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A MODELLING APPROACH FOR THE PRIORITISATION OF CHEMICALS UNDER THE WATER FRAMEWORK DIRECTIVE

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EXECUTIVE SUMMARY

This is the report of a feasibility study in which a model-based prioritisation methodology was developed in support of the implementation of the Water Framework Directive. The approach focuses on aquatic ecosystems and takes into account the intrinsic hazards of chemicals as well as their exposure levels. The prioritisation approach also takes into account hazards due to secondary poisoning, bioaccumulation through the food chain and potential human health effects, e.g. due to consumption of fish or drinking water. A list comprising 2034 compounds provided by Member States, Stakeholders and Non-Governmental Organisations was evaluated according to pre-defined hazard and exposure criteria. Then 78 compounds considered to be "of high concern" were analysed and ranked in terms of their PEC/PNEC risk ratio (Predicted Environmental Concentration/Predicted No-Effect Concentration). In the interests of reproducibility, the tools employed in a model-based prioritisation process should ideally be freely accessible; however in this study this was not entirely possible due to the tight schedule and the fact that some estimation/calculation procedures were not available and thus needed to be developed. Nevertheless, the proposed approach constitutes a first step in for the establishment of an open modular tool that could eventually be used to support future prioritisation exercises.

ABBREVIATIONS AND ACRONYMS

BCF	bioconcentration factor
BMF	biomagnification factor
bw	body weight
CAS	Chemical Abstracts Service
ClassLab	Working database which includes classifications and labelling of substances or groups of substances according to the criteria in Directive 67/548/EEC
COMMPS	Combined Modelling and Monitoring Prioritisation Strategy
EC	effect concentration
	European Commission
ECHA	European Chemicals Agency
ECB	European Chemicals Bureau
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EEB	European Environmental Bureau
EEC	European Economic Community (replaced by EU)
EINECS	European inventory of existing commercial chemical substances
EPI	estimation programs interface
EQS	environmental quality standard
ERC	Environmental Release Categories
ESIS	European Chemical Substances Information System
EU	European Union
IAWR	International Working Group Rhine Waterworks
ICPDR	International Commission for the Protection of the Danube River
INERIS	Institut National de l'Environnement Industriel et des Risques (France)
IUCLID	International Uniform Chemical Information Database
IUPAC	International Union of Pure and Applied Chemistry
*K*oc	organic carbon adsorption coefficient
*K*ow	octanol/water partition coefficient
LCx	effect concentration at which x% lethality is observed, generally LC50 and LC10 are calculated
LD50	dose that is lethal to 50% of the tested animals
LRT	Long Range Transport
LRTP	Long Range Transport Potential
min	minutes
mo	months
NOEC	no observed effect concentration
oc	organic carbon
OECD	Organisation for Economic Co-operation and Development
om	organic matter
OSPAR	The Convention for the Protection of the Marine Environment of the North-East Atlantic (OSPAR replaced both the Oslo and Paris Conventions)
PAH	polycyclic aromatic hydrocarbon
PCB	polychlorinated biphenyl
PEC	Predicted Environment Concentration
PNEC	Predicted No Effect Concentration
QSAR	Quantitative Structure–Activity Relationship
RAR	Risk Assessment Report
RCR	Risk Characterisation Ratio
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RIVM	National Institute for Public Health and the Environment
SCTEE	Scientific Committee for Toxicology, Ecotoxicology and Environment
SIDS	screening information dataset

SMILES	simplified molecular input line entry system
SPIN	Substances in preparations in Nordic countries
TC-NES	Technical Committee for New and Existing Substances under Regulation EEC 793/93
TGD	Technical Guidance Document
US	United States
w	weeks
WHO	World Health Organization
y	years

CONTENTS

1. INTRODUCTION

Article 16 of the Water Framework Directive (WFD; EC, 2000) requires the setting out of a list of priority substances (PS) and priority hazardous substances (PHS) presenting a significant risk to or via the aquatic environment. Substances should be prioritised taking into account: i) risk assessments carried out under existing chemically-relevant EU Directives and Regulations (Bodar et al., 2002; ECHA, 2008a; EC, 1998; EC, 1991); ii) targeted risk-based assessments focusing on aquatic ecotoxicity and human toxicity via the aquatic environment; iii) simplified risk-based assessments based on intrinsic hazards, widespread environmental contamination, production volumes and use patterns. PHS are defined as substances that are persistent, bioaccumulative and toxic (i.e. PBT) or that give rise to an equivalent level of concern (e.g. endocrine disruptors).

In recent years there has been a considerable development in the number of chemical risk assessments available due to the development of several pieces of EU legislation on the assessment and management of biocides, industrial chemicals and pesticides (EC, 1998; EC, 2001b; EFSA, 2007). These assessments can be incorporated in the prioritisation exercise as well as in the development/revision of the Environmental Quality Standards (EQS) for the selected PS and PHS to provide a solid basis for the prioritisation exercise. Furthermore, the development of new analytical techniques has increased the number of monitored chemicals and decreased the limit of detection, providing EU-wide monitoring datasets that were not available when the first prioritisation exercise was performed (Klein et al., 1999). In addition, according to the EQS Directive (EC, 2008) a further revision of the PS list and their EQS must be completed by 13 January 2011.

With the development of the WFD (EC, 2000) and its Daughter Directive on EQS (EC, 2008), there is a need to revise the list of PS and PHS developed more than 8 years ago (EC, 2001a) on the basis of a simplified risk-based assessment procedure (Klein et al., 1999).

After extensive discussions and consultations with experts from the Member States (MS), the Commission decided to run in parallel two exercises, one monitoring-based and the other modelling-based (Fig. 1). This was decided because even though experimental data from EU water bodies would provide a clearer picture of the environmental conditions of the aquatic ecosystems, there was still the possibility that relatively new substances which are not routinely monitored could not be detected and properly assessed (SCTEE, 2004).

The monitoring-based exercise was carried out by INERIS (Bonnomet and Alvarez, 2006; James et al., 2009) using environmental data provided by MS authorities. They developed a prioritisation methodology based on the COMMPS (combined monitoring-based and modelling-based priority setting procedure; IUCT, 1999). The COMMPS monitoring database has evolved from ~ 700000 analysis of 314 substances from 15 countries, to the current monitoring status with ~14000000 analysis

of 1153 substances from 28 countries, and which consists of: a) the establishment of a manageable list; b) the design of procedures for data collection, processing and treatment; c) the selection of relevant parameters to consider; d) the development of algorithms for substance's prioritisation; and e) the expert review of the results (James et al., 2009). Based on this methodology, a list of 316 substances for which there were monitoring data from more than three countries in water, sediment and/or biota was selected as candidates for prioritisation. The Predicted Environmental Concentration (PEC) and Predicted No-Effect Concentration (PNEC) were calculated (see James et al., 2009 for the approach) and based on the risk ratio, PEC/PNEC, the compounds were ranked and a list of 41 compounds was produced with another of 21 compounds considering water for human consumption (James et al., 2009).

A prioritisation process should consider two aspects, the first concerns the hazard of a given chemical and the second its exposure levels. In the case of the WFD, the hazard is focused on the aquatic ecosystem, but since the definition of EQS is "*the concentration of a particular pollutant or group of pollutants in water, sediment or biota that should not be exceeded in order to protect human health and the environment*", it should also consider hazards due to secondary poisoning, bioaccumulation through the food chain and potential human health effects, e.g. due to the consumption of fish or drinking water. The exposure of a chemical is related to its use and its tonnage, as well as its partitioning into water.

In the modelling-based approach, the risk scoring was adapted from the UK methodology (Wilkinson et al., 2007), which depends on the integration of hazard and exposure assessments and ranges from 1 to 5. A value of 1 indicates the highest priority and a value of 5 the lowest. The hazard assessment is based on the PBT (Persistence, Bioaccumulation and Toxicity) approach developed in the REACH Guidance (2008b), whereas the exposure assessment is based on production and use data obtained from the IUCLID and SPIN databases. To rank all compounds classified with a score of 1 (78 compounds) a PNEC value was estimated using experimental data and a QSAR model and a tool developed by ECETOC and the Long Range Transport Potential (LRTP) OECD tool was used to calculate a PEC value. The risk ratio, PEC/PNEC, was then calculated and a ranked list of the 78 compounds developed.

It is recommended that this exercise be followed up with an expert review of the applied methodology and the results obtained; therefore one of the main objectives of this report is to provide the reader with a comprehensive view of the steps taken and the criteria applied during the process. As far as possible, one of the main requirements for the tools employed was that they should be freely accessible to interested parties; however this has not always been possible due to the tight schedule of the process and the fact that some estimation/calculation procedures were not available and needed to be developed at the JRC. A long term objective was also to set the basis for an open modular tool that

could be used for the next prioritisation exercises when more data on physico-chemical properties, toxicity and production levels for substances of concern will become available. The proposed approach constitutes the first step in this direction, but further work will be necessary to develop such a tool.

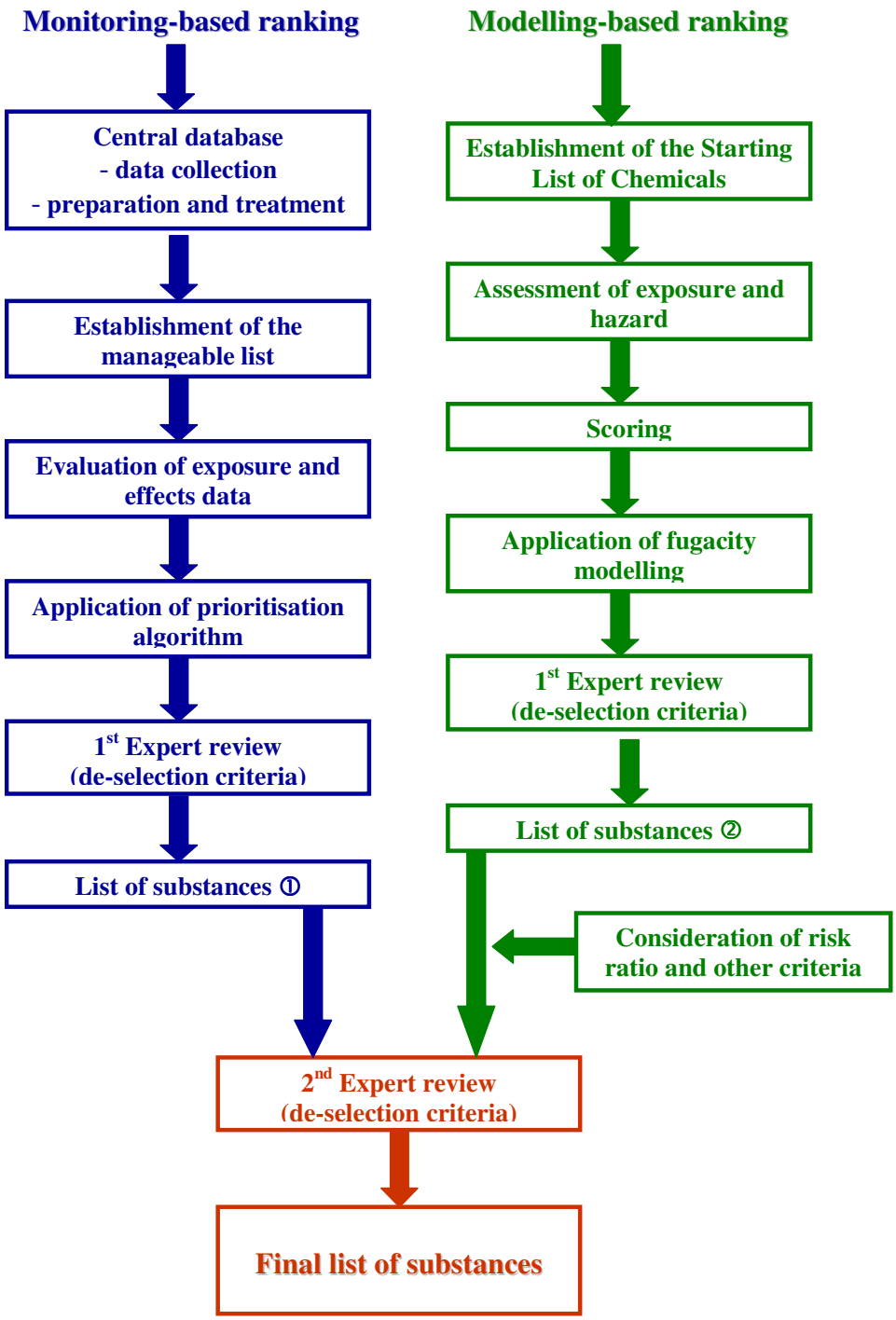

Figure 1. Outline of the parallel prioritisation approach including the monitoring- and modelling-based exercises.

2. IDENTIFICATION OF CANDIDATES FOR PRIORITISATION

The Starting List of Chemicals (SLoC) was based on inputs from Member States (MS), the European Parliament (EP), stakeholders, research consortiums, international organizations and several EU lists of substances of possible concern such as PBT, possible endocrine disruptors, plant protection products, etc.

Specifically the following lists were merged, see Fig. 2:

- all substances in the list of monitoring data provided by Member States (922 compounds);
- indications from MS: DK (R50-53 list), SK, SV and UK after a general call for substances to be analyzed for prioritisation (712 compounds);
- list of substances included by the EP for further investigation (34 compounds);
- compounds included by stakeholders: EEB (European Environmental Bureau) (25 compounds), Greenpeace which indicated OSPAR lists of substances for priority action and of substances of possible concern (331 compounds), IARW (International Working Group Rhine Waterworks) (25 compounds), ESR (Existing Substances Regulation; EC, 93) (141 compounds);
- compounds indicated by research consortiums: the Network of reference laboratories for monitoring of emerging environmental pollutants (NORMAN, http://www.norman-network.net/index_php.php) provided a list of Emerging Substances (ES) of concern derived from scientific literature and expert judgment as well as a monitoring database (422 compounds);
- compounds indicated by international organizations: OSPAR (http://www.ospar.org/) lists of substances for priority action and of substances of possible concern (331 compounds) and ICPDR (International Commission for the Protection of the Danube River, http://www.icpdr.org/jds) compounds monitored during the second Joint Danube Survey (JDS2) in surface water and sediments (310 compounds);
- EU lists of substances from the JRC Website (http://ecb.jrc.ec.europa.eu/): PBT (TC-NES working group), RAR, IUCLID, ClassLab, and potential endocrine disruptor data base (ED lists 1 and 2, http://ec.europa.eu/environment/endocrine/strategy/short_en.htm).

After several interactions with the WG-E Working Group on Prioritisation, the initial SLoC list contained 2034 compounds. Specifically several points were raised:

- Banned Plant Protection Products: it was argued that PPP which are already banned and they are not any longer produced or placed on the European market should not be considered. However, it was pointed out that looking from an ecosystem health perspective they still pose a risk. Of course, if we look at risk management measures they should not be considered. Finally, it was agreed to keep these compounds in the SLoC.
- Emerging chemicals: it was emphasized that emerging substances (ES) for which less monitoring data is available should be included. The NORMAN network provided their list.

- Pharmaceuticals: the EEB list of pharmaceuticals and IAWR list were included in the SLoC even though European legislation managing pharmaceuticals already exists. Pharmaceutical compounds were also included in the NORMAN project.

- Grouping of Chemicals: a strategy is needed for grouping chemicals for specific substances having congeners (e.g. PAH – Polycyclic Aromatic Hydrocarbons -, PBDE - Polybrominated Diphenyl Ethers-, PCB - Polychlorinated Biphenyls-, PCDD/F - Polychlorinated Dibenzo-p-Dioxins and Polychlorinated Dibenzofurans-). However, there was no clear conclusion on this aspect and it was decided to run first the prioritisation process and then to study the possibility of grouping on a case by case basis.

