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An intelligent data collection tool for chemical safety/risk assessment

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Abstract

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) is the new European chemical legislation which aims to assess risk or safety of tens of thousands of chemicals to improve the protection of human health and the environment. The chemical safety assessment process is of an iterative nature. First, an initial, worst-case assessment is conducted after which refinements are made until no risk has been estimated or the risk is adequately controlled. Wasting time and resources on additional testing and implementing risk management measures with low effect on risk conclusions should be avoided as much as possible. This paper demonstrates the usefulness of an intelligent data collection strategy based on a sensitivity (and uncertainty) analysis on the risk assessment model EUSES to identify and order the most important "within-EU-TGD-reducible" input parameters influencing the local and regional risk characterisation ratios. The ordering can be adjusted for the costs involved in additional testing (e.g. ecotoxicity, physico-chemical properties, emission estimates, etc.). The risk refinement tool therefore reduces the resources needed to obtain a realistic risk estimate (both less conservative and less uncertain) as efficient as possible.

Keywords: EUSES; Sensitivity analysis; Uncertainty; REACH; Exposure scenario

1. Introduction

The European risk assessment principles for new and existing chemicals are laid down in Commission Directive 93/67/EEC and 1488/94 (EC, 2003), respectively. Increasing concern that these EC regulations do not provide sufficient protection and that less than hundred high priority substances underwent a risk assessment in the past 10 years led to a review of the current policy on chemicals. A new system called REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) has recently been adopted (EC, 2006). The aim of REACH is to improve the protection of human beings (comprising of workers, consumers, and humans indirectly exposed via the environment) as well as ecosystems in the aquatic (water and sediment) and terrestrial compartments (including top predators) from adverse effects of chemicals while maintaining the competitiveness and enhancing the innovative capability of the EU chemicals industry. Within the context and scope of REACH, there is a need to be able to efficiently perform risk assessments on thirty thousands chemicals manufactured in or imported into Europe. The exposure and hazard assessment require many data acquisitions in accordance with the EU Technical Guidance Document (TGD; EC, 2003) or via EUSES software and consequently can absorb considerable time and resources.

The chemical risk/safety assessment process is of an iterative nature. First, an initial, worst-case assessment with conservative input parameters and assumptions is conducted. Recently, ECETOC developed a pragmatic and adequately conservative (i.e. no false negatives) approach that shares the same fundamental principles as the TGD (and EUSES) but allows for a ready identification of substances of very low or no immediate concern (Verdonck et al., 2005). If the substance does not pass this lower tier

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approach or an initial risk assessment based on a tentative exposure scenario, it is required to (1) collect further information and/or testing or (2) to implement risk management measures (RMM). This iterative procedure continues until no risk is estimated or the risk is adequately controlled.

Wasting time and resources on additional testing and implementing RMMs with low effect on risk conclusions should be avoided as much as possible in these iterative processes. There is therefore a need for techniques that optimises additional testing. This paper will demonstrate the usefulness of an efficient risk refinement tool (based on sensitivity and uncertainty analysis on the EUSES model) to check whether further refinement is worthwhile and if so, to identify and order the most important within-EU-TGD-reducible input parameters and RMMs influencing the local and regional risk characterisation ratios. The ordering can also be adjusted to the costs involved in additional testing or implementation of RMMs. Focus in this paper is given on the environmental side although the general concepts are also applicable for human health risk assessment.

2. Methodology

2.1. Environmental chemical risk/safety assessment

An environmental chemical risk/safety assessment usually proceeds in the following sequence: hazard assessment, exposure assessment and risk characterisation.

In the hazard assessment, reliable and relevant long-term (chronic) ecotoxicity data for organisms belonging to different trophic levels are gathered. For a limited effects database, the predicted no effect concentration (PNEC) is calculated by applying an assessment factor (AF), reflecting sources of uncertainty, to the lowest ecotoxicity value observed. For a sufficiently large effects database, a species sensitivity distribution (SSD) can be used to derive the PNEC value. The 5th percentile is used as the PNEC estimate, after application of an AF between one and five to cover remaining uncertainties (EC, 2003).

In the exposure assessment, a distinction is made between different spatial scales (EC, 2003). The local scale considers the vicinity of a point source and the local predicted environmental concentration (PEClocal) is calculated. The regional scale assesses the exposure levels due to diffuse/widespread releases in a larger region (PECregional). The PECregional acts as the background concentration for the local assessment. The technical principles, described in the EU TGD (EC, 2003), are implemented in the computer program EUSES (EC, 1998). EUSES first calculates releases of chemicals based on the volume produced or imported, the use pattern, and the physico-chemical properties of the chemical concerned. These release estimates are subsequently translated into PECs for each environmental compartment (air, water, sediment, soil) based on the transport and fate of the substance. For metals in sediment, a bioavailability correction can be made for metals bound to acid volatile sulfides (AVS) (ICMM, 2007). In general, however, preference is given to measured, representative input parameters or PECs where available. If not available, conservative, worst-case assumptions need to be used. Jager et al. (1998) identified several of these conservative input parameters/modules: release estimation, biodegradation, the exposure scenario. The estimation of partition coefficients and BCFs was found to be realistic and the regional distribution model may be characterised as best case.

