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# Uncertainty analysis of EUSES: Improving risk management by probabilistic risk assessment

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# PREFACE

Risk assessment for new and existing chemicals is based on a deterministic comparison between an exposure level and an effect or no-effect level. This report advocates a transition from this deterministic approach to a probabilistic risk assessment and demonstrates how this may improve risk management. This study is not meant to be a mathematical exercise. Instead, this report is written for risk assessors and risk managers working in the framework of chemical legislation. The details on the parameter distributions which were used for the example calculations are therefore given in an appendix for the interested readers. We hope that this report can increase familiarity with the concept of probabilistic risk assessment and that it may serve as a discussion document in updating the methods of the Technical Guidance Documents for new and existing chemicals and the decision-support system EUSES.

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# ABSTRACT

In risk assessment of new and existing substances, it is current practice to characterise risk using a deterministic quotient of the exposure concentration, or the dose, and a no-effect level. Feelings of uncertainty are tackled by introducing worst-case assumptions in the methodology. Since this procedure leads to an assessment with an unknown degree of conservatism, it is therefore advisable to deal quantitatively with uncertainties. This report is a discussion document describing the advantages and possibilities to be had with a probabilistic risk assessment framework. Several options for probabilistic risk assessment are illustrated with sample calculations.

# SUMMARY

The methods for risk assessment of new and existing chemicals are harmonised between the EU Member States and laid down in Technical Guidance Documents (TGD). To ensure rapid and transparent assessments, the methodology of the TGD is implemented in a computerised system: the European Union System for the Evaluation of Substances (EUSES). The measure of risk that is used in this framework is a point estimate; for environmental endpoints the PEC/PNEC ratio (quotient of the Predicted Environmental Concentration and the Predicted No-Effect Level for an endpoint) and for human populations a MOS (Margin Of Safety, quotient of a toxicity measure and the exposure level). Point estimates like these quotients may be efficient in a first stage to narrow the scope, but the disadvantage is that it is generally not possible to determine where a point estimate lies in the range of possibilities. Furthermore, the use of point estimates may mislead risk managers by producing falsely precise estimates. It is advisable to take uncertainty in the assessment explicitly into account in the decision-making process. With uncertainty analysis, parameters are characterised by probability distributions, leading to a probability distribution of the risk estimate. A risk manager can then base decisions upon an "acceptable" level of certainty. Apart from being closer to the truth (the real world is inherently uncertain), probabilistic risk assessment has the advantage that it includes all information available so that risk managers and the general public can see the full range of possibilities. Another advantage is that the main sources of uncertainty in the final result can be identified, thereby offering an efficient way to refine the assessment.

This report is a discussion document, describing the advantages and possibilities of a probabilistic risk assessment framework. Risk is generally defined as an "impact" times the probability that this impact will actually occur. In chemical risk assessment, we cannot usually define a risk in the strictest sense because the probabilities are not routinely quantified, and first of all, because impacts are not properly quantified. Analysing uncertainties in the exposure assessment is relatively straightformward leading to a probability distribution for the PEC, but if true risks are to be characterised, the effects assessment is the critical stage. The following options are available to revise the effects assessment in order to deal with uncertainties in the risk characterisation stage. In order preference:

A. Establish some kind of dose-effect relationship for human populations and ecosystems. The result of the risk characterisation stage will then be a probability distribution of *effects*. Decisions can be based on an acceptable level of effects.
B. Revise the assessment factors in the effects assessment to yield a median, or most likely, PNEC instead of a safe estimate and attach uncertainty to these factors. The result of the risk characterisation will be a probability distribution of *PEC/PNEC ratios*.
C. Leave the effects assessment as it is now. In that case, only uncertainty in the exposure estimate can be quantified. The result of the risk characterisation will be a probability that PEC exceeds a fixed, worst-case, PNEC.

These three options are discussed and worked out in example calculations of a new chemical. More information is presented to the risk managers to base decisions on which is both powerful as well as potentially confusing. We hope that this report helps to familiarise risk managers as well as risk assessors with probabilistic methods. It is the intention of the authors to discuss this report with a larger group of experts (scientists and risk managers) in 1998. After these discussions, a proposal will be drafted for the EU Technical Meeting which can be entered in the discussions for a future update of the TGDs and EUSES.

# SAMENVATTING

De methoden voor risicobeoordeling van nieuwe en bestaande stoffen zijn geharmoniseerd tussen de EU-lidstaten en vastgelegd in technische leidraden (TGD). Om een snelle en transparante beoordeling te garanderen is de TGD-methodologie geïmplementeerd in een gecomputeriseerd systeem: the European Union System for the Evaluation of Substances (EUSES). De risicomaat die wordt toegepast in dit kader is een puntschatting; voor het milieu de PEC/PNEC ratio's (het quotiënt van een voorspelde concentratie in het milieu en een geen-effect niveau) en voor humane populaties een MOS (veiligheidsmarge, het quotiënt van een toxiciteitsmaat en een blootstellingsniveau). Puntschattingen zoals deze quotiënten kunnen efficiënt zijn in een eerste stadium om de reikwijdte van een beoordeling te verkleinen maar het nadeel is dat het i.h.a. onmogelijk is om vast te stellen waar een puntschatting ligt in het scale van mogelijkheden. Verder kan het gebruik van puntschattingen risicomanagers misleiden door een ongerechtvaardigde mate van nauwkeurigheid te pretenderen. Het is daarom aan te bevelen om onzekerheden in de beoordeling expliciet te overwegen in de besluitvorming. Met onzekerheidsanalyse worden paramaters beschreven door kansverdelingen, wat leidt tot een kansverdeling van de risicoschatting. Een risicomanager kan zijn besluiten baseren op een "acceptabel" niveau van zekerheid. Behalve dat dit dichter bij de waarheid ligt (de echte wereld is inherent onzeker) heeft probabilistische risicobeoordeling als voordeel dat het alle beschikbare informatie meeneemt zodat risicomanagers en het grote publiek de volle omvang van de mogelijkheden kunnen zien. Een ander voordeel is dat de belangrijkste bronnen van onzekerheid geïdentificeerd kunnen worden wat een efficiënte manier is om een beoordeling te verfijnen.

Dit rapport is een discussiedocument dat de voordelen en mogelijkheden van een probabilistisch risicokader beschrijft. Risico wordt algemeen gedefinieerd als een "impact" maal de kans dat deze impact echt voorkomt. In risicobeoordeling van stoffen kunnen we meestal geen risico in strikte zin bepalen omdat de kansen niet routinematig bepaald worden en, belangrijker nog, dat impacts niet goed gekwantificeerd zijn. Onzekerheidsanalyse aan de blootstellingskant is redelijk helder te bepalen en leidt tot een kansverdeling van de PEC's. Echter, de effectbeoordeling is de kritieke stap als echte risico's bepaald moeten worden. De volgende opties zijn beschikbaar om de effectbeoordeling aan te passen om met onzekerheden in de risicokarakterisering om te gaan. In volgorde van voorkeur:

A. Bepaal een soort dosis-effect relatie voor humane populaties en ecosystemen. Het resultaat van de risicokarakterisering is een kansverdeling van *effecten*. Besluiten kunnen worden gebaseerd op een acceptabel effectniveau.
B. Reviseer de "assessmentfactoren" om een mediane, of meest waarschijnlijke, PNEC op te leveren in plaats van een veilige schatting en bevestig onzekerheid aan deze factoren. Het resultaat van de risicokarakterisering is een kansverdeling van *PEC/PNEC-ratio's*.
C. Laat de effectbeoordeling zoals hij is. In dat geval kan alleen de onzekerheid in de blootstellingsschatting worden meegenomen. Het resultaat van de risicokarakterisering is de kans dat PEC een vaste, worst-case, PNEC overschrijdt.

Deze drie opties worden besproken en uitgewerkt in voorbeeldberekeningen van een nieuwe stof. De risicomanager krijgt meer informatie om een beslissing op te baseren wat zowel krachtig als potentieel verwarrend is. We hopen dat dit rapport helpt om risicomanagers en risicobeoordelaars vertrouwd te maken met probabilistische methoden. Het is de bedoeling van de auteurs om dit rapport in 1998 in bredere kring te bespreken (met zowel wetenschappers als risicomanagers). Na deze discussie zal een voorstel opgesteld worden voor

de EU Technische Vergadering dat gebruikt kan worden bij de discussies rond toekomstige nieuwe versies van de TGD's en EUSES.

# 1. INTRODUCTION

Chemical risk assessment tries to protect humans and the environment from the possible adverse effects of substances. The methods for risk assessment of new and existing chemicals are harmonised between the EU Member States and laid down in Technical Guidance Documents (TGD) (EC, 1996). To ensure rapid and transparent assessments, the methodology of the TGD is implemented in a computerised system: the European Union System for the Evaluation of Substances (EUSES) (EC, 1996; Vermeire *et al.*, 1997). This system is able to perform calculations for, in principle, all chemicals, based on a relatively limited amount of available data (e.g. the EC Base Set for new chemicals). The assessment should protect ecosystems and human populations from unacceptable risks. For pragmatic reasons, several groups are explicitly defined for which a risk estimate is made; the so-called protection targets or endpoints as shown in Table 1.

*Table 1 protection targets in EUSES.*

| |
|---|
| **Human populations:** |
| • Workers |
| • Consumers |
| • Humans exposed via the environment |
| **Ecological systems and populations** |
| • Micro-organisms in sewage treatment systems |
| • Aquatic ecosystems |
| • Terrestrial ecosystems |
| • Sediment ecosystems |
| • Top predators |

The measure of risk that is used in this framework is a point estimate; for environmental endpoints the PEC/PNEC ratio (quotient of the Predicted Environmental Concentration and the Predicted No-Effect Level for an endpoint) and for human populations a MOS (Margin Of Safety, quotient of a toxicity measure and the exposure level). Point estimates like these quotients may be efficient in a first stage to narrow the scope in an assessment challenged by many contaminants and many potential risks (Bartell, 1996), but the disadvantages are numerous (Table 2).