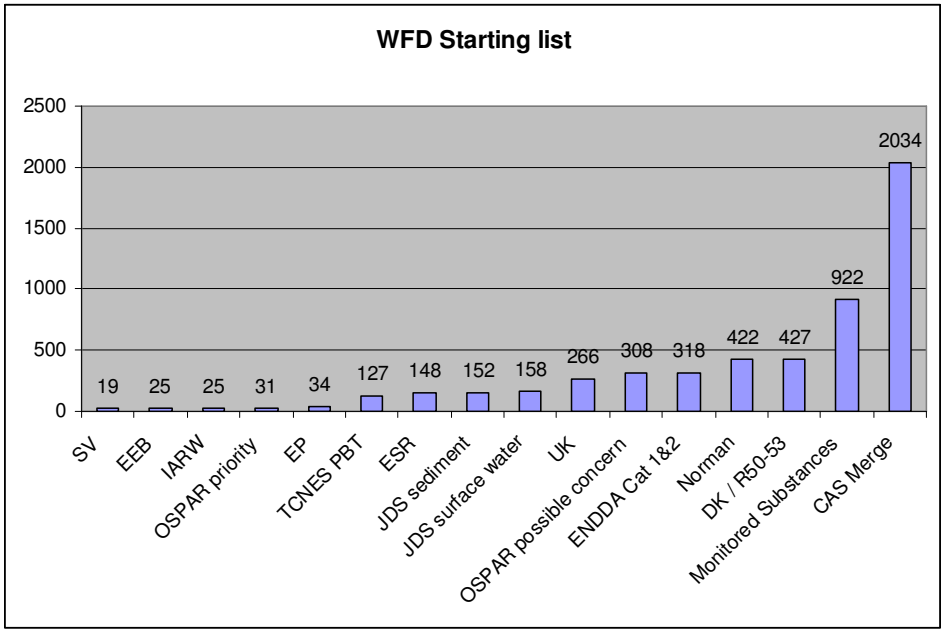

Figure 2. Starting list of Chemicals (SLoC): Contribution from different sources.

After combining all the lists, merged by CAS number, and eliminating repeated compounds, the final list contained 2034 compounds. Afterwards, for 1872 substances, the SMILES[1] codes were generated (see Fig. 3). In this step, a set of codes for substance identification was generated, if appropriate:

- Names: chemical names provided by the nominator, source database, IUPAC Name
- Identification Numbers: CAS, EINECS
- Chemical Structure: SMILES (http://www.daylight.com/dayhtml/doc/theory/theory.smiles.html), InChI (http://www.iupac.org/inchi/)

[1] The SMILES notification describes the molecular structure in short ASCII strings. Typically, a number of equally valid SMILES can be written for a molecule. Pipeline Pilot includes algorithms to ensure that the same SMILES is generated for a molecule regardless of the order of atoms in the structure. This SMILES is unique for each structure and is termed the Canonical SMILES.

The chemical structures were mainly taken from the Pre-registered substances (PRS) list – processed file (Daginnus, 2009). Substances that could not be identified by CAS within the PRS-list, were processed with ACD Name to generate the structure from the chemical name or data-mined from the Chemspider database (http://www.chemspider.com/).

Using the generated structures, the SMILES, InChI and the IUPAC names were generated with ACD Name (Advanced Chemistry Development, Inc, ON, Canada).

A "Parent SMILES" was generated and used as a standard input for the QSAR software by following a procedure using Pipeline Pilot (Accelrys; http://accelrys.com/): keep the largest fragment, protonated acids, de-protonated bases, canonical SMILES.

It was noticed that the SLoC merged by CAS includes some duplicates in structures identified by the Canonical SMILES substance and the Canonical SMILES parent.

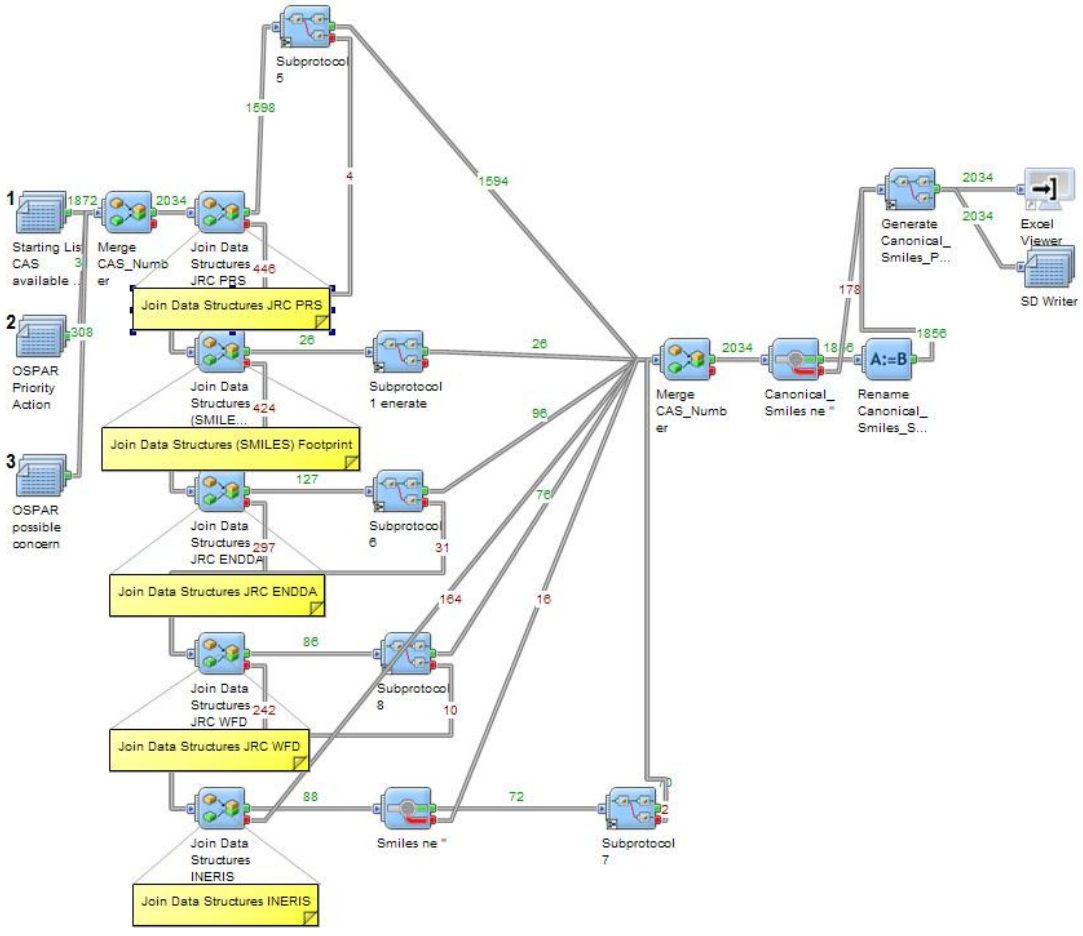

Figure 3. Algorithm for the generation of SMILES codes and the merging of compounds with the same CAS number (numbers in the links refers to the number of compounds).

Even though metals and organometallic compounds were present in the list, the majority of the tools developed for the estimation of physical, chemical and toxicological properties have been developed to

deal with organic compounds. Therefore, metals were not been treated with this approach, and only organometallic compounds for which experimental data were available were prioritised since correlations applied are out of the validity domain for which they were developed.

3. MODELLING-BASED PRIORITISATION APPROACH

3.1. OUTLINE

As discussed above, the risk scoring in the modelling-based prioritisation exercise is based on the integration of two separated scores provided after hazard and exposure assessment, plus an additional ranking step based on the PEC/PNEC ratios.

The scoring scheme for hazard assessment, which is a modified version from Wilkinson et al. (2007) after the discussion and comments from the WG-E Working Group on Prioritisation, is calculated as:

$$\text{Total Score} = Score_P + Score_B + Score_T + Score_{ED} \quad (1)$$

where P stands for Persistent (0/1), B= Bioaccumulative (0/1), T=Toxic (0/1) and ED = priority list of Endocrine Disruptors Cat. 1 and 2 (0/1). If the substance fulfils the criteria or fulfils all the screening assigned criteria for P or B or T or ED, +1 was added to the score. If the substance fulfils the vPvB (v = very) criteria or fulfils the screening assignment criteria the score is set to 4. In particular, the maximum hazard score is 4 which corresponds to a substance classified as PBT or vPvB, while the minimum score is 0, if the substance does not present P, B, T or ED characteristics.

The hazard assessment is preferably based on experimental data for the endpoints of bioaccumulation (B) and aquatic toxicity (T). For many substances the available data may not allow a definitive conclusion on PBT or vPvB properties. In this case so called screening criteria were used as surrogate information to decide whether a substance may fulfill the PBT or vPvB criteria. The screening criteria often include the application of non-testing methods like QSAR. According to Annex XI of the REACH regulation, QSAR results may be used instead of testing when all of the following conditions are met:

- The results are derived from a QSAR model whose scientific validity has been established.
- The substance falls within the applicability domain of the QSAR model.
- The results are adequate for the purpose of the risk assessment.
- Adequate and reliable documentation of the applied method is provided.

QSARs are generally valid for organic substances; metals and organometallic substances are generally out of the applicability domain of the QSARs employed here and therefore cannot be assessed.

The scoring scheme for exposure assessment, modified from Wilkinson et al. (2007), after the discussion and comments from the WG-E Working Group on Prioritisation, is shown in Table 1.

The exposure assessment score is obtained by calculating the annual use as:

$$\text{Use Assessment} = \text{Total Production} \cdot \text{Use Index} \quad (2)$$

Each contribution to Eq. (2) is explained in Table 2.

In this step, it was decided not to include the monitoring data provided by Member States to INERIS to avoid a bias in the results by using the same dataset as the monitoring-based prioritisation exercise.

Table 1. Exposure assessment scores. See Eq. (2) for the calculation.

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

Table 2. Release assessment.

Contribution	Index	Approach
A. How much is produced/ imported annually in EU?	Ton/year	Data from IUCLID and SPIN databases (Nordic Countries)
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

The final Risk scoring is obtained by combining the hazard and exposure assessment results using Table 3 (Wilkinson et al., 2007).

Table 3. Risk scores obtained by combining the hazard and exposure assessment results.

		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

Finally all the compounds classified with a value of "1" were ranked according to the PNEC/PEC ratio. The PNEC was obtained from existing experimental values or estimated using QSAR algorithms developed at the JRC (see below), whereas the PEC was calculated by applying the ECETOC Targeted Risk Assessment (TRA) tool and/or the OECD LRTP multimedia tool to calculate the distribution in water and the following equation:

$$PEC = Total\_production \cdot Use\_Index \cdot distribution\_in\_water / 25 \cdot 10^{9} \quad (3)$$

The value $25 \cdot 10^9$ refers to the $m^3 \cdot year^{-1}$ proposed in R.16 (Environmental exposure estimation) REACH Guidance (2008b) and applied in the ECETOC TRA tool to calculate PEC for several wide dispersive outdoor releases scenarios. In principle, this value should provide an upper bound to the PEC value.

This process has produced a ranked list of 78 compounds which should now be merged with the monitoring-based ranking as shown schematically in Fig. 1.

3.2. HAZARD ASSESSMENT

The hazard assessment was developed as a PBT assessment following the REACH Guidance on Information Requirements and Chemical Safety Assessment:

- Part B - Hazard Assessment
- Part C - PBT & vPvB assessment

or according to scientific progress when it was not clear how to distinguish between some categories, i.e. P or vP.

The Hazard Scoring was performed as:

- Total Score (PBT) = Score P (0/1) + Score B (0/1) + Score T (0/1) + Score ED (0/1)
- If the substance has been classified as P or B or T or is listed as endocrine active substance (CAT1&2), +1 has been added to the score.
- Total Score (vPvB) = 4

3.2.1 Persistence

To estimate the Persistence (P) of a compound in the environment we have followed the approach proposed in the ECHA Guidance (2008b) based on half-lives in water and sediment; whereas to estimate vP, we have used the OECD P_{ov} (overall persistence) and LRTP Screening Tool (Klasmeier et al. 2006; Scheringer et al., 2006).

Table 4 summarizes the criteria for assessing the persistency (P) or very persistency (vP) of a substance following ECHA (2008b) and the OECD tool.

Table 4. P and vP assessment criteria (TGD 2003; ECHA 2008b; Scheringer et al., 2006).

Criteria	Classification
P	Fresh(estuarine) water $t_{1/2}$>40 d, or marine water $t_{1/2}$>60 d, or Fresh (estuarine) sediment $t_{1/2}$> 120 d, or marine sediment $t_{1/2}$>180 d.
vP	P_{ov} >195 d and *CTD* >5097 km or *TE*> 2.25%. (see text for the explanation of parameters)

- <u>P screening</u>

For the P assessment, BIOWIN or BIOHCWIN, from the EPI suite™ v4.0 tool (Syracuse Research Corporation, NY, USA), were used to calculate persistence (see Fig. 4 for the Pipeline Pilot workflow). This approach is also mentioned in the ECHA Guidance (2008b) for assigning a screening P value. BIOHCWIN estimates the half life prediction of petroleum hydrocarbons, whereas BIOWIN estimates the rapid aerobic biodegradation of an organic compound in the presence of mixed populations of environmental microorganisms. In this aspect the ECHA Guidance (2008b) states that the screening assignment for substances is P, if:

- BIOWIN 3 < 0.5 (low probability of fast biodegradation) and BIOWIN 6 < 2.2 (ultimate biodegradation timeframe is equal or greater than months).

The BIOHCWIN was used for the P assessment of hydrocarbons because this module was specifically designed for these substances as recommended by ECHA Guidance (2008b, 2008c). The SMILES (Parent SMILES) was used as an input for the EPISUITE modules.

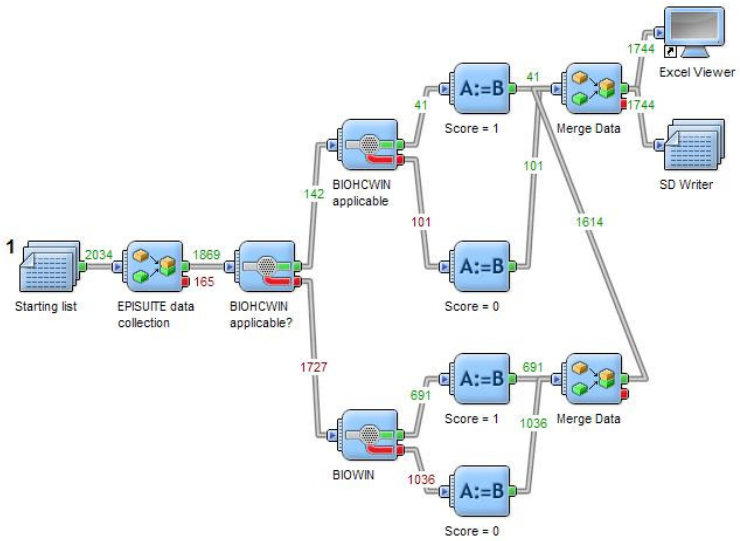

Figure 4. Pipeline Pilot workflow for the estimation of persistence scores.

Figure 4 shows that for 1869 substances a persistence score (0 or 1) was generated. The module BIOHCWIN was applicable to 142 substances from which 41 substances got a P assignment, whereas from 1727 in BIOWIN, 691 were assigned as P.

Moreover, the BIOWIN module (ECHA Guidance 2008b) was used to assess the ready biodegradability of substances, if:

- BIOWIN 3 is equal or greater than 2.75 (e.g. days or days to weeks) and
- BIOWIN 6 is equal or greater than 0.5 (the probability is high that the substance biodegrades fast)

This estimation was used as an input data for the exposure estimation using the ECETOC TRA tool (see Section 3.5).

- vP screening

For screening vP, the OECD P_{ov} and LRTP Screening Tool was employed. This tool requires the molecular weight, the octanol-water partition coefficient, K_{ow}, the air-water partition coefficient (Henry's law constant), K_{aw}, and the degradation half-lives for soil, marine water and air. The OECD Screening Tool provides the P_{ov} value which is the overall residence time of the chemical in the entire model system and two metrics for the LRTP: the first is the characteristic travel distance, *CTD* (km), which indicates the distance from a point source at which the chemical's concentration has dropped to 37% (e^{-1}) of its initial concentration; the second is the transport efficiency, *TE* (%), that estimates the percentage of emitted chemical that is deposited to surface media after transport away from the region of release.

