Results of the modelling-based prioritisation exercise

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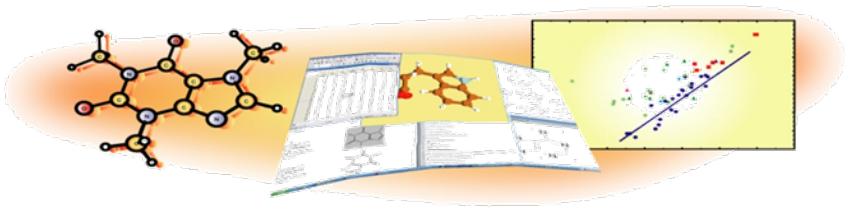
Expert group on Review of WFD Priority Substances List

http://ecb.jrc.ec.europa.eu/qsar/

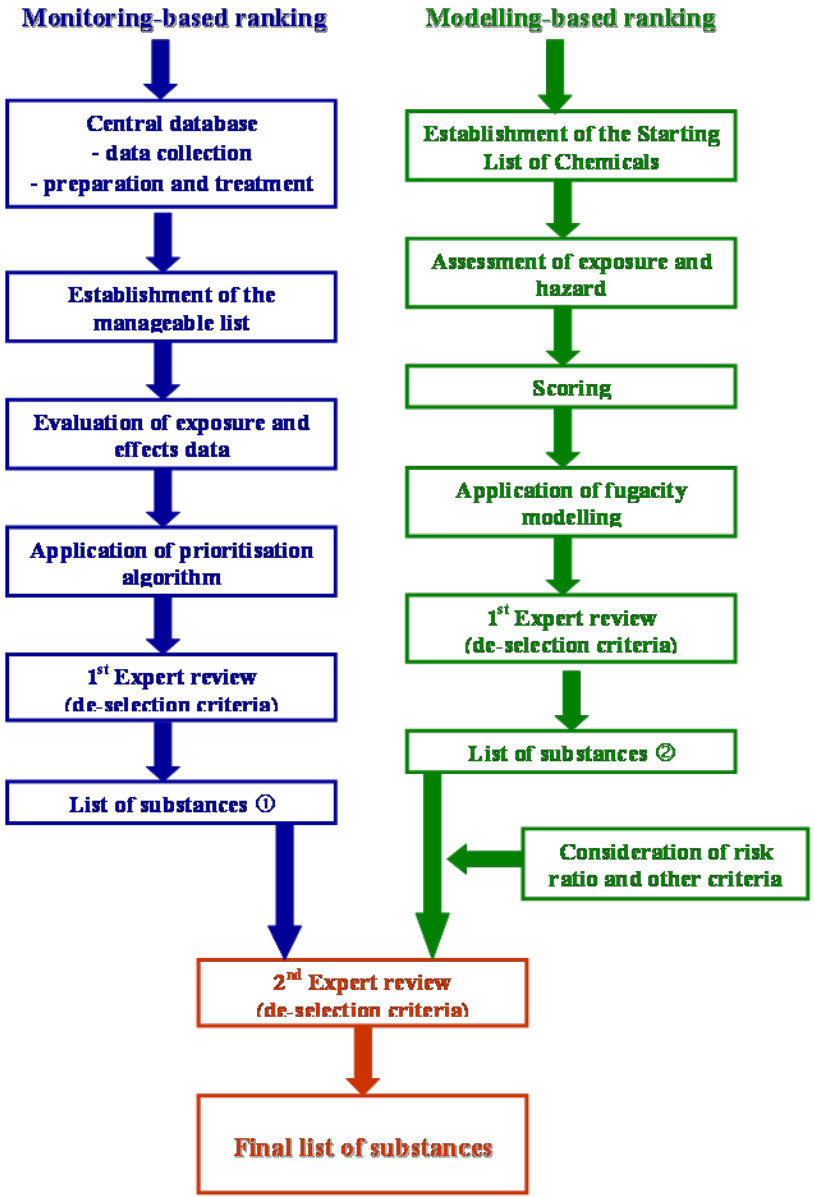


OUTLINE

- Introduction
- Identification of candidates for prioritisation
- Process overview
- Preliminary screening
  - Hazard assessment
    - Persistence
    - Bioaccumulation
    - Toxicity
  - Exposure Assessment
- Final Ranking
  - PNEC estimation
  - PEC estimation
    - ECETOC TRA Tool
    - Multimedia modelling
- Results
- Conclusions
- Next Steps

