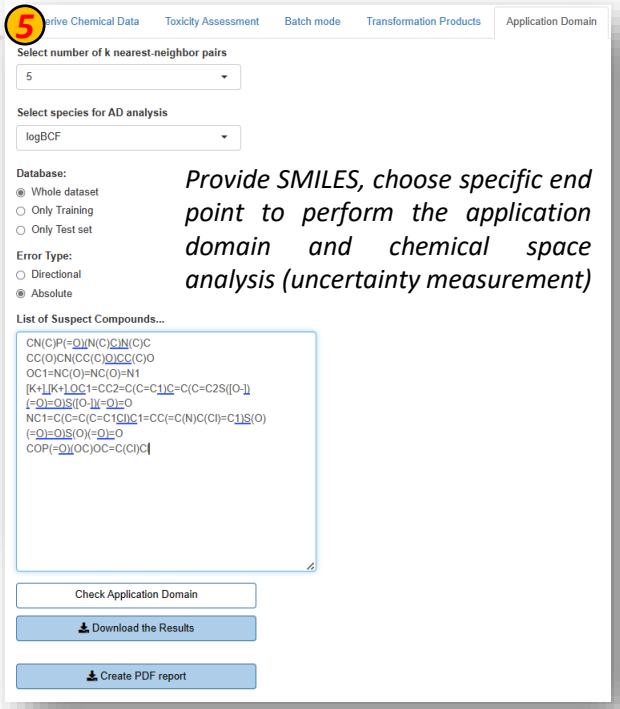


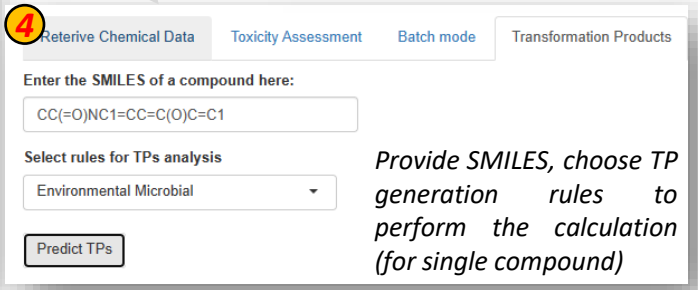
Provide CAS number to retrieve the chemical identifiers



Provide SMILES to perform the calculation (for a single compound)







ToxAI; *All 105 end points calculated for input compound*

1 *Single chemical calculation*

Marine Salt water

Saltwater

Americamysis Bahia — 9.16 mg/L

Artemia Salina — 537.85 mg/L

Hyalella Azteca — 108.64 µg/L

Single cell

Tetrahymena Pyriformis — $pIGC_{50}$(48 hours): -0.39

Aliivibrio fischeri (Microtox assay) — IBC50= 213.31 mg/L

Terrestrial Plants

Glycine max — 3.51 (Al lb/acre)

Zea Mays — 1.71 (Al lb/acre)

Avena sativa — 0.19 (Al lb/acre)

Lactuca sativa — 0.53 (Al lb/acre)

Brassica oleracea — 0.38 (Al lb/acre)

Mammals

Rat (oral dose) — 2220.54 mg/kg

Guinea Pig intraperitoneal LD_{50} — 515.97 mg/kg

Rabbit intraperitoneal LD_{50} — 2716.08 mg/kg

Dog Intravenous LD_{50} — 1766.8 mg/kg

Amphibian

Cyprinodon variegatus — 8.64 mg/L

Xenopus Laevis — 85.97 mg/L

Soil

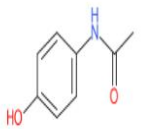
Earthworm (*Eisenia Fetida*) — 1.04 g/L

Insects

Aedes Aegypti — 1.154 g/L

Honey Bees (*Apis Mellifera*) — 34.18 µg/bee

Chemical Structure:



λmax (solvent)

H_2O: 327 nm
ACN: 306 nm
THF: 311 nm
EtOH: 377 nm
MeOH: 303 nm
DMSO: 298 nm
DMFA: 351 nm
CH_2Cl_2: 323 nm
EtOAc: 335 nm
Hexane: 294 nm
Acetone: 392 nm
Chloroform: 321 nm
Cyclohexane: 313 nm
1,4- Dioxane: 394 nm

Yale University · Umwelt Bundesamt · National and Kapodistrian University of Athens

Abraham Solvation Equation

Desc. A: 0.713 Desc. B: 0.829 Desc. E: 1.23 Desc. L: 6.2 Desc. S: 1.1 Desc. V: 1.18

Chemical Smell

Fruity: 6.9% Floral: 0% Woody: 0% Green Grassy: 91% Meaty Sulfurous: 0%
Fatty: 0% Nutty: 0% Minty: 0% Faint & balsamic: 0% Miscellaneous: 2%

Chemical Tastant

Sweetness: 0% Bitterness: 100% Umaminess: 0% Sourness: 0% Multitaste: 0%
Tastelessness: 0% Non-sweetness: 0% Miscellaneous (e.g. burning, tingling etc.): 0%

Chemical Properties

MW: 151.1
pka: 9.424 (acidic) 5.663 (Basic)
logKow: 0.1715
logBCF: 0.243 L/kg
logKoa: 9.52
logKoc: 1.6 L/kg (Mobile in Soil)
logBBB: -0.384
logHL: -8.79414
$log(kNO_3)$: -11.352
$logD_{(pH=7.4)}$: 0.527
Boiling point: 335.2 °C at 760mmHg
Melting point: 196.5 °C at 760mmHg
Water Solubility: 4.295 g/L
Ethanol Solubility: 154.227 g/L
Abiotic degradation (logAOH): -10.026
Caco-2 cell logPapp(cm/s): -4.766
Biodegradation: Readily biodegradable (Prob= 99.7%)

Human

Liver Injury: Unsafe (Prob= 99.8%)
Androgen Activity: Inactive (Prob= 100%)
Carcinogenic: Carcinogenic (Prob= 100%)
Eye Corrosion: Non-Corrosive (Prob= 100%)
Eye irritation: Non-Irritant (Prob= 98.7%)
Cardiotoxicity: Unsafe (Prob= 71.7%)
Skin Sensitisation: Sensitising Agent (Prob= 79.5%)
AMES Mutagenicity: Non-Mutagenic (Prob= 99.6%)
Respiratory Disease: Unsafe (Prob= 100%)
Endocrine Receptor — Agnostic: Inactive (Prob= 85.9%); Binding: Inactive (Prob= 91.4%)
Teratogenicity: Teratogenic (Prob= 62.6%)
Intestinal Absorption: Active (Prob= 99.8%)
CYP450 Receptor — CYP3A4: Inactive (Prob= 100%); CYP2C9: Inactive (Prob= 100%)
Maximum Recommended Daily Dose [log(mg/kg/day)]: 1.69
Exposure Limits (long-term 8h [$mg.m^{-3}$]): 10.11

Avian

Colinus Virginianus — 183.71 mg/kg

Anas Platyrhynchos — 31.03 mg/kg

Coturnix Japonica — 2593.64 (ppm/diet)

Mode of toxic action MOA

Reactivity: 0%
Neurotoxicity: 0%
Narcosis: 100%
Electron transport inhibition: 0%
AChE inhibition: 0%
Iono / Osmoregulatory / Circulatory impairment: 0%

Water Hazard Classes (WGK)

Not hazardous: 0%
Slightly hazardous to water: 100%
Hazardous to water: 0%
Extremely hazardous to water: 0%

Fresh Water

Skeletonema — 335.37 µg/L

Anabaena Blue Green — 605.93 µg/L

Lemna — Gibba: 1.21 mg/L; Minor: 295.42 µg/L

Pseudokirchneriella Subcapitata — 72 hours: 574.38 µg/L

Daphnia Magna — Chronic: 2.79 mg/L; 48 hours: 41.96 mg/L

Gammarus Fasciatus — 13.75 mg/L

Oncorhynchus Mykiss — Chronic: 700.12 µg/L; 4 days: 789 µg/L; 2 days: 3.41 mg/L

Ceriodaphnia Dubia — 19.19 mg/L

Pimephalas Promelas — 96 hours: 487.92 mg/L; Chronic: 699.41 µg/L

Oryzias Latipes — 3.72 mg/L

Leuciscus idus — 135.28 mg/L

Poecilia Reticulata — 4.71 mg/L

Carassius Auratus — 254.64 mg/L

Zebrafish (*Danio rerio*) — Chronic: 96 hours: 3.91 mg/L

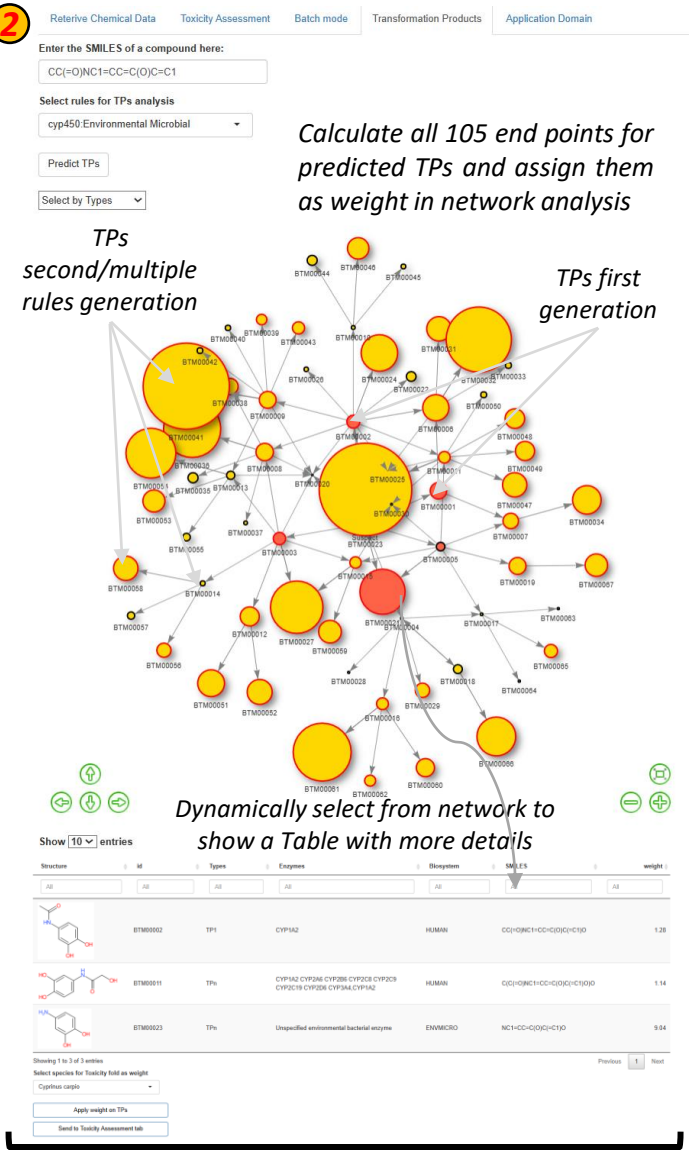
Zebrafish Embryo — 48 hours: 2.39 mg/L

Lepomis Macrochirus — 15.05 mg/L

Cyprinus Carpio — 10.52 mg/L

Ictalurus Punctatus — 3.62 mg/L

2



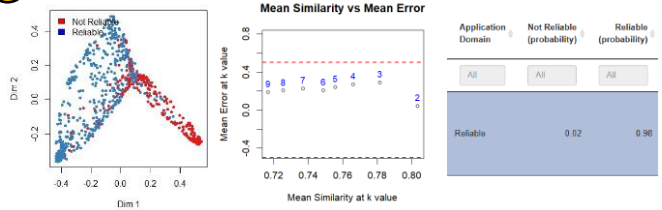
Calculate all 105 end points for predicted TPs and assign them as weight in network analysis

TPs second/multiple rules generation

TPs first generation

Dynamically select from network to show a Table with more details

3 *Provides uncertainty values toward all 105 end points*



Preparing JPA 2024

WG-1 Prioritisation

New development in the prioritisation tool

Implementation of the online prioritisation tool linking:

- target monitoring data (EMPODAT)
- suspect screening data (EMPODAT-SUSPECT under construction)
- PNEC values (ECOTOXICOLOGY database)
- Bioassays, Bioactivity database? etc.