The boundaries for the identification of a chemical as Persistent Organic Pollutant (POP)-like or non-POP-like are based on the values obtained for ten reference chemicals: six with high environmental half-lives and empirically known transport to remote regions, i.e. PCBs 28, 101, 180; hexachlorobenzene (HCB); α-hexachlorocyclohexane (α-HCH) and carbon tetrachloride; and four chemicals with low half-lives and less pronounced (or no) occurrence at remote locations, i.e. p-cresol, atrazine, biphenyl, aldrin. Using these reference values, four regions were identified; see fig. 5 (Scheringer et al., 2006):

- Region A: High persistence, High LRTP
- Region B: Low persistence, High LRTP
- Region C: High persistence, Low LRTP
- Region D: Low persistence, Low LRTP

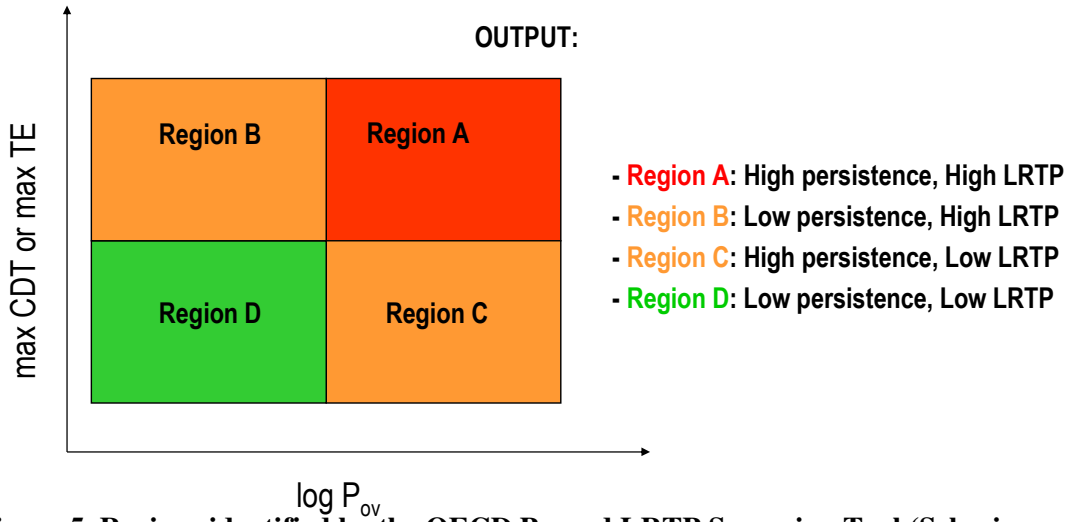

Figure 5. Regions identified by the OECD P_{ov} and LRTP Screening Tool (Scheringer et al. 2006).

3.2.2 Bioaccumulation

According to EC (2003) and ECHA (2008b), bioaccumulation assessment should be based preferably on the measurement of the bioconcentration factor (*BCF*) in aquatic species (normally fish) and the *BMF* (biomagnification factors). The criteria are (EC, 2003; ECHA, 2008b):

- BCF > 2000 L kg^{-1} BCF< 5000 L kg^{-1} → B
- BCF > 5000 L kg^{-1} →vB

In addition if the measured BMF is higher than one this implies convincing evidence of bioaccumulation through the food chain (ECHA, 2008b). According to ECHA (2008b), the standard test to study the BCF in fish is the OECD 305 bioconcentration test guideline (OECD, 1996).

If no data are available, the substance can be considered as not B and not vB if it has a log $K_{ow} \leq 4.5$ and no specific mechanisms of uptake (ECHA 2008c). In addition to log K_{ow}, non-testing data such as the molecular size (average maximum diameter and maximum molecular length), molecular weight and octanol solubility, may be used in a weight of evidence approach for the assessment. (ECHA, 2008b). Furthermore, QSARs may be used provided that the model is appropriate for the chemical class (ECHA, 2008c).

After a discussion by the WG-E Working Group of Prioritisation, it was proposed to use experimental BCF values when available (Arnot BCF database in EPISUITE contained 307 experimental data points, whereas Footprint database contained 312) and to apply QSAR models when no experimental data existed using the worst case QSAR estimated values for this screening phase.

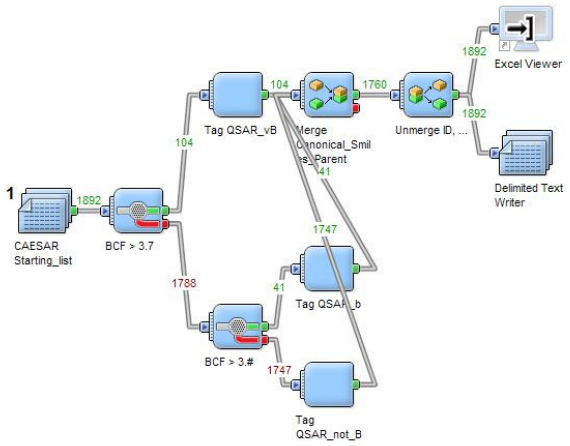

Figure 6. Pipeline Pilot workflow for the calculation of Bioaccumulation.

Three modelling approaches were applied to estimate BCF: EPI Suite™ (BCFBAF), CAESAR[2] bioaccumulation (http://www.caesar-project.eu/index.php?page=results&section=endpoint&ne=1) and

[2] CAESAR is an EU funded project, which was specifically dedicated to develop QSAR models for the REACH legislation. Five endpoints are addressed in CAESAR; one is the bio-concentration module

a JRC BCF model[3] (see Fig. 6). These QSAR models represent the state-of-the-art for QSAR bio-concentration models. They are not (yet) covered in the REACH guidance, because they appeared later in time. The error of prediction for all the models, about 0.5 log units, is in the range of experimental variability.

In all cases, the Canonical Smiles Parent of the substances were used to generate the predictions. A BCF_{max} was generated and used to assign a score, BCF_{mean} and BCF_{StdDev} were used to assess the coherence of the prediction.

3.2.3 Toxicity

According to the REACH legislation (Annex XIII), a substance is considered to fulfill the toxicity criterion (T) when:

- the long-term no-observed effect concentration (NOEC) for marine or freshwater organisms is less than 0.01 mg L^{-1}, or
- the substance is classified as carcinogenic (category 1 or 2), mutagenic (category 1 or 2), or toxic for reproduction (category 1, 2 or 3), or
- there is evidence of chronic toxicity, as identified by the classifications: T, R48, or Xn, R48 according to Directive 67/548/EEC.

For the determination of a definitive criterion for T, chronic tests must be performed. The standardised chronic tests on fish, daphnia and algae are preferred to assess the NOEC. Only a few QSAR models predicting chronic aquatic toxicity are available but further research on the QSAR prediction of chronic toxicity may increase their predictive capacities. Therefore at the current state of the art, QSAR models seem not to be applicable for the definitive assessment of the T criteria (ECHA Guidance 2008c).

Table 5. Toxicity assessment.

Type of data	Criterion	Screening assignment	Definitive assignment
Short-term aquatic toxicity	EC50 or LC50 $\geq$ 0.1 mg·L^{-1}	presumably not T	-
Short-term aquatic toxicity	EC50 or LC50 < 0.1 mg·L^{-1}	potentially T	-
Short-term aquatic toxicity	EC50 or LC50 < 0.01 mg·L^{-1}	-	T

A substance is considered to potentially meet the criterion for T classification when an acute E(L)C50 value from a standard E(L)C50 toxicity test (REACH Annexes VII to X) is less than 0.1 mg L^{-1}. The toxicity criterion (T) for PBT assessment cannot be decided on the basis of acute studies alone. If the screening criterion is met, the substance is referred to definitive T testing, and then chronic studies are required regardless of the tonnage band unless the E(L)C50 < 0.01 mg L^{-1}. Table 5 summarizes the approach. At preliminary stages in the assessment, in cases where no acute or chronic toxicity data are

[3] The JRC BCF QSAR model was generated by ADMET predictor software using the experimental data in the EPISUITE PhysProp database, 307 compounds.

available, the assessment of the T criterion at a screening level can be performed using data obtained from QSARs for acute aquatic toxicity (ECHA, 2008b).

For this exercise, in addition to the analysis of existing data from several databases, i.e. Footprint (http://www.eu-footprint.org, chronic/acute data various taxa pesticides), ECETOC Technical Report 91 (http://www.ecetoc.org/, chronic/acute data various taxa), DSSTOX (http://www.epa.gov/ncct/dsstox/, acute toxicity data for fish), four QSAR models were applied.

The structure of the workflow for the toxicity prediction combining experimental estimated values is represented in Fig. 7. The workflows were generated to follow the priorities: chronic over acute data, experimental data over QSAR estimation.

The QSAR models were generated by the ADMET modeler software (Simulations Plus, CA, USA; http://www.simulations-plus.com).[4]

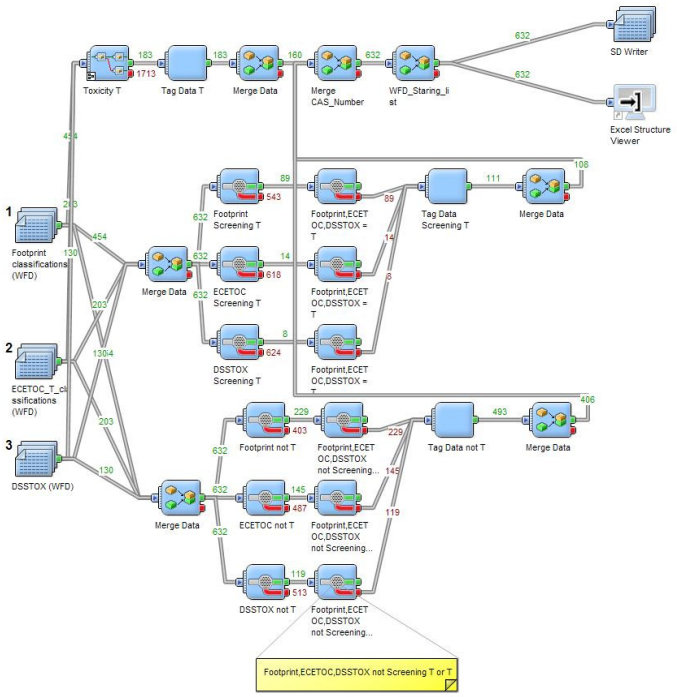

Figure 7. Pipeline Pilot flowchart for the screening of toxicity from the SLoC.

[4] ADMET modeller is an integrated part of the ADMET predictor software that automates the difficult and tedious process of making high quality predictive structure-property models from sets of experimental data. It works seamlessly with ADMET Predictor structural descriptors as its inputs, and appends the selected final model back to ADMET Predictor as an additional predicted property.

ADMET Modeler automates each of the following steps necessary to build high quality predictive models:

- Filtering descriptors to eliminate those that are underrepresented, those with very small variance, and those that are highly correlated with other descriptors.
- Clustering of compounds to identify similar structures and ensure intelligent selection of training, verification, and test sets (Kohonen map)
- Rank ordering descriptors to select the best ones to use for a particular model architecture (Sensitivity Analysis)
- Training a matrix of model ensembles to allow selection of the most appropriate architecture
- Automatic selection of the best ensemble to use as the final predictive model

The ADMET modeler software was used to generate 3 JRC acute aquatic toxicity models using the DSSTOX dataset using 577 experimental data (EPA fathead minnow acute toxicity database), generated by different modeling methods (multi-linear regression, kernel partial least squares regression, artificial neural network) and the DSSTOX dataset to generate the QSAR model. Additionally the ADMET predictor proprietary model for aquatic toxicity – based on the DSSTOX dataset – was used to assign screening scores in a consensus approach, see Fig. 8.

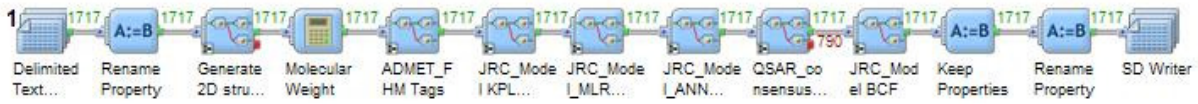

Figure 8. Screening T consensus approach plus data for bioaccumulation, generated by the ADMET predictor software.

The screening assignment T was assigned in a consensus approach, if 3 or 4 QSAR models classifications agree on the T classification.

3.3. EXPOSURE ASSESSMENT

To complement the monitoring-based approach which depends on the availability of monitoring data, with the consequent risk of missing substances that are not subject to monitoring programmes by Member States, and therefore increasing the risk of false negatives, we have developed a parallel approach based on the use assessment.

As a first step data DG-ENV requested to ECHA data from ECHA/SIEFs registration process. However the data is not available yet, therefore other sources of data have been used. In particular an algorithm to extract data from IUCLID (http://iuclid.echa.europa.eu/) was implemented as well as data from SPIN[5] (http://www.spin2000.net/), the Nordic database on the use of substances in products which was provided by their curators.

The IUCLID database contains data which were collected through an obligation put on producers and importers of high production volume chemicals and low production volume chemicals by the Existing Substances Regulation EEC 793/93 (Allanou 1999; accessible from http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=hpv).

A workflow was generated to merge IUCLID with the SLoC, to calculate the sum of the production volumes for the last reported year and to extract the use and type of use of the substances.

The IUCLID-SloC-CAS-merge contains more than 15000 dossiers, merged to 931 substances. The data collection covers data in the time period from 1990 to 2005. The use patterns (see Table 2) were

[5] 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.

applied to generate the release index. In case of reported uses as pesticides, cosmetics and pharmaceuticals the release index was set to 1. The maximum and minimum release indices were calculated, the use assessment score is based on the release $index_{max}$. Figure 9 shows the results of the exposure scoring using IUCLID data.

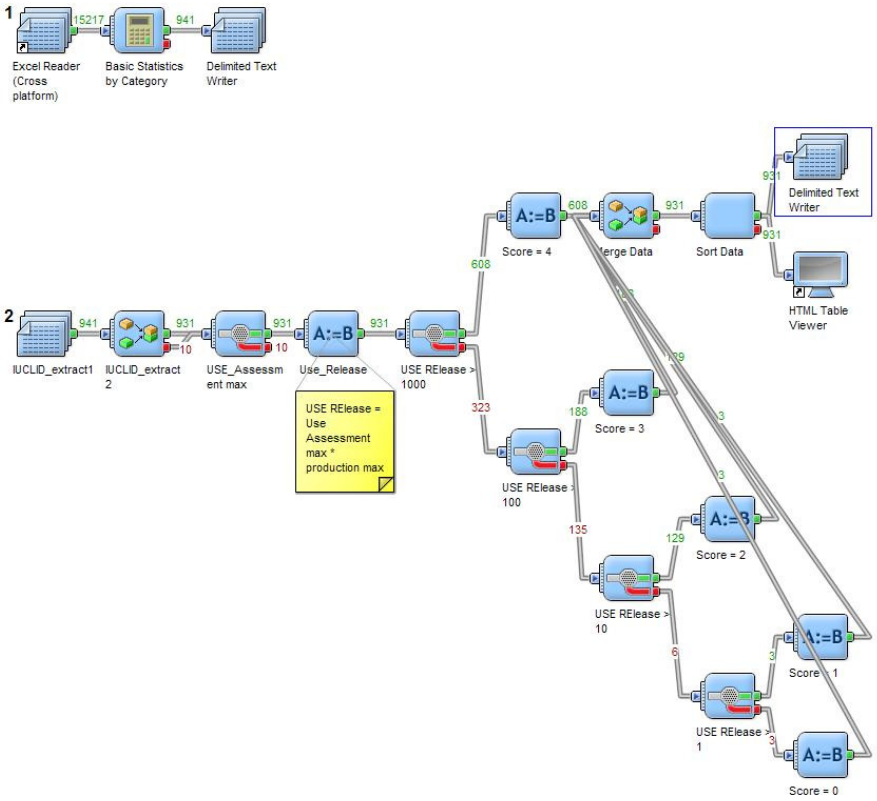

Figure 9. Pipeline Pilot workflow for the generation of use assessment scores.

Moreover the SPIN database was data-mined (Skov, 2009). SPIN collects data from the use of substances in products in the Nordic countries. Production volumes from 2006 and 2007 were collected, divided by 2 and multiplied by 20 (population factor) to estimate the use of substances at the European scale. Information on the industrial use of the use categories was translated to IUCLID types of uses and IUCLID uses to assign a release index to the substance. Figure 10 shows the exposure scoring by using SPIN data. Compared to IUCLID there are less data available. In the later case, when no information is available from IUCLID, tonnages from SPIN were extrapolated to European scale to be comparable with IUCLID data. Of course, depending of the use of chemicals this factor should be evaluated on a case by case basis. However, since we were performing a first screening and also because IUCLID data is relatively old (1999-2005), making the intercomparison between both databases difficult, it was felt that when recent data from ECHA will become accessible, after December 2010, a more accurate calculation could be performed.