***Table 2** Disadvantages of point estimates in risk assessment (Thompson & Graham, 1996).*

| |
|---|
| 1. It is generally not possible to determine precisely where a point estimate lies in the range of possibilities. |
| 2. Use of point estimates may mislead risk managers by producing falsely precise estimates. |
| 3. Use of point estimates may lead to non-optimal decisions. |
| 4. Use of point estimates eliminates the incentives for conducting research that might reduce uncertainty. |
| 5. Use of point estimates ignores variability in the population and thus precludes discussion and consideration of inequity in the distribution of risk in the exposed population. |

Clearly, the results from systems like EUSES must be accompanied by a fair amount of uncertainty, caused by (Etienne, 1996):

1. Uncertainty due to natural variability in time or space. The world around us is inherently variable which will also affect the risk for the protection targets. As an example: the flow rate of a river will vary between different rivers but also according to seasonal influences. In contrast with the following categories, uncertainty caused by variability cannot be reduced by further research, it can only be more accurately characterised.
2. Uncertainty due to ignorance: imperfect or incomplete knowledge of things that could be known. This can be said about model parameters but also for the model formulation itself (e.g. the assumption of well-mixed compartments in multi-media models).
3. Uncertainty due to error: mistakes in execution of assessment activities (e.g. measurement errors).

4. Uncertainty due to choices: decisions about the system and situation to be modelled (e.g. the definition of the standard environment and selection of the protection targets).

It is advisable to take this uncertainty in the assessment into account in the decision-making process. From a scientific point of view, it is advisable to do this explicitly instead of relying on point estimates. Up till now, risk assessors have reacted upon a sense of uncertainty by introducing worst case assumptions in the methodology. As an example, the extrapolation of the results of standard biodegradation tests to rate constants in the environment is very uncertain. The EU expert meeting on biodegradability therefore agreed on a rather worst-case extrapolation procedure for the TGD (e.g. a substance characterised as "readily biodegradable" will receive a half life in surface water of 15 days). An accumulation of worst cases like this could eventually lead to unrealistic assessments which is neither transparent, nor efficient when too many chemicals are flagged as potentially dangerous. Chemicals may be judged as very dangerous just because of the large uncertainty in the assessment, not because of the risk they pose. This makes a risk-based comparison of chemicals, or priority setting, virtually impossible.

Uncertainty analysis is a tool that can be used to tackle uncertainty in a more efficient and scientific manner. With uncertainty analysis, parameters are not characterised by a single value (point estimate) but by probability distributions. The effect of these distributions on the model's results is calculated, leading to a probability distribution of the risk estimate. A risk manager can then base decisions upon an "acceptable" level of certainty. In this way, the probabilistic approach places the responsibility for determining who should be protected and how much with the risk manager, where it belongs (Thompson & Graham, 1996). Probabilistic methods are well defined mathematically and are well established in other disciplines including physics, chemistry, biology, engineering, economics and finance (see Burmaster, 1996). No nuclear power plant is built without a probabilistic risk assessment. We are not absolutely certain about our risk assessments and distributions represent reality better than point estimates. Risk managers may argue that they have to set arbitrary cut-off levels for distributions but relatively "arbitrary" cut-off values were defined before in the field of chemical risk assessment:

- I.e. the PEC/PNEC>1 represents a cut-off value.
- For new chemicals the PEC/PNEC cut-offs of 10, 100, 1000 were set to decide whether to ask for further testing immediately, wait for the next tonnage trigger or to request risk reduction measures (see EC, 1996).
- The 95% species protection level in statistical extrapolation methods (see e.g. Van Leeuwen, 1990).
- The maximum permissible and negligible risk levels for chemicals without thresholds (VROM, 1989).

Nevertheless, before a risk manager can interpret probability distributions, it has to be clear what the distribution actually represents. This challenges risk assessors and scientists to provide sufficient transparency to avoid *arbitrary* cut-offs. In effect, decisions or cut-offs can be based on a deliberation of the costs of type I and type II errors (see Table 3) and the expected effects of the chemical (for a genotoxic carcinogen, one may desire more certainty than for a compound causing irritation). The advantages of probabilistic risk assessment are summarised in Table 3.

*Table 3 Advantages of probabilistic risk assessment.*

**The probabilistic framework of risk (Burmaster, 1996):**

1. Honours the definition of risk.
2. Includes all information available about uncertainty and variability inherent in the assessment.
3. Reveals the compounded conservatism in the deterministic framework. Risk managers and the general public can see the full range of possibilities.
4. Reveals the nature and the extent of professional judgement in a risk assessment.
5. Can indicate the main sources of uncertainty in the final result, thereby offering an efficient way to refine the assessment.
6. Re-establishes the now blurred boundary between risk assessment and risk management. Too often risk assessors use exaggerated point values so the risk manager can ignore the complexities and cost-effectiveness of measures. Allows the risk manager to make a trade-off between the costs of type I errors (rejecting a harmless substance) and type II errors (accepting a harmful substance).
7. Ultimately saves money as the results are generally less conservative, yet fully protective.
8. Is closer to the truth. The output is a distribution of potential risk. Getting closer to the truth is preferable to the world of fiction created when distributions are replaced by single numbers.

**And additionally:**

9. Allows for comparing chemicals with different degrees of uncertainty.
10. Acts to reward the input of measured data. Even when additional data lead to higher PEC/PNEC ratios, their uncertainty may be lower which may therefore result in an assessment with greater confidence.

There are numerous example studies were the power of quantitative uncertainty analysis is demonstrated in risk assessment of chemicals (McKone & Ryan, 1989; De Nijs & De Greef, 1992; Dakins *et al.*, 1994; Copeland *et al.*, 1993; Thompson *et al.*, 1992; Traas *et al.*, 1996a; Traas *et al.*, 1996b). Nevertheless, the application of uncertainty analysis to decision making is far from routine as virtually all decisions are still based on point estimates of exposure and effects. One of the reasons for the reluctance of regulators to accept probabilistic risk assessment is the lack of proper guidance and policy (Finley *et al.*, 1994). A summary of the reasons for reluctance for probabilistic approaches is given in Table 4. Apart from the technicalities of uncertainty analysis, the presentation and interpretation of uncertain end results should therefore receive proper attention.

The purpose of this report is to investigate how chemical-risk management can benefit from probabilistic risk assessment. The discussion on whether to use uncertainty analysis in risk assessment cannot be pursued without discussing the most appropriate way to express "risk". In Chapter 3, several options are worked out to illustrate how uncertainty analysis can be used to characterise risk and how these distributions must be interpreted. These options are illustrated with example calculations. These alternatives should be seen as means to broaden the perspective on risk analysis rather than actual proposals for immediate implementation. It should be noted that the technicalities of uncertainty analysis will not be discussed in much detail in this report. We believe that, at this moment, it is better to concentrate on the possibilities and (dis)advantages of probabilistic risk assessment so that risk assessors and risk managers in the EU are better informed and, perhaps, can feel more confident about these methods. Probability distributions for parameters were not investigated in detail and the technicalities are therefore moved to Appendix I. Reasonable distributions were selected based on (limited) data sets or expert judgement (from RIVM colleagues). These distributions must be seen as illustrative, but may provide a starting point for discussion or further research.

***Table 4*** *Disadvantages or costs of probabilistic risk assessment.*

**Explanations for the limited use of probabilistic risk assessment (Thompson & Graham, 1996):**

1. Lack of (EPA) guidance.
2. The existence of established point estimates for some inputs (e.g., the Exposure Factors Handbook).
3. Inexperience with using probabilistic results.
4. Increased legal challenge.
5. Mistrust and suspicion. Risk managers may suspect that outcome will favour industry (perhaps just by delaying decisions by endless discussion) or may be worried that the assessment contains hidden assumptions or hard-to-detect errors.
6. Difficulties in risk communication.

**Costs of probabilistic risk assessment (Burmaster, 1996):**

1. Probabilistic methods need more measured data to estimate the variability or uncertainty in a stochastic variable.
2. Probabilistic methods need many input distributions.
3. To work in the probabilistic framework, risk assessors, toxicologists and regulators need to learn new skills. It takes serious study to learn how to develop, manipulate, and interpret stochastic variables and equations.
4. Risk management decisions are harder to make. The risk manager must consider the character, location, and spread of the whole distribution of risk.
5. Risk communication hinges on the continued development of visual and graphical tools to convey the results.
6. Risk assessors must make sure that guidance manuals do not impede the growth and advancement of their discipline.

It is the intention of the authors to discuss this report with a larger group of experts (scientists and risk managers) in 1998. After these discussions, a proposal will be drafted for the EU Technical Meeting which can be entered in the discussions for a future update of the TGDs. This report deals with the following steps:

1. Defining the scope of the analysis: which uncertainties are quantified and which not (Chapter 2).
2. Used uncertainty to characterise "risk": alternatives for the fixed PEC/PNEC quotient (Chapter 3).
3. Defining parameter distributions (probability density functions). Chapter 4 discusses some frequently used distributions and their backgrounds but the technicalities of distributions used for the example calculations are given in Appendix I.
4. Several example calculations to compare the deterministic approach to the results of uncertainty analysis and different expressions of "risk" (Chapter 5).
5. Conclusions are provided in Chapter 6.

This study departs from two earlier reports (Jager & Slob, 1995; Jager, 1995) in which preliminary work is done for uncertainty analysis of USES 1.0 (RIVM *et al.*, 1994), the predecessor of EUSES. General conclusions from this study were:

1. Monte Carlo analysis[1] is the most applicable technical method for this system. This method has become increasingly popular in recent years and as a result, Monte Carlo analysis is now almost synonymous with uncertainty analysis. Advantages are its ease of use and the wide range of applicability, disadvantage is the time consumption. This

[1] In Monte Carlo analysis, point estimates in a model are replaced by probability distributions. Samples are randomly taken from the distributions and the model's results are combined, usually in the form of a probability density distribution or a cumulative density function.

method is especially useful when data or theory exist to properly specify the model equations and the input distributions (Moore, 1996).

2. Uncertainties in the model's results depend on the properties of the chemical. This means that the analysis must be done for each chemical separately and that some substances can be assessed with greater confidence than others.
3. Uncertainties or variability in typical scenario choices are extremely difficult to quantify.
4. Uncertainties in the effects assessment were not addressed but require further consideration.

# 2. CHOICE OF UNCERTAIN PARAMETERS (SCOPE)

Uncertainty about the value of a parameter can be caused by lack of knowledge (e.g. emission estimates), measurement errors (e.g. vapour pressure) or natural variability (e.g. river flow rate, dilution factors). The type of uncertainties that are included in an uncertainty analysis will also affect the interpretation of the resulting risk distribution (Table 5).