The risk characterisation comprises of a quantitative comparison of the PEC, for most substances under REACH estimated through modelling, with the PNEC. The risk characterisation ratio (RCR), or PEC/PNEC ratio, larger or equal to one signifies that there is a potential risk of adverse effects occurring. A RCR smaller than one signifies no need for further information and/or testing and/or implementing RMMs.

2.2. Sources of uncertainty

All exposure and effects related EUSES input parameters are characterised by uncertainty. The sources of uncertainty can be further subdivided into irreducible and reducible uncertainty, also called respectively variability and uncertainty (Verdonck et al., 2007). Variability represents inherent heterogeneity or diversity in a well-characterised population. Examples are the temporal and spatial variations of the chemical concentrations, inter-species sensitivity, intra-species variability, differences in endpoints (reproduction, growth, survival...). Sources of reducible uncertainty in risk assessment are sampling uncertainty (i.e. uncertainty related to a limited sample size), representativeness of the selected species,...

For some input parameters, sources of uncertainty are a trigger for using AFs and worst-case assumptions in the exposure and effects assessment in order to avoid false-positives (unsafe chemicals that are assessed to be safe). Schematically visualised in Fig. 1, an upper percentile of the

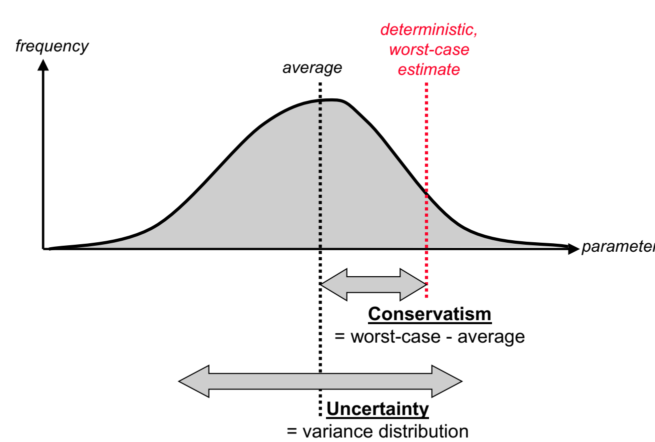

Fig. 1. Concepts of uncertainty and conservatism.

uncertainty distribution of an input parameter can act as the deterministic, worst-case estimate. For example in the TGD, a dilution factor of 10 is assumed for a local industrial or municipal plant's effluent discharging to the receiving river. Note that in this example, a lower percentile is the worst-case estimate. The difference between the reasonable worst-case dilution factor of 10 and the average dilution factor of all European discharges can be considered as a measure of conservatism. For other input parameters, it is not possible to determine a priori the worst-case value (e.g. a high partition coefficient may be worst-case for one environmental compartment but best-case for another compartment). The spread or variance of the uncertainty distribution can be considered as a measure of uncertainty. For some input parameters, characterised by an uncertainty distribution, no conservatism is introduced and an average estimate is used for further consideration. For example, an average or median is typically considered for physico-chemical input parameters (vapour pressure, water solubility, partition coefficients...). Those input parameters are characterised by uncertainty but typically not by conservatism. A proper distinction between conservatism and uncertainty is needed for further sensitivity analysis.

Not all input parameters can be considered to reduce the conservatism or uncertainty within the legislative context. The environmental input parameters of the multimedia model in EUSES, for example, are "fixed" in the TGDs (e.g. the area of a region). These input parameters are not readily allowed to be changed and therefore their uncertainty is built-in the assessment. Those input parameters are usually not substance-specific. The analysis conducted in this paper focuses on those input parameters that are readily allowed to be changed, i.e. substance-specific input parameters as emissions, physico-chemistry,... These input parameters will be named readily within-EU-TGD-reducible input parameters hereafter. For a more elaborate sensitivity analysis covering more EUSES input parameters, the reader is referred to the literature (e.g. Schwartz et al., 2000).