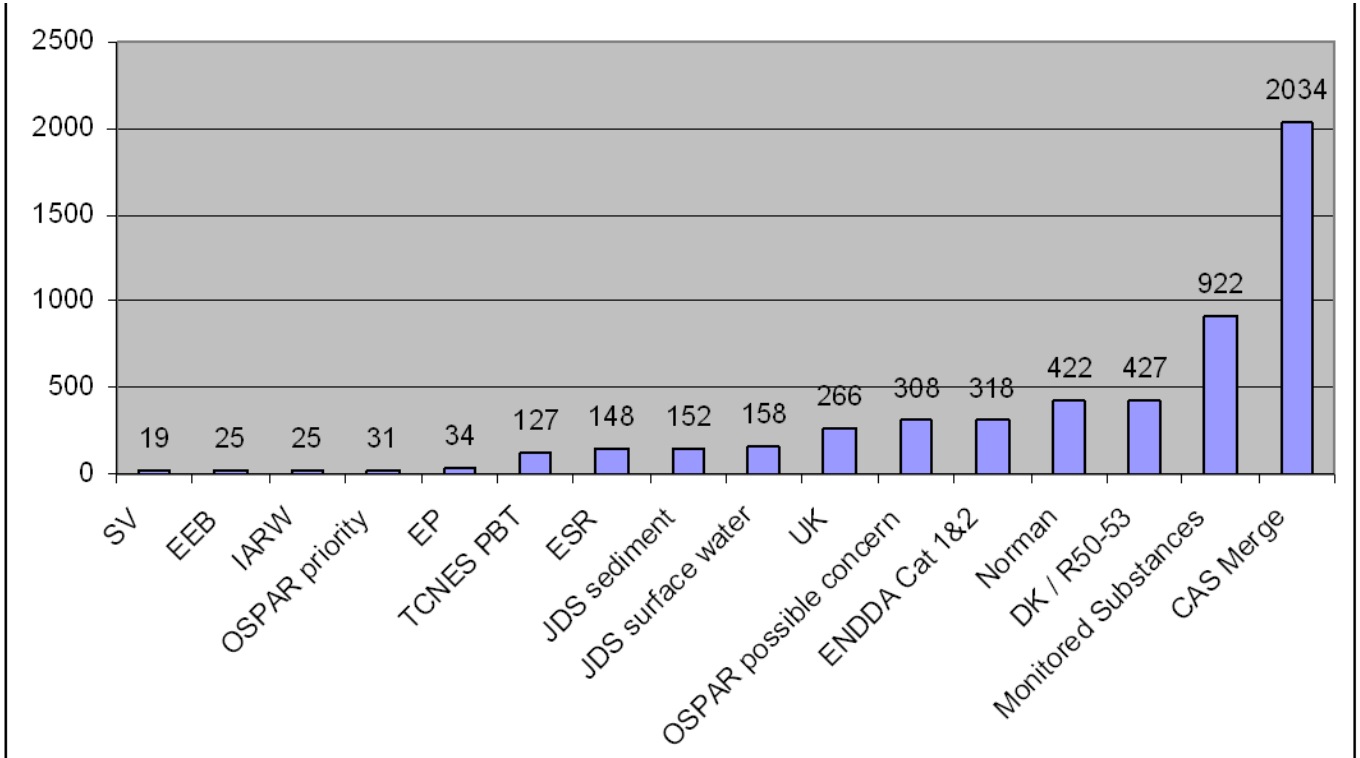
Outline of the prioritisation approach (two steps):

- **Screening** (2034 compounds)
- **Ranking** (78 compounds)



Starting list of Chemicals

- Updated list agreed on last meeting (15/9/09) after the addition of proposals from: EEB, Greenpeace, TC-NES PBT working group, EU endocrine disruptors database (lists 1 & 2, DG-ENV), OSPAR, Joint Danube Survey and NORMAN to the existing list proposed by JRC.
- CAS merge: 2034 substances.