DSFP Digital Sample Freezing Platform

Home | Search[beta] | Data | Contributors | About

Deep Search

Instant Search

Instant Search

LIFE APEX

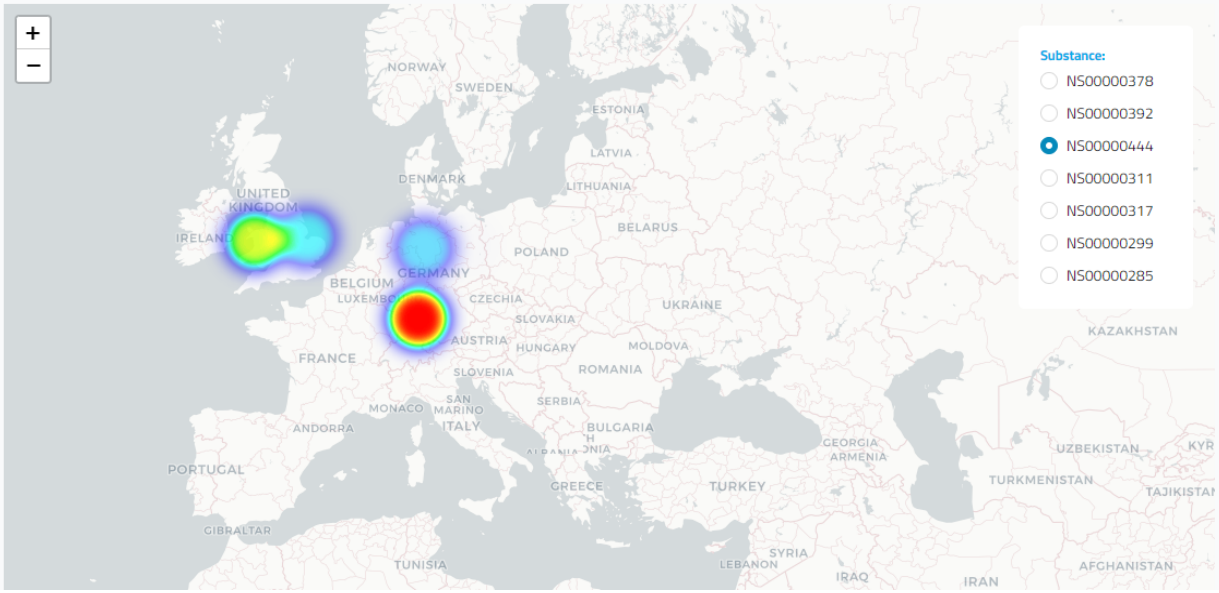
All methods

1998-01-01 → 2021-02-02

Propazine × Metoclopramide × Lenacil × Sebuthylazine × Pethoxamid × Naphthalene-2-sulfonic acid × Fenofibrate ×

Search samples

Download CSV | Tabular | Map



EMPODAT-Suspect

NORMAN WEBSITE | NORMAN DATABASE SYSTEM | HOME | LOGIN

SEARCH STATISTICS DCT DOWNLOAD

NORMAN EMPODAT - SUSPECT Database

Update Search / New Search / Results

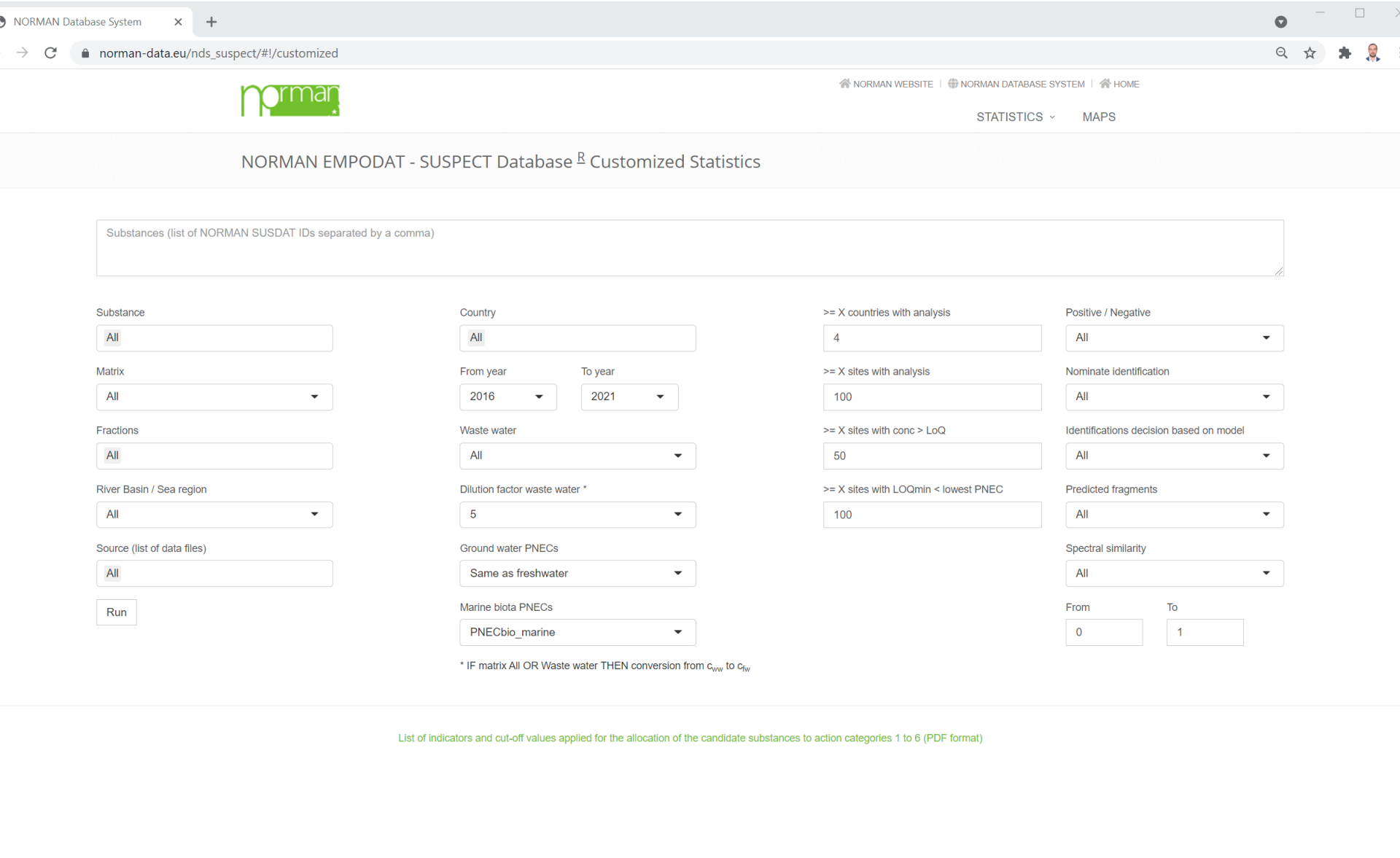
Export to CSV

Show 200 entries

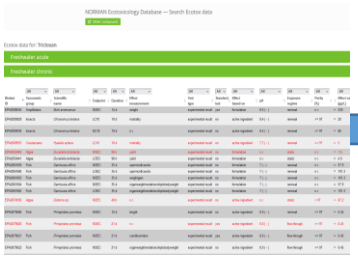
	ID	Substance	Concentration	Unit	Ecosystem/Matrix	Sampling Site/Station	Sampling Date	Country
Reset	Set	Set	Set	Set	Set	Set	Set	Set
	2236809	Caffeine	0.007	µg/l	Waste water - Municipal	Effluent wastewater from Uzhgorod	2019/08/27	Ukraine
	2236810	Caffeine	0.001	µg/l	Waste water - Municipal	Effluent wastewater from Vratsa	2019/08/26	Bulgaria
	2236811	Caffeine	0.003	µg/l	Waste water - Municipal	Effluent wastewater from Giurgiu	2019/08/26	Romania
	2236812	Caffeine	0.002	µg/l	Waste water - Municipal	Effluent wastewater from Sabac	2019/08/26	Serbia
	2236813	Caffeine	0.013	µg/l	Waste water - Municipal	Effluent wastewater from Zupanja	2019/08/26	Croatia
	2236814	Caffeine	0	µg/l	Waste water - Municipal	Effluent wastewater from Novo Nesto	2019/08/26	Slovenia
	2236815	Caffeine	0.001	µg/l	Waste water - Municipal	Effluent wastewater from Gyor	2019/08/26	Hungary
	2236816	Caffeine	0.002	µg/l	Waste water - Municipal	Effluent wastewater from Bratislava	2019/08/26	Slovakia
	2236817	Caffeine	0.002	µg/l	Waste water - Municipal	Effluent wastewater from Hodonin	2019/08/26	Czech Republic

Suspect screening prioritization exercises

https://norman-data.eu/nds_suspect/#!/customized



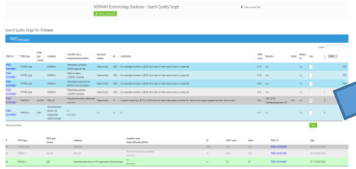
Analogy of Ecotox Module and the new Bioactivity DB Module



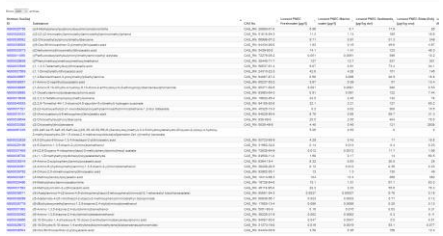
Ecotox data Sub-Module:
Raw ecotox data

CRED Sub-Module:
evaluate key study

PNEC derivation Sub-Module:
Derive your own PNEC



Quality Target Sub-Module:
Compilation of existing thresholds



Lowest PNEC – Sub-Module:

Bioactivity Sub-Module:
Raw bioassay data

(to be developed)

CRED Bioassay Sub-Module:
evaluate assay results

(to be developed)

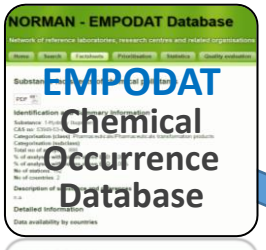
Potency / EBT Derivation Sub-

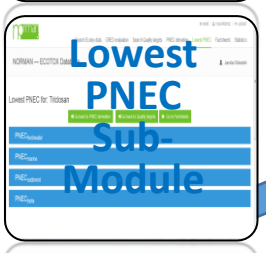
(to be developed)

Existing Potency / EBT Sub-Module

„Lowest“ Potency / EBT – Sub-Module

Analogy of Risk Modelling and Iceberg Modeling and link to Prioritisation





MEC_{site}
MEC_{95}

PNEC

Risk Characterisation Ratio (RQR) – Calculation Module

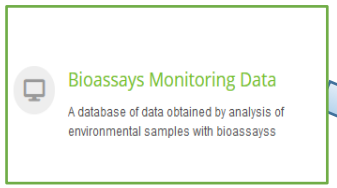
(currently in background)

FoE
EoE

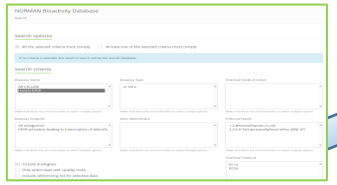
MRC

DSFP

MEC_{sample}



$Effect_{sample}$



EBT

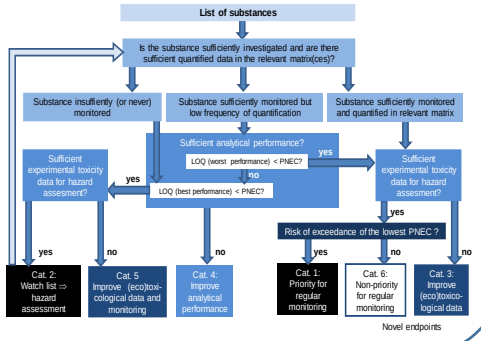
„Lowest“ Potency / EBT Sub-Module

Iceberg – Modelling Module

Which chemicals explain the observed effect?
(to be developed)