***Table 5** What does the risk distribution represent (Thompson & Graham, 1996)?*

| |
|---|
| **Case 1.** Risk is variable but not uncertain. The distribution represents risk differences between individuals in the population (human risk assessment) or differences between ecosystems in structure, sensitivity or exposure level. |
| **Case 2.** Risk is uncertain but not variable. The risk for every individual or for every ecosystem is the same unknown number. The distribution represents the uncertainty about the actual value. |
| **Case 3A.** Risk are uncertain and variable - uncertainty and variability combined. The distribution represents the uncertain risk to a random individual or ecosystem. |
| **Case 3B.** Risk are uncertain and variable - uncertainty and variability distinguished. The results may be thought of as a "two-dimensional" distribution. Uncertainty could be characterised by upper and lower confidence intervals around the distribution representing the variability between different individuals or ecosystems. |

Risk assessments in the framework of the TGDs are not performed for an existing location but for a so-called standard environment by using a "reasonable worst-case" exposure scenario. The uncertainty or variability in this scenario is extremely difficult to quantify. For example, all the fish for human consumption is caught at the point of complete mixing of the STP effluent with a dilution factor of 10. The dilution is quite variable between locations but also in time, but also the behaviour of the fish plays a role. A fish does not spend all its time at the point of complete mixing, but may swim closer or further from the release point. Furthermore, humans do not generally consume all of their fish from the same location, but if there are more point sources, the probability increases that a fish from the vicinity of a point source is consumed. Summarising, the uncertainty in this concentration in fish will be extremely difficult to quantify in a transparent manner. Natural variability may very well be a dominant source of uncertainty and should therefore preferably be included in the assessment. The influence of uncertainty and variability should, however, be considered separately and could be pursued by an analysis in two dimensions (see e.g. Hoffman & Hammonds, 1994).

Another source of uncertainty which is extremely difficult to quantify is the uncertainty caused by the simplifications in a model concept (e.g. the assumption of well-mixed boxes in the regional model). A model is always a simplification of reality and therefore model calculations can only approximate reality.

There are specific situations where variability tends to average out in subsequent calculations. An example are the consumption rates of individual cows. Clearly, the feeding habits differ between individual cows. Humans, however, do not generally consume their milk and meat from one cow, but from many different cows. Since our time scale of interest is chronic exposure, these inter-individual differences tend to average out. In fact, we may want to include the *uncertainty* about the *average* grass consumption, but not the *variability* of the consumption between individual cows. The same argumentation can be followed for the properties of fish, earthworms and crops.

To avoid the problems with natural variability and uncertainty in model concepts as outlined previously, we restrict the analysis in this report to uncertainty in chemical-specific parameters: e.g. physico-chemical properties, emissions, partition coefficients, degradation rates, bioconcentration factors. The characteristics of the environment can be defined as "scenario properties", thereby ignoring any uncertainty or variability in them. This must be seen as an initial, pragmatic solution for the example calculations, which has the benefit of transparency. Insight in the influence of the variability in this scenario can, however, be visualised by performing assessments with alternative, equally plausible scenarios.

In many cases, this distinction between chemical-specific and scenario properties is not completely straightforward: many parameters depend both upon properties of the chemical as well as on the environment (e.g. biodegradation rates which depend also on properties like soil temperature or available bacterial populations). In these cases and whenever possible, it must be attempted to distinguish between these sources of uncertainty. The uncertainty analysis outlined in this chapter will result in a probability distribution of "risk levels" *given* the selected exposure scenario (i.e. comparable to Case 2 in Table 5). Although the variability in the environment is ignored, the advantage of this assessment is its transparency. In further development of the uncertainty analysis or in higher tiers of the risk assessment, Case 3 approaches may be pursued.

# 3. INTEGRATING UNCERTAINTY IN RISK CHARACTERISATION

Risk assessments based on limited information will always be accompanied by considerable uncertainties. It is advisable to take the uncertainties into account in the decision-making process and therefore quantify them in the risk characterisation stage. In this stage, results of exposure and effects assessment are compared to give an indication of "risk". Risk is generally defined in the scientific community as an "impact" times the probability that this impact will actually occur[1]. For example, when discussing the risk associated with flying, the risk may be expressed as the number of casualties when the plane crashes (a measure of impact), multiplied with the probability that a crash occurs (the frequency). In chemical risk assessment, we cannot usually define a risk in the strictest sense because the probabilities are not routinely quantified, and first of all, because impacts are not properly quantified. We can only indicate how much a "no-effect level" (the PNEC or an NOAEL) is exceeded (a "quotient approach"). The quotient may serve as a first step in characterising risk, but little more (Bartell, 1996) and the impact of a certain exceedance remains unknown. As inheritance from the methods for setting "safe" environmental quality standards, we are left with a tendency to aim for "no-effect levels" rather than quantifying actual impacts. Only for the human health assessment of genotoxic carcinogens, an acceptable risk or impact level is set (in the Netherlands and the US). This is required as it is assumed that no safe exposure level exists for these substances (one or just a few molecules are sufficient to develop a tumour). In the Netherlands, an additional probability of $1{:}10^6$ per year to die of cancer is taken as acceptable (the Maximum Permissible Risk level, which is a true risk) (VROM, 1989).

In contrast with flying by aeroplane where the impact of an accident can be clearly imagined, (eco)toxicological impacts are less clearly defined. What is lacking in chemical risk assessment is a kind of "dose-effect" curve for ecosystems and human populations. If such a relation could be established, we would be able to attach an effect level to a certain exposure level. Uncertainty about the exposure level will thus result in a probability distribution of effect levels, in other words: a risk in the strict sense. For human populations, the type of effect that can be expected is usually evident from animal studies (although this does not necessarily mean that the same effect occurs in humans or that it is the most sensitive effect) but there is a lack of reliable dose-effect information. For ecosystems, our scientific knowledge is still too limited to predict the nature and the extent of the impacts that chemicals may have (Power & McCarthy, 1997). Although the effect of a chemical on a single species can be tested in the laboratory, the impact in the field cannot simply be extrapolated from these tests. In the field situation, organisms will interact with others in an often complex manner. Clearly, if true risks are to be characterised, the effects assessment is the critical stage.

Current practice in the TGD (EC, 1996) for ecological effects assessment is to apply assessment factors of 10-1000 on the result of the most sensitive single-species toxicity test. The resulting PNEC may be regarded as a safe level[2]. These factors are rather arbitrary and based on limited scientific argumentation. Nevertheless, they serve a purpose as there is a

[1] This definition is not only used in the scientific community. Also in risk analysis for insurance purposes risk is defined in terms of: "how often does *it* occur (frequency)" and "when *it* occurs, how much will it cost to us."

[2] The TGD avoids the use of the term "safe level" but describes the PNEC as "A concentration below which an unacceptable effect will most likely not occur."

broad consensus on these factors, at least for screening purposes, and there is a general feeling that these factors are in the right order of magnitude. The problem with these factors is that they are probably on the conservative side, but the degree of conservatism is unknown. This can hamper risk managers to appraise possible risks as the impact of any exceedance of this PNEC is unknown. Even a qualitative comparison between two chemicals sharing the same PEC/PNEC ratio cannot be made as the shape of the hypothetical dose-effect curve of the ecosystem is not known. Nevertheless, in the risk characterisation for new substances, the decision scheme is based on the *absolute* value of the PEC/PNEC ratio[1] (EC, 1996). Another disadvantage of the safety factor approach is that it does not explicitly reward input of more toxicity data, as more data will generally only lead to lower PNECs[2]. For human effects assessment, there is not even an extrapolation to no-effect levels. The available effects data from a mammalian laboratory test or a human epidemiological study are used directly in comparison with the exposure level. This effect parameter may be an NOAEL, LOAEL, NOEC, LOEC, LD50, etc. The resulting Margin Of Safety (MOS) is evaluated on the basis of expert judgement. Although this process leaves a lot of freedom for interpretation, it lacks transparency. The TGD furthermore provides no quantitative guidance in the interpretation of the MOS and this procedure may thus lead to inconsistency in the risk assessments of individual Member States (see also Vermeire *et al.*, In prep.).

Analysing uncertainties in the exposure assessment is relatively straightforward (see Jager & Slob, 1995), which leads to a probability distribution for the PEC. The following options are available to revise the effects assessment in order to deal with uncertainties in the risk characterisation stage. In order preference (in view of the definition of "risk"):

A. Establish some kind of dose-effect relationship for human populations and ecosystems (the uncertainties in this relationship can also be quantified and may include extrapolation from laboratory species to field species or humans). The result of the risk characterisation stage will then be a probability distribution of *effects*. Decisions can be based on an acceptable level of effects.

B. Revise the assessment factors in the effects assessment to yield a median, or most likely, PNEC instead of a safe estimate and attach uncertainty to these factors (e.g. instead of a factor of 1000 use an assessment factor of 100 with a factor of 10 uncertainty). The distributions of the assessment factors can also be based on the total data set, thereby using all available information. The result of the risk characterisation will be a probability distribution of *PEC/PNEC ratios* (see e.g. Bartell, 1996)).

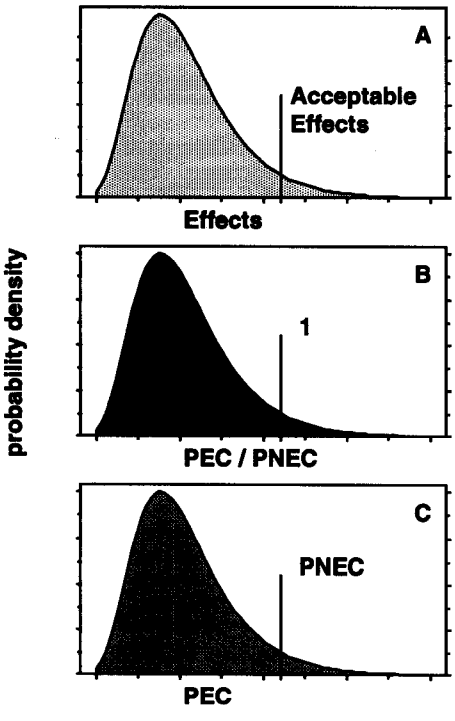



***Figure 1** Example of the three options for representing uncertainty in risk characterisation.*

[1] The decision scheme uses threshold PEC/PNEC ratios of 10, 100 and 1000 to decide whether to test at the subsequent tonnage level, ask for immediate further testing or to immediately go to risk reduction measures.

[2] The amount and the quality of the data will be used in the risk assessment to decide upon a PNEC but this will be done on the basis of professional judgement.

C. Leave the effects assessment as it is now. In that case, only uncertainty in the exposure estimate can be quantified. The result of the risk characterisation will be a probability that PEC *exceeds* a fixed, worst-case, PNEC. This option was worked out earlier (Jager & Slob, 1995; Jager, 1995) and is easy to perform and interpret. The uncertainties in the effects assessment can, however, be quite large and should preferably also be included in a risk characterisation.

These options result in different interpretations of the final "distribution of risk" that the risk managers are confronted with. The distributions are schematically drawn in Figure 1. Options A and B are discussed in more detail in the following sections.