Screening: Hazard Assessment

$$\text{Total Score} = Score_P + Score_B + Score_T + Score_{ED}$$

P stands for Persistent (0/1)
B= Bioaccumulative (0/1)
T=Toxic (0/1)
ED = priority list of Endocrine disruptors Cat. 1 and 2 (0/1)

modified from Wilkinson et al. (2007)

Screening: Exposure Assessment

Use Assessment = Total Production · Use Index

Contribution	Index	Approach
A. How much is produced/ imported annually in EU?	**Ton/year**	**Data from IUCLID and SPIN (Nordic Countries) databases**
B. What is the use pattern?	**Use Index (0.1-1)**	**A factor is applied to Ton/year based on use pattern: 0.1 Controlled system (isolated intermediate) 0.2 Industrial (non dispersive) use or use resulting in inclusion into/onto matrix 0.5 Wide dispersive use (mainly diffusive sources) 1.0 Used in the environment**

Exposure score	Definition
0	**Annual use: 0-1 tons**
1	**Annual use: 1-10 tons**
2	**Annual use: 10-100 tons**
3	**Annual use: 100-1000 tons**
4	**Annual use: >1000 tons**

modified from Wilkinson et al. (2007)

Screening: Risk (Hazard & Exposure) Assessment

First step

	Exposure assessment score					
Hazard Assessment score		**4**	**3**	**2**	**1**	**0**
	4	**1**	**1**	**2**	**3**	**5**
	3	**1**	**2**	**2**	**3**	**5**
	2	**2**	**2**	**3**	**4**	**5**
	1	**3**	**3**	**4**	**4**	**5**
	0	**5**	**5**	**5**	**5**	**5**

Second step

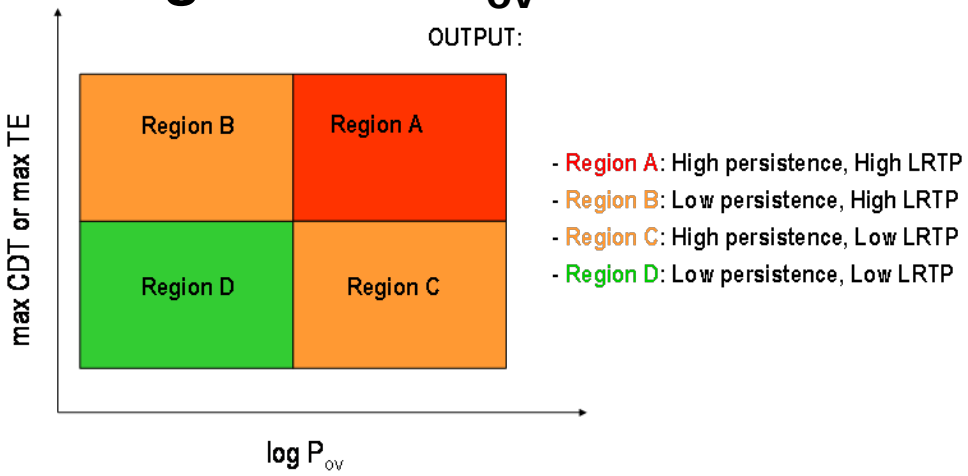
Only for substances with value 1

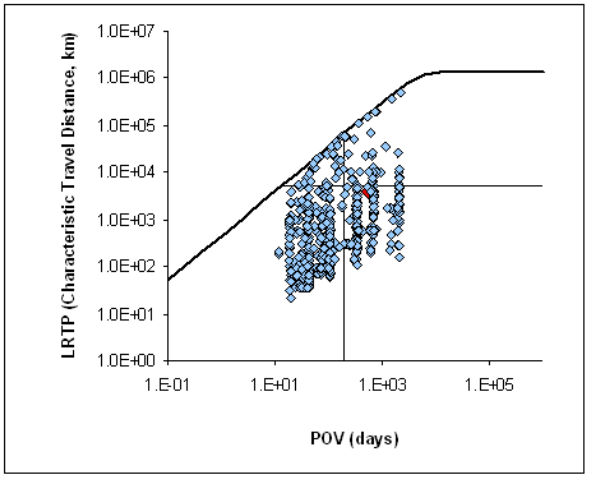
- **PEC estimation**
- **PNEC estimation**
- **Risk ratio=PEC/PNEC**