Explained Effect

NORMAN Prioritisation tool



Lists of priority substances

New development in the prioritisation tool

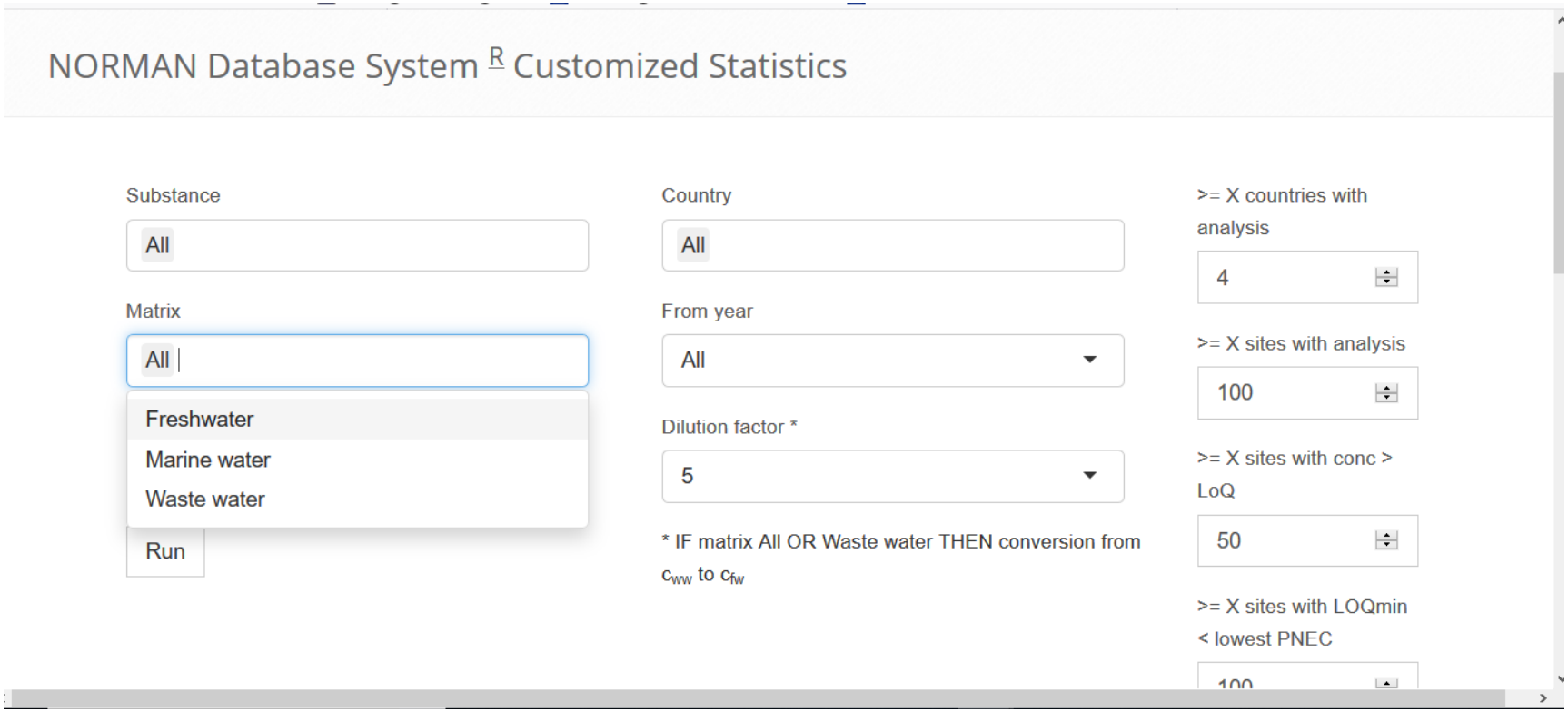
- Improving the interface of the target prioritisation tool
- Visualisation features
- Defining your own categories based on criteria and associated indicators (PARC)

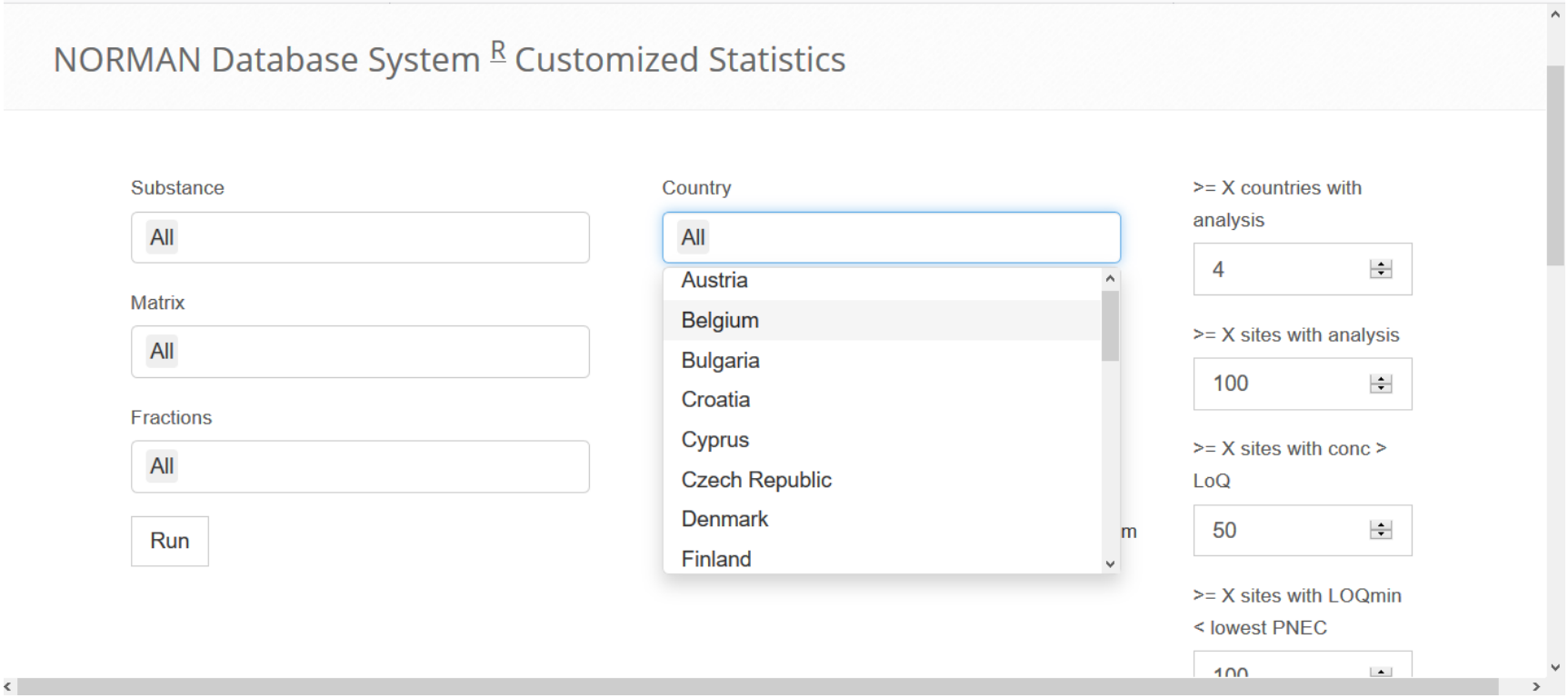
Automated tool for prioritisation of substances based on target monitoring data

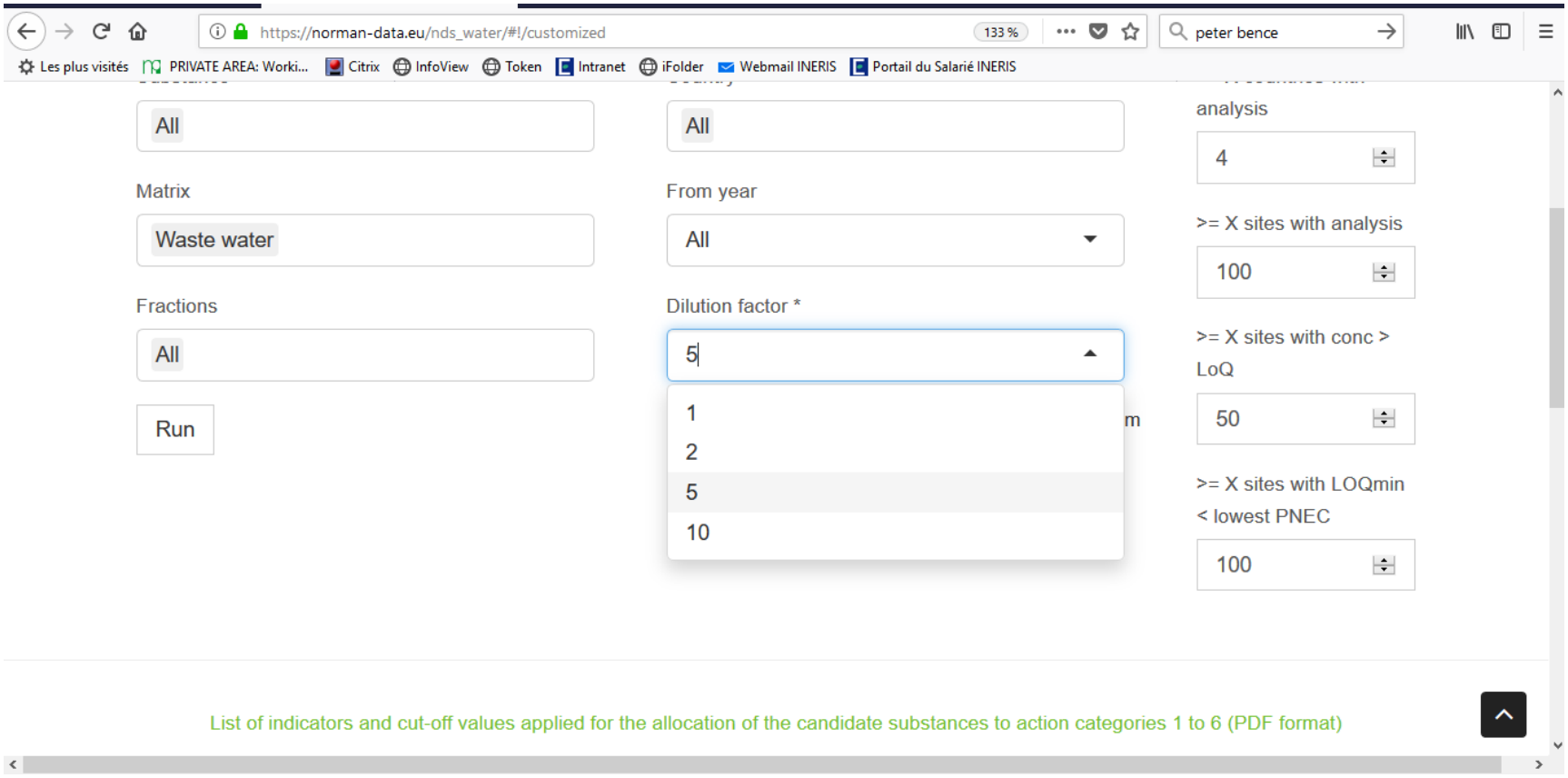
Prioritisation workflow for target monitoring data is implemented in an automated prioritisation module (see demonstration)