### 3.1. Uncertainty in assessment factors

Ecosystems

A PNEC for ecosystems is calculated by application of fixed assessment factors of 10-1000 to the lowest available NOEC or LC50. These factors were chosen to reflect (EC, 1996):

1. Intra- and inter-laboratory variation of toxicity data (i.e. measurement errors).
2. Intra- and inter-species variations (biological variance).
3. Short-term to long-term toxicity extrapolation.
4. Laboratory data to field impact extrapolation (including mixture toxicity).

This interpretation of the assessment factors is quite vague as the size and contribution of each factor is unknown. The TGD factors are however very similar to those established by the EPA and modified by Slooff (1992). These were explicitly chosen according to the 10x10x10 principle: a factor of 10 for acute to chronic, 10 for inter-species differences, and 10 to extrapolate from the laboratory to ecosystems. Although still arbitrary, this procedure at least increases transparency. The total assessment factor is given by the multiplication of these factors and is applied on the lowest LC50 or NOEC. As each of these factors is aiming at a relatively "safe", upper-percentile estimate, the multiplication of these factors may lead to an unwanted worst case[1]. Furthermore, only the lowest LC50 or NOEC is used, other available data are ignored.

It is assumed in the TGD that "ecosystem sensitivity depends on the most sensitive species" (EC, 1996)[2]. The aim of the complete set of factors is therefore probably to arrive at the NOEC for the most sensitive species of the ecosystem. In view of this aim, the assessment factor approach could be interpreted as indicated in Table 6. Each factor will undoubtedly yield a distribution of values which can be combined with, for example, Monte Carlo sampling.

[1] If each factor of 10 would represent the 90th percentile of its distribution, the multiplication of these distributions would yield an overall distribution in which the factor 1000 would be at a much higher percentile.

[2] The dangers of this concept are discussed by Power & McCarthy (1997).

***Table 6** Alternative assessment factor approach for ecological effects assessment.*

**The proposed approach can be summarised as follows:**
1. Select NOECs for each basic taxonomic group: algae, crustaceans and fish.
2. For the missing NOECs: convert LC50 to NOEC with an assessment factor (acute-chronic).
3. Extrapolate from NOEC to the lowest NOEC for each group with an assessment factor (inter-species).
4. Extrapolate from lowest NOEC from the most sensitive group to PNEC using an assessment factor (lab-field).

**For predators, a similar approach can be followed:**
1. Take NOEC for mammalian species (these are usually given for industrial chemicals).
2. Apply an assessment factor to extrapolate to chronic toxicity (subacute-chronic or subchronic-chronic).
3. Extrapolate from the mammalian NOEC to the lowest NOEC for birds and mammals with an assessment factor (inter-species).
4. Extrapolate from the lowest NOEC to the field NOEC using factors to correct for differences in metabolic rate and caloric content of the food (see Jongbloed *et al.*, 1994) (lab-field).

Humans

The difference between human and ecological risk assessment lies in the protection target. For ecological risk assessment we aim to protect *species* whereas human risk assessment protects *individuals* of one species. In the TGD, human risk characterisation relies heavily on expert judgement and no attempt is made to extrapolate laboratory studies to no-effect levels for humans. This procedure leaves little room for quantitative uncertainty analysis in the effects assessment. The margin between the exposure and the laboratory test results (the Margin Of Safety or MOS) needs to be judged considering (EC, 1996):

1. The uncertainty arising from, among other factors, the variability in the experimental data and intra- and interspecies variation.
2. The nature and severity of the effects.
3. The human population to which the quantitative and/or qualitative information on exposure applies.
4. The differences in exposure (route, duration, frequency and pattern).
5. The dose-response relationship observed.
6. The overall confidence in the database.

Quantitative guidance on the weight of these factors is, however, lacking. Currently, a proposal for default assessment factors for human health is being prepared (Vermeire *et al.*, In prep.). The required factors are summarised in Table 7. This proposal also includes the definition of probabilistic assessment factors (see also Slob & Pieters, 1997). With these probabilistic factors, options A and B as described in Section 3 can be realised. The result of an uncertainty analysis of type B would be the probability that exposure exceeds the no-effect level of the "most sensitive individual" of the population.

*Table 7 Assessment factors for human health effects assessment.*

| Proposed assessment factors for (Vermeire *et al.*, In prep.): |
|---|
| 1. Inter-species extrapolation (laboratory mammal to human) |
| 2. Intra-species differences (variability among the individuals in the population) |
| 3. Extrapolation to a chronic time scale from sub-acute or sub-chronic data |
| 4. Extrapolating from LOAEL to an NOAEL |

## 3.2. Dose-effect curves for ecosystems and human populations

Ecosystems

An alternative to the use of assessment factors is to use the variability in sensitivity of the test species as a measure of the variability of all species in the ecosystem. By fitting a continuous distribution (e.g. log-normal or log-logistic) through the data (usually NOECs), an exposure level can be derived at which a theoretical percentage of the species is fully protected, i.e. is exposed below its NOEC. These statistical approaches for effects assessment are described by several authors (Van Straalen, 1990; Van Straalen & Denneman, 1989; Aldenberg & Slob, 1993; OECD, 1992). The approach of Aldenberg & Slob is also applied in the derivation of environmental quality criteria in the Netherlands and is advised in the TGD (EC, 1996) as additional method to support the effects assessment with factors. Instead of deriving a PNEC as a certain percentile of the NOEC distribution, the same distribution can also be used to calculate the fraction of species exposed above its NOEC at a given exposure level. This fraction is called the Potentially Affected Fraction or PAF (Hamers *et al.*, 1996)[1]. The relation between the PAF approach and the statistical derivation of a PNEC is shown in Figure 2. The NOEC distribution can be viewed as a kind of dose-effect curve for the ecosystem and the affected fraction as an impact or effect level (as required in option A of the previous section). So instead of the relative amount with which PEC exceeds PNEC, (semi-)quantitative impacts can now be calculated.

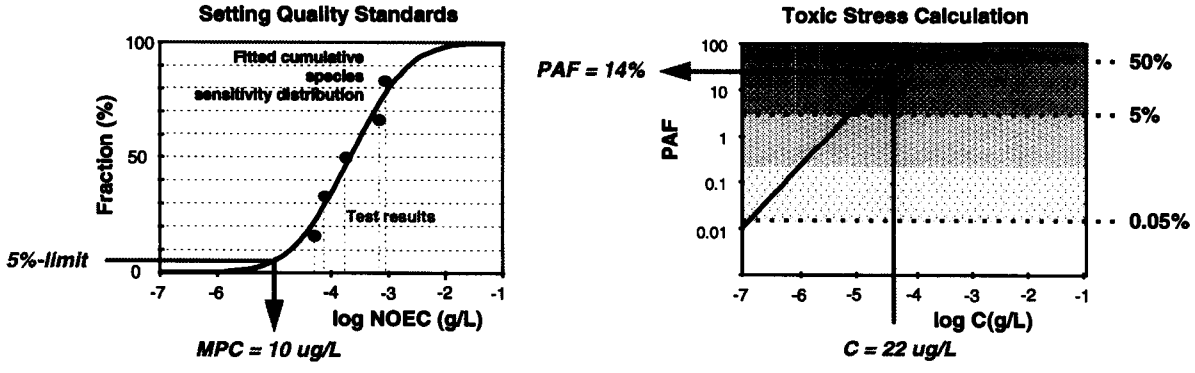



*Figure 2 The relationship between the PAF approach and the method for deriving environmental quality standards (MPC=Maximum Permissible Concentration).*

[1] This approach is also applied in the Dutch environmental outlooks for geographical mapping of risks for chemical substances. The PAF approach is described in more detail in a series of reports (Klepper & Van de Meent, 1997; Luttik *et al.*, 1997; Bakker & Van de Meent, 1997; Roghair *et al.*, 1997) and the ways to investigate the ecological consequences are discussed by Traas *et al.* (1997).

The PAF can be seen as a kind of quantitative risk level although the impact of a PAF on ecosystem structure and function is unknown. These and other limitations of the application of the PAF approach to general risk assessment are summarised in Table 8. Generally, it is considered acceptable when the NOEC is exceeded for less than 5% of the species (see also OECD, 1992; Health Council of the Netherlands, 1988). Even though the impact of a given PAF remains unknown, it gives quantitative information which can very well be applied to risk reduction or comparison of chemicals. This is illustrated in Figure 3: substance A and B have the same lowest NOEC, and therefore the same PNEC (according to standard extrapolation procedures with factors). For substance A, the experimental NOECs are further apart. Because of this higher variability, it is likely that species exist that are more sensitive species for this chemical than for substance B. This is reflected in the fact that the 5% line is exceeded at a lower PEC for this compound. On the other hand, if the exposure concentration is above the lowest NOEC, the PAF for compound B will be higher than for compound A. This shows that a more quantitative risk estimate can be obtained when the entire curve is taken into account.

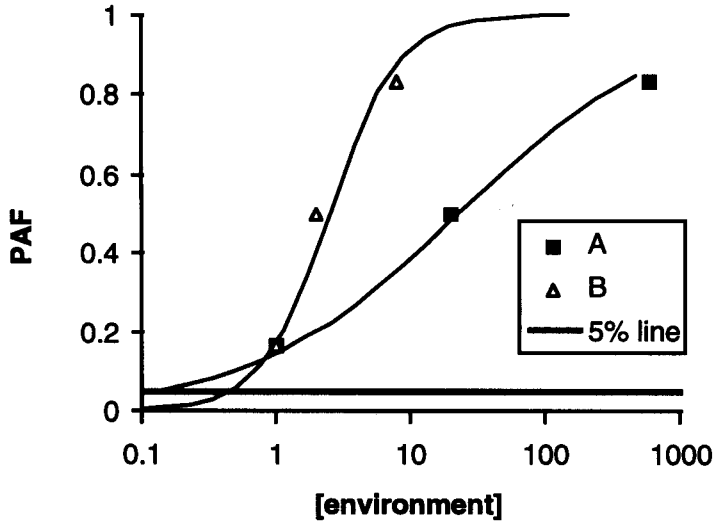



*Figure 3 Example of PAF curves for two substances with the same lowest NOEC but different variation in sensitivities.*

With the PAF approach, the variability in sensitivities between species in the ecosystem is accounted for. When the PEC is uncertain, we have to deal with two different distributions: an NOEC distribution caused by variability, and a PEC distribution caused by uncertainty (variability in the exposure was ignored by defining a standard scenario). There are in principle three ways to combine these two distributions in a risk measure:

1. Define an acceptable effect level (e.g. the 5th percentile of the NOEC distribution) and calculate the probability that PEC exceeds this level (conform case 2 in Table 5).
2. Draw randomly from both distributions and calculate PEC/NOEC. From the distribution of PEC/NOEC, the probability can be calculated that PEC>NOEC which can be interpreted as the probability that for a random species, its NOEC is exceeded (conform case 3A in Table 5). This approach was proposed by Van Straalen (1990).
3. Draw random PECs and calculate for each the corresponding PAF. The risk distribution is in this case a probability distribution of PAFs for a chemical. This can be interpreted as a case 3B risk distribution (see Table 5), at least for the variability in the effects assessment.