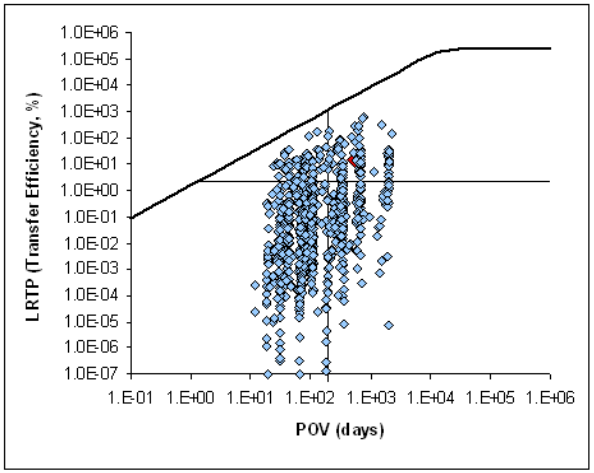
modified from Wilkinson et al. (2007)

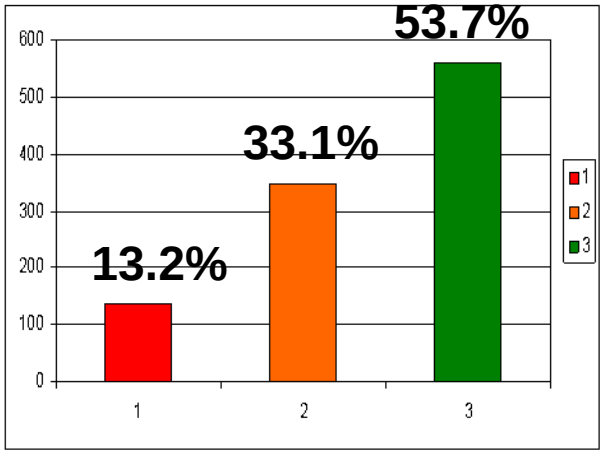
Hazard Assessment: Persistence (Screening)

- P screening: BIOWIN or BIOHCWIN (EPI suite™)
- vP screening: OECD P_{ov} and LRTP screening tool