To assess exposure information on overall tonnage used in the area of concern (EU preferably for this exercise), as well as to estimate fractions of this tonnage going to particular uses and emissions by

simplified categories using Table 3 as a first approximation, the use of substances in products was assessed considering information from both databases (see results). When several uses were possible, the more dispersive was selected.

The cases in which both information on monitoring and tonnage/uses were available, allowed the development of a combined single score.

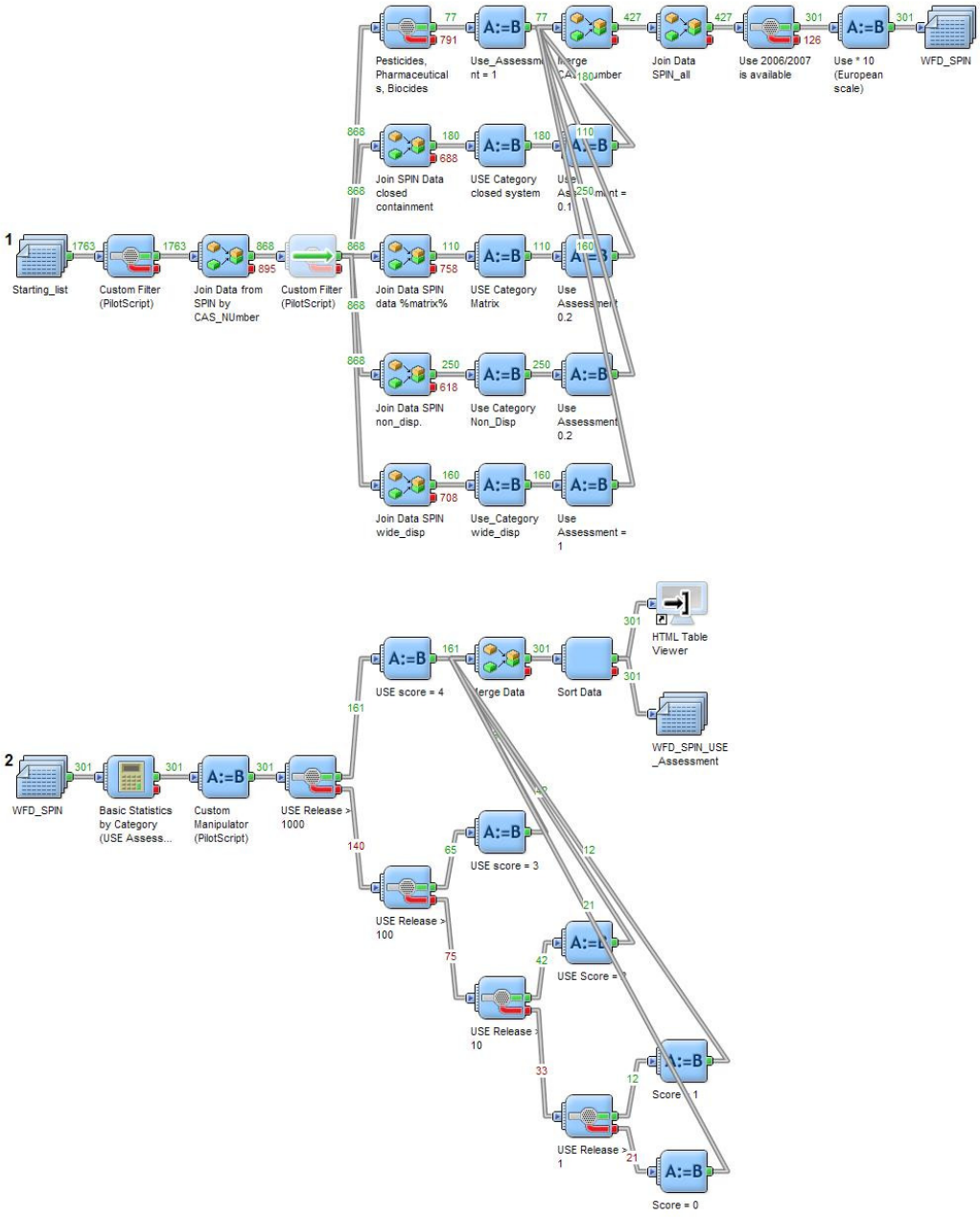

Figure 10. Pipeline Pilot workflow for exposure scoring by using the SPIN database.

3.4. PEC CALCULATION: MULTIMEDIA MODELLING

To calculate Predicted Environmental Concentrations (PEC) in the water compartment and to have a ranking of substances characterized by a risk score equal to 1, a simple multimedia model has been

implemented (Figure 11). Multimedia models predict the distribution of a chemical between several environmental compartments. In this modelling-based prioritisation exercise the model considers air, water and soil compartments and it is the one incorporated in the OECD P_{ov} and LRTP Screening Tool. The model provides the percentage of distribution between these compartments on the fraction of the emitted tonnage.

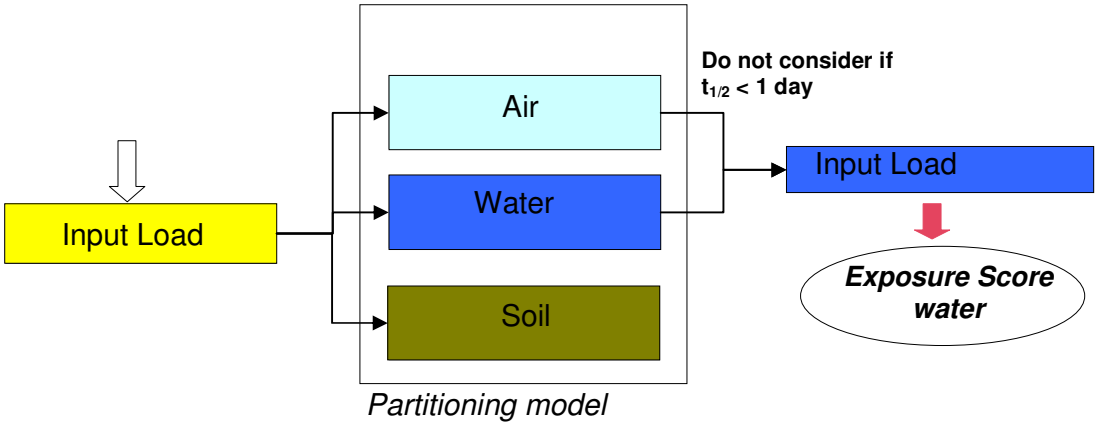

Figure 11. Modelling-based exposure scoring.

This approach calculates PEC in water compartment by multiplying the annual tonnage of each substance by two parameters, i.e. the percentage of distribution in water in relation to soil and air provided by the OECD multimedia model and the Use Index used in the Exposure assessment (see Table 2) and by dividing the result by the water volume of 25.109 m3 suggested in the REACH guidance chapter R.16 (ECHA, 2008d).

The results from this approach have been used as comparison with the outcomes provided by the ECETOC TRA tool based on pre-defined and conservative exposure scenarios (see Section 3.5).

3.5. PEC CALCULATION: ECETOC TRA TOOL

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

- **Tier 0**: to screen chemicals and conditions of no immediate concern out of the process and to identify chemicals and conditions where further targeting risk assessment is required.
- **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)

In addition a tool in Excel was developed to implement and apply this approach. The tool contains the user interface and the datasheets to perform risk assessment for workers and consumers and to predict

the environmental concentration (PEC) in water, soil and sediment compartments. The tool is freely downloadable after registration from the ECETOC website (http://www.ecetoc.org/tra).

In this work we were interested only in the algorithms that estimate the environmental concentrations, and specifically the concentrations in fresh water. In this case, the minimal amount of data necessary to run the tool (i.e. mandatory input) is reported in Table 6.

Table 6. Mandatory input required by ECETOC TRA tool to estimate PEC in local freshwater compartment. ERC = Environmental Release Category.

ECETOC mandatory input		Measurement unit
Substance identification	IUPAC name	
	CAS number	
	Sector of use (SU)	
Physico-chemical properties	Molecular weight	g/mol
	Vapor pressure	Pa or hPa
	Water solubility	mg/L
	Partition coefficient octanol/water	Kow or logKow
	Biodegradability test result	
Environmental exposure scenario	Tonnage	tons/year
	Fraction of tonnage to region	
	ERC code	

Figure 12 shows, as an example, the user interface for the application of the ECETOC TRA tool.

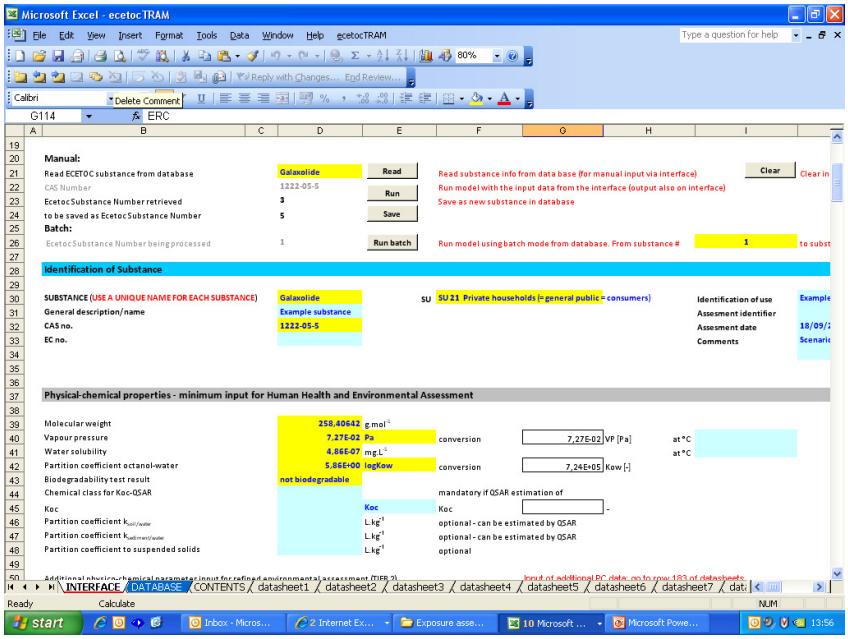

Figure 12. Example of application of ECETOC TRA tool.

3.6. PNEC CALCULATION

PNECs were calculated with preference for experimental data over QSAR and NOEC over EC50. Several databases were mined to find toxicological data, see Section 3.7. When no PNEC was

accessible, the data were combined in a developed algorithm to estimate a value for each specific compound.

For substances having experimental data, $PNECs_{aquatic}$ were calculated according to the TGD 2003 (EC,2003) as:

$$PNEC_{aquatic} = aquatic\ toxicity\ /\ Assessment\ factor\ (AF) \quad (4)$$

Assessment factors were based also on TGD 2003, see Table 7. In case of data gaps and the application of QSAR provisional PNECs were calculated using the mean of the predicted EC50 from the 4 modules and the assessment factor 1000.

Table 7. Assessment factors for aquatic toxicity

Available data	Assessment factor (AF)
At least one L(E)50 from each trophic level from the base set (fish, daphnia and algae)	1000
One long term NOEC (either fish or daphnia)	100
Two long term NOECs from two trophic levels (fish and/or daphnia and/or algae)	50
Long term NOECs from each trophic level from the base set (fish, daphnia and algae)	10

3.7. DATA COLLECTION

Experimental data were employed whenever possible. For this reason, several databases were screened. When no experimental data were available several algorithms to estimate physico-chemical and toxicological properties were applied and, if no method was available, QSAR approaches were specifically developed for some parts. QSAR models are being introduced in the QSAR Model Database operated by the Joint Research Centre (http://ecb.jrc.ec.europa.eu/qsar/); in this database, QSARs are documented in accordance with OECD validation principles (OECD, 2007).

Figures 13-16 summarize the workflow developed to query several databases and to merge the results for the model-based prioritisation exercise. In particular, we have used the experimental values in EPI Suite™ concerning several physico-chemical properties and we have queried Footprint (NOECs, EC50 for pesticides), ECETOC (NOECs, EC50) and DSSTOX (EC50) for mining experimental data. In addition, Fig. 17 shows, as an example the type and number of data we got from these databases.

As an example, Fig. 14 shows how the ECETOC database was data-mined:

- Step 1
    - Filter the following taxa: algae, daphnia and fish
    - Filter NOECs and
    - Filter EC50s

Calculate Statistics (number of values including the maximum, minimum and mean values)

- Step 2
    - Merge data (with preference to chronic data)
    - Join data (with SLOC)

- Classifications (based on minimum values)

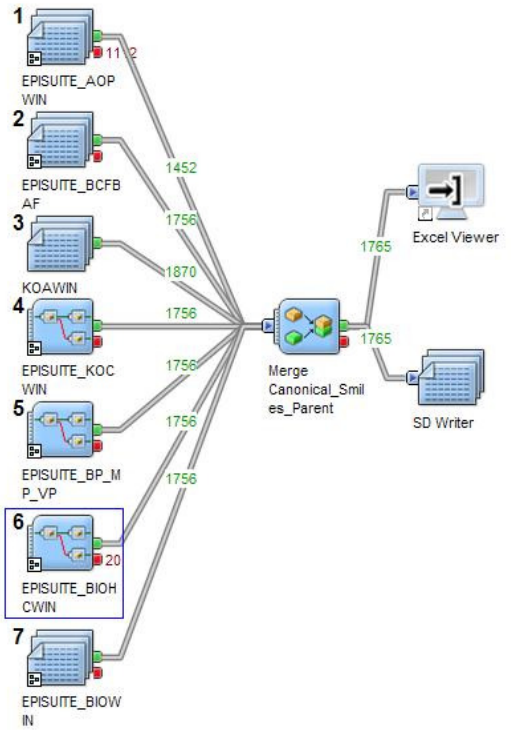

Figure 13. Pipeline Pilot workflow for EPI Suite™ data collection.

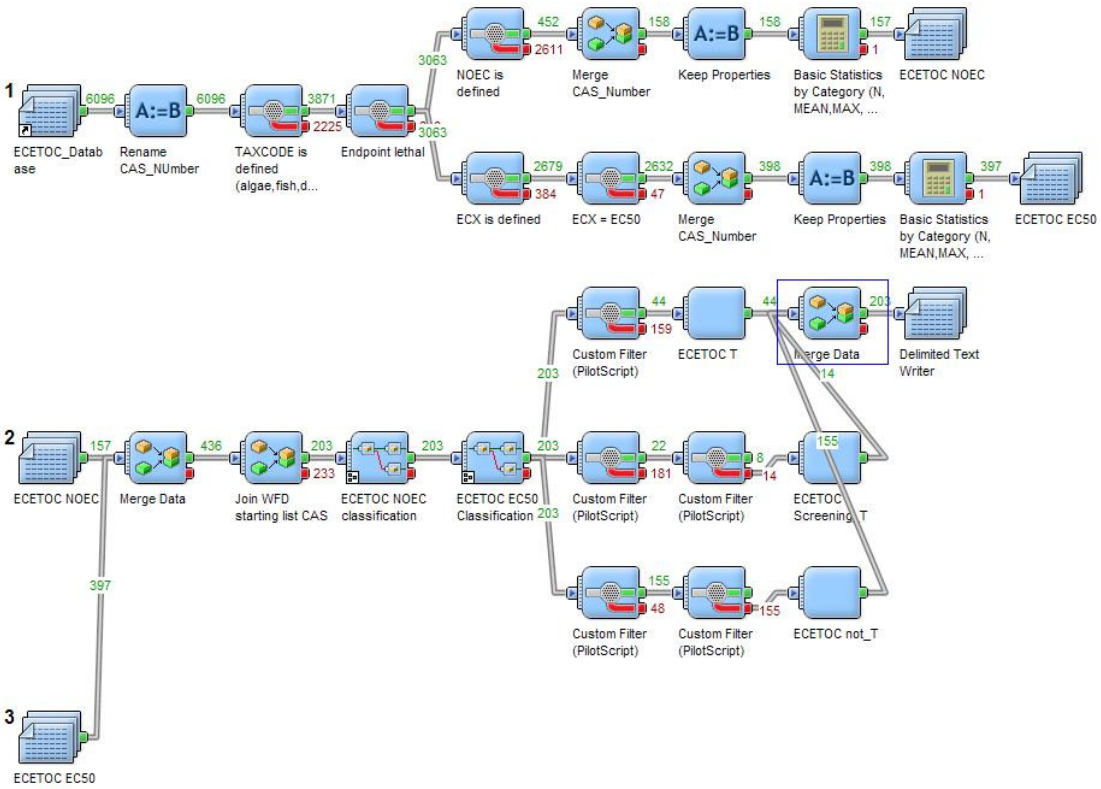

Figure 14. Pipeline Pilot workflow for ECETOC data mining, merging and classification.