***Table 8** Limitations of the PAF approach.*

1) There are generally insufficient data available to estimate a reliable NOEC distribution (the Dutch Health Council advises to use at least four NOECs (Health Council of the Netherlands, 1988). The minimum required data set for new substances includes only three aquatic LC50s. Advantage of the PAF approach is that more information will give a more precise distribution and, generally, lower risk estimates. The problem of lack of NOECs can be tackled as follows (Hamers *et al.*, 1996):
   - LC50s can be extrapolated to NOECs (using a historical distribution of LC50/NOEC ratios, see e.g. Roghair *et al.*, 1997). The added uncertainty of this extrapolation step can be included in the assessment.
   - Equilibrium partitioning can be applied to convert aquatic toxicity data to the sediment or terrestrial environment (adding the uncertainty in the partition coefficient). This assumes that all species are exposed via the porewater or a related route. There are, however, also possibilities to address food-exposed animals (see e.g. Klepper & Van de Meent, 1997; Traas *et al.*, 1997).
   - NOAELs for rats or NOECs in food can be extrapolated to NOECs based on environmental concentrations using bioconcentration factors, feeding rates, and possibly, correction factors for caloric contents of the food etc. The resulting NOECs can then be included in the NOEC distribution for the ecosystem.
2) The method assumes laboratory species to be representative, random samples from the ecosystem. This assumption is questionable since laboratory species are usually selected on the basis of there ease of culture and handling in the laboratory, but also on their sensitivity (the species must be sensitive enough to express toxic effects). Furthermore, the tested species are usually derived from laboratory cultures which are genetically less heterogeneous than field populations.
3) The method assumes a type of distribution of species sensitivity (e.g. log logistic). For the main part of the range, the shape of the distribution will not have a major effect. Care must be taken for estimates in the tails of the distribution (which will depend heavily on the assumed shape) and for chemicals with a specific mode of action (e.g. insecticides or herbicides).
4) The ecological impact of a given PAF is unknown. Work is currently in progress to address this item (see also Traas *et al.*, 1997).

These risk measures all have their merits. The first method corresponds best with the current practice of deriving fixed PNEC values, the third method probably corresponds best to the notion of "ecosystem damage". The second approach is interesting as it returns ecological risk as a single number. However, a 5% probability that the NOEC is exceeded for a randomly drawn species could mean that 5% of the species is exposed above their NOEC (narrow PEC distribution, broad NOEC distribution). It could however also mean that for all species there is a 5% probability that their NOEC is exceeded (broad PEC distribution, narrow NOEC distribution). Option 3 is worked out in the example calculation. It should be noted that the NOEC distribution in itself is also uncertain, depending on the number and quality of the available NOECs. When NOECs are derived from LC50s, the resulting NOEC distribution will be more uncertain than when it is based on 20 chronic toxicity studies. This uncertainty must also be incorporated in the assessment (this is worked out preliminary in Appendix I.9).

Humans

Human risk assessment aims to protect individuals. For human effects assessment, a dose-effect relationship like the PAF approach discussed previously, should therefore not reflect variation in sensitivities between species but inter-individual differences. For ecological risk assessment, the laboratory data are assumed to be representative for real species, for human risk assessment, data for one species (e.g. rats or mice) must be extrapolated to another (humans). We don't want to protect a certain percentage of all mammalian species, but we want to protect a certain percentage of the population of one species which is a fundamentally different problem. Current practice (explicit or implicit) is to apply a factor of 10 to account for differences in sensitivity within the population between average and sensitive individuals.

In this way, it is considered unlikely that the most sensitive individuals are more than ten times as sensitive as the average human. Slob & Pieters (1997) proposed a lognormal distribution for this assessment factor. The variation in the assessment factor for intra-species differences can also be used to define a sensitivity distribution comparable to the PAF curve. In this manner, a theoretical percentage of the population can be calculated that is exposed above its no-effect level (type A as described in Section 3). However uncertain this percentage is, it may still provide valuable (semi-)quantitative information especially in the comparison of different chemicals.

A further advantage of this dose-effect approach would be that variability is distinguished from uncertainty. Human individuals differ in sensitivity (which is variability) but we are also uncertain about the extrapolation from the experimental data to human NOAELs. These sources of uncertainty in risk assessment can thus be treated separately which is important as they are fundamentally different. First, experimental results can be extrapolated to the average human using probabilistic assessment factors for inter-species differences, sub-acute to chronic time scales, and LOAELs to NOAELs (see Table 7). Subsequently, inter-individual differences are represented in an "individual sensitivity distribution" comparable to the NOEC distribution for ecosystems.

When uncertainty in the PEC (i.e. the daily dose) is included, the same type of risk characterisation for humans can be performed as for the ecosystem Apart from the added transparency, these kind of risk characterisations also secure comparability between human and ecological risk assessment which currently leaves much to be desired.

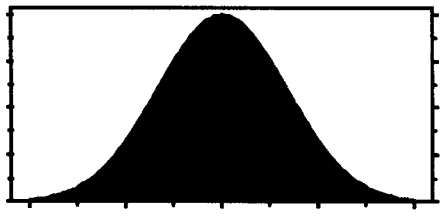
# 4. TYPES OF DISTRIBUTIONS

For the uncertain parameters, probability distributions must be defined. The difficulty of selecting appropriate parameter distributions may be another reason for lack of acceptance of probabilistic risk assessment among regulators (Finley & Paustenbach, 1994). The final distribution of risk may depend strongly upon the shape and magnitude of the input distributions but, nevertheless, even limited information about the distribution of an input parameter is better than assuming a single value for an entire population (Anderson & Yuhas, 1996). A strategy for defining distributions is given in Table 9 and several popular distributions are discussed briefly in this chapter.

***Table 9** Strategy in characterising input distributions (Haimes et al., 1994, as adapted by Moore, 1996).*

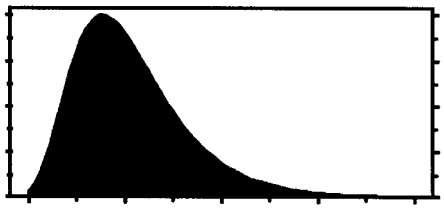
| |
|---|
| 1. Will the variable have an important influence on the output? If not, don't worry about it. |
| 2. Is the distribution for the input variable known? |
| 3. If not, are there sound theoretical reasons for assigning a specific distribution to the input variable? |
| 4. If not, are the data adequate for fitting a distribution? |
| 5. If not, do appropriate surrogates exist? If yes, repeat 2-4. |
| 6. If not, do data exist addressing components of the variable? If yes, repeat 2-4. |
| 7. If not, solicit expert opinion. |

## 4.1. The normal distribution



The normal distribution is probably the most popular distribution since many natural phenomena like people's height can be satisfactory described by it. The distribution is symmetrical and extends from minus infinity to plus infinity. The normal distribution is characterised by a mean and a standard deviation. As a rule of thumb, approximately 68% of the values are within one standard deviation from the mean and 95% within 2 standard deviations.

## 4.2. The lognormal distribution



There are strong theoretical and empirical considerations to assume a lognormal distribution *a priori* for many physical entities (Slob, 1987; Seiler & Alvarez, 1996). The lognormal distribution is positively skewed, and has a domain ranging from zero to infinity. These properties make the lognormal distribution less suited for parameters which have a physical upper limit like fractions which are usually smaller than 1. The distribution can be characterised by the median and a measure for the variation. A convenient measure is the "dispersion factor" or $k$ which is defined as follows: 95% of the values is within a factor of $k$ from the median (Slob, 1994). This dispersion factor has the advantage of

being readily interpretable and can be simply related to the standard deviation or coefficient of variation (see Table 10).

***Table 10** Characterising lognormal distributions.*

Lognormal distributions are characterised by a dispersion factor ($k$) defined such that e.g. 95% of the values of a stochastic variable ($X$) is within a factor of $k$ from the median, $M(X)$ (Slob, 1994):

$$p\left(\frac{M(X)}{k} > X > kM(X)\right) = 0.95$$

This factor is related to the standard deviation on log scale ($\sigma_{log\,X}$) by:

$$k = \exp\left(1.96\sigma_{\log X} \ln b\right)$$

Where $b$ denotes the base of the logarithm used to calculate the standard deviation. When comparing estimated data with measured values, the required standard deviation can be derived from the residuals on log scale. In case of log-linear QSAR regressions, the sd of the residuals can be used directly in the equation above. However, in case the average of the residuals is not zero (e.g. when comparing an estimation routine with independent measured data), the standard deviation of the residuals cannot be used. What is required is the deviation of the measured data from the estimate (and not from the average deviation); i.e. the sum of squares:

$$\sigma_{\ln X} = \sqrt{\frac{\sum\left(\ln x_{\text{expected}} - \ln x_{\text{measured}}\right)^2}{n-1}}$$

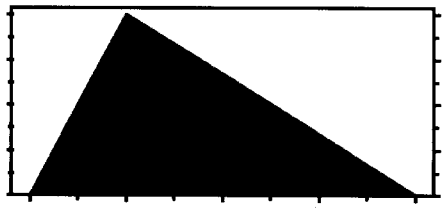
Other measures which are sometimes given in the literature for the spread of the lognormal distribution are the coefficient of variation ($CV$) and the geometric standard deviation ($GSD$). These can be related to a dispersion factor $k$ by the following equations:

$$\sigma_{\ln X} = \ln GSD$$

$$\sigma_{\ln X} = \ln\left(CV^2 + 1\right)$$

$$k = \exp\left(1.96\sigma_{\ln X}\right)$$

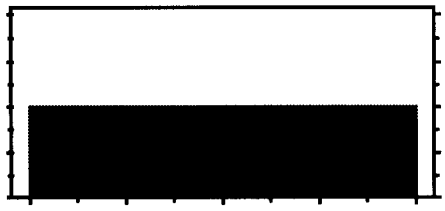
## 4.3. The triangular distribution



The normal and lognormal distribution are less suited for parameters which have an upper or lower limit like fractions. An alternative is the triangular distribution which is characterised by a mode and a lower and upper limit. The parameter values near the mode have a higher probability than the values in the tails. Triangular distributions can be viewed as a conservative characterisation of a truncated normal or lognormal distribution (Finley *et al.*, 1994). From theoretical considerations, it is highly unlikely that the actual distribution of a parameter in risk assessment is triangular (Seiler & Alvarez, 1996). Nevertheless, this distribution may be used as initial assumption to represent

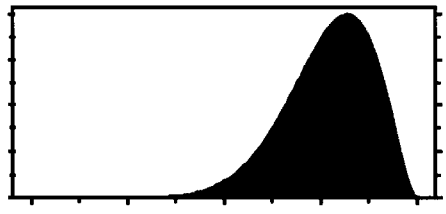
the currently available data when little is know except upper and lower limits and a mode (Whitmyre *et al.*, 1992).