2.3. Impact of sources of uncertainty in risk

2.3.1. Procedure

An initial risk assessment (with tentative exposure scenario) is based on limited data and therefore, works protective through the use of conservative (default) values for exposure and effects input parameters. The combination of uncertain and sometimes conservative input parameters leads to an initial, worst-case (overestimated) and uncertain risk estimate (see Fig. 2 on the left). As more information or data become available, AFs and worst-case assumptions/values are reduced; and the resulting risk estimate becomes more realistic (usually lower because of the conservative nature of the initial exposure and effect assessment). The most realistic risk estimate can be obtained by collecting and using as much data and information as possible (see Fig. 2 on the right).

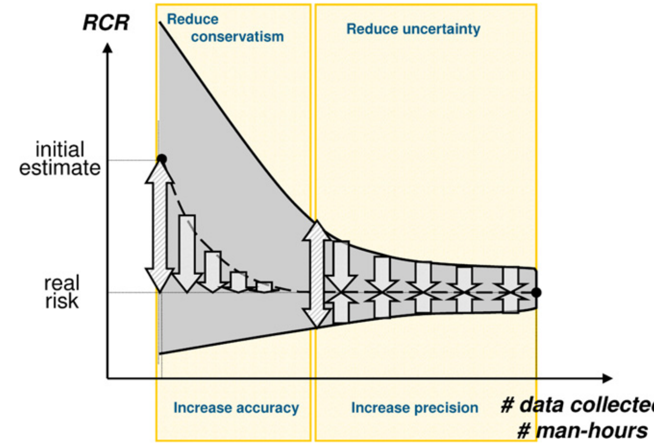

Fig. 2. Data collection leads to more accurate and precise risk estimates (RCR: risk characterisation ratio).

In the development of the risk refinement tool, it was chosen to first reduce the conservatism (see Fig. 2 left part) and then to reduce the uncertainty (see Fig. 2 right part). Note that reducing conservatism automatically also leads to reduced uncertainty. Following the constraints of the EU TGD in adjusting input parameters of the EUSES model, there will remain an "irreducible" built-in conservatism and uncertainty due to TGD constraints (e.g. the uncertainty in the environmental dimensions of the EUSES model).

The risk refinement tool, developed in this paper, identifies those input parameters that are most conservative and uncertain in relation to the conservatism and uncertainty of the RCR of concern. These input parameters are the "low hanging fruit" to obtain a realistic risk as soon as possible. Such an input parameter ordering can be obtained through sensitivity analysis.

2.3.2. Sensitivity analysis

Several methods are available to conduct sensitivity analysis (Saltelli et al., 2000; Janssens et al., 1992). The Monte Carlo based method on linear regression was found to be the most suitable method because it is easy to use and understand. The general idea is to approximate the often complicated relation between an output variable Y (dependent variable, the RCR of concern) and the input parameters X_i (independent variables) by a simple linear regression:

$$Y = \sum_{i=1}^{n} \hat{\beta}_i \cdot X_i + \hat{\beta}_0$$

with $\hat{\beta}_i$ the regression coefficients and $\hat{\beta}_0$ the intercept. The observations $(X_1, X_2, \ldots X_i,\ Y)$ are generated by a Monte Carlo simulation on the uncertainty distributions of the input parameters of EUSES. The following standardised quantity

$$S_i = \hat{\beta}_i \cdot \frac{s_{X_i}}{s_Y}$$

with s_{X_i} and s_Y respectively the estimated standard deviation of the input parameters and the output, is a measure for the sensitivity of the uncertainty in the output relative to the uncertainty in the input parameters (also called SRC or standardised regression coefficients). This sensitivity measure can, therefore, identify the input parameters with the largest contribution to the output uncertainty. This sensitivity measure can, however, not detect the most conservative input parameters because the definition does not contain any measure of conservatism as defined in Fig. 1. For this reason, the following standardised quantity was developed:

$$S_i = \hat{\beta}_i \cdot \frac{|X_{i,\mathrm{wc}} - \bar{X}_i|}{Y_{\mathrm{wc}} - \bar{Y}}$$

with $X_{\boldsymbol{i},\mathrm{wc}}$ and Y_{wc} respectively the "worst case" estimates of the input parameters and the resulting output, and $\bar{X}_i$ and $\bar{Y}$ respectively the mean estimates of the input parameters and the output. This new quantity is consequently a measure for the sensitivity of the conservatism of the output relative to the conservatism of the input parameters (called here wcRC or worst case regression coefficients).

The sensitivity measures for uncertainty and conservatism will not result in a different ordering in case the uncertainty and conservatism of an input parameter are dependent (i.e. when the uncertainty is estimated based on the conservatism or vice versa e.g. more conservatism results in more uncertainty). In case conservatism and uncertainty are estimated independently (e.g. a very uncertain parameter and small conservatism or vice versa), the sensitivity measures for uncertainty and conservatism will result in a different ordering.