In addition, to apply the ECETOC TRA tool, we have collected also data concerning use assessment for 827 and for 301 substances of the SLoC from IUCLID and SPIN, respectively.

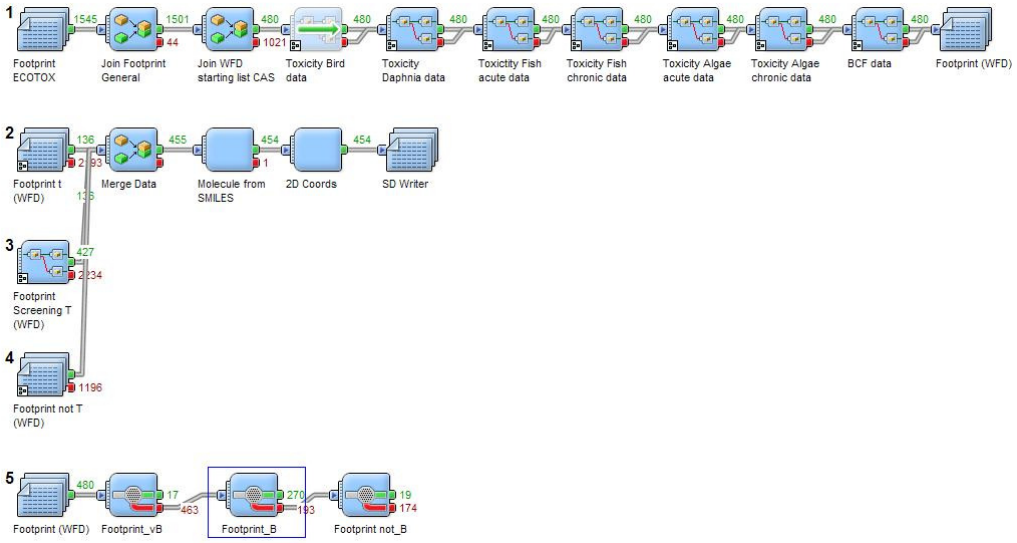

Figure 15. Pipeline Pilot workflow for Footprint data mining, merging and classification.

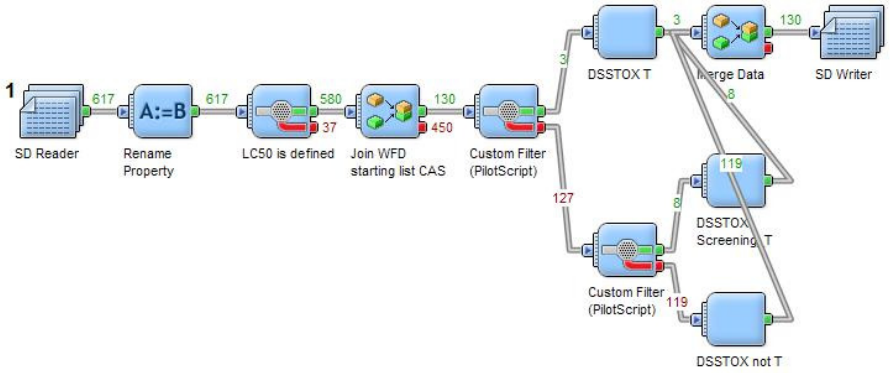

Figure 16. DSSTOX data mining, merging and classification.

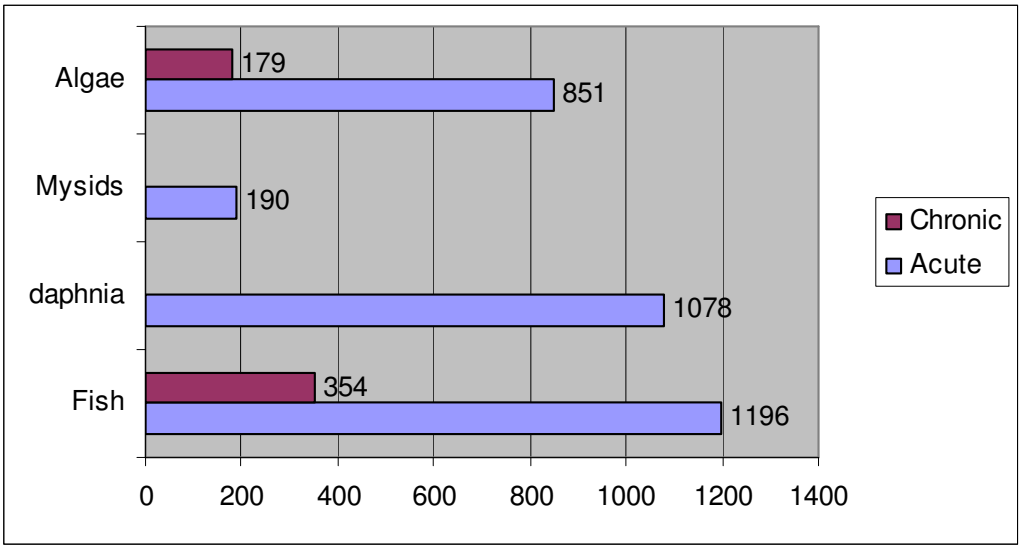

Figure 17. Toxicity data availability in the Footprint database as an example.

4. RESULTS OF THE MODELLING-BASED PRIORITISATION EXERCISE

Excel files containing the main results obtained during the model-base exercise are attached in an accompanying CD. The interested reader can consult the files for the results.

4.1. RESULTING LIST OF CANDIDATE (RANGED) SUBSTANCES

Excel files containing the main results obtained during the model-base exercise are attached in an accompanying CD. The interested reader can consult the files for the results.

The risk ranging procedure is presented in Fig. 18. The first part represents the PBT assessment, whereas the last part contains the exposure assessment. Red lines in the work flow and numbers indicated there represent the substances that could not be assessed on each part of the process. As can be observed from the initial 2034 substances, the risk ranging process could be performed for 737 substances. The main bottleneck in this process was the production and use data which were not available for a considerable proportion of the substances in the SLoC. It is foreseen that with REACH more data will become available after December 2010 and therefore, the approach will cover a major number of substances. We should also highlight that IUCLID data sometimes referred to the beginning of 00's and therefore certain values could not be representative of the actual situation.

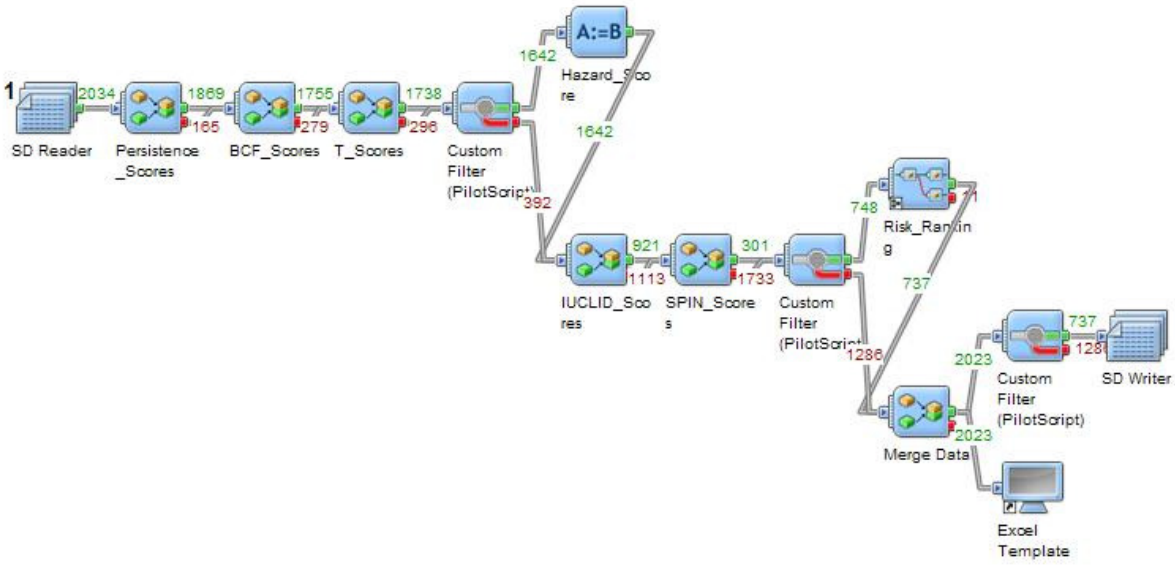

Figure 18. Risk ranging procedure and output.

4.2. RESULTING LIST OF RANKED (RISK RATIO) SUBSTANCES

A summary of the 2034 SLoC substances as well as their physico-chemical properties is provided in the excel file in the accompanying CD: WFD_prioritization_summary.xls. The results of the model-based prioritisation are summarized in the Excel file: WFD_Risk_ranking_1.xls. The first page

contains the parameters, units and definitions of the columns in the Excel file. The final list ranked according the risk ratio, PEC/PNEC, for the 78 compounds classified as 1, is provided as supporting material on the above mentioned Excel file (second sheet called Risk_Ranking_1). The use of the chemical their application and the type of industry using it is provided in the Excel file: WFD_IUCLID_Industry_TYPE_Use.xls. The related RCR (Risk Characterisation Ratio) of each substance was calculated by dividing the PEC by the PNEC value. The calculations as well as the results are reported in the Excel file: ECETOC_application_Score1_PECvsPNEC_October2009.xls. The results of the application of the different methodologies and tools are discussed in Section 5.

5. DISCUSSION

During the model-based prioritisation exercise, several comparisons between the results obtained with different estimation methods and existing experimental results were performed to check the validity of the approaches. However, due to time constraints and the large number of compounds, it was not possible to perform a detailed analysis on a case by case basis. Here we present several results that provide an assessment of the global validity of the proposed approach. In principle, experimental data were preferred over estimation algorithms and they were used to compare with the predictions, and to analyze which method provided a better alternative for the SLoC list of compounds.

5.1. APPLICATION OF THE OECD P_{ov} AND LRTP SCREENING TOOL

To calculate the parameters needed for the application of the tool, the following considerations were made:

- Octanol-Water partition coefficient (K_{ow}):

The estimation of K_{ow} has been performed using EPI suite™ v4.0 when no data was available. In case of experimental values these has been inserted, approx. 895. Figure 19 shows comparison between the estimated $\log_{10}K_{ow}$ versus measured values.

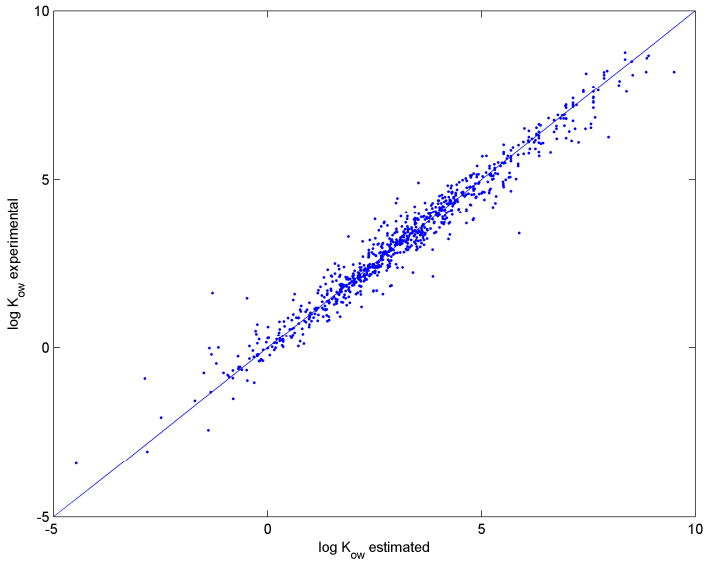

Figure 19. Measured versus estimated $\log_{10}K_{ow}$ using EPI suite v4.0 for the SLoC.

- Air-water partition coefficient (K_{aw})

This value can be calculated from Henry's law constant, H, as:

$$K_{aw} = \frac{H}{R \cdot T} \tag{5}$$

where R is the ideal gas constant and T is a reference temperature (298.16 K). The Henry law constant was calculated using the bond method (Hine and Mookerjee, 1975) in EPI suite™ v4.0.

- Water half-life

The water half-life was assigned based on BIOWIN3 output using the correction proposed by Aroson et al. (2006) and summarized in Table 8.

Table 8.Default water half-live values from BIOWIN3 output (correction proposed by Aroson et al., 2006).

BIOWIN3 category		
Descriptor	**Model output**	**Water half live (h)**
Hours	>4.75	4.1
Hours-days	4.25-4.75	30
days	3.75-4.25	56
Days-weeks	3.25-3.75	208.1
Weeks	2.75-3.25	360
Weeks-months	2.25-2.75	900
months	1.75-2.25	2880
recalcitrant	1.25-1.75	5760
recalcitrant	<1.25	17280

- Air half-life

The air half-life was estimated using the estimated atmospheric oxidation value calculated in EPI suite™ v4.0

- Sediment half-life

The sediment half-life was estimated applying default values as defined in EPI suite™ by doubling the water half life values.

- Preliminary screening

A preliminary screening produced the following results. There were 16 chemicals for which the calculation was not possible because EPI suite™ was not able to provide a log K_{aw} estimate or for which the air half-life was set to zero. Examples of these are:

a) Not log K_{aw} estimate: fentin chloride; chlorotrioctylstannane; trichlorooctylstannane; chlorotricyclohexylstannane; dichlorodioctylstannane; dibutyltin oxide; dibutylbis(pentane-2,4-dionato-O,O')tin, etc.

b) Zero air half-life: hexachloroethane; carbon tetrachloride; 1,1,2-trichlorotrifluoroethane; chlordecone, etc.

c) Both problems: potassium 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulphonate; Perfluorooctane sulphonic acid potassium salt; potassium heptadecafluorooctane-1-sulphonate; Perfluorooctane sulphonic acid; lithium salt; lithium heptadecafluorooctanesulphonate, etc.

In addition, there were more than 130 chemicals for which the calculated values (mainly for log K_{ow} and log K_{aw}) were outside the range considered by the software which are:

- $-11 < \log K_{aw} < 2$
- $-1 < \log K_{ow} < 10$

- 10^{-4}< air $t_{1/2}$ <10^{10}
- 10^{-4}< water $t_{1/2}$ <10^{10}
- 10^{-4}< soil $t_{1/2}$ <10^{10}

To allow the calculation for all chemicals log K_{aw} was set to -45 (lower value calculated) and air $t_{1/2}$ to 10^{-6} hours.

- Preliminary results

If we classify chemicals as persistent and long range transport as those that have a P_{ov} >195 days, and a CTD> 5097 km or a TE > 2.25%; and non-persistent and non LRTP as those that have a P_{ov} <195 days, and a CTD< 5097 km and a TE < 2.25% and intermediate those that are between these values, we obtain the following results (see Fig. 20):

1. Persistent: 138 compounds (13.2%)
2. Intermediate 346 compounds (33.1%)
3. Non-persistent: 561 compounds (53.68%)

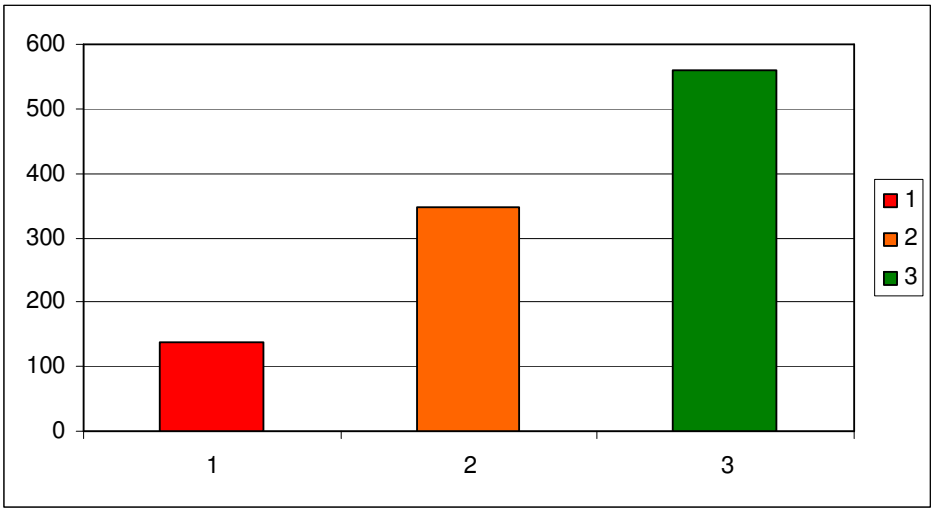

Figure 20. Chemicals classified according with their persistence and LRTP.