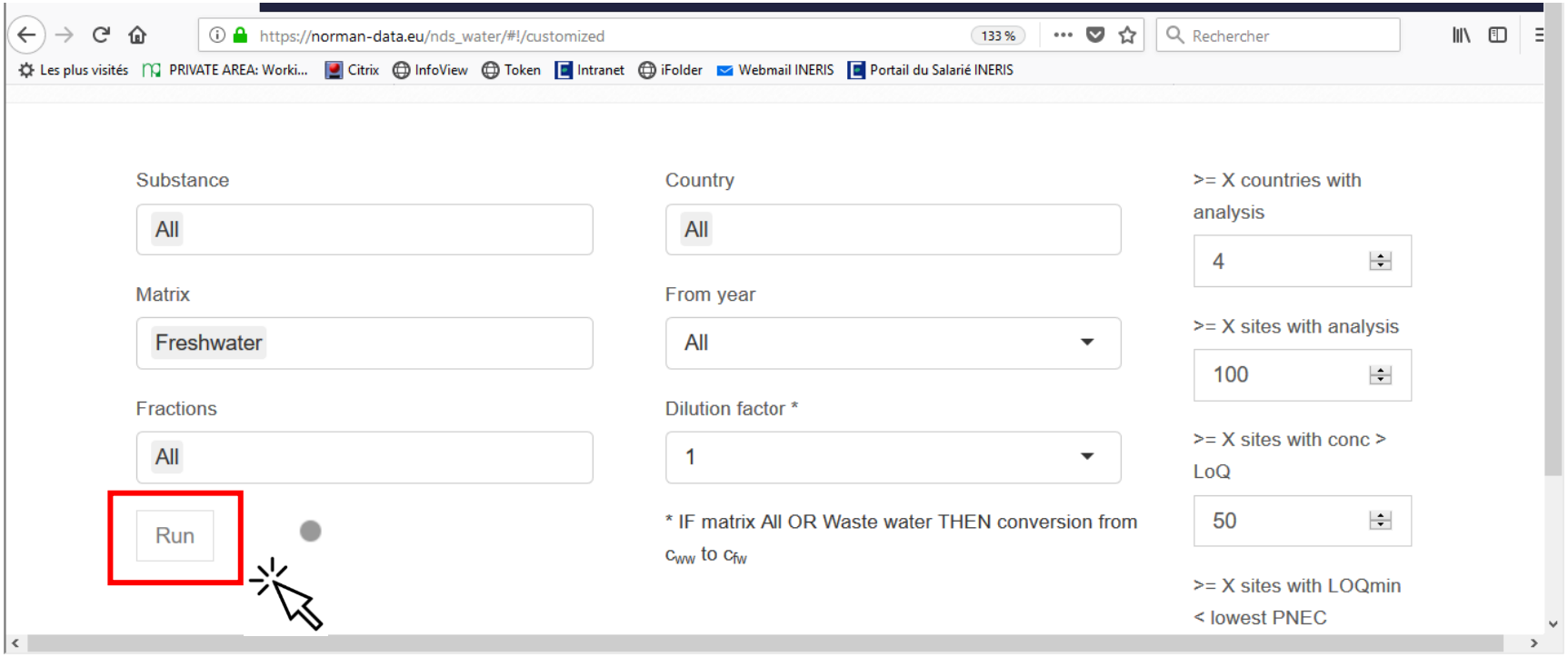
The system is connected with the NDS's modules

Customised for application to one environmental compartment but there is high flexibility of the query system


NORMAN Database System R Customized Statistics
Substance
All
Matrix
All
Freshwater
Marine water
Waste water
Run
Country
All
From year
All
Dilution factor *
5
* IF matrix All OR Waste water THEN conversion from c_{ww} to c_{fw}
>= X countries with analysis
4
>= X sites with analysis
100
>= X sites with conc > LoQ
50
>= X sites with LOQmin < lowest PNEC


NORMAN Database System R Customized Statistics
Substance
All
Matrix
All
Fractions
All
Run
Country
All
Austria
Belgium
Bulgaria
Croatia
Cyprus
Czech Republic
Denmark
Finland
>= X countries with analysis
4
>= X sites with analysis
100
>= X sites with conc > LoQ
50
>= X sites with LOQmin < lowest PNEC
100


https://norman-data.eu/nds_water/#!/customized
133 %
peter bence
Les plus visités
PRIVATE AREA: Worki...
Citrix
InfoView
Token
Intranet
iFolder
Webmail INERIS
Portail du Salarié INERIS
All
All
analysis
4
Matrix
From year
Waste water
All
>= X sites with analysis
100
Fractions
Dilution factor *
All
5
>= X sites with conc > LoQ
50
Run
1
2
5
10
>= X sites with LOQmin < lowest PNEC
100
List of indicators and cut-off values applied for the allocation of the candidate substances to action categories 1 to 6 (PDF format)


https://norman-data.eu/nds_water/#!/customized
133 %
Rechercher
Les plus visités
PRIVATE AREA: Worki...
Citrix
InfoView
Token
Intranet
iFolder
Webmail INERIS
Portail du Salarié INERIS
Substance
All
Matrix
Freshwater
Fractions
All
Run
Country
All
From year
All
Dilution factor *
1
* IF matrix All OR Waste water THEN conversion from c_{ww} to c_{fw}
>= X countries with analysis
4
>= X sites with analysis
100
>= X sites with conc > LoQ
50
>= X sites with LOQmin < lowest PNEC

Substance	SusDat ID	CAS no.	Lowest PNEC	Matrix	No. of Analyses	No. of Analyses with conc > LoQ	No. of Basins	No. of Countries	No. of Sites	No. of Years	Category	FoE score	EoE score	Final RISK score	Final HAZARD score	Final EXPOSURE score	Final score
All	All	All		A	Al	Al		All			1				A	All	
1,3,5-Triazin-2(1H)-one, 4-((1,1-dimethylethyl)amino)-6-(ethylamino)-	NS00000294	CAS_RN: 66753-07-9	0.0073	Freshwater	711	455	66	12	136	3	1A	0.61	0.25	0.86	0.5	0.74	2.1
Ibuprofen	NS00000214	CAS_RN: 15687-27-1	0.011	Freshwater	536	346	66	12	142	3	1A	0.5	0.25	0.75	0.52	0.64	1.9
Diclofenac	NS00000212	CAS_RN: 15307-86-5	0.05	Freshwater	893	704	83	12	166	3	1A	0.34	0.25	0.59	0.56	0.81	2
Nicosulfuron	NS00008411	CAS_RN: 111991-09-4	0.0087	Freshwater	337	129	50	12	116	3	1A	0.34	0.25	0.59	0.5	0.62	1.7
Chlorpyrifos (Chlorpyrifos-ethyl)	NS00000445	CAS_RN: 2921-88-2	0.00046	Freshwater	692	255	33	13	125	3	1A	0.33	0.1	0.43	0.69	0.61	1.7
Perfluorooctanesulfonic acid (PFOS)	NS00010280	CAS_RN: 1763-23-1	0.002	Freshwater	364	241	25	12	109	3	1A	0.29	0.1	0.39	0.5	0.71	1.6
Metazachlor	NS00000249	CAS_RN: 67129-08-2	0.02	Freshwater	1130	571	73	12	169	3	1A	0.22	0.1	0.32	0.62	0.69	1.6
Diflufenican	NS00008837	CAS_RN: 83164-33-4	0.01	Freshwater	1120	321	81	12	174	3	1A	0.21	0.1	0.31	0.44	0.26	1
Imidacloprid	NS00000361	CAS_RN: 138261-41-3	0.013	Freshwater	500	243	41	12	114	3	1A	0.18	0.1	0.28	0.5	0.72	1.5
Di(2-ethylhexyl)phthalate (DEHP)	NS00010909	CAS_RN: 117-81-7	1.3	Freshwater	1033	879	77	11	162	3	1A	0.14	0.1	0.24	0.28	0.57	1.1
Terbutylazine	NS00000258	CAS_RN: 5915-41-3	0.22	Freshwater	1493	1120	88	12	185	3	1A	0.13	0.1	0.23	0.5	0.84	1.6
Metolachlor	NS00000248	CAS_RN: 51218-45-2	0.2	Freshwater	1294	817	75	12	169	3	1A	0.11	0.1	0.21	0.38	0.81	1.4
Flufenacet	NS00000324	CAS_RN: 142459-58-3	0.048	Freshwater	596	200	64	12	159	3	1A	0.11	0.1	0.21	0.44	0.5	1.2
Bisphenol A	NS00008865	CAS_RN: 80-05-7	0.24	Freshwater	972	800	74	12	157	3	1A	0.076	0.1	0.18	1	0.9	2.1

From data to info

Visualisation of the results

- What is already possible today:
  - Downloadable Excel file with the list of susbstances by category and associated scores
- What could be improved (short-term, long-term)?
  - Heatmaps (overview of results by compartment, by year, by sector of use)
  - Mapping of substances against selected indicators
  - Focus on individual substances (e.g. star / spider-web charts)

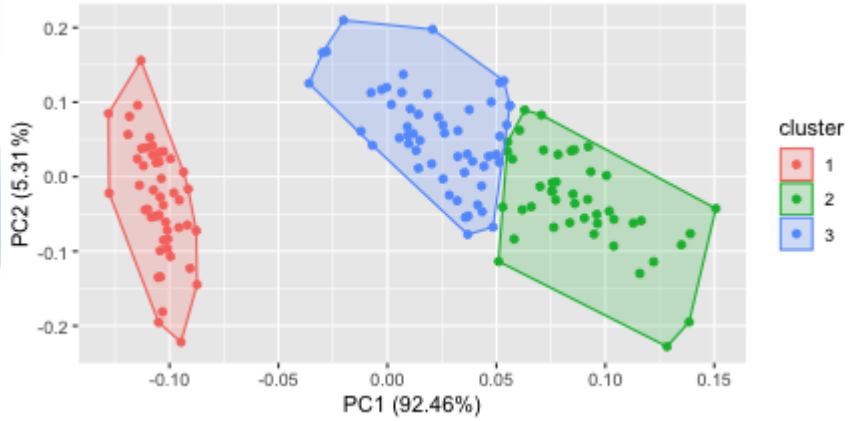
From data to info

The prioritisation system

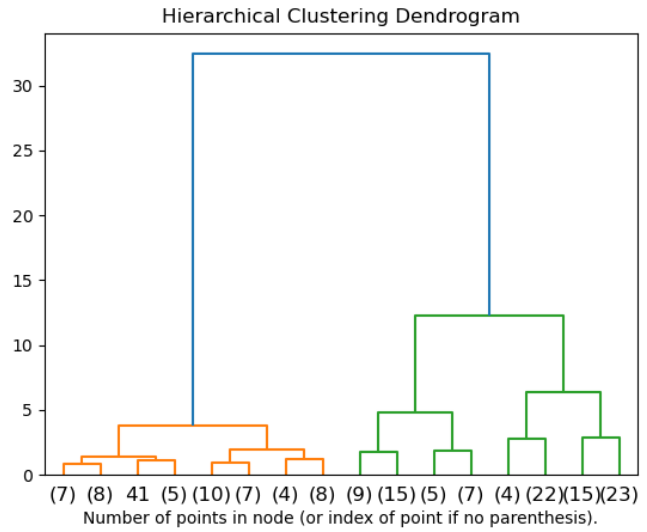
- Today
  - Customised query for prioritisation of CECs in a single environmental compartment + identification of substances which cannot be evaluated due to current knowledge gaps
- What could be improved:
  - User is in controls of the queries and list of indicators
  - Unsupervised mapping of substances

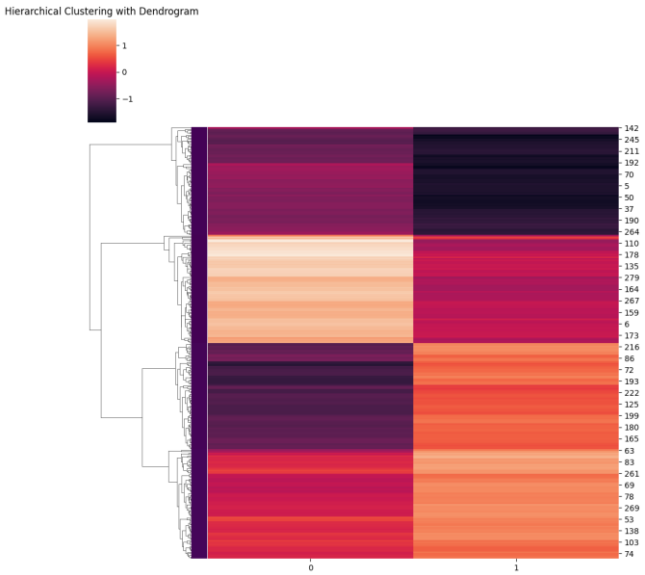
Unsupervised clustering

PCA (scores, scree, loading plots)