A rank transformation of the input parameters and output can be conducted if linear regression results in a bad fit due to a strong non-linear relationship (Janssens et al., 1992). In a rank transformation, the samples of each input parameter are sorted and for each sample, the rank within the sorted list is determined. The two measures of sensitivity for uncertainty and conservatism are then respectively called SRRC (standardised ranked regression coefficients) and wcRRC (worst case ranked regression coefficients).

The final order of the input parameters is done in so-called tornado plots. A tornado plot is a convenient means of graphically depicting which input parameters in a model are the most influential. The graph is called a "tornado plot" because of the tornado-like appearance of the graph when factors are arrayed from most influential at the top to least influential at the bottom (for example, see Fig. 5).

A highly sensitive input parameter indicates that collection of an additional measurement (or additional information) on that input parameter is likely going to have the most significant effect on the RCR of concern. This leads to a more realistic RCR estimate. Note that the ordering of the input parameters in the tornado plot assesses the effect of adding one additional measurement only. The effect of multiple, additional measurements for the same or different input parameters require a more complex algorithm.

The EUSES simulations were conducted in batch mode. First, random samples for subsequent Monte Carlo simulation were generated in the @Risk software package (Palisade corporation, 1997) and saved in several EUSES input files. Second, these input files were entered in the batch mode of EUSES 2.0 (EC, 1998). The output from EUSES was then statistically analysed.

2.3.3. Cost-sensitivity analysis

The proposed input parameter order in the tornado plots is the basis for the development of a subsequent data collection strategy. However, the most influential input parameters may not be the cheapest ones to collect. Therefore, a sensitivity ordering relative to the cost of each input parameter collection may be found more useful. The cost can refer to financial resources (expressed in euro) or to human resources (e.g. number of working days/weeks). The cost-sensitivity can be calculated as:

$$\mathrm{CS}_i = \frac{S_i}{\mathrm{Cost}_i}$$

with $S_{\boldsymbol{i}}$ and $\mathrm{Cost}_{\boldsymbol{i}}$ respectively the sensitivity (based on conservatism or uncertainty) and the cost of input parameter i.

2.4. Case study

2.4.1. Introduction

A case study will illustrate the concepts, the feasibility and the usefulness of the developed intelligent data collection tool. A substance was selected that is currently undergoing an environmental risk assessment under the EU New and Existing Substances Directive and will feed into REACH. The substance will be named X for confidentiality reasons. The significance of the case as such is less important as the developed risk refinement tool is applicable for any substance (or group of substances).

The substance of concern is produced and consumed in more than hundred sites covering several industrial sectors following the life-cycle of the substance. For this paper, one generic scenario and one site-specific scenario of a processing sector were selected. Generic scenarios need to be conducted to cover all sites for which no site-specific information is available.

2.4.2. Data collection and estimation of uncertainty and conservatism

The data on input parameters were collected from the ongoing risk assessment. The parameter estimator can vary in risk assessment from the 10th percentile (e.g. for flow), mean or median (e.g. effluent discharge, solids–water partition coefficients) to the 90th percentile (effluent concentration, local production/consumption tonnage in a generic scenario).

The conservatism was estimated as the absolute value of the difference between the parameter estimate (following

TGD practise, usually realistic worst case) and the average estimate of all input parameters. This difference gives zero for those parameters where no conservatism is introduced.

The method for estimating uncertainty is depending on the data/information availability. The selection of the distribution was largely based on the best fitting distribution using the BestFit software (Palisade corporation, 1997) and expert judgement. If multiple data points were available for an input parameter, both variability and uncertainty were quantified using the parametric bootstrap method (Verdonck et al., 2001). The estimated uncertainty distribution of the estimator can be interpreted as sampling uncertainty. Sampling uncertainty reflects the degree to which sample results represent actual conditions for the population sampled. If no data are available (e.g. because the variability is not relevant or unknown) but data (and an estimated probability distribution) are available for the same input parameter on a different scale, then these data and their estimated probability distribution can be used as surrogate for the input parameter of interest. For example, no data were available for the emission factor to water/air for the generic scenario, and the probability distribution based on the emission factors of the other sites was used as surrogate uncertainty distribution. If absolutely no data are available, then expert judgement can be used to estimate the uncertainty. For example, the regional and continental emissions of X were based on a detailed analysis of all sources. However, no data are available to estimate the uncertainty.

For the ecotoxicity related input parameters, only the effect of additional tests for the existing, available number of species and endpoints was assessed. The effect of testing additional species and endpoints was not assessed due to the complex hierarchical dependency structure of individuals, endpoints and species in the derivation of a PNEC.