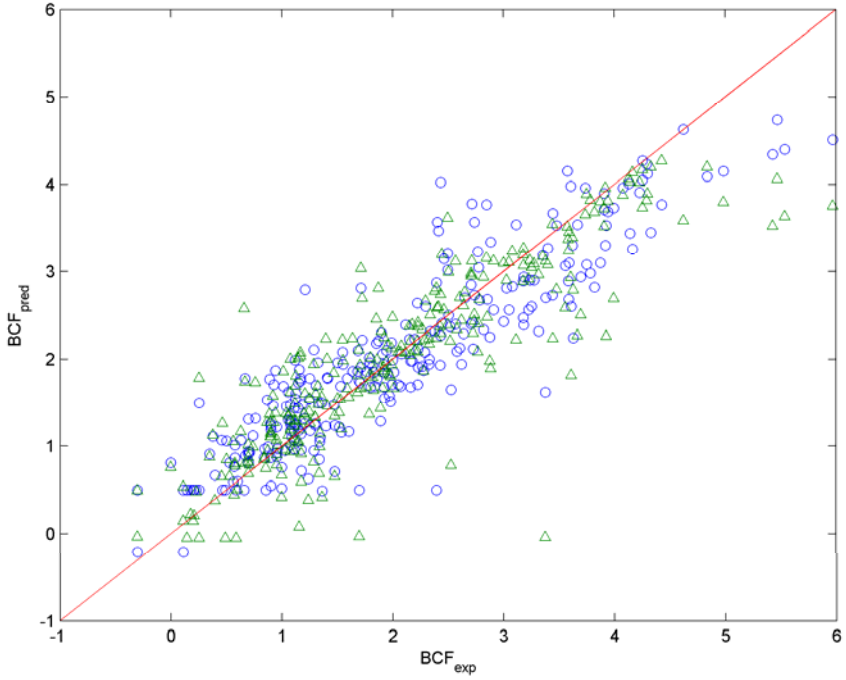


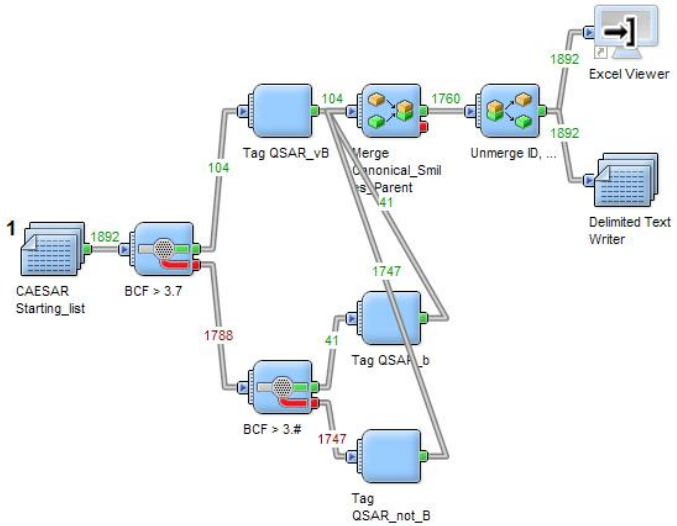




Hazard Assessment: Bioaccumulation (Screening)

- **BCF values (Arnot BCF and Footprint databases)**
- **QSAR, EPI Suite (BCFBAF),CAESAR bioaccumulation and JRC tool (error ~ 0.5 log units)**

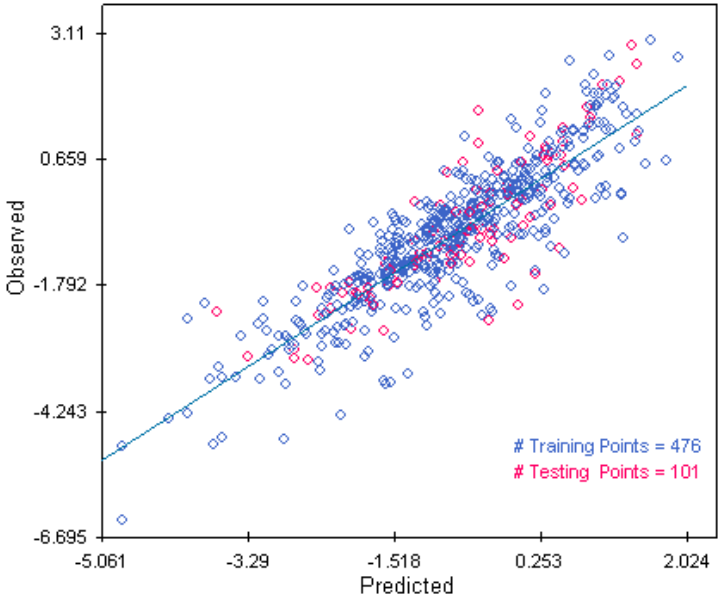




Hazard Assessment: Toxicity (Screening)

- **Footprint (NOECs, EC50 pesticides), ECETOC (NOECs, EC50) DSSTOX (EC50) data- mined for experimental data**

- **4 QSAR models (ADMET Predictor proprietary model, 3 JRC models) were run to estimate toxicity using a consensus approach**



ALL: Slp=1.029 Int=0.03 QSqd=0.74 RMSE=0.695 MAE=0.518
TEST: Slp=1.039 Int=0.047 QSqd=0.715 RMSE=0.705 MAE=0.515

Exposure Assessment (Screening)

- **An algorithm to extract data from IUCLID was implemented (http://iuclid.echa.europa.eu/) as well as data from SPIN[1] (http://www.spin2000.net/) provided.**
- **Use and type of use of substances from IUCLID (if several uses maximum value was chosen)**
- **Problems: IUCLID has old data, data for 56% compounds not found**

[1]SPIN (Substances in preparations in Nordic countries) is a database on the use of Substances in Products in the Nordic Countries. The database is based on data from the Product Registries of Norway, Sweden, Denmark and Finland. The database is financed by the Nordic Council of Ministers, Chemical group.