### 4.4. The uniform distribution



The uniform distribution is characterised by an upper and a lower limit. All parameter values have equal probability. This distribution is popular when there is very limited knowledge about the actual distribution of the probabilities. As with the triangular distribution, the theoretical background is doubtful and the use of this type of distribution in risk assessment should be quite rare (Seiler & Alvarez, 1996). Physical processes will not show this type of discontinuous behaviour. As an initial and conservative assumption, this distribution may be used but the limitations and theoretical suspicions must be kept in mind.

### 4.5. The beta distribution



The beta distribution is a continuous and very flexible distribution commonly used to represent variability over a fixed range (e.g. for percentages and fractions). This distribution is advised by Seiler & Alvarez (1996) as the simplest alternative for discontinuous distributions like the uniform or triangular ones. The beta distribution can take a wide variety of shapes but is always confined between zero and a positive value. The methods for determining the parameters of the distribution are, however, complex.

### 4.6. Non-parametric distribution

Apart from parametric distributions, it is also possible to use the original data in a non-parametric representation (e.g. cumulative percentiles). Finley *et al.* (1994) recommend this approach as parametric distributions can result in implausible or even physically impossible values. They propose to use parametric distributions only when they are demonstrated to fit the original data.

### 4.7. Summary and pragmatic approach

From the discussion by Seiler & Alvarez (1996), it can be concluded that the normal, lognormal and beta distribution are most appropriate for the purpose of risk assessment. A normal distribution may be assumed *a priori* when available data suggest a symmetrical distribution around the mode and a lognormal distribution when the frequency distribution is positively skewed (Whitmyre *et al.*, 1992). Monte Carlo analysis requires a precise characterisation of parameter distributions, even when the underlying empirical information is actually insufficient. This characterisation is usually done using "a combination of professional judgement, limited empirical information, and blind faith" (Moore, 1996).

In Appendix I the uncertainty in the chemical-specific parameters (see Chapter 2) is characterised for the example calculations in Chapter 5. It should be noted that this quantification is by no means complete: no extensive literature searches or extensive consultation of experts was conducted. Nevertheless, the presented quantification is used as a "order of magnitude" estimate for the example calculations and may provide a starting point for further discussion. A summary of the selected distributions is presented in Table 11. In the summary table, the following symbols are used to characterise the type of distribution:

L Lognormal. Defined by a median (the median value is usually clear, otherwise it is denoted by M) and an uncertainty factor k (95% of the parameter values is within a factor *k* from the median)

U Uniform. Defined by an upper and lower limit.

T Triangular. Defined by an upper and lower limit and a mode. Not that this mode can differ extremely from the median or the average in case the triangular distribution is skewed.

***Table 11** Summary of the parameter distributions for the EUSES local model.*

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| **Physico-chemical properties** | All data from handbooks (Etienne, 1996; Howard, 1990; Mackay, 1995; Verschueren, 1983; Weast *et al.*, 1985) | | |
| Octanol-water partition coefficient | Kow<br>log Kow≤4<br>log Kow 4-5.5<br>log Kow>5.5 | <br>L (k=2.8)<br>L (k=12)<br>L (k=24) | Different uncertainty for low, medium and high *Kow* values |
| Water solubility | SOL<br>SOL≤1 mg/L<br>SOL>1 mg/L | <br>L (k=12)<br>L (k=2.4) | Different uncertainty for low and high solubility. Correlated to uncertainty in *Kow*, (corr. coeff.= -0.96 on log scale) |
| Vapour pressure | VP<br>VP≤1 Pa<br>VP>1 Pa | <br>L (k=60)<br>L (k=1.9) | Different uncertainty for low and high vapour pressure. Correlated to *Kow* (corr. coeff.= -0.87 on log scale) |
| Melting point | TEMPmelt | U (+- 3°) | Judged from residuals |
| **Emission estimation** | All data from P. van der Poel (pers. comm.) | | |
| Release fraction | $F_{air}$ / $F_{water}$ | Triangular | Several tables in App. I.2 |
| Fraction of the local main source | Fmainsource | Triangular | Several tables in App. I.2 |
| Number of emission days | Temission | Triangular | Several tables in App. I.2 |
| **Partition coefficients** | | | |
| Organic-carbon normalised partition coefficient | Koc<br>log Kow 1-4<br>log Kow 4-7 | <br>L (k=3.2)<br>L (k=14) | Calculated from original data Sabljic *et al.* (1995) |
| Henry's law constant | HENRY | L (k=16) | Data from handbooks. Only relevant when measured |
| Constant of Junge equation | CONjunge | L (M=0.4, k=3.3) | Derived from observations Noordijk & De Leeuw (1991) |
| **Biodegradation rates** | All data from J. Struijs (pers. comm.) | | |
| Biodegradation rates in STP, surface water, soil and sediment | $DT50bio_{stp}$<br>$DT50bio_{water}$<br>$DT50bio_{soil}$<br>$DT50bio_{sed}$ | L (M and k depend on characterisation of biodegradability) | See Appendix I.4 |
| **Environmental distribution** | | | |
| Standard deposition flux of gaseous compounds | $DEPstd_{gas}$ | L (k=10) | Toet & De Leeuw (1992) and A. van Pul (pers.comm.) |
| Standard deposition flux of aerosol-bound compounds | $DEPstd_{aer}$ | L (k=5) | (Toet & De Leeuw, 1992) and A. van Pul (pers.comm.) |

| **Exposure assessment predators/humans** | | | |
|---|---|---|---|
| BCF for fish | $BCF_{fish}$<br>log Kow 1-6<br>log Kow 6-10 | L (k=20)<br>L (k=185) | From experimental data (Devillers *et al.*, 1996; Nendza, 1991) |
| Worm-porewater partition coeff. | $K_{worm\text{-}porew}$ | L (k=17) | From experimental data (Connell & Markwell, 1990) |
| Transpiration stream conc. Fact. | TSCF | T (0-1) | Estimate taken as mode (based on data Briggs *et al.*, 1982; Polder *et al.*, 1995) |
| Conductance | $g_{plant}$ | L (k=4.1) | From experimental data (Riederer, 1995) |
| Biotranfer factor for meat | $BAF_{meat}$ | L (k=64) | From experimental data (Travis & Arms, 1988) |
| Biotranfer factor for milk | $BAF_{milk}$ | L (k=36) | From experimental data (Travis & Arms, 1988) |
| Purification factor drinking water | Fpur | T (M 0.15, range 0-0.65) | Based on F. van Gaalen (pers. comm.) |
| Respirable fraction of the inhaled substance | Fresp | U (range 0-1) | T. Vermeire (pers. comm.) |
| Bioavailability for inhalation | BIOinh | U (range 0-0.75) | T. Vermeire (pers. comm.) |
| Bioavailability for oral uptake | BIOoral | U (range 0-1) | T. Vermeire (pers. comm.) |
| **Effects assessment** | | | |
| Acute LC50 to chronic NOEC | $AF_{ac\text{-}chr}$ | L (M=5, k=10) | Roghair *et al.* (1997) and D. de Zwart (pers. comm.) |
| NOEC to most sensitive species | $AF_{inter}$ | 1+L (M=6.3, k=23) | Data set D. de Zwart (pers. comm.) |
| Lab to field systems | $AF_{lab\text{-}eco}$ | L (M=1, k=10) | From data of Emans *et al.* (1993) |
| Mammals 28 day to chronic | $AFpred_{subac\text{-}chr}$ | L (M=3.5, k=23) | Proposed by (Vermeire *et al.*, In prep.) |
| Sub-chronic to chronic | $AFpred_{subchr\text{-}chr}$ | L (M=2, k=15) | Proposed by (Vermeire *et al.*, In prep.) |
| Mammals to most sensitive from birds and mammals | $AFpred_{inter}$ | 1+L (M=7.4, k=15) | Experimental data (Romijn *et al.*, 1991) |
| Mammals lab to field | $AFpred_{lab\text{-}fld}$ | L (M=10, k=2.5) | Data Jongbloed *et al.* (1994) |
| Inter-species extrapolation from rat to human | $AFhuman_{inter}$ | L (M=4, k=34) | Proposed by Vermeire *et al.* (In prep.) |
| Intra-species extrapolation | $AFhuman_{intra}$ | 1+L (M=3, k=2.3) | Slob & Pieters (1997) |
| Sub-chronic to chronic | $AFhuman_{subchr\text{-}chr}$ | L (M=2, k=15) | Proposed by Vermeire *et al.* (In prep.) |
| Sub-acute to chronic | $AFhuman_{subac\text{-}chr}$ | L (M=3.5, k=23) | Proposed by Vermeire *et al.* (In prep.) |

# 5. EXAMPLE CALCULATIONS

The benefits of probabilistic risk assessment are illustrated in this chapter with example calculations. Actual data for a new chemical was taken (a chemical intermediate, input values are given in Appendix II). The approaches A (dose-effect curve), B (uncertainty in PEC and PNEC) and C (only uncertainty in PEC) of Chapter 3 are worked out separately. In the last section, the same chemical is assessed for a "borderline-risk" situation: the releases to the environment are divided by a fixed factor so that EUSES predicts a PEC/PNEC ratio of one for the aquatic compartment. These calculations are just illustrations of the possibilities of probabilistic risk assessment. In interpreting these results, the scope of the analysis and the assumptions in the preliminary distributions must be kept in mind. Furthermore, it should be noted that these results indicate a risk *given* the worst-case exposure scenario.

For now, only a risk assessment for the local scale is examined, since this scale usually dominates for new chemicals. The regional model is ignored for now (see e.g. the work of Etienne, 1996). The exposure routes of EUSES for the different endpoints are shown in Figure 4 to Figure 6. Calculating these routes with parameter distributions leads to probability distributions for the PECs and the dose for human exposure.