Eight-teen and third-teen input parameters were selected for respectively the regional and two local exposure analyses (regional/local emissions, partition coefficients, regional background concentrations for several compartments, effluent concentrations, river flows, removal efficiencies,...). The EUSES model was used to calculate the PECs. Ninety-five individual aquatic, sediment and terrestrial chronic ecotoxicity tests were collected for the effects assessment. SSDs were used to calculate the PNECs. For this, the best fitting distribution was determined using the BestFit software (Palisade corporation, 1997) and expert judgement. The resulting deterministic risk characterisation ratios (RCRs) for the scenarios and the compartments under study (water, sediment and soil) can be found in Table 1.

3. Results

3.1. Estimation of uncertainty and conservatism

Lessmann et al. (2005) found that the distributional shape of input parameters can greatly influence the variance of the EUSES output in uncertainty analysis. It is expected that sensitivity analysis is more robust towards deviations from distributional shape compared to uncertainty analysis because the sensitivity measures are relative measures of input and output uncertainties. Nevertheless, the uncertainty and conservatism were carefully estimated for all selected input parameters and the results can be found in the online appendix. For most input parameters (except for emissions), the uncertainty and conservatism estimates of the exposure and effects are based on data and can therefore be considered as reliable estimates. Lognormal, gamma, normal, weibull and mainly uniform distributions were used to characterise the uncertainty of the input parameters.

The uncertainty and conservatism estimates of the emissions are based on expert judgement (this includes a comparison of emission estimates with other studies and a mass balance exercise). Uncertainty ranges of 15–90% were selected. These ranges are therefore uncertain themselves. Only the uncertainty and conservatism of the main contributing emission sources was assessed and it was found however that no major sources of uncertainty or conservatism can be identified based on the available information. Note that several conservative assumptions were made on estimates of minor contributing emission sources. These have, however, no significant impact on the total emissions.

Table 1
Results of deterministic risk characterisation ratios (RCRs), presence of readily "within-EU-TGD-reducible conservatism" and sensitivity measure for the scenarios and compartments under study

Scenario	Compartment	Deterministic RCR	Presence of "within-EU-TGD-reducible" conservatism?	Sensitivity measures
Regional	Water	0.034	No	SRC
	Sediment	1.66	No	SRRC
	Soil	0.20	No	SRC
Local: GenericSite	Water	0.041	Yes	wcRRC, SRRC
	Sediment	57.6	Yes	wcRRC, SRRC
	Soil	0.2	Yes	wcRRC, SRRC
Local: SiteSpecific	Water	0.03	Yes	wcRC, SRC
	Sediment	58.2	Yes	wcRRC, SRRC
	Soil	0.20	No	SRC

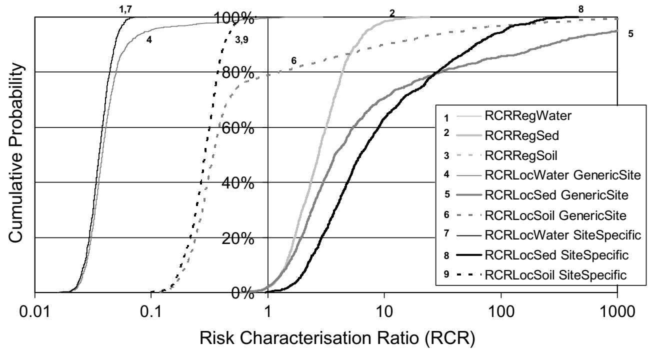

Fig. 3. Readily within-EU-TGD-reducible uncertainty of the risk characterisation ratio (RCR) for the scenarios and compartments under study (Note that RCRRegWater and RCRLocWater SiteSpecific coincide and RCRRegSoil and RCRLocSoil SiteSpecific coincide).

The readily within-EU-TGD-reducible uncertainty of the RCR for the scenario and compartments under study are visualised in Fig. 3. The uncertainty distributions of the sediment RCR are largely located above one. The uncertainty distributions of the water RCR are largely below one. The uncertainty distribution of the soil RCR (for the generic scenario) is partly below and partly above one. This is useful information to assess the potential to change risk conclusions by collecting additional information (see further in Section 4).

3.2. Contributions of input parameters to conservatism and uncertainty

A risk refinement can be initiated if a risk is identified or if more certainty on the risk outcome is desired. For the case study, potential risks were identified for the sediment compartment and sensitivity analysis was conducted for those scenarios. No acceptable linear fit was obtained. For this reason, a rank transformation was conducted.

3.2.1. Sensitivity of conservatism

The tornado plots analysing the sensitivity of conservatism for the sediment compartment of the two local scenarios can be found in Fig. 4. There are more conservative input parameters in the generic compared to the site-specific scenario. The most important input parameters influencing the conservatism of the local, generic and site-specific scenario for the sediment compartment are the AVS correction and the dilution factor.