Screening results

- **78 compounds classified with Risk Score 1**

- **Next step, Ranking:**

Obtain a risk ratio (PEC/PNEC) for these compounds relevant databases for Toxicity and

  - **PNEC estimation**
  - **PEC estimation**

PNEC Estimation (Ranking)

- **PNECs were calculated with preference for experimental data over QSAR and NOEC over EC_{50}.**
- **Several databases were mined to find toxicological data,**
- **When no PNEC was accessible, the data were combined in a developed algorithm to estimate a value for each specific compound.**
- **In case of data gaps and when a QSAR estimation was applied provisional PNECs were calculated using the mean of the predicted EC_{50} from the 4 modules and the assessment factor (AF) 1000.**

PEC Estimation: ECETOC TRA tool (Ranking)

Proposed application to estimate PEC/PNEC ratio for substances with risk score = 1

ECETOC has developed a tiered approach for calculating the exposure and related risks to consumers, workers and the environment caused by chemicals implementing REACH Guidance:

- **Tier 1**: based on pre-defined and conservative use scenarios corresponding to Environmental Release Categories (ERC) described under REACH Guidance (Chapter R.16)
- **Tier 2**: detailed risk assessment on previously identified uses (additional more realistic exposure input)

Developed in Excel, contains the user interface and the datasheets

Freely downloadable after registration from: ***http://www.ecetoc.org/tra***

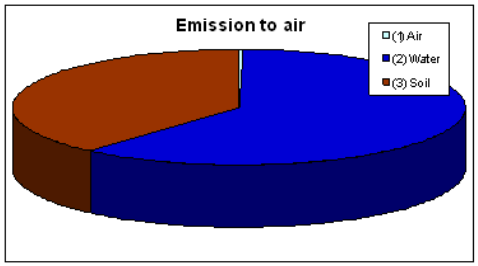
PEC Estimation: Multimedia modelling (Ranking)

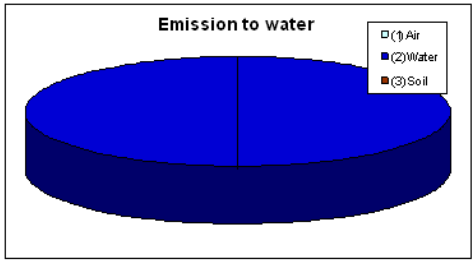
$$PEC = Total\_production \cdot Use\_Index \cdot distribution\_in\_water / 25 \cdot 10^{9}$$

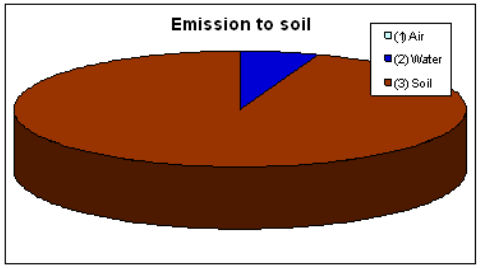
from REACH Guidance

Distribution in water from OECD LRTP:

http://www.oecd.org/env/riskassessment







Alachlor (example):