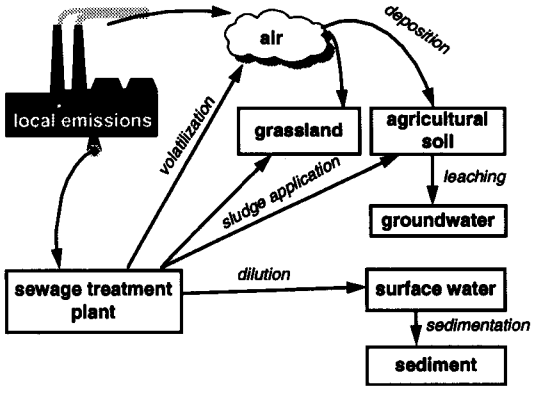



*Figure 4 Local emission and distribution routes in EUSES.*

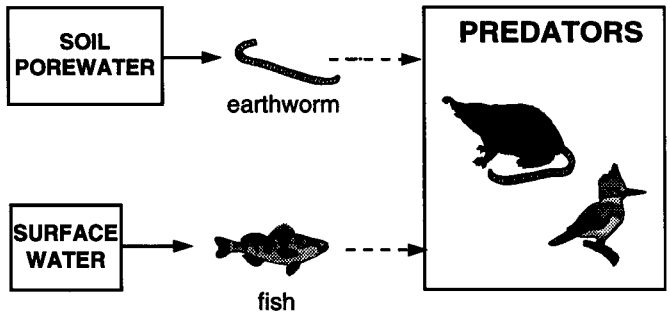



*Figure 5 Generic food chains for predating birds and mammals.*

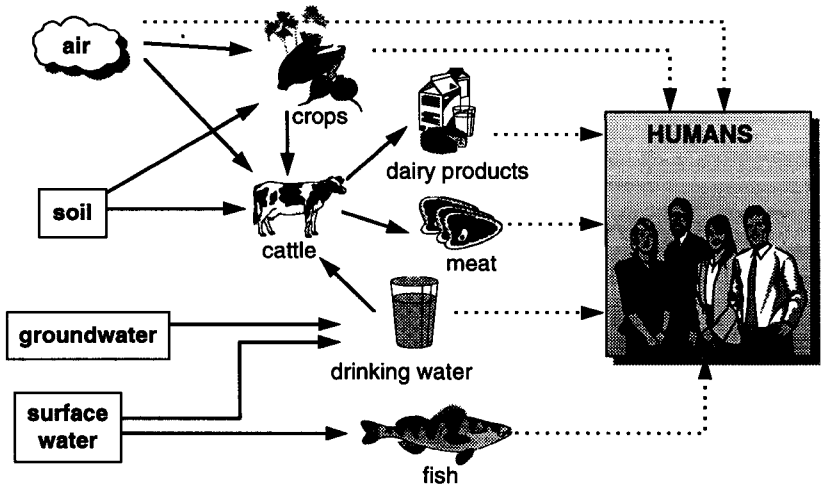



***Figure 6** Exposure routes for humans via the environment as applied in EUSES.*

For the effects assessment, the three options discussed in Chapter 3 are calculated. The calculation steps are schematically drawn in Figure 7 and Figure 8, a more detailed description is provided in Appendix I.9 and I.10.

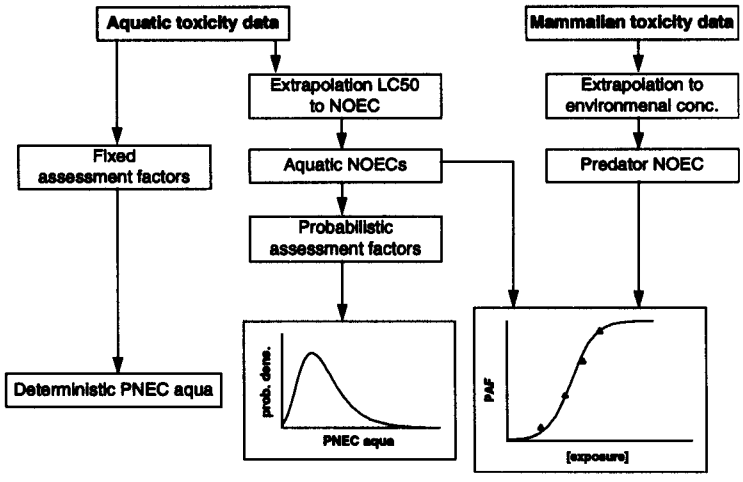



*Figure 7 Schematic representation of the three options for aquatic effects assessment. The approach for the terrestrial ecosystem is comparable using equilibrium partitioning to estimate toxicity data.*

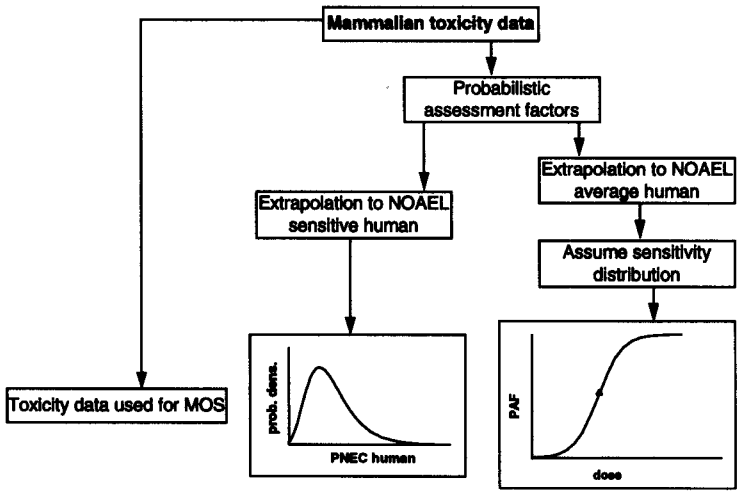



*Figure 8 Schematic representation of the three options for human effects assessment.*

The results will be presented graphically (cumulative probability distributions) and in tables as explained in Table 12. For the quotient approaches, not all endpoints will be shown in the Tables. Only the results for the aquatic ecosystem, the fish-eating predators and humans are reported. More detailed results are given in Appendix II.

*Table 12 Explanation of the table format used in the subsequent sections.*

| | Endpoints |
|---|---|
| **EUSES** | Results calculated with the standard EUSES settings. |
| **Results of uncertainty analysis** | |
| 50% | 50th percentile of the risk estimate's distribution. This is the median risk level. |
| 80% | 80th percentile of the risk estimate's distribution. |
| 90% | 90th percentile of the risk estimate's distribution. |
| 95% | 95th percentile of the risk estimate's distribution. |
| Prob RCR>1 | Probability that PEC exceeds PNEC. |
| Prob MOS<100 | Probability that the Margin Of Safety is less than 100. |
| Prob MOS<1000 | Probability that the Margin Of Safety is less than 1000. |
| EUSES perc. | The percentile of the risk distribution which equals the risk estimate as given by EUSES. This indicates the degree of conservatism of the EUSES quotient. |
| **Main uncertainties** | |
| | Main source of uncertainty for each protection target. In order of importance. |

All calculations were performed with an Excel™ spreadsheet of EUSES. Monte Carlo sampling was performed with Crystal Ball™ using 1000 runs and Latin Hypercube sampling. Test results indicated that less than 500 runs is sufficient. More runs were performed to obtain smoother distributions.

## 5.1. Approach C: Fixed PNEC, uncertain PEC

This risk estimate compares the uncertain PEC to the PNEC derived according to the TGD assessment factors. The results of the uncertainty analysis are summarised in Table 13. The median risk estimate is usually lower than the figure given by EUSES. For the fish-eating predator, it is higher which is caused by the shape of the distribution of the emission factor to water. In this triangular distribution, the probability that a value is sampled above the mode is very high. The shape of the distribution should therefore be carefully considered. The risk estimate produced by EUSES for the other end-points lies at the 77-94th percentile of the distribution. For the human MOS, this percentile is highest, indicating that the EUSES MOS is more conservative than the ecosystem RCRs for this compound.

The cumulative probability distributions for the RCRs and the MOS are shown in Figure 9 and Figure 10, respectively. From Figure 9 it is clear that the RCRs for predators are more uncertain (lower slope) than those of the terrestrial and aquatic ecosystem. From these figures, it can be judged how much the RCR must be decreased or the MOS must increased to obtain an acceptable risk estimate.

The main sources of uncertainty are also shown in Table 13. The release figures are prominently present in these lists, as well as the biodegradation rates in the STP and soil. These parameters would therefore be the first to receive in-depth attention.

*Table 13 Summarised results of uncertainty analysis with a fixed PNEC.*

| | Water | Fish-eater | MOS |
|---|---|---|---|
| **EUSES RCR** | 413 | 1.17 | 23.3 |
| **Fixed PNEC** | | | |
| 50% RCR | 204 | 1.7 | 140 |
| 80% RCR | 466 | 7.7 | 54 |
| 90% RCR | 719 | 17 | 35 |
| 95% RCR | 982 | 28 | 21 |
| Prob RCR>1 | 100 | 62 | - |
| Prob MOS<100 | - | - | 39 |
| Prob MOS<1000 | - | - | 94 |
| EUSES perc. | 77 | 42 | 94 |
| **Main uncertainties** | | | |
| | em. days | $BCF_{fish}$ | em. days |
| | $kbio_{stp}$ | $kbio_{stp}$ | $DT50bio_{soil}$ |
| | $Femiss_{water}$ | $Femiss_{water}$ | $Femiss_{water}$ |
| | $F_{mainsource}$ | $F_{mainsource}$ | VP |
| | | | $BCF_{fish}$ |