Figure 21 shows the distribution of all analyzed compounds in the classes defined in the OECD LRTP screening tool. Similar calculations has been carried out for the list of Plant Protection Products (PPP, Directive 91/414/EEC, 889 compounds) and corresponding registered chemicals (60384 compounds) with the following percentages: persistent: 6.5 and 9.1%, intermediate: 31.1 and 22.7% and non-persistent: 62.4 and 68.2%, respectively. In general terms, the results seem to agree with our expectations in the sense than the SLoC contains higher percentages of persistent chemicals indicating therefore that the preliminary selection has been done properly.

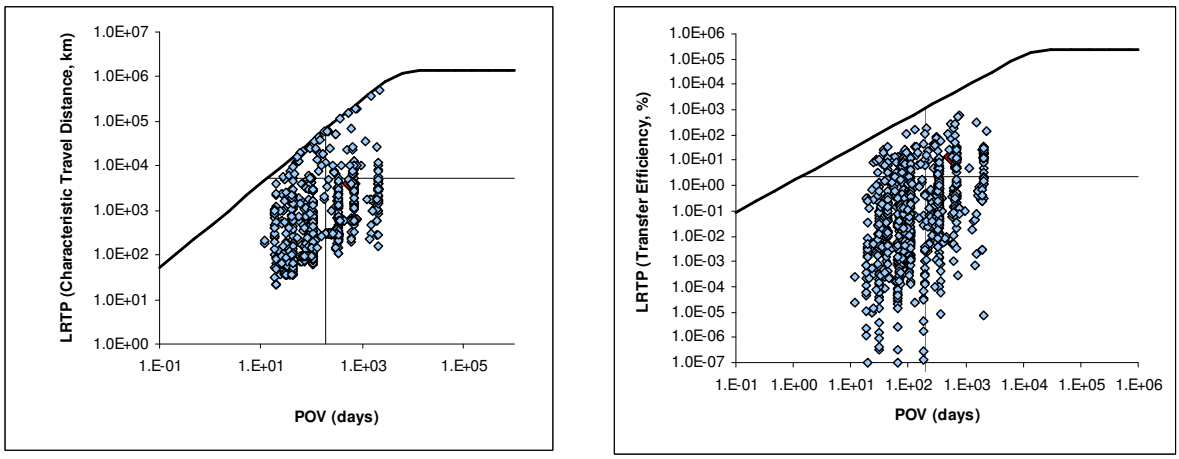

Figure 21. Example of results on the classification of Persistence and Long Range Transport for the SLoC.

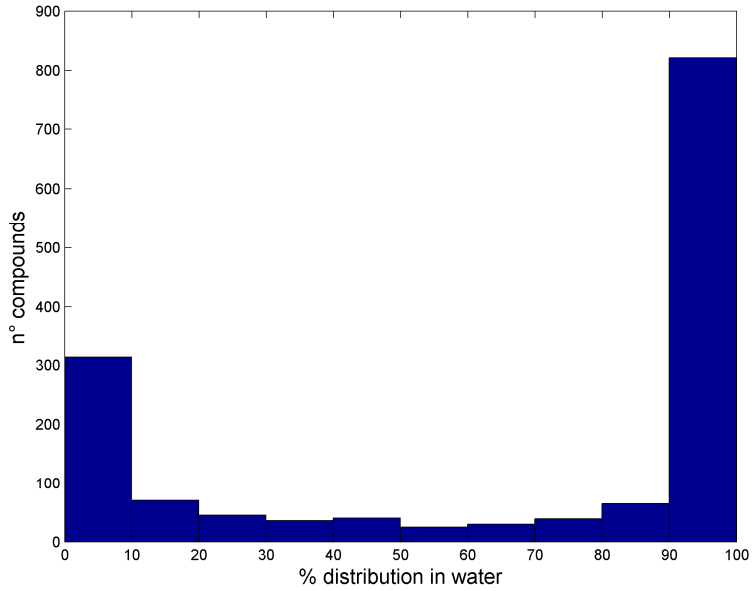

Figure 22. Percentage of distribution in water calculated using the OECD P_{ov} and LRTP Screening Tool.

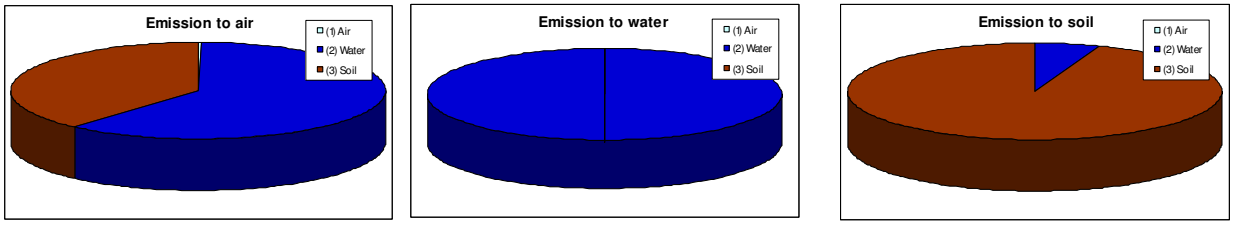

Figure 23. Example of distribution results of the multimedia model as a function of emissions scenarios for Alachlor (Emission to air: P_{ov} = 64 days; CDT = 90 km; Emission to water: P_{ov} = 173 days; CDT = 298 km; Emission to soil: P_{ov} = 328 days; Overall: P_{ov} = 328 days CDT = 298 km).

Figure 22 shows the histogram of the distribution of the percentage in water as a function of the number of compounds in the SLoC. As can be observed, there are two main groups at the extremes, highly hydrophobic and highly hydrophilic compounds. In the first case, these compounds will tend to be attached to organic matter and stay in soil/sediments, but normally they will tend to bioaccumulate in the food web. Typically, these are industrial chemicals. In the second case, the compounds will tend to dissolve in water and therefore high concentrations may be expected, but normally these compounds tend to degrade fast than the other group. Plant protection products typically fall in this category. The multimedia model was used to calculate the percentage distribution between air, water and soil and the water value used to estimate a high limit PEC value, see Eq. (2). Figure 23 shows, as an example, the results obtained for Alachlor.

5.2. BIOCONCENTRATION FACTOR ASSESSMENT

The BCFWIN program from EPI Suite™ has several estimation methods for the *BCF* of organic compounds from its log K_{ow} with specific rules for ionic compounds taking into account biotransformation rates in fish (Arnot et al., 2008). For example Figure 24 shows predicted *BCF*s, by the regression-based estimate (Meylan et al., 1999) and the Arnot-Gobas upper trophic level including biotransformation rates estimates (Arnot and Gobas, 2003), and experimental *BCF*s. Also several correlations based on log K_{ow} has been proposed. For example, the correlation of Veith et al. (1979), $\log BCF = 0.85 \cdot \log K_{ow} - 0.7$, was indicated in EC (2003).

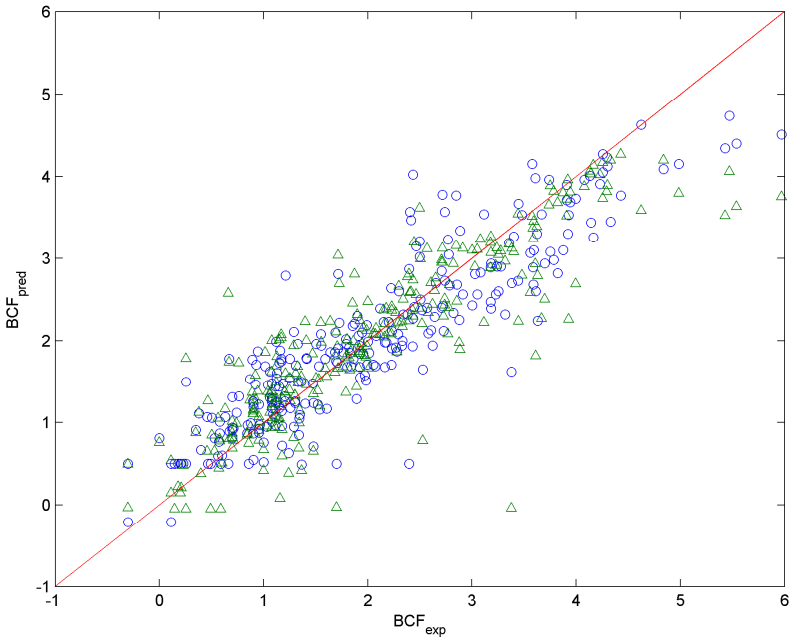

Figure 24. Predicted BCFs using the regression-based estimate method (circles) and the Arnot-Gobas upper trophic level (triangles) in BIOWIN (EPI Suite™) for the SLoC. The first method is approximately 22% more accurate.

5.3. TOXICITY ASSESSMENT

In a recent study (Crane et al., 2008) on the application of non-testing methods to characterize chemicals, it was concluded that the sole reliance on Quantitative Structure-Activity Relationships (QSARs) to estimate acute and chronic toxicity is not recommended and toxicological data are still necessary. However, in the absence of these data a combined approach using several methodologies could be useful in a first screening phase to assess if a substance is potentially toxic. For example Figure 25 shows the application of several software packages to estimate different type of toxic effects.

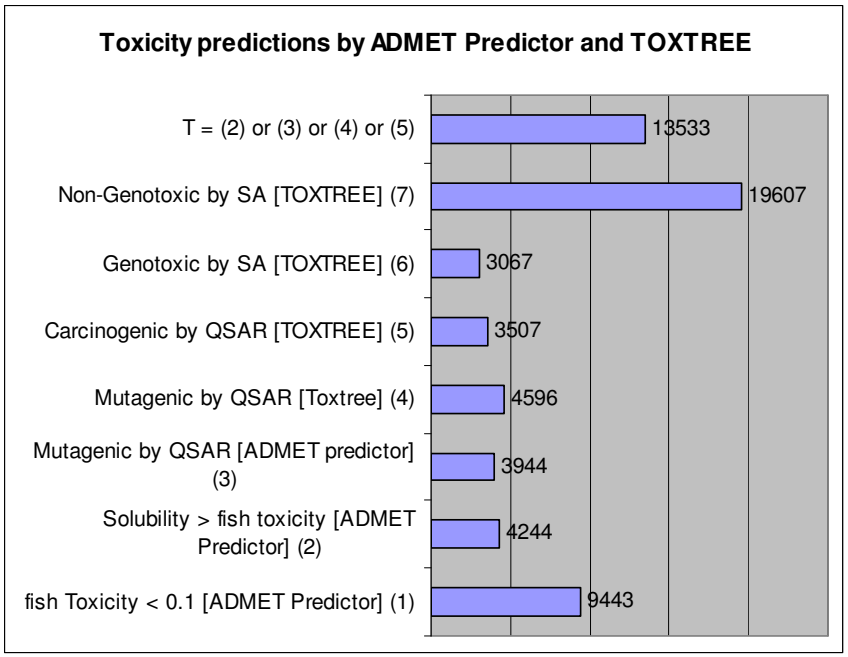

Figure 25. Examples of combined toxicity prediction for Pre-Registered Substances.

In this work, when toxicological information was not available, several QSARs were developed to estimate toxicity for the screening of the substances as well as for the calculation of PNEC values. Figure 26 shows for example the statistical data for the QSAR model (observed/predicted LC_{50}), generated by an artificial neural network. The QSAR models are going to be reported in a separate publication.

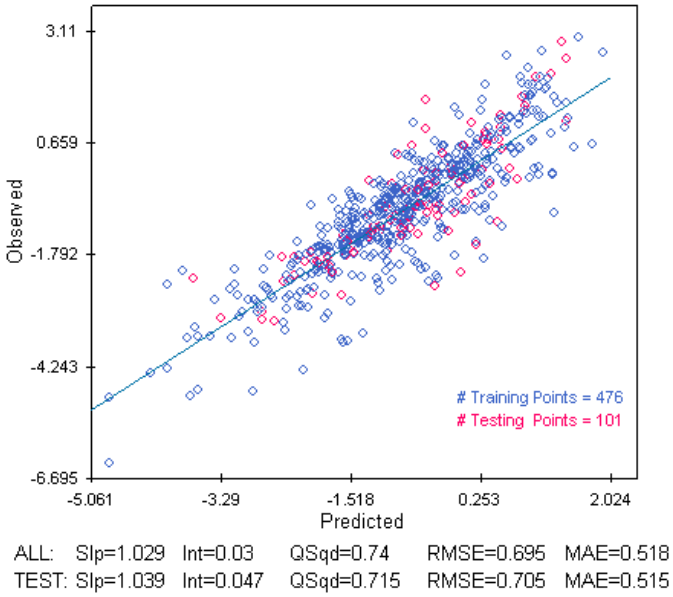

Figure 26. Example of an "in-house" developed QSAR to predict toxicity.

5.4. PEC CALCULATION

A summary of input data entered into the ECETOC TRA tool for the group of substances (i.e. 78) characterized by a risk score of 1 are reported in Table 9a-c (these data are also in the accompanying CD, file ECETOC_application_Score1_PECvsPNEC_October2009.xls).

As far as physico-chemical properties are concerned, experimental data were preferred to QSAR-predicted data if available. Information on industrial activity, use type, use pattern and annual production volume of each substance was extracted from the IUCLID database (Allanou et al, 1999).

This information allowed selecting the most appropriate Sector of Use (SU) from a list of options reported on the REACH guidance chapter R.12 (ECHA, 2008c). The tonnage per year required by ECETOC TRA tool was calculated by summing up data on production volumes of the same substance provided by all industries in Europe for the most recent year. A fraction of 1 (100%) or 0.1 (10%) can also be selected in line with the REACH Guidance chapter R.16 (ECHA, 2008d) reporting that "The most conservative assumption is that 100 % of the manufacturers or importers tonnage per year is applied at one site (i.e. fraction = 1). If it is known that the production or processing sites are numerous, various in size and randomly distributed over Europe, a 10 % rule can be applied by assuming that 10 % of the amount produced or imported is used at the local scale (i.e. fraction = 0.1)". Accordingly in the modelling-based prioritisation exercise a fraction of 0.1 was applied to the annual tonnage assuming that production and/or processing sites are quite distributed all over Europe. The most appropriate ERC code of each substance was selected from a drop menu referring to the REACH guidance chapter R.16 (ECHA, 2008d), where a short description of each exposure scenario and related parameters are provided.

Table 9a. Input data to the ECETOC TRA tool for considered substance. MW= Molecular Weight, VP=Vapour Pressure, S=Solubility, K_{ow}= octanol/water partitioning coefficient; SU=Sector of Use; ERC=Environmental Release Category.