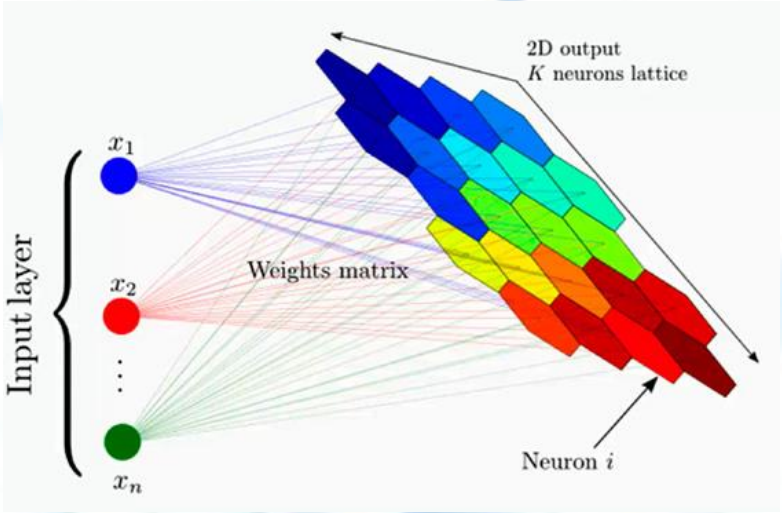


Hierarchical clustering



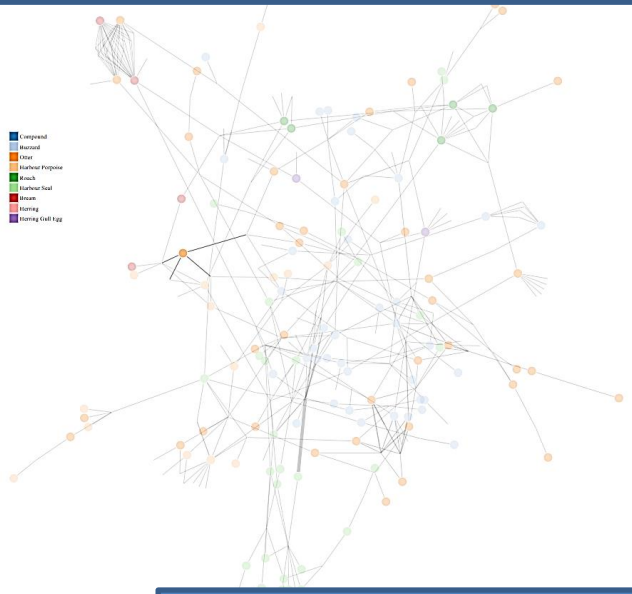


Self-organizing maps

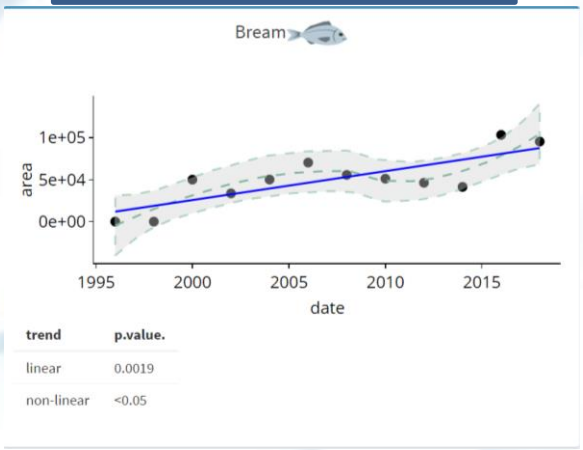


Visualisations

Network analysis

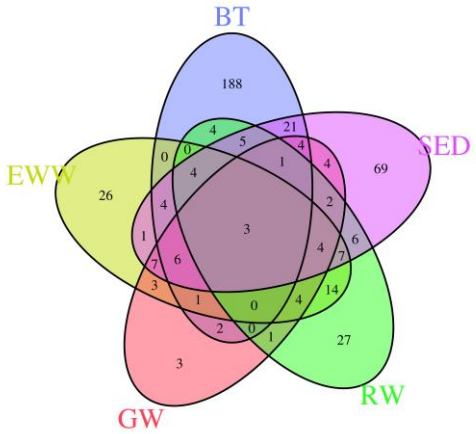


Trend analysis

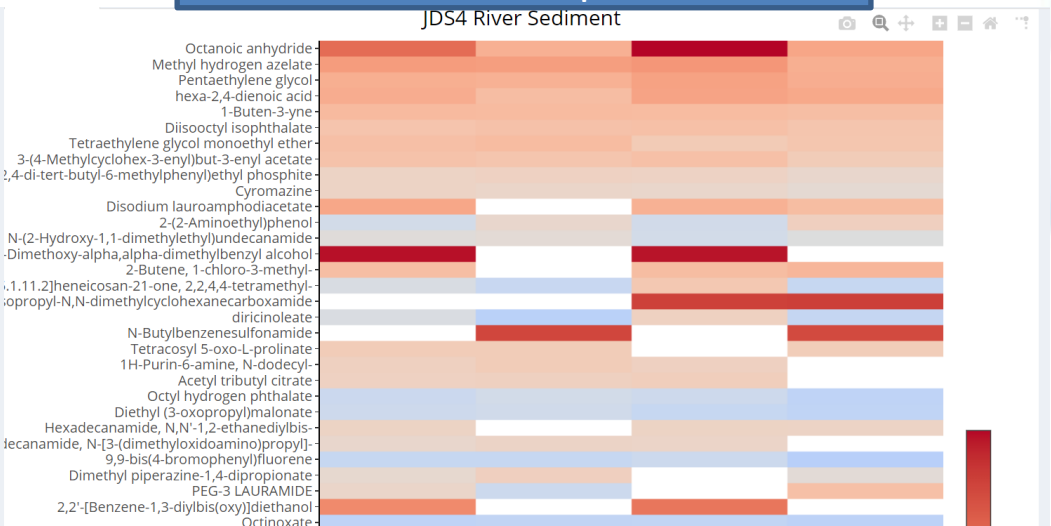


trend	p.value.
linear	0.0019
non-linear	<0.05

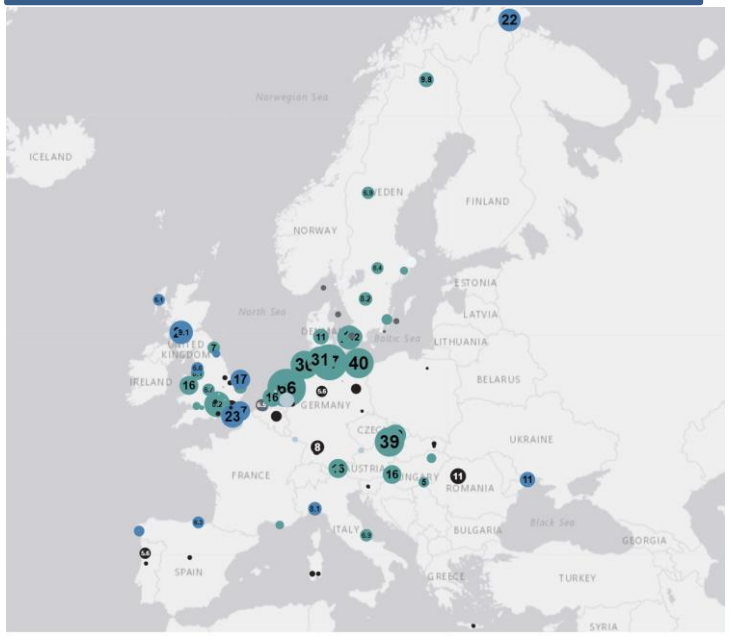
Venn diagrams



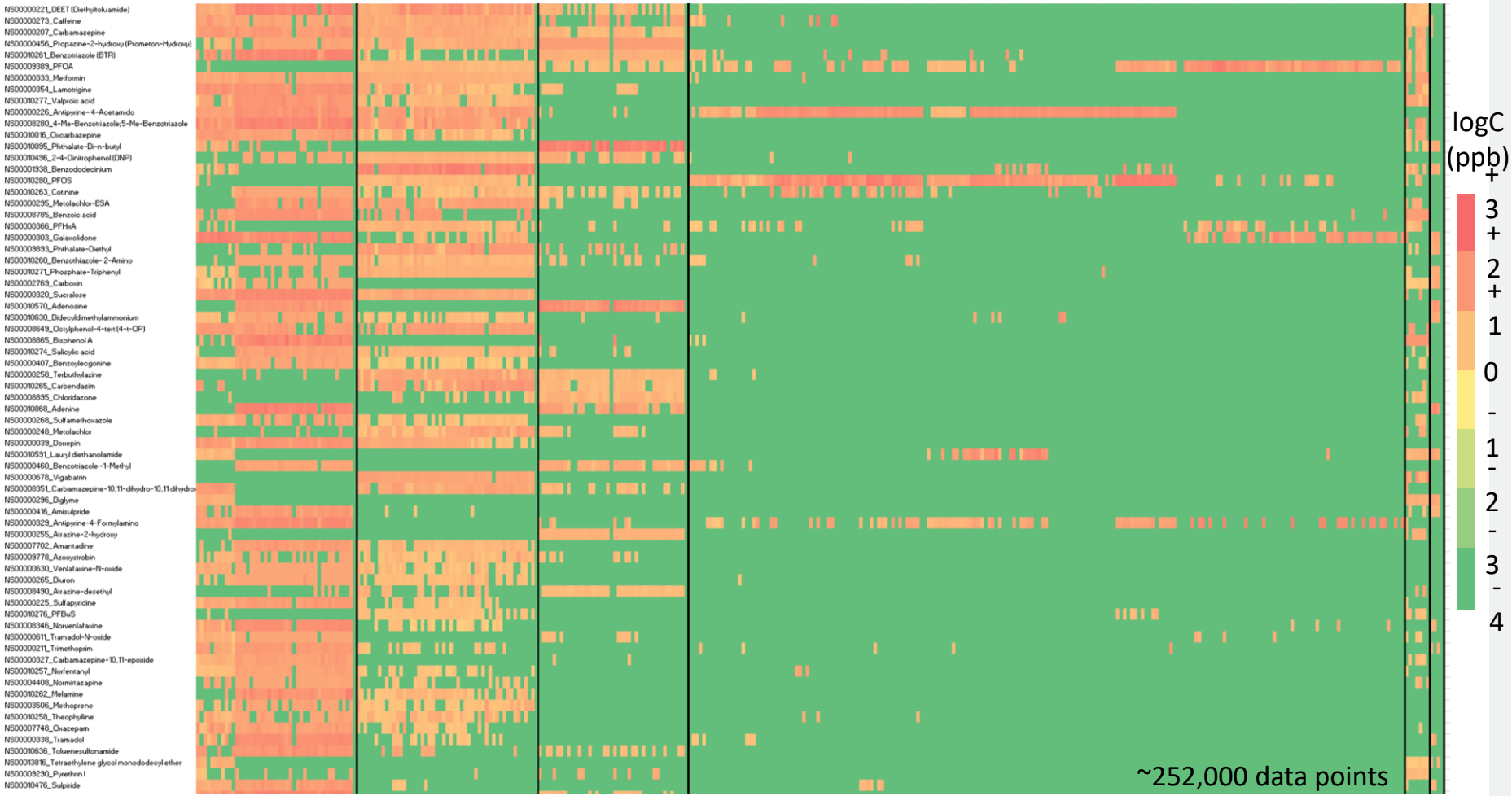
Heatmaps



Georgaphical distribution maps

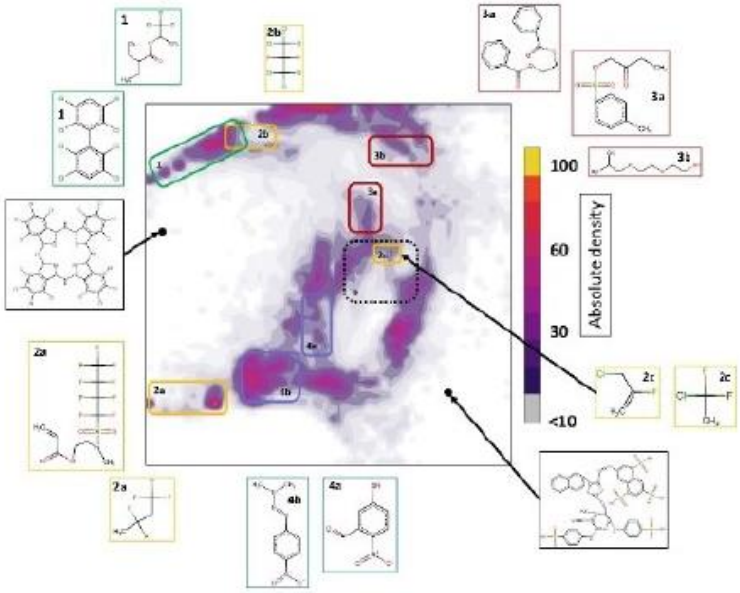