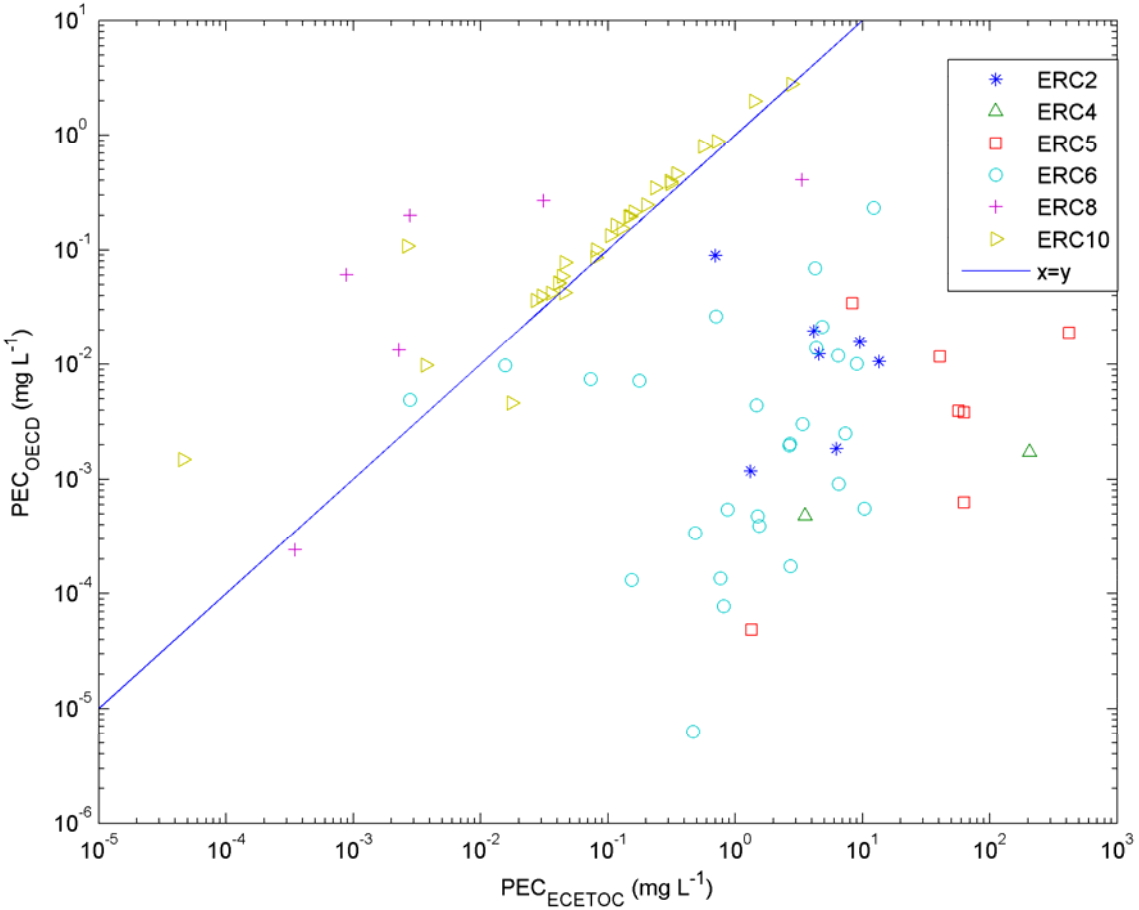
Emission to air: Pov = 64 days; CDT = 90 km;
Emission to water: Pov = 173 days; CDT = 298 km;
Emission to soil: Pov = 328 days;

Overall: Pov = 328 days CDT = 298 km.

Distribution in water (equilibrium) = 98.86%

Pov (Overall Persistence)
CDT (Characteristic Travel Distance)

PEC calculation: ECETOC- Multimedia



- Good agreement for wide dispersive chemicals
- ECETOC gave too high values for non dispersive chemicals
- Solubility is required in ECETOC but not considered for PEC

RANKED RESULTS (Top 20)

CAS	Name
2921-88-2	chlorpyrifos
834-12-8	ametryn (ECPA-S: not used anymore in EU)
1085-98-9	Dichlofluanide
7287-19-6	prometryn (ECPA-S: not used anymore in EU)
55283-68-6	ethalfluralin
886-50-0	terbutryn (ECPA-S: modelling PNEC values lower)
52315-07-8	alpha-cyano-3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
5598-13-0	chlorpyrifos-methyl (DAS: low production, PEC, PNEC values)
42576-02-3	methyl 5-(2,4-dichlorophenoxy)-2-nitrobenzoate
118-82-1	2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol (TBMD) (CEFIC: Tonnage lower)
1897-45-6	chlorothalonil (ECPA-S: modelling PNEC values lower, biodegradable)
79-94-7	2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol (RAR concern aquatic compartment: yes)
1582-09-8	trifluralin (DAS: PEC, PNEC values)
107-64-2	Dimethyldioctadecylammonium chloride (RAR concern aquatic compartment: no)
74070-46-5	2-chloro-6-nitro-3-phenoxyaniline
2312-35-8	propargite
77-47-4	hexachlorocyclopentadiene (RAR concern aquatic compartment: no)
67747-09-5	N-propyl-N-[2-(2,4,6-trichlorophenoxy)ethyl]-1H-imidazole-1-carboxamide
115-32-2	Dicofol
1861-40-1	benfluralin

Comments from Chem. Industry

- **New production levels for 3 compounds**
- **New Physico-chem. properties for one compound**
- **PEC/PNEC risk ratio recalculated for these compounds**

RANKED RESULTS (Top 20)

After comments from Chem. Ind.