CAS	Name	MW	VP (Pa)	S (mg/L)	log Kow	Biodegradability	Industrial activity	SU	Use type	Use pattern	Use Index	Tonnage	ERC
101-05-3	Anilazine	275.52	8.27E-07	8.00E+00	3.92	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	5000	ERC10b
107-64-2	Dimethyldioctadecylammonium chloride	551.06	1.17E-14	5.25E-02	10.75	Not readily	Chemical Industry: used in sinthesis	SU9	Wide dispersive	Antistatic agents	1	183150	ERC2
1085-98-9	Dichlofluanide	333.23	1.49E-05	1.30E+00	3.38	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	10000	ERC10b
1120-36-1	Tetradecene	196.38	2.00E+00	1.62E-02	7.49	Readily	Chemical industry: used in sinthesis	SU8	Wide dispersive	Intermediates	0.5	156000	ERC6a
115-32-2	Dicofol	370.49	5.31E-05	8.00E-01	5.24	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	5550	ERC10b
1163-19-5	Bis(pentabromophenyl) ether	959.22	6.23E-10	2.50E-02	9.46	Not readily	Polymers industry	SU8	Inclusion into matrix	Flame retardants and fire preventing agents	0.2	50500	ERC6d
118-74-1	Hexachlorobenzene	284.78	2.40E-03	6.20E-03	5.71	Not readily	Chemical industry: used in sinthesis	SU8	Non dispersive Closed systems	Intermediates	0.2	15000	ERC6a
118-82-1	2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol	424.67	2.90E-06	3.92E-06	9.63	Readily	Polymers industry	SU8	Inclusion into matrix	Lubricants and additives	0.5	1000	ERC2
119-47-1	6,6'-di-tert-butyl-2,2'-methylenedi-p-cresol	340.51	3.31E-07	2.00E-02	7.04	Not readily	Polymers industry	SU8	Inclusion into matrix Wide dispersive	Stabilizers	0.5	77660	ERC6C
120-82-1	1,2,4-trichlorobenzene	181.45	61.33	4.90E+01	4.13	Not readily	Chemical Industry: used in sinthesis	SU8	Closed systems	Intermediates	0.2	16000	ERC6a
1222-05-5	4,6,6,7,8,8-hexamethyl-1,3,4,6,7,8-hexahydrocyclopenta[g]isochromene	258.41	7.27E-02	4.86E-04	5.86	Not readily	Personal and domestic use (cosmetics)	SU21	Wide dispersive	Odour agents Cleaning/washing agents and disinfectants	1	27475	ERC8a
122-34-9	simazine	201.66	2.95E-06	6.20E+00	2.34	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	9450	ERC10b
128-69-8	isochromeno[4',5',6':6,5,10]anthra[2,1,9-def]isochromene-1,3,8,10-tetrone	392.33	1.09E-11	7.03E-05	3.20	Not readily	Paints, lacquers and varnishes industry Chemical Industry: used in synthesis	SU9	Wide dispersive	Intermediates	0.5	4550	ERC8c
133-49-3	pentachlorobenzenethiol	282.4	6.76E-04	1.21E-03	5.69	Not readily	Polymers industry	SU11	Inclusion into a matrix	Mastication agents for natural or synthetic rubber	0.2	5000	ERC6d
13356-08-6	bis(tris(2-methyl-2-phenylpropyl)tin) oxide	1052.71	3.01E-19	1.14E-02	13.63	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	3050	ERC10b
135-91-1	4,4'-methylenebis[N,N-diethylaniline]	310.486	7.81E-05	5.29E+00	6.22	Not readily	Chemical industry: used in synthesis	SU8	Non dispersive use	Intermediates	0.2	1600	ERC6a
13680-35-8	4,4'-methylenebis[2,6-diethylaniline]	310.486	6.19E-07	1.87E+00	5.18	Not readily	Chemical industry: used in synthesis	SU8	Non dispersive use	Intermediates	0.1	50	ERC6a
1461-25-2	tetrabutyltin	347.18	0.259974	6.40E-05	9.37	Not readily	Chemical industry: used in synthesis	SU8	Non dispersive use	Intermediates	0.2	5000	ERC6a
1582-09-8	trifluralin	335.285	6.11E-03	1.84E-01	4.76	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	145900	ERC10b
1861-40-1	benfluralin	335.285	8.71E-03	1.00E-01	4.90	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	100	ERC10b
1897-45-6	chlorothalonil	265.914	7.60E-05	6.00E-01	3.65	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	11650	ERC10b
1912-24-9	atrazine	215.687	3.85E-05	3.47E+01	2.76	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	21860	ERC10b
2082-79-3	octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	530.881	4.51E-11	3.72E-02	12.00	Not readily	Polymers industry	SU8	Non dispersive use	Stabilizers	0.2	74305	ERC6c
21725-46-2	cyanazine	240.697	1.84E-05	1.70E+02	2.08	Not readily	Agricultural industry	SU1	Non dispersive use	Other	0.2	13500	ERC10a

Table 9b. Input data to the ECETOC TRA tool for considered substance. MW= Molecular Weight, VP=Vapour Pressure, S=Solubility, K_{ow}= octanol/water partitioning coefficient; SU=Sector of Use; ERC=Environmental Release Category.

CAS	Name	MW	VP (Pa)	S (mg/L)	log Kow	Biodegradability	Industrial activity	SU	Use type	Use pattern	Use Index	Tonnage	ERC
21850-44-2	1,1'-(isopropylidene)bis[3,5-dibromo-4-(2,3-dibromopropoxy)benzene]	943.663	8.48E-13	2.16E-03	9.84	Not readily	Chemical industry: used in synthesis	SU9	Non dispersive use	Flame retardants and fire preventing agents	0.2	3500	ERC6a
2303-17-5	tri-allate	304.668	1.60E-02	4.00E+00	4.51	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	10150	ERC10b
2312-35-8	propargite	350.48	4.00E-05	5.00E-01	4.65	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	5150	ERC10b
25103-58-6	tert-dodecanethiol	202.404	41.19588	9.54E+00	5.57	Not readily	Polymers industry	SU8	Use in closed system	Process regulators	0.2	43500	ERC4
25637-99-4	hexabromocyclododecane	641.731	2.64E-06	1.52E-02	7.43	Not readily	Textile processing industry	SU5	Non dispersive use	Flame retardants and fire preventing agents	0.2	23500	ERC6a
2921-88-2	chlorpyrifos	350.589	2.71E-03	1.12E+00	4.81	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	65050	ERC10b
294-62-2	cyclododecane	168.324	3.119688	6.59E-02	6.09	Not readily	Chemical industry: used in synthesis	SU9	Use in closed system	Intermediates	0.1	200000	ERC6a
31565-23-8	di(tert-dodecyl) pentasulphide	498.985	7.60E-07	1.96E-02	12.00	Not readily	Metal extraction, refining and process	SU2	Non dispersive use	Lubricants and additives	0.2	5000	ERC4
31570-04-4	tris(2,4-ditert-butylphenyl) phosphite	646.94	6.32E-12	3.23E-03	12.00	Not readily	Polymers industry	SU8	Use resulting in inclusion into or onto	Stabilizers	0.2	357005	ERC5
3194-55-6	1,2,5,6,9,10-hexabromocyclodecane	613.677	1.32E-05	7.05E-02	5.88	Not readily	Polymers industry	SU8	Use resulting in inclusion into or onto matrix	Flame retardants and fire preventing agents	0.2	40000	ERC5
32534-81-9	diphenyl ether, pentabromo derivative	564.717	4.13E-06	1.63E-02	7.45	Not readily	Polymers industry	SU8	Use resulting in inclusion into or onto matrix	Flame retardants and fire preventing agents	0.2	3550	ERC5
32536-52-0	diphenyl ether, octabromo derivative	801.421	4.91E-09	2.03E-03	8.72	Not readily	Polymers industry	SU8	Use resulting in inclusion into or onto matrix	Flame retardants and fire preventing agents	0.2	39200	ERC5
3520-72-7	4,4'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[2,4-dihydro-5-methyl-2-phenyl-3H-pyrazol-3-one]	623.505	1.01E-18	5.19E-05	6.56	Not readily	Paints, lacquers and varnishes indust	SU10	Use resulting in inclusion into or onto matrix	Colouring agents	0.5	51400	ERC2
38521-51-6	2,3,4,5,6,alpha-hexabromotoluene	565.548	8.45E-05	2.62E-02	6.37	Not readily	Chemical industry: used in synthesis	SU8	Use in closed system	Intermediates	0.1	1000	ERC6a
3861-47-0	4-cyano-2,6-diiodophenyl octanoate	497.115	3.09E-05	5.18E-01	5.71	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	1050	ERC10b
42576-02-3	methyl 5-(2,4-dichlorophenoxy)-2-nitrobenzoate	342.137	1.33E-05	3.98E-01	4.34	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	1000	ERC10b
469-61-4	[3R-(3alpha,3abeta,7beta,8aalpha)]-2,3,4,7,8,8a-hexahydro-3,6,8,8-tetramethyl-1H-3a,7-methanoazulene	204.358	1.84E-02	2.35E-01	6.29	Not readily	Personal and domestic use	SU21	Wide dispersive	Cosmetics	1	4000	ERC8c
470-90-6	chlorfenvinphos	359.575	1.00E-03	1.24E+02	4.09	Not readily	Agricultural industry	SU1	Wide dispersive	Pesticides	1	1500	ERC10b
4979-32-2	N,N-dicyclohexylbenzothiazole-2-sulphenamide	346.56	8.239176	1.17E+00	6.02	Not readily	Polymers industry	SU8	Non dispersive use	Vulcanizing agents	0.2	13050	ERC6a
50-29-3	clofenotane	354.492	2.13E-05	5.50E-03	6.58	Not readily	Chemical industry: used in synthesis	SU9	system	Intermediates	0.1	5000	ERC6a
5102-83-0	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxobutyramide]	685.614	6.16E-21	2.38E-02	6.02	Not readily	Paints, lacquers and varnishes indust	SU10	inclusion into or onto matrix	Colouring agents	0.2	16200	ERC2
5216-25-1	alpha,alpha,alpha,4-tetrachlorotoluene	229.922	3.319668	3.27E+00	4.63	Not readily	Chemical industry: used in synthesis	SU9	Non dispersive use	Intermediates	0.2	15505	ERC6a
52315-07-8	alpha-cyano-3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate	416.307	0.173316	4.00E-03	6.07	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	3100	ERC10b
52434-90-9	1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione	728.725	1.57E-13	3.40E+01	3.64	Not readily	Polymers industry	SU8	Use resulting in inclusion into or onto matrix	Flame retardants and fire preventing agents	0.2	500	ERC5
52-68-6	trichlorfon	257.439	1.04E-03	1.20E+05	0.88	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	1050	ERC10b

Table 9c. Input data to the ECETOC TRA tool for considered substance. MW= Molecular Weight, VP=Vapour Pressure, S=Solubility, K_{ow} = octanol/water partitioning coefficient; SU=Sector of Use; ERC=Environmental Release Category.

CAS	Name	MW	VP (Pa)	S (mg/L)	log Kow	Biodegradability	Industrial activity	SU	Use type	Use pattern	Use Index	Tonnage	ERC
52740-90-6	1-amino-N-(3-bromo-9,10-dihydro-9,10-dioxo-2-anthryl)-9,10-dihydro-9,10-dioxoanthracene-2-carboxamide	551.361	5.85E-18	4.53E-03	4.61	Not readily	Chemical industry: used in synthesis	SU8	Non dispersive use	Intermediates	0.2	1700	ERC6a
5468-75-7	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxobutyramide]	657.56	2.73E-20	2.98E-02	5.39	Not readily	Paints, lacquers and varnishes indust	SU10	inclusion into or onto matrix	Colouring agents	0.2	51250	ERC2
55283-68-6	ethalfluralin	333.269	1.17E-02	3.00E-01	4.51	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	4000	ERC10b
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]	818.502	2.40E-23	9.57E-03	5.17	Not readily	Paints, lacquers and varnishes indust	SU10	inclusion into or onto matrix	Colouring agents	0.2	65350	ERC2
5598-13-0	chlorpyrifos-methyl	322.535	5.60E-03	4.76E+00	4.16	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	325	ERC10b
56-35-9	bis(tributyltin) oxide	596.12	1.00E-03	1.00E+02	3.84	Not readily	Paints, lacquers and varnishes indust	SU10	Wide dispersive use		1	5100	ERC8f
5915-41-3	terbuthylazine	229.714	1.49E-04	8.50E+00	3.28	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	3350	ERC10b
60207-90-1	1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole	342.227	5.60E-05	1.10E+02	3.43	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	2550	ERC10b
61213-25-0	3-chloro-4-(chloromethyl)-1-[3-(trifluoromethyl)phenyl]pyrrolidin-2-one	312.12	4.40E-04	3.51E+01	3.72	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	1000	ERC10b
629-59-4	tetradecane	198.395	1.546512	2.20E-03	7.85	Readily	Chemical industry: used in synthesis	SU9	Non dispersive use	Intermediates	0.2	15000	ERC6a
63449-39-8	Paraffin waxes and Hydrocarbon waxes, chloro	411.456	1.05E-03	1.23E-01	6.65	Not readily	Chemical industry: used in synthesis	SU8	Wide dispersive use	fluds, lubricants, falme	0.5	51150	ERC2
64131-85-7	O,O,O-tris(4-nitrophenyl) thiophosphate	477.348	2.75E-06	3.79E-01	5.48	Not readily	Chemical industry: used in synthesis	SU8	Use in closed system	Intermediates	0.1	1000	ERC6a
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	1177.66	9.84E-29	3.15E-01	12.00	Not readily	Polymers industry	SU12	Non dispersive use	Stabilizers	0.2	77255	ERC6a
67747-09-5	N-propyl-N-[2-(2,4,6-trichlorophenoxy)ethyl]-1H-imidazole-1-carboxamide	376.672	1.51E-04	3.40E+01	4.20	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	5550	ERC10b
67774-74-7	undecylbenzene	232.412	0.171	1.00E-02	7.91	Not readily	Personal and domestic use	SU21	Wide dispersive use	Cleaning/washing agents and disinfectants	0.5	2492100	ERC8d
68442-68-2	4-(1-phenylethyl)-N-[4-(1-phenylethyl)phenyl]aniline	377.533	8.59E-08	3.99E-03	8.18	Not readily	Polymers industry	SU12	Wide dispersive use	Stabilizers	0.5	6600	ERC6C
7287-19-6	prometryn	241.36	2.66E-04	3.30E+01	3.51	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	1300	ERC10b
731-27-1	N-{[dichloro(fluoro)methyl]sulfanyl}-N',N'-dimethyl-N-(4-methylphenyl)sulfuric diamide	347.259	2.66E-02	9.00E-01	3.90	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	2000	ERC10b
732-26-3	2,4,6-tri-tert-butylphenol	262.438	8.81E-02	3.50E+01	6.06	Not readily	Fuel industry	SU8	Non dispersive use	Fuel additives	0.2	705	ERC2
74070-46-5	2-chloro-6-nitro-3-phenoxyaniline	264.67	1.60E-05	2.50E+00	4.04	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	5000	ERC10b
77-47-4	hexachlorocyclopentadiene	272.774	7.9992	1.80E+00	5.04	Not readily	Chemical industry: used in synthesis	SU9	Wide dispersive use	Flame retardants and fire preventing agents	0.5	55000	ERC5
79-94-7	2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol	543.897	4.61E-09	6.19	6.87	Not readily	Polymers industry	SU12	Non dispersive use	Flame retardants and fire preventing agents	0.2	42500	ERC6a
81-15-2	5-tert-butyl-2,4,6-trinitro-m-xylene	297.269	8.47E-05	5.39	3.48	Not readily	Personal and domestic use	SU21	Wide dispersive use	Cosmetics	1	1670	ERC8c
834-12-8	ametryn	227.333	3.65E-04	2.09E+02	2.91	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	6150	ERC10b
84852-53-9	1,1'-(ethane-1,2-diyl)bis[pentabromobenzene]	971.277	2.53E-11	3.22E-03	10.11	Not readily	Polymers industry	SU12	Non dispersive use	Flame retardants and fire preventing agents	0.2	500	ERC5
87-68-3	hexachlorobuta-1,3-diene	260.762	29.3304	3.20E+00	4.66	Not readily	Chemical industry: used in synthesis	SU9	Non dispersive use	Heat transferring agents	0.2	2500	ERC6a
886-50-0	terbutryn	241.36	2.25E-04	2.50E+01	3.46	Not readily	Agricultural industry	SU1	Wide dispersive use	Pesticides	1	1300	ERC10b
93-46-9	N,N'-di-2-naphthyl-p-phenylenediamine	360.461	1.91E-09	3.00E-04	7.58	Not readily	Polymers industry	SU8	Non dispersive use	Antioxidants	0.2	500	ERC6c
96-69-5	6,6'-di-tert-butyl-4,4'-thiodi-m-cresol	358.546	2.89E-08	0.442	7.24	Not readily	Polymers industry	SU8	Non dispersive use	Stabilizers	0.2	5100	ERC6c

Based on input data in Table 9a-c a PEC value in freshwater was calculated for each substance as reported in the following Table 10a-b. In case the estimated PEC value turned out to be higher than the solubility value, the latter one was chosen as value to be used for prioritisation purposes, i.e. for calculation of RCR (Risk Characterisation Ratio).

The selection of an appropriate ERC for each compound was not an easy task and needs expert assessment. Moreover we encountered some problems in their application (see next section). For some compounds, the production volumes extracted by IUCLID were old (1999-2005) so more realistic data (if available) should be considered in a future revision phase. Moreover for some compounds having a risk score of 1, no production volumes were available which prevented us from completing the prioritisation process.