Occurrence of contaminants in the environment



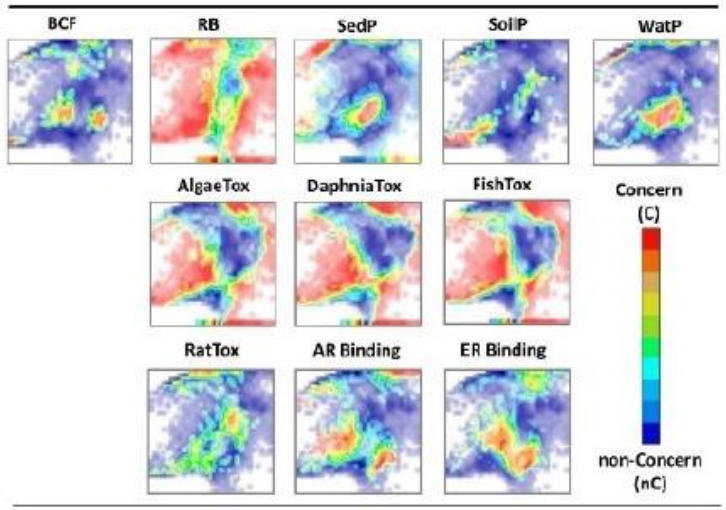
Mapping of properties based on similar structures

Chemical space



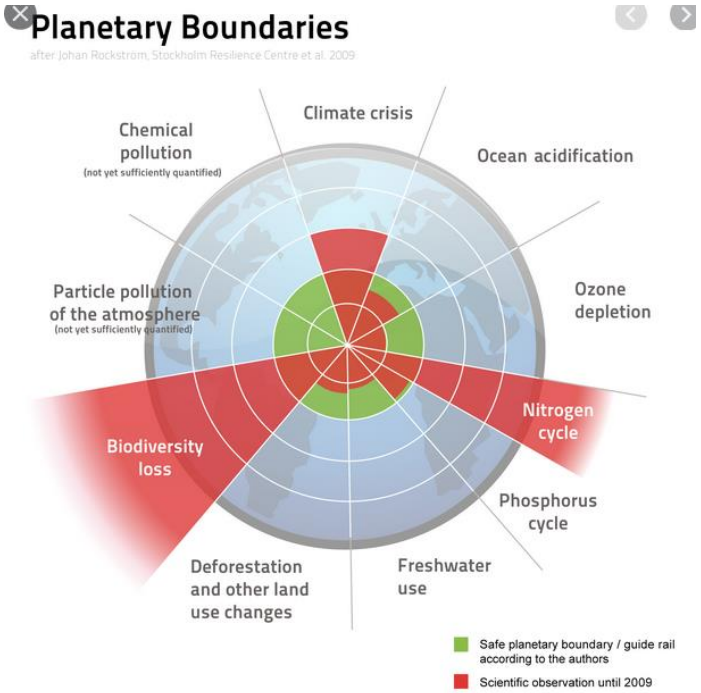
Lunghini et al., 2020
DOI: 10.1002/minf.202000232

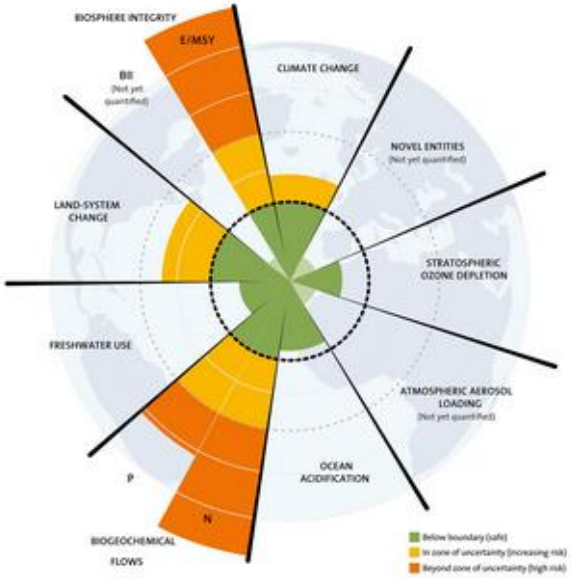
Endpoints / properties scaled from 0 (non-concern) to 1 (concern)



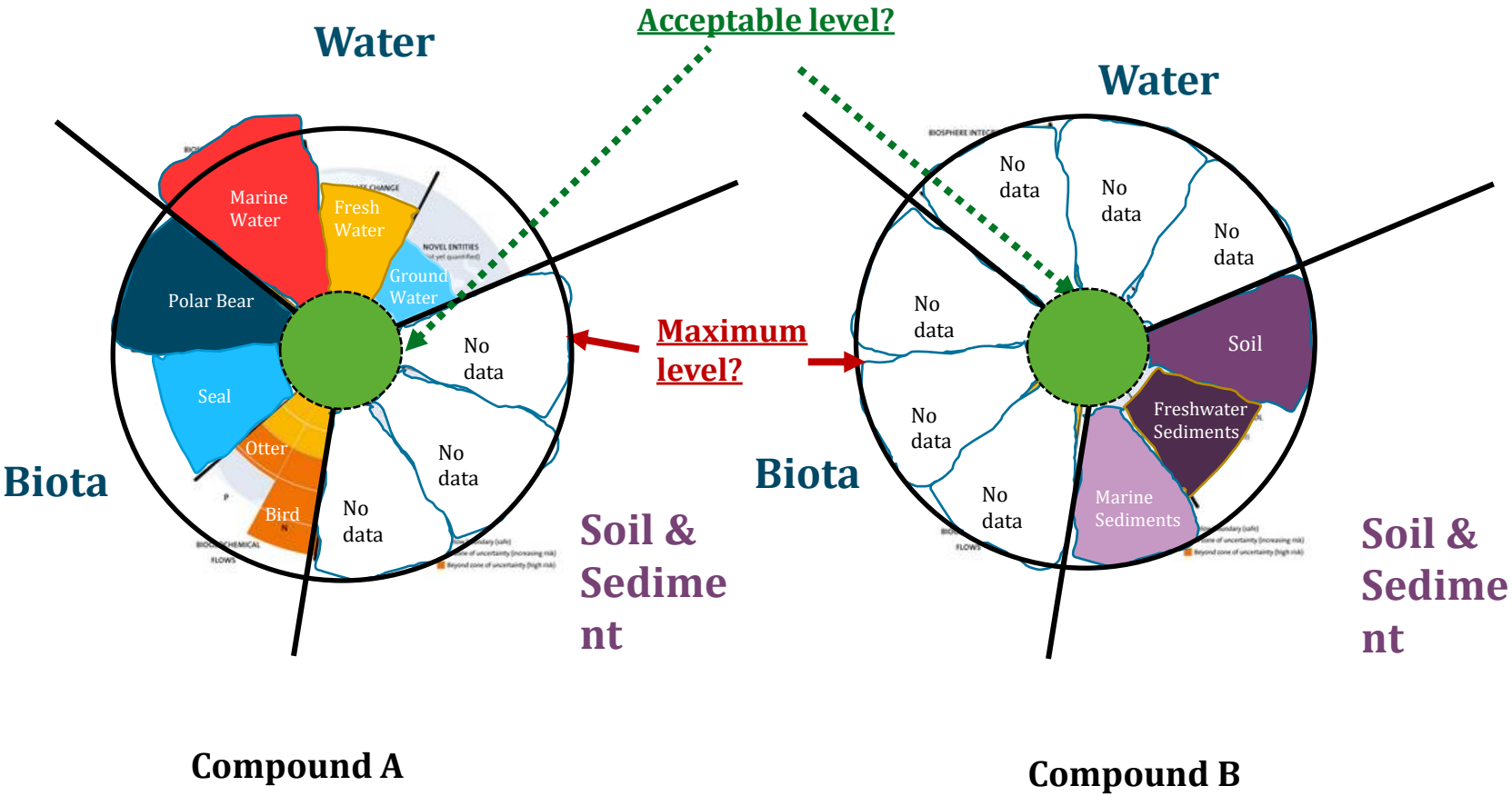
It is possible to derive
Overall score = SUM of the scores of the different endpoints

Idea to use a „Star“ or „Spider-web“ Chart, based on the concept of„planatory boundaries“