CAS	Name
2921-88-2	chlorpyrifos
834-12-8	ametryn
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1582-09-8	trifluralin
107-64-2	Dimethyldioctadecylammonium chloride
74070-46-5	2-chloro-6-nitro-3-phenoxyaniline
2312-35-8	propargite
77-47-4	hexachlorocyclopentadiene
67747-09-5	N-propyl-N-[2-(2,4,6-trichlorophenoxy)ethyl]-1H-imidazole-1-carboxamide
115-32-2	Dicofol
50-29-3	clofenotane
5102-83-0	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxobutyramide]
5468-75-7	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxobutyramide]

CONCLUSIONS

- **A model-based approach for chemical prioritization under the WFD has been developed**
- **Two phases: First screening (2034 compounds) and second PEC/PNEC estimation (78 compounds)**
- **Positive points: Complements monitoring data (no use of the database developed by the monitoring approach)**
- **Drawbacks: Estimated data and properties (PBT assessment possible for 76%), hard to find data on production levels (46% compounds) and use assessment, no data on emissions (eg. chemicals produced by combustion), PEC/PNEC uncertain (only for internal ranking).**

NEXT STEPS

- **Short term:**
  - **Combining lists (DG-ENV proposal)**
  - **Expert review**
  - **Replacement of estimated data/parameters by experimental values for finally selected compounds (Dossiers)**
- **Long term:**
  - **Develop an workflow task/package for subsequent prioritisation exercises (open source tool) that is accessible to all interested parties**

Score	CAS	Name
21	50-29-3	clofenotane
22	5102-83-0	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxobutyramide]
23	5468-75-7	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxobutyramide]
24	1120-36-1	Tetradecene
25	96-69-5	6,6'-di-tert-butyl-4,4'-thiodi-m-cresol
26	63449-39-8	Paraffin waxes and Hydrocarbon waxes, chloro (LCCP) (CEFIC:not PBT/vPvB)
27	52-68-6	trichlorfon
28	1912-24-9	atrazine
29	2082-79-3	octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
30	119-47-1	6,6'-di-tert-butyl-2,2'-methylenedi-p-cresol
31	2303-17-5	tri-allate
32	56-35-9	bis(tributyltin) oxide
33	6683-19-8	3-{[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propanoyl]oxy}-2,2-bis({[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propanoyl]oxy}methyl)propyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propanoate
34	120-82-1	1,2,4-trichlorobenzene (RAR concern aquatic compartment: yes)
35	731-27-1	N-{[dichloro(fluoro)methyl]sulfanyl}-N',N'-dimethyl-N-(4-methylphenyl)sulfuric diamide (ECPA-S: Lower tonnage)
36	4979-32-2	N,N-dicyclohexylbenzothiazole-2-sulphenamide
37	67774-74-7	undecylbenzene (RAR concern aquatic compartment: no)
38	32534-81-9	diphenyl ether, pentabromo derivative
39	68442-68-2	4-(1-phenylethyl)-N-[4-(1-phenylethyl)phenyl]aniline
40	135-91-1	4,4'-methylenebis[N,N-diethylaniline]
41	31570-04-4	tris(2,4-ditert-butylphenyl) phosphite
42	5567-15-7	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(4-chloro-2,5-dimethoxyphenyl)-3-oxobutyramide]
43	64131-85-7	O,O,O-tris(4-nitrophenyl) thiophosphate
44	294-62-2	cyclododecane (CEFIC: not SVHC)
45	25637-99-4	hexabromocyclododecane (RAR concern aquatic compartment: yes)
46	3194-55-6	1,2,5,6,9,10-hexabromocyclodecane (RAR concern aquatic compartment: yes)
47	732-26-3	2,4,6-tri-tert-butylphenol