Finally even though the ECETOC TRA tool provides a choice of several life cycle stages, the same stage (i.e. “use”) was chosen for all substances due to a lack of information.

Table 10a. PEC values estimated by the ECETOC TRA tool for 78 substances.

CAS	Name	ECETOC PEC (mg/L)	Solubility Corrected ECETOC PEC (mg/L)
101-05-3	Anilazine	1.49E-01	1.49E-01
107-64-2	Dimethyldioctadecylammonium chloride	6.98E-01	5.25E-02
1085-98-9	Dichlofluanide	3.09E-01	3.09E-01
1120-36-1	Tetradecene	1.54E+00	1.62E-02
115-32-2	Dicofol	1.15E-01	1.15E-01
1163-19-5	Bis(pentabromophenyl) ether	2.78E-03	2.78E-03
118-74-1	Hexachlorobenzene	4.33E+00	6.20E-03
118-82-1	2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol	3.18E-02	3.92E-06
119-47-1	6,6'-di-tert-butyl-2,2'-methylenedi-p-cresol	1.22E+01	2.00E-02
120-82-1	1,2,4-trichlorobenzene	4.81E+00	4.81E+00
1222-05-5	4,6,6,7,8,8-hexamethyl-1,3,4,6,7,8-hexahydrocyclopenta[g]isochromene	3.12E-02	4.86E-04
122-34-9	simazine	3.11E-01	3.11E-01
128-69-8	isochromeno[4',5',6':6,5,10]anthra[2,1,9-def]isochromene-1,3,8,10-tetrone	2.28E-03	7.03E-05
133-49-3	pentachlorobenzenethiol	1.56E-02	1.21E-03
13356-08-6	bis(tris(2-methyl-2-phenylpropyl)tin) oxide	4.62E-05	4.62E-05
135-91-1	4,4'-methylenebis[N,N-diethylaniline]	2.70E+00	2.70E+00
13680-35-8	4,4'-methylenebis[2,6-diethylaniline]	1.54E-01	1.54E-01
1461-25-2	tetrabutyltin	7.68E-01	6.40E-05
1582-09-8	trifluralin	2.77E+00	1.84E-01
1861-40-1	benfluralin	1.60E-03	1.60E-03
1897-45-6	chlorothalonil	3.45E-01	3.45E-01
1912-24-9	atrazine	7.19E-01	7.19E-01
2082-79-3	octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	1.76E-01	3.72E-02
21725-46-2	cyanazine	2.66E-03	2.66E-03
21850-44-2	1,1'-(isopropylidene)bis[3,5-dibromo-4-(2,3-dibromopropoxy)benzene]	4.85E-01	2.16E-03
2303-17-5	tri-allate	2.35E-01	2.35E-01
2312-35-8	propargite	1.29E-01	1.29E-01
25103-58-6	tert-dodecanethiol	2.06E+02	9.54E+00
25637-99-4	hexabromocyclododecane	3.37E+00	1.52E-02
2921-88-2	chlorpyrifos	1.41E+00	1.12E+00
294-62-2	cyclododecane	2.72E+00	6.59E-02
31565-23-8	di(tert-dodecyl) pentasulphide	3.55E+00	1.96E-02
31570-04-4	tris(2,4-ditert-butylphenyl) phosphite	8.33E+00	3.23E-03
3194-55-6	1,2,5,6,9,10-hexabromocyclodecane	4.20E+02	7.05E-02
32534-81-9	diphenyl ether, pentabromo derivative	6.28E+01	1.63E-02
32536-52-0	diphenyl ether, octabromo derivative	6.26E+01	2.03E-03
3520-72-7	4,4'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[2,4-dihydro-5-methyl-2-phenyl-3H-pyrazol-3-one]	4.56E+00	5.19E-05
38521-51-6	2,3,4,5,6,alpha-hexabromotoluene	1.50E+00	2.62E-02
3861-47-0	4-cyano-2,6-diiodophenyl octanoate	1.75E-02	1.75E-02
42576-02-3	methyl 5-(2,4-dichlorophenoxy)-2-nitrobenzoate	2.71E-02	2.71E-02

Table 10b. PEC values estimated by the ECETOC TRA tool for 78 substances.

CAS	Name	ECETOC PEC (mg/L)	Solubility Corrected ECETOC PEC (mg/L)
469-61-4	[3R-(3alpha,3abeta,7beta,8aalpha)]-2,3,4,7,8,8a-hexahydro-3,6,8,8-tetramethyl-1H-3a,7-methanoazulene	3.49E-04	3.49E-04
470-90-6	chlorfenvinphos	4.38E-02	4.38E-02
4979-32-2	N,N-dicyclohexylbenzothiazole-2-sulphenamide	7.07E-01	7.07E-01
50-29-3	clofenotane	6.49E+00	5.50E-03
5102-83-0	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxobutyramide]	6.24E+00	2.38E-02
5216-25-1	alpha,alpha,alpha,4-tetrachlorotoluene	4.23E+00	3.27E+00
52315-07-8	alpha-cyano-3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate	3.72E-03	3.72E-03
52434-90-9	1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione	5.67E+01	3.40E+01
52-68-6	trichlorfon	3.58E-02	3.58E-02
52740-90-6	1-amino-N-(3-bromo-9,10-dihydro-9,10-dioxo-2-anthryl)-9,10-dihydro-9,10-dioxoanthracene-2-carboxamide	6.43E+00	4.53E-03
5468-75-7	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxobutyramide]	9.54E+00	2.98E-02
55283-68-6	ethalfluralin	8.04E-02	8.04E-02
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]	1.35E+01	9.57E-03
5598-13-0	chlorpyrifos-methyl	8.50E-03	8.50E-03
56-35-9	bis(tributyltin) oxide	2.78E-03	2.78E-03
5915-41-3	terbuthylazine	1.05E-01	1.05E-01
60207-90-1	1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole	8.12E-02	8.12E-02
61213-25-0	3-chloro-4-(chloromethyl)-1-[3-(trifluoromethyl)phenyl]pyrrolidin-2-one	3.04E-02	3.04E-02
629-59-4	tetradecane	4.66E-01	2.20E-03
63449-39-8	Paraffin waxes and Hydrocarbon waxes, chloro	4.16E+00	1.23E-01
64131-85-7	O,O,O-tris(4-nitrophenyl) thiophosphate	2.66E+00	3.79E-01
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	7.32E-02	7.32E-02
67747-09-5	N-propyl-N-[2-(2,4,6-trichlorophenoxy)ethyl]-1H-imidazole-1-carboxamide	1.60E-01	1.60E-01
67774-74-7	undecylbenzene	3.36E+00	1.00E-02
68442-68-2	4-(1-phenylethyl)-N-[4-(1-phenylethyl)phenyl]aniline	7.34E+00	3.99E-03
7287-19-6	prometryn	4.07E-02	4.07E-02
731-27-1	N-{[dichloro(fluoro)methyl]sulfanyl}-N',N'-dimethyl-N-(4-methylphenyl)sulfuric diamide	4.61E-02	4.61E-02
732-26-3	2,4,6-tri-tert-butylphenol	1.32E+00	1.32E+00
74070-46-5	2-chloro-6-nitro-3-phenoxyaniline	1.45E-01	1.45E-01
77-47-4	hexachlorocyclopentadiene	4.06E+01	1.80E+00
79-94-7	2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol	9.00E+00	6.19E+00
81-15-2	5-tert-butyl-2,4,6-trinitro-m-xylene	8.83E-04	8.83E-04
834-12-8	ametryn	2.02E-01	2.02E-01
84852-53-9	1,1'-(ethane-1,2-diyl)bis[pentabromobenzene]	1.35E+00	3.22E-03
87-68-3	hexachlorobuta-1,3-diene	8.67E-01	8.67E-01
886-50-0	terbutryn	4.07E-02	4.07E-02
93-46-9	N,N'-di-2-naphthyl-p-phenylenediamine	8.11E-01	3.00E-04
96-69-5	6,6'-di-tert-butyl-4,4'-thiodi-m-cresol	1.04E+01	4.42E-01

5.5. PEC CALCULATION: ECETOC TRA AND MULTIMEDIA MODEL

To compare the PEC results obtained using ECETOC TRA tool, we applied the values obtained from the multimedia model concerning the distribution of the compound between air, water and soil. The hypothesis was that the values obtained using Eq. (3) should be an extreme in the calculation of the PEC, i.e. PEC_{OECD}>PEC_{ECETOC}. Figure 27 shows the results obtained. As it can be observed for case of ERC10 and in a lesser measure ERC8, the predictions are confirmed since most of the points fail in the top half of the figure and the predictions with both approaches are quite similar. ERC (Environmental Release Categories, Appendix R.16-1, REACH Guidance, Chapter R.16) number 10 corresponds to wide dispersive outdoor use, whereas number 8 corresponds to wide dispersive indoor use. Conversely, from ERC2 to ERC6 the results were the opposite, i.e. the PEC_{ECETOC} >>PEC_{OECD} which is unrealistic since these scenarios are not wide dispersive. For this reason, it was decided to run the same scenario ERC10 for all compounds. The new results obtained are shown in Fig. 28. As it can be observed, in this case the differences still persist, but they have decreased considerably.

Finally, the selection of PEC values was done case by case basis between PEC_{ECETOC} and PEC_{OECD}, and limited to the solubility of the compound in water, i.e. if PEC was higher than solubility then this last value was selected as PEC (27 cases from the 78 selected compounds).

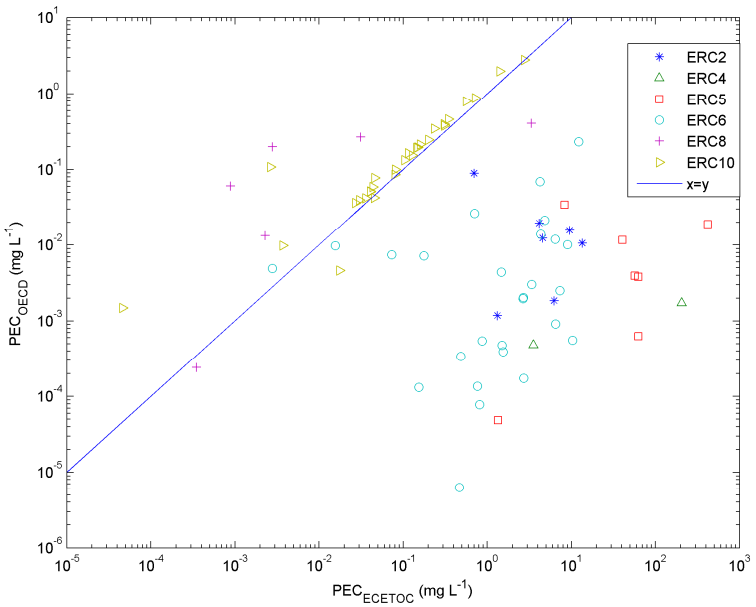

Figure 27. Comparison between PEC estimated using ECTOC and Eq. (3).ERC = Environmental Release Categories (Appendix R.16.1, REACH Guidance).

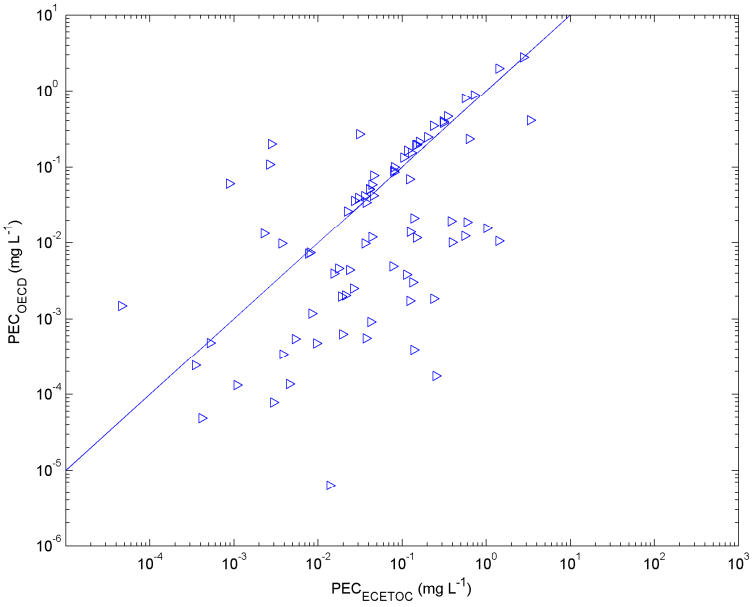

Figure 28. Comparison between PEC estimated using ECTOC and Eq. (3) assuming only environmental release scenarios categories 8 and 10.

6. CONCLUSIONS AND NEXT STEPS

In this study, a modelling-based prioritisation scheme has been developed and implemented. The approach was intentionally kept separate from the monitoring-based prioritisation scheme for the use of experimental data to be able to take into account substances for which monitoring data were not available in Member State monitoring programmes and which could pose a risk to aquatic ecosystems and to human health. However, the approach was merged with the monitoring-based prioritisation exercise in a final step by the calculation of modeled risk ratios (PEC/PNEC). In this way, results from both approaches could be compared. However, caution should be exercised since predicted environmental concentrations need to be assessed experimentally on a case by case basis.

As far as possible, the approach made use of public domain tools (e.g. EPI suite^{TM}, OECD P_{ov} and LRTP Screening Tool, ECETOC TRA, etc.) to make the approach accessible to all parties. However, this was not always possible and, in some cases, in-house models were developed and commercial software was used. The main reason for this was due to the tight schedule of the process and the amount of information to gather and process. Automated workflows were developed using the Pipeline Pilot software since a preliminary analysis of PBT compounds from the REACH PRS list had already been performed. However, the open source software (e.g. KNIME) could also be used to develop such workflows.

The present approach did not consider metals and, in some cases (when experimental physico-chemical and toxicological data were not available) organometalic compounds. This is due to the fact that most of the existing correlations have been developed for organic chemicals and the predictions of some properties for these chemicals are not valid using existing approaches. To consider these families of compounds would have required an additional effort that was not possible with the time and resource constraints of the project, but a parallel approach could be developed. However, due to the reduced number of substances, when compared with organic chemicals, a case by case study should be considered.

Another open question concerns the treatment of mixtures. In some cases, we believe that this is the approach to consider, since for some families an analysis of all congeners is not feasible. This is probably an issue that should be tackled after the present prioritisation exercise if some compounds that are part of one of these families are included in the next WFD Priority Substances list.

A future option for the next prioritisation exercises could consist of the development of an open source tool able to re-calculate as a function of the increase of data (e.g. REACH registration, new monitoring programmes, toxicological data, etc.) or new analytical tools (e.g. multimedia models, QSAR models, etc.) or emergent pollutants, all the parameters to re-assess the risk ratio. This would be a coherent approach, but it would require an effort for the development of the tool and clear documentation that could be used to check and assess the validity of the results. The current exercise should be considered

as a first step in this direction – a feasibility study showing that the approach is possible and worthwhile.

However, irrespective of the degree of automation in the process and the amount of information it is possible to deal with (all inventory of chemical substances could be introduced in the process when data become available), an expert review should always be the last step in all prioritisation exercises. This is recommended as the next step after combining the monitoring and modelling-based prioritisation lists before the new list of Priority Substances is developed.

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Abstract. This is the report of a feasibility study in which a model-based prioritisation methodology was developed in support of the implementation of the Water Framework Directive. The approach focuses on aquatic ecosystems and takes into account the intrinsic hazards of chemicals as well as their exposure levels.. The prioritisation approach also takes into account hazards due to secondary poisoning, bioaccumulation through the food chain and potential human health effects, e.g. due to consumption of fish or drinking water. A list comprising 2034 compounds provided by Member States, Stakeholders and Non-Governmental Organisations was evaluated according to pre-defined hazard and exposure criteria. Then 78 compounds considered to be "of high concern" were analysed and ranked in terms of their PEC/PNEC risk ratio (Predicted Environmental Concentration/Predicted No-Effect Concentration). In the interests of reproducibility, the tools employed in a model-based prioritisation process should ideally be freely accessible; however in this study this was not entirely possible due to the tight schedule and the fact that some estimation/calculation procedures were not available and thus needed to be developed. Nevertheless, the proposed approach constitutes a first step in for the establishment of an open modular tool that could eventually be used to support future prioritisation exercises.

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