It can also be observed that the AF is inversely related to RCR. This is counter-intuitive because an increasing AF results per definition in an increasing RCR. This means that in linear regression of the sensitivity analysis, an inverse correlative relationship was, by coincidence, observed. However, these coincidental correlations are typically negligible and not significant to the RCR of concern. They are therefore an indication for the point in the tornado plot under which the input parameters are no longer significant (have negligible influence on the RCR of concern).

3.2.2. Sensitivity of uncertainty

The tornado plots analysing the sensitivity of uncertainties for the sediment compartment of all three scenarios can be found in Fig. 5. The most important input parameters influencing the uncertainty of the regional scenario for the sediment compartment are the NOECs (No Observed Effect Concentration) on *Gammarus pulex* (endpoint growth) and *Hyalella azteca* (endpoint reproduction), the regional emission to agricultural soil and the NOECs on *G. pulex* (endpoint survival), *Lumbriculus variegatus* (endpoint reproduction) and *Tubifex tubifex* (endpoint reproduction). The most important input parameters influencing the uncertainty of the local, generic scenario for the sediment compartment are the AVS correction, the fraction of X released to the surface water, the local effluent discharge rate and the dilution factor. The most important input parameters influencing the uncertainty of the local site-specific scenario for the sediment compartment are the AVS correction and the dilution factor.

Note that some input parameters can pop up in the tornado plots that have no causal relationship with the RCR of concern, e.g. the NOEC of *Senecio vulgaris* is a

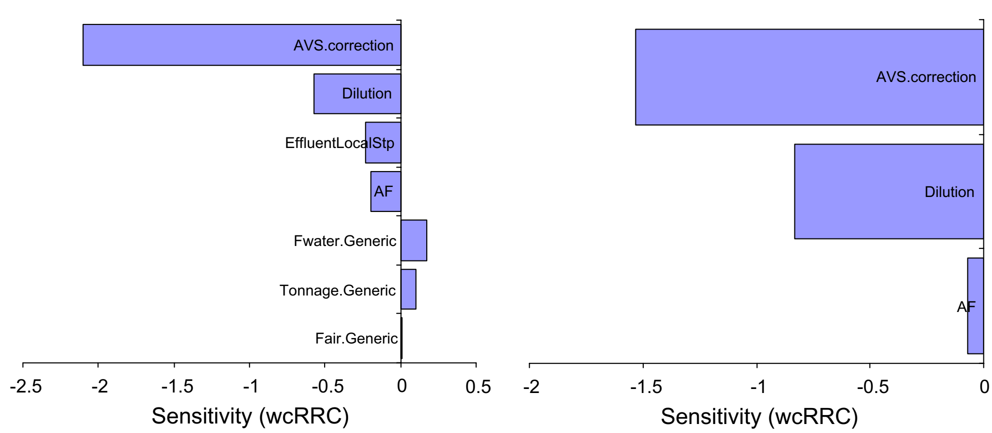

Fig. 4. Tornado plots of the regional, local generic and site-specific scenarios (Left: RCRLocSed.GenericSite, Right: RCRLocSed.SiteSpecific) for the sediment compartment, testing the sensitivity of conservatism.