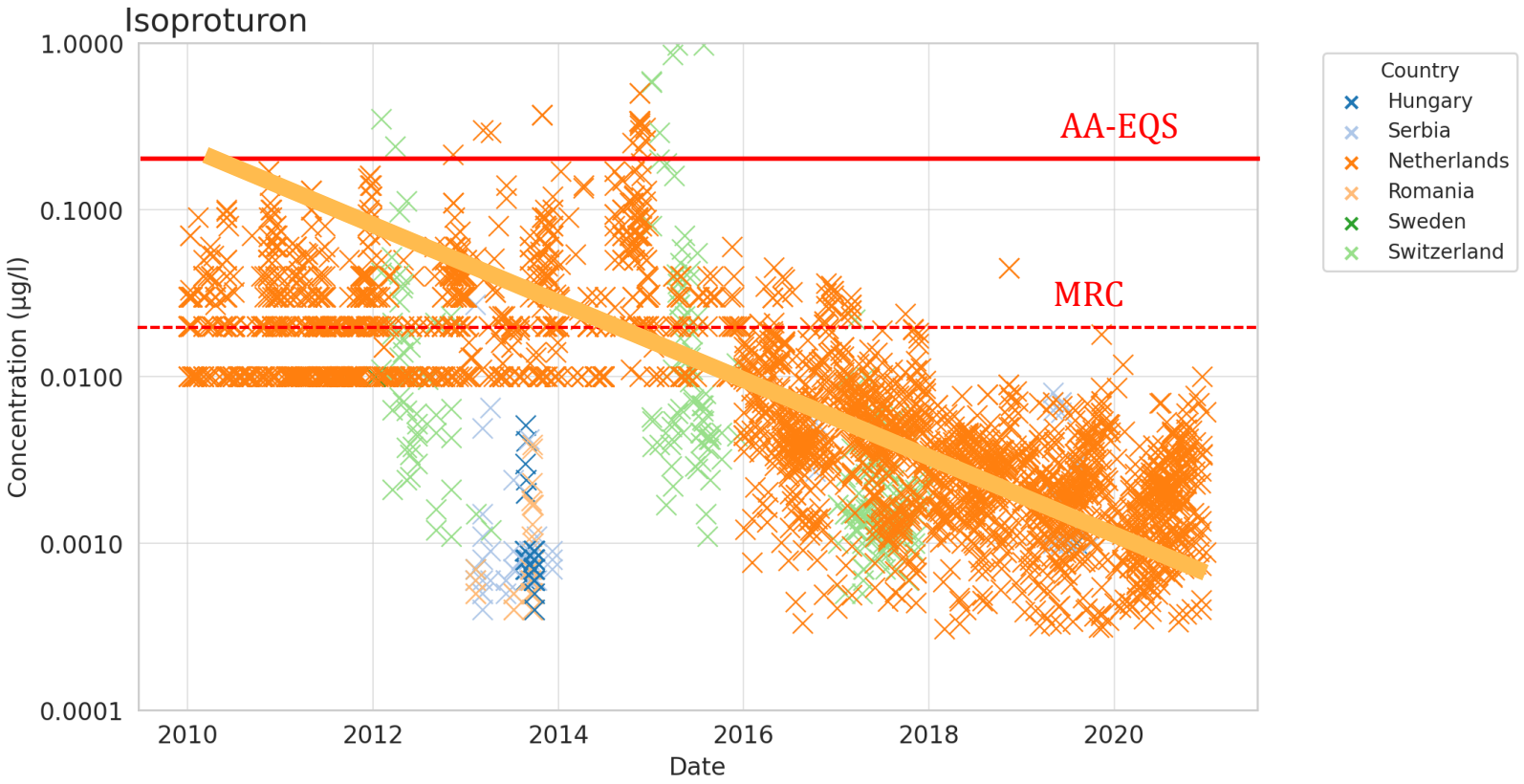




Theoretical Example: exceedance for marine data



Visualisation of Exceedances and Timetrends

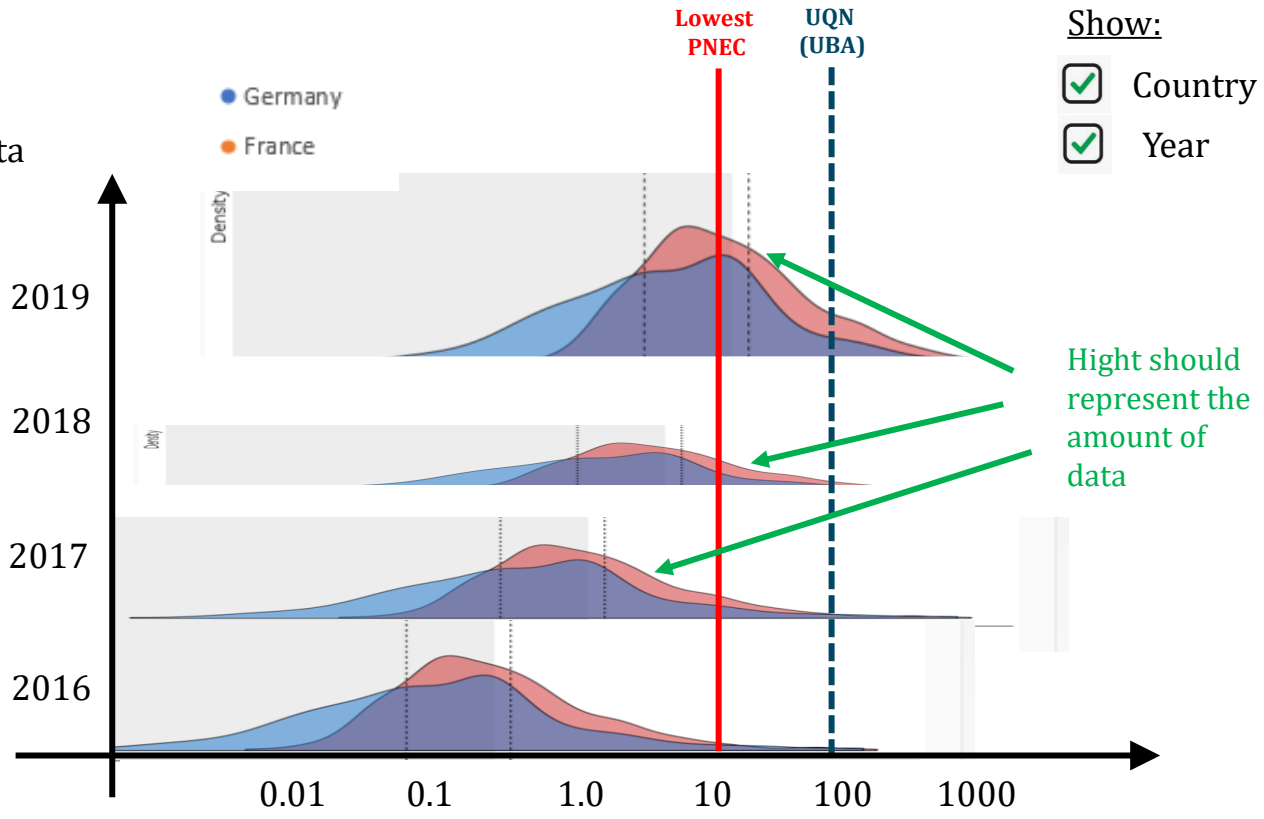


In one view: number of exceedances (recent or old), contribution to mixture risks as well as estimated trends

Different Visualisation

Example: fictive

- Normal distribution – no raw data
- Different „countries“ with colors
- All PNEC´s can be shown
- Time trends



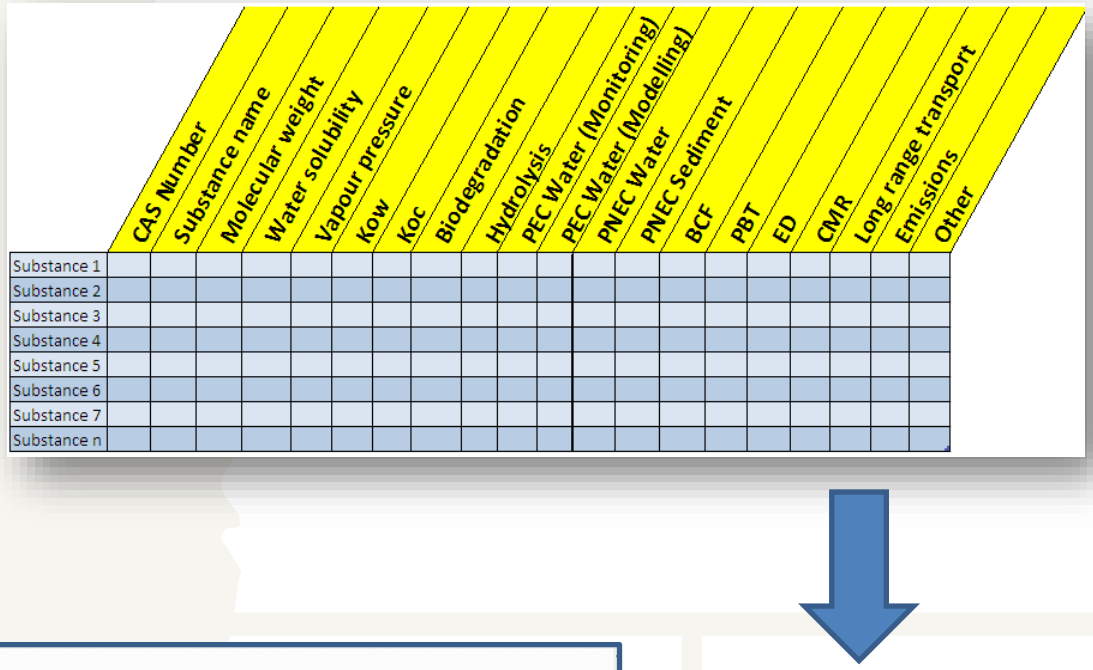
Prioritisation scheme

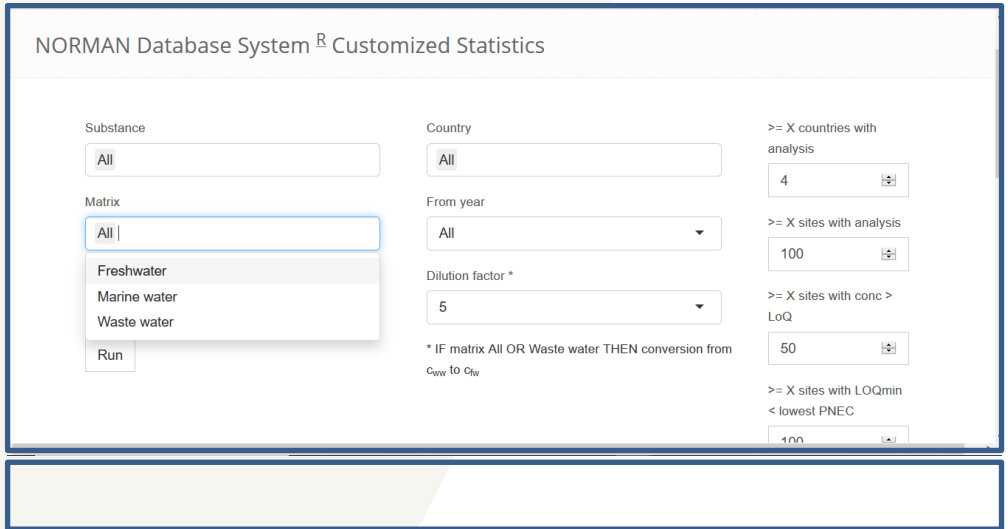
UPGRADING THE SYSTEM

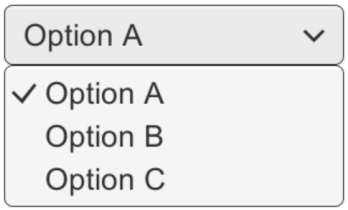
COLLABORATION WITH PARC

PARC Workshop 12-13 October: main conclusions

- Consensus about the categorisation concept
- System flexible for new prioritisation queries (regulatory and research needs)
- Extending the list of indicators
- The user can customise:
  - the list of indicators
  - the weight of each indicator for the scoring





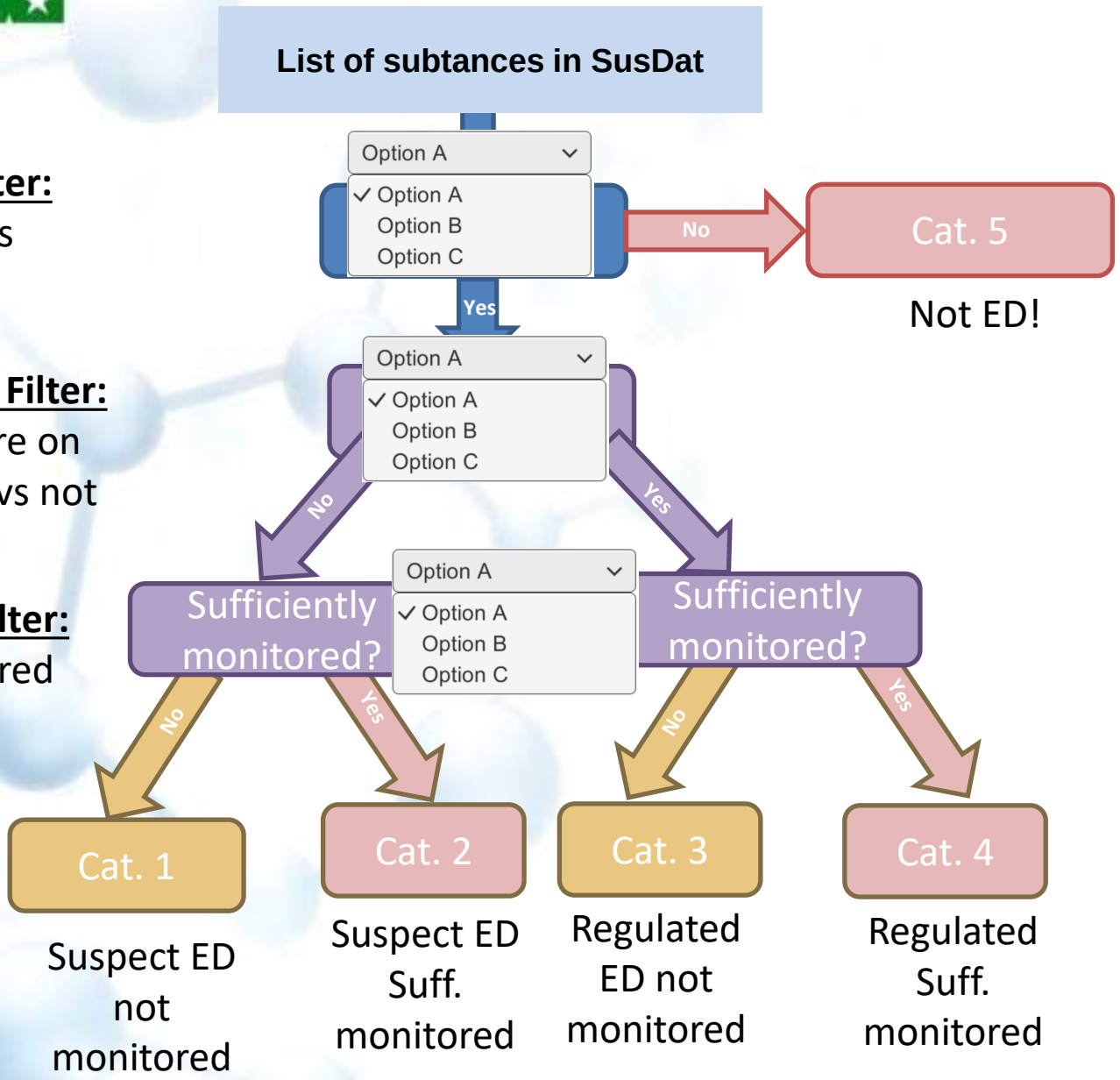


Example: Insufficiently monitored ED

First Indicator / Filter:
Exclude compounds that are not ED

Second Indicator / Filter:
Compounds that are on regulatory ED lists vs not

Third Indicator / Filter:
Sufficiently monitored



Conclusions for next JPA?