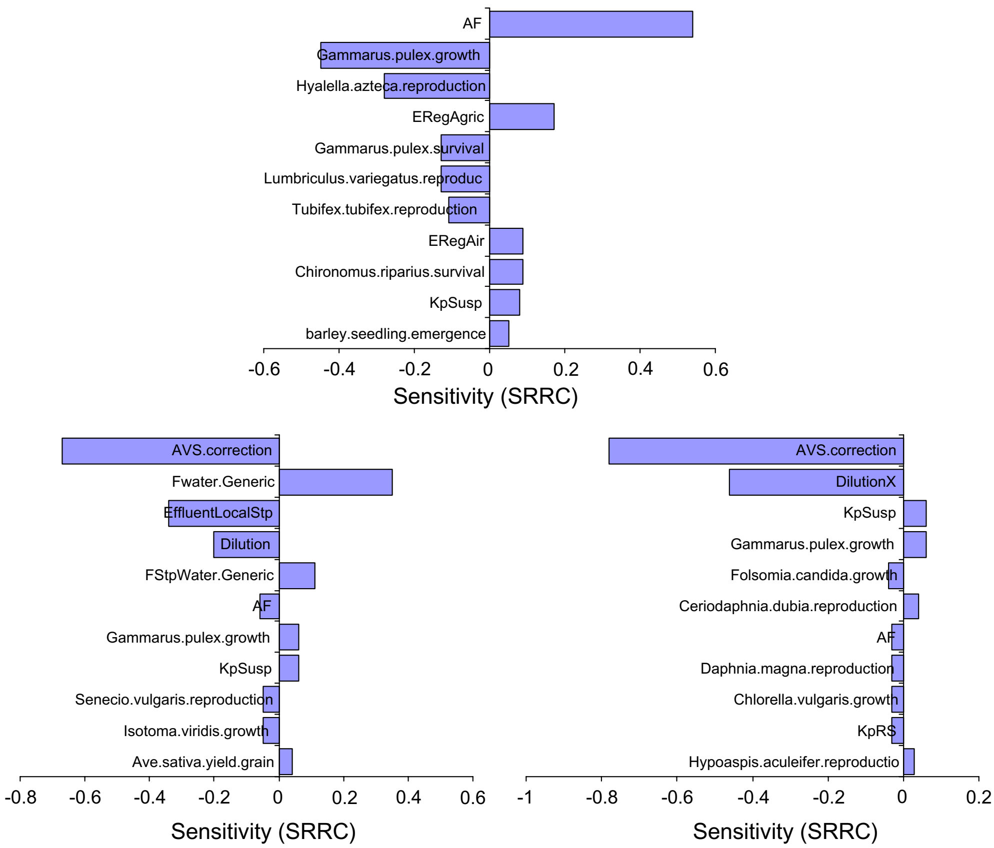

Fig. 5. Tornado plots of the regional, local generic and site-specific scenarios (Top: RCRRegSed, Bottom left: RCRLocSed.GenericSite, Bottom right: RCRLocSed.SiteSpecific) for the sediment compartment, testing the sensitivity of uncertainty.

terrestrial ecotoxicity input parameter that is not used in the estimation of the RCR for sediment. This means that in the sensitivity analysis, some correlative relationship was, by coincidence, observed. However, these coincidental correlations are typically negligible and not significant to the RCR of concern. These coincidental correlations can be avoided by conducting a priori a mechanistic analysis and by selecting those parameters that are expected to have an influence on the RCR of concern.

For the other compartments under study, the following observations can be made (tornado plots not shown). For the regional and local site-specific RCRs of the water compartment, the background concentration and subsequently aquatic ecotoxicity values are the most influential input parameters. For the regional and local site-specific RCRs of the soil compartment, the regional emission to air and subsequently terrestrial ecotoxicity values are the most influential input parameters. Only for the local, generic

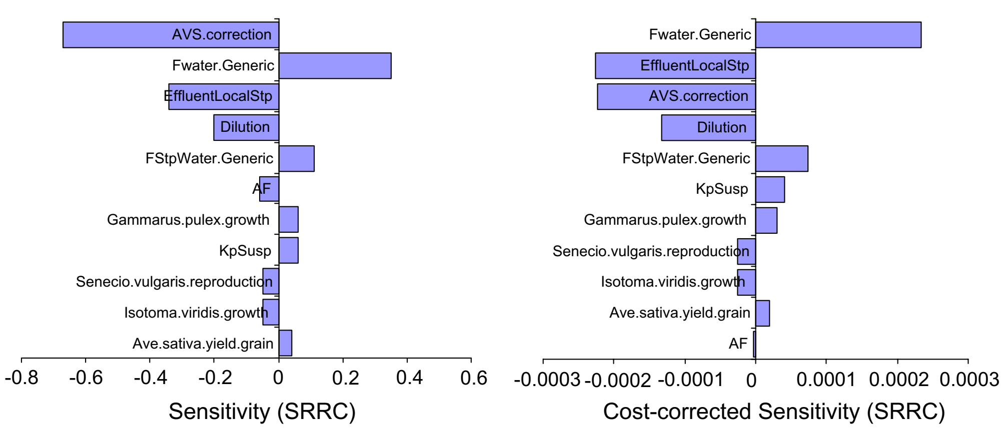

Fig. 6. Tornado plots of the local generic scenario for the sediment compartment, testing the sensitivity of uncertainty (left) and the sensitivity corrected for costs (right).

scenario, a combination of exposure input parameters (background concentration, effluent discharge rate, dilution factor, fraction emission to water, presence/absence STP) and effects input parameters (ecotoxicity values) was found to be influential.

3.3. Cost-sensitivity of input parameters

The cost-sensitivity analysis is illustrated for the local generic scenario in the sediment compartment (results, see Fig. 6). For this, the effects related input parameters were estimated to cost 2000 € each and the exposure related input parameters were estimated to cost 1500 € each (except AVS correction 3000 €, AF involves field testing estimated at 20,000 €). These amounts are for illustrative purposes only. It was assumed that it is cheaper to collect exposure related data through sending a questionnaire to the industrial sites of concern than to conduct laboratory ecotoxicity tests. This, of course, very much depends on the number of sites of concern, the species to be tested, etc. Fig. 6 evidently shows that costly input parameters decrease in importance and less costly input parameters increase in importance.

4. Discussion

4.1. Worthwhile to refine?

The RCR uncertainty distributions enable the risk assessor to assess whether there is potential to change the risk conclusions by updating the input parameters or, in other words, whether it is worthwhile to refine the assessment.

In this case study, a potential risk is identified for the sediment compartment in all three scenarios. Input parameter refinements can possibly decrease the conservatism and decrease the uncertainty of the RCR estimate. However, further refinements of the considered readily "within-EU-TGD-reducible" input parameters for the sediment compartment will most likely not turn a "potential risk" into a "no risk" outcome because the RCR uncertainty distribution is located largely above one (see Fig. 3). Similarly, further refinements for the water compartment will not turn a "no risk" into a "potential risk" outcome. Further refinements can, however unlikely, turn a "no risk" into a "potential risk" outcome for the soil RCR (for the generic scenario).

Based on the assessment above, a risk assessor may decide not to conduct additional risk refinements but to choose directly for implementation of RMMs for the risk scenarios. In this paper for illustrative purposes, it was decided to use the risk refinement tool for the sediment RCR anyway.

4.2. Which input parameters to refine?

In the proposed intelligent data collection strategy, the goal is to reduce the conservatism first (or increase the accuracy), and then to reduce the uncertainty (or increase the precision) by collecting additional information or conducting one additional test for the "readily-within-TGD-reducible" input parameters.

The most conservative input parameter relative to the RCR to refine is the AVS correction and the dilution factor in both local scenarios. In the site-specific scenario, information on dilution factor requires information on the effluent discharge rate and the river flow rate. This can be obtained through search and collection of flows of nearby gauging stations or by conducting flow measurements at the site. In the generic scenario, this would require the collection of additional information of all non-covered sites. This is a more resource-demanding effort. Measurements on AVS in the sediment can be conducted at the site or at all non-covered sites. Collection of these input parameters should result in a decrease in conservatism and consequently a decrease of the RCR (at least if the initial input parameter values are indeed conservative enough).

The most uncertain input parameters relative to the RCR to refine come from both the exposure and effect assessment. Generally speaking in this case study, one observes the presence of more exposure input parameters in generic scenarios and more effect input parameters in site-specific/regional scenarios because in the latter exposure information is typically more abundant.

The ecotoxicity input parameters pop up in the tornado plots of every scenario and are therefore an important opportunity for refinement. The most important ecotoxicity input parameter appears to be the species mean for *G. pulex* on growth. This is not the most sensitive species (*H. azteca* is) but the species mean for *G. pulex* on growth is based on a smaller number of data points (laboratory tests, references from literature) than the *H. azteca* input parameter. Consequently, the order of ecotoxicity input parameters is a combinatorial effect of both influential (very sensitive species have a large effect) and the uncertainty (less samples for a specific species and endpoint have large effect).

The most important exposure input parameters in all scenarios are related to the emissions (the actual emissions or the emission factors). A subsequent data collection strategy would therefore be to collect more information on emissions related input parameters (such as influent/effluent concentration) or information on the actual industrial process (for example, which RMMs are taken to reduce losses during the processing). In the generic scenario, local input parameters as dilution factor and effluent discharge rate are also important.

The tornado plots are found to be a suitable visualisation of input parameter ordering and refinement that forms the basis for the development of an intelligent data collection strategy. If budget is important to consider, the cost of additional testing and its influence on the input parameter ordering can be included. The sensitivity measures are a combination of the input parameter sensitivity towards the RCR as such (which can remain the same for the same type of substances) and input parameter uncertainty/conservatism (which is different for each substance and even within the phase of data collection of the same substance, it is solely dependent on data availability).

Once additional data are collected for one or more influential input parameters, the iterative process of recalculating RCR and identification of the most influential/uncertainty input parameters can continue until no further refinement is needed/possible. Further refinement steps relate to the non-readily "within-EU-TGD-reducible" input parameters and the EUSES model structure and assumptions. However, this requires approval of the competent authorities as the regular procedure is modified through such changes.

5. Conclusions

This paper demonstrated the usefulness of an efficient risk refinement tool (based on sensitivity and uncertainty analysis on the risk assessment model EUSES) to check whether further refinement is worthwhile and if so, to identify and order the most conservative and uncertain "within-EU-TGD-reducible" input parameters influencing the local and regional risk characterisation ratios. The ordering can also be adjusted to the costs involved in additional testing. Although this risk refinement tool initially requires more effort, it can have its merit in the iterative nature of the risk assessment process especially under the new chemical EU policy, REACH, which aims to assess tens of thousands of chemicals.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.chemosphere.2007.08.072.

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