Environmental status indicators

- Proposals for status indicators:
  - Number of chemicals exceeding the PNEC (MRC, FoE)
  - Extent of exceedance (RQ_sum)
  - Other proposals?

Indicators for Prioritisation of substances vs Indicators of Environmental status

$$FoE_i = \frac{Nb\ sites\ where\ substance\ i\ shows\ RQi > 1}{Nb\ sites\ where\ substance\ i\ was\ monitored}$$

$$MRC\_i = \frac{Nb\ sites\ where\ substance\ i\ shows\ 0.1 \leq RQi < 1}{Nb\ sites\ where\ substance\ was\ monitored}$$

Prioritisation of risk drivers

FoE + MRC = Risk Score

➔ Ranking of substances

$$FoE\_status = \frac{Nb\ sites\ where\ RQmax \geq 1}{Nb\ sites\ monitored}$$

$$MRC\_status = \frac{\text{Nb } sites\ where\ RQsum > 1\ and\ RQmax < 1}{\text{Nb } sites\ monitored}$$

Environmental Status

FoE_status + MRC_status = Total Risk sites

➔ Risks associated to single substances and mixtures at each site

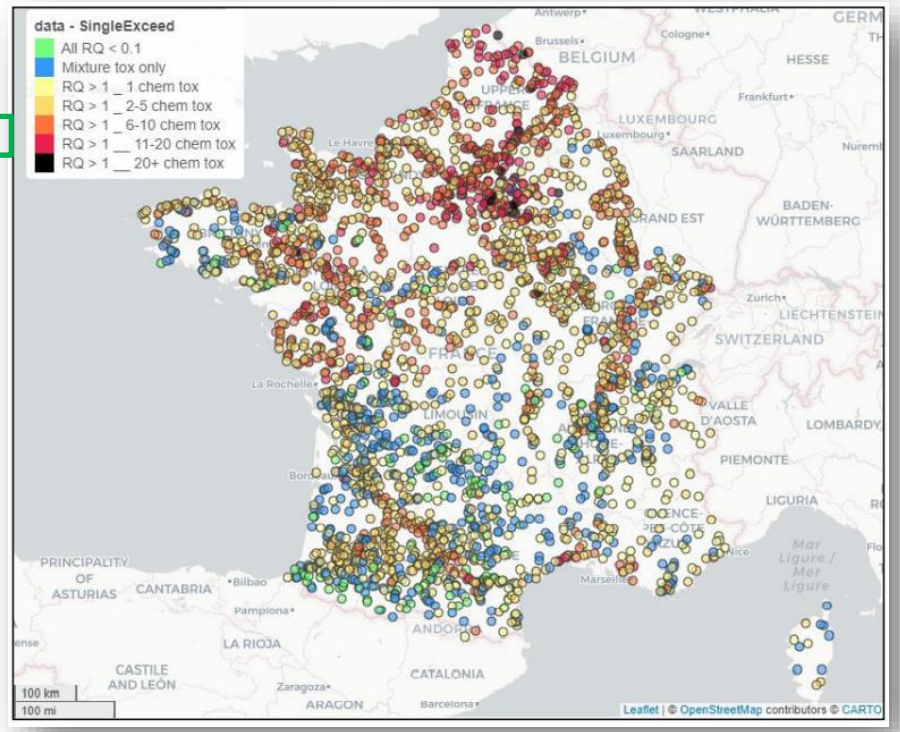
➔ Improvement of the environmental status

Priority Candidates based on single Exceedence and Contributions to Mixture Risk

Substance prioritisation indicators

Name	FoE	MRC	FoQ
Benzo(a)pyrene	0,56	0,00	0,32
Pyrene	0,47	0,08	0,17
Chrysene	0,41	0,15	0,23
Perfluorooctanesulfonic acid (PFOS)	0,37	0,00	0,19
Diflufenican	0,28	0,25	0,40
Formaldehyde	0,27	0,00	0,08
Nicosulfuron	0,22	0,02	0,08
Dibenz(a,h)anthracene	0,21	0,25	0,26
Benzo(g,h,i)perylene	0,20	0,50	0,39
Propyzamide	0,20	0,26	0,18
Metolachlor	0,18	0,34	0,37
Flufenacet	0,18	0,18	0,10
Diclofenac	0,18	0,27	0,26
1,3,5-Triazin-2(1H)-one, 4-((1,1-dimethylethyl)amino)-6-(ethylamino)-	0,16	0,02	0,09
Benzo(b)fluoranthene	0,15	0,50	0,40
Benz(a)anthracene	0,14	0,44	0,21
Metazachlor	0,13	0,21	0,14
Carbamazepine	0,13	0,39	0,40
Dimethenamid	0,11	0,28	0,21
Butylated hydroxytoluene	0,09	0,00	0,01
Imazamox	0,08	0,04	0,03
Chlorate	0,08	0,36	0,22
Iobitridol	0,07	0,01	0,06
2-Ethylhexyl-2-cyano-3,3-diphenylacrylate	0,07	0,00	0,02
Iopromide	0,06	0,04	0,06
Imidacloprid	0,06	0,04	0,03
Benzo(k)fluoranthene	0,05	0,39	0,26
Bisphenol A	0,05	0,33	0,15

Environmental status indicators

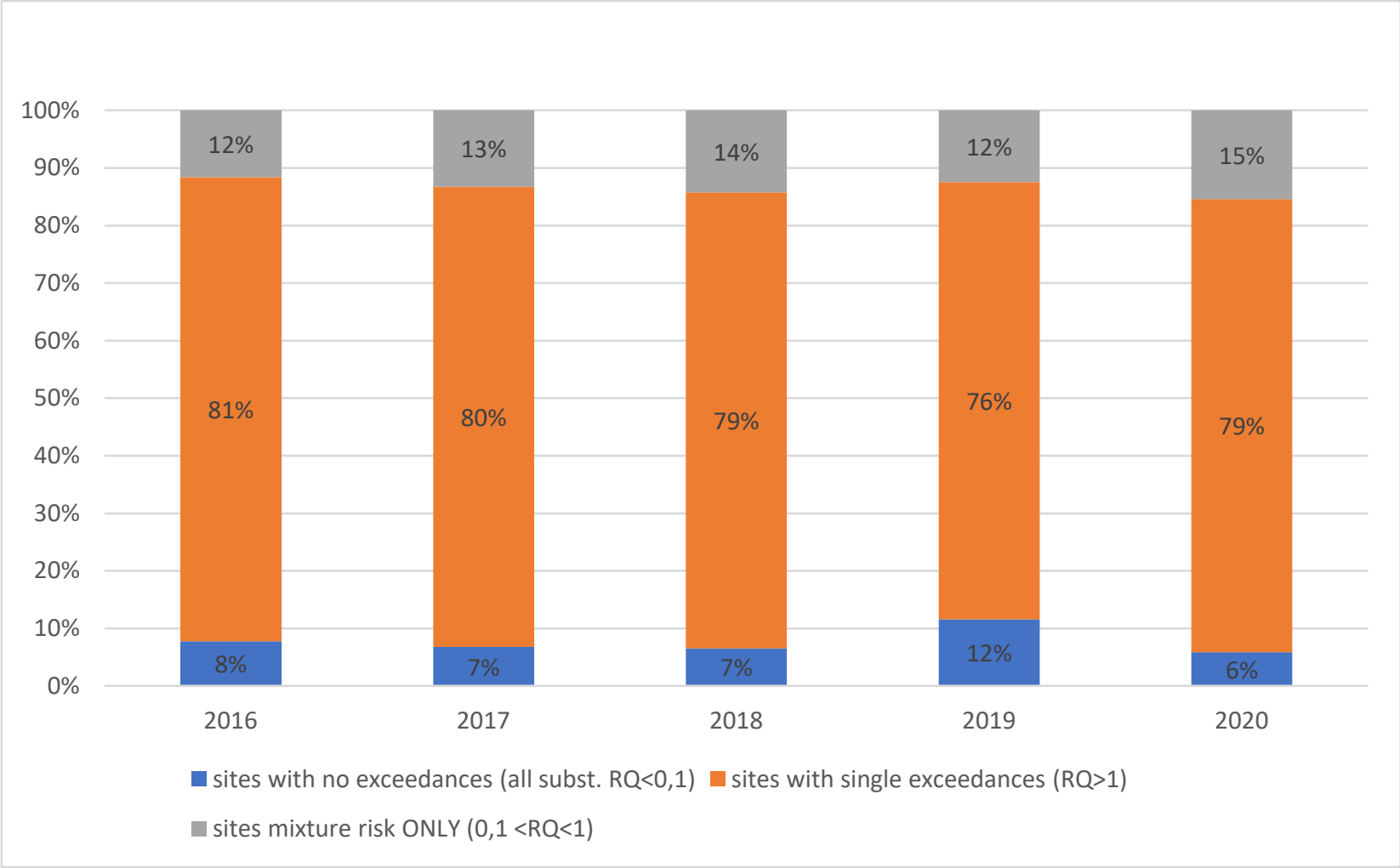


Example: France river monitoring 2020

Number of compounds: ***1200***

Number of sites: ***3000***

Percentage of sites with no risk of exceedances, with risk of exceedance for individual substances or with mixture risks only – sites with ≥ 15 substances monitored (overview per year)



Other examples of environmtal status indicators ?

- Number of chemicals exceeding the PNEC (MRC, FoE)
- Extent of exceedance (RQ_sum)
- Number of samples and substances measured at each sites
- Number of detected substances / Total measured substances
- Other proposals?

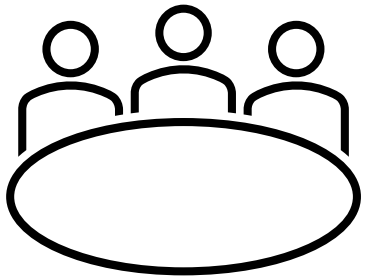
Conclusions for next JPA?

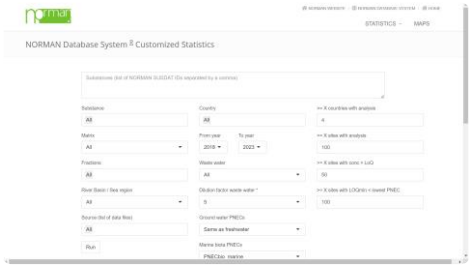
Factsheets

- How to deal with **multiple values** (predicted/experimental) – creation of DCT and modules (important also for the Factsheets)

Conclusions for next JPA?

- How to deal with multiple values (predicted/experimental) – creation of DCT and modules (important also for the Factsheets)





Any other business