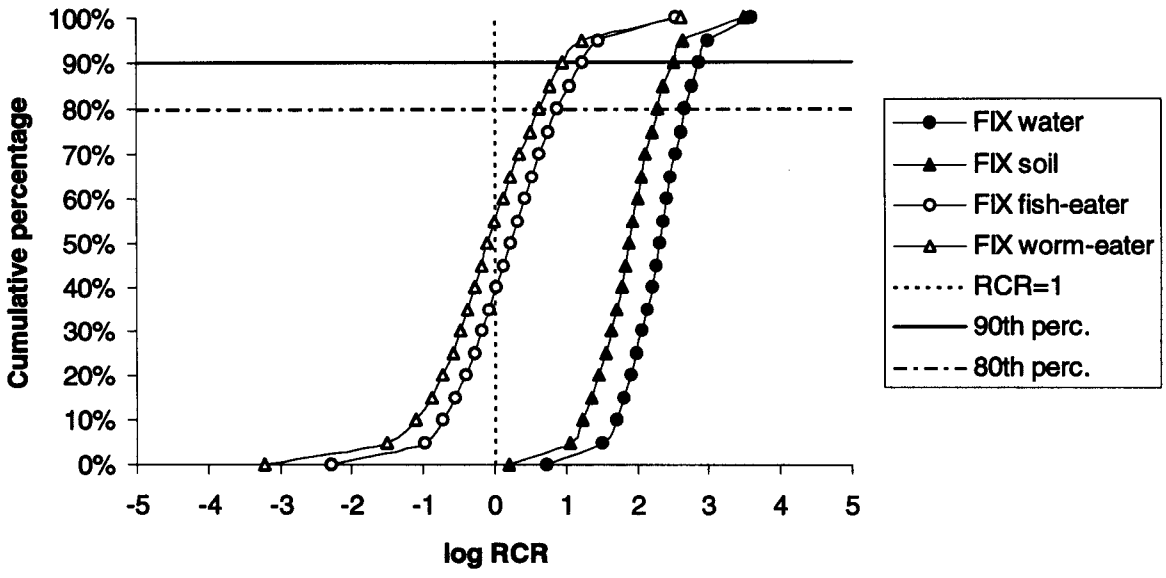



***Figure 9** Cumulative probability distribution for the RCR with PNEC calculated using the fixed assessment factors of the TGD. The RCR is denoted by "FIX" in the legend.*

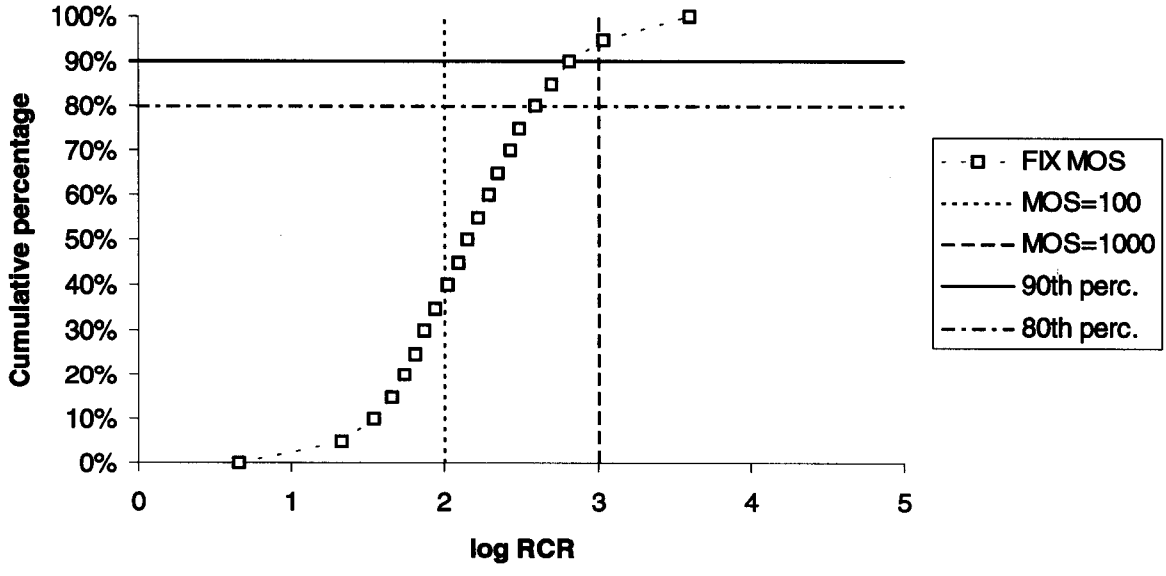



***Figure 10** Cumulative probability distribution for the MOS using a fixed NOAEL.*

## 5.2. Approach B: Uncertainty in PEC and PNEC

This risk estimate compares the uncertain PEC to the PNEC derived using uncertain assessment factors (see Appendix I.9). The results of the uncertainty analysis are summarised in Table 14. The median risk estimate is generally much lower than the EUSES figure. Only for predators it is similar or higher. This is caused by the fact that the proposed extrapolation of the NOEC includes the lab-field difference in caloric content of the food and metabolism rates. These factors are ignored in the TGD procedure. The risk estimate produced by EUSES for the other end-points lies at the 88-90th percentile of the distribution. For humans, also an RCR is calculated using uncertain assessment factors to arrive at a No-Effect Level (NEL) for a sensitive human individual (see Appendix I.10).

The cumulative probability distributions for the RCRs and the MOS are shown in Figure 11. The distribution of the MOS using an uncertain NOAEL is not shown as it is nearly identical to the distribution shown in Figure 10. From these figures, it can be judged how much the RCR must be decreased to obtain an acceptable risk estimate.

The main sources of uncertainty are also shown in Table 14. The release figures are present in these lists, but the list is dominated by the uncertainty in the assessment factors. Toxicity testing may therefore receive in-depth attention. This kind of information could not be derived using the previous approach using fixed assessment factors.

*Table 14 Summarised results of uncertainty analysis with uncertain PEC and PNEC.*

| | Water | Fish-eater | Sens. human | MOS |
|---|---|---|---|---|
| **EUSES RCR** | 413 | 1.17 | - | 23.3 |
| **Uncertainty** | | | | |
| 50% RCR | 37 | 5.2 | 0.39 | 141 |
| 80% RCR | 190 | 56 | 3.5 | 43 |
| 90% RCR | 523 | 176 | 10 | 23 |
| 95% RCR | 1140 | 430 | 32 | 12 |
| Prob RCR>1 | 97 | 74 | 36 | - |
| Prob MOS<100 | - | - | - | 41 |
| Prob MOS<1000 | - | - | - | 90 |
| EUSES perc | 88 | 28 | - | 90 |
| **Main uncertainties** | | | | |
| | em. days | $AF_{subac-chr}$ | $AFhum_{inter}$ | UF NOEC |
| | $AF_{inter}$ | $BCF_{fish}$ | $AF_{subac-chr}$ | em. days |
| | $AF_{lab-eco}$ | $AFpred_{inter}$ | em. days | $DT50bio_{soil}$ |
| | $AF_{ac-chr}$ | $Femiss_{water}$ | $DT50bio_{soil}$ | log VP |
| | $kbio_{stp}$ | $AF_{lab-field}$ | $Femiss_{water}$ | $Femiss_{water}$ |

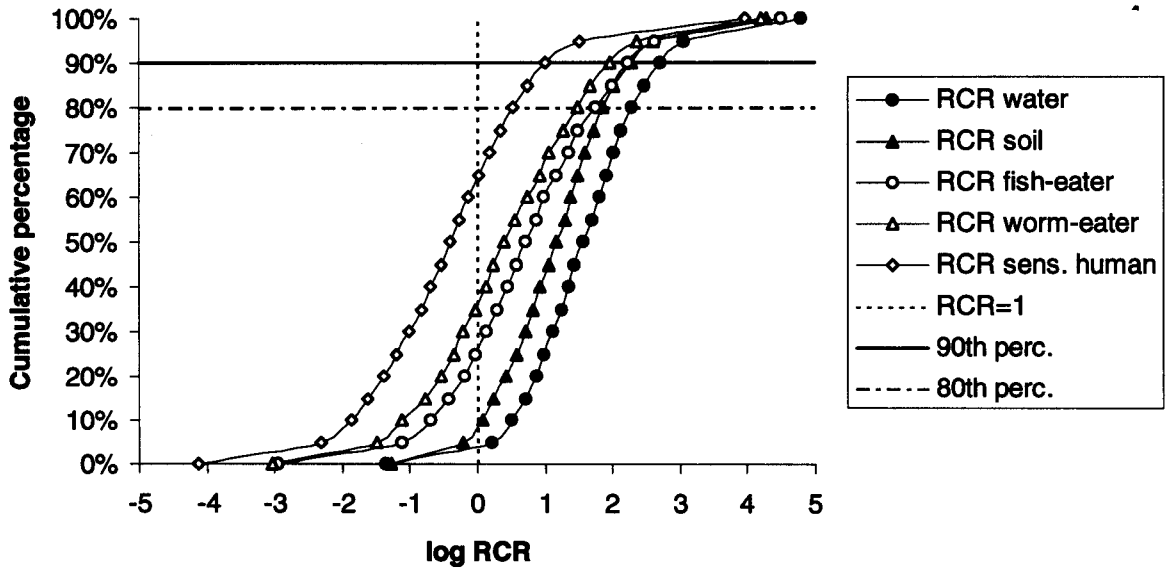



***Figure 11*** *Cumulative probability distribution for the RCR with PNEC calculated using uncertain assessment factors.*

## 5.3. Approach A: Dose-effect approach (PAF)

This risk estimate gives the fraction of the species which is expected to be exposed above it's NOEC. For humans, this is the fraction of the individuals in the population exposed above their NOAEL. The approach is described in detail in Appendix I.9. The assessment of predators is included in the ecosystem PAF. In this way, four NOECs are available to construct a species-sensitivity distribution. For each PEC in the PEC probability distribution, a corresponding PAF can be derived. This procedure results in a probability distribution of PAFs which is drawn in a cumulative form in Figure 12. This figure also shows the 95% protection line as example of an "acceptable risk level", and the 80th and 90th percentiles.

For the aquatic and terrestrial system, the PAFs are high, also resulting in a large probability that the PAF exceeds 5%. For humans, the distribution is highly skewed: the median PAF is low (1%), but the 80th percentile is already at a PAF of 41%. Figure 17 in Appendix II shows the sensitivity curves in more detail.

***Table 15** Summarised results of uncertainty analysis with the dose-effect approach (PAF).*

| | Water | Soil | Sens. human |
|---|---|---|---|
| **EUSES** | 413 | 286 | - |
| **PAF** | | | |
| 50% | 0.56 | 0.29 | 0.01 |
| 80% | 0.80 | 0.56 | 0.41 |
| 90% | 0.88 | 0.70 | 0.86 |
| 95% | 0.95 | 0.79 | 0.98 |
| Prob PAF>5% | 97 | 88 | 36 |
| **Main uncertainties** | | | |
| | No emiss. | No emiss. | $AFhum_{inter}$ |
| | $kbio_{stp}$ | $AF_{subac\text{-}chr}$ | $AF_{subac\text{-}chr}$ |
| | $BCF_{fish}$ | $K_{worm\text{-}porew}$ | No emiss. |
| | $AF_{subac\text{-}chr}$ | $Femiss_{water}$ | $DT50bio_{soil}$ |
| | $F_{mainsource}$ | LC50 | $Femiss_{water}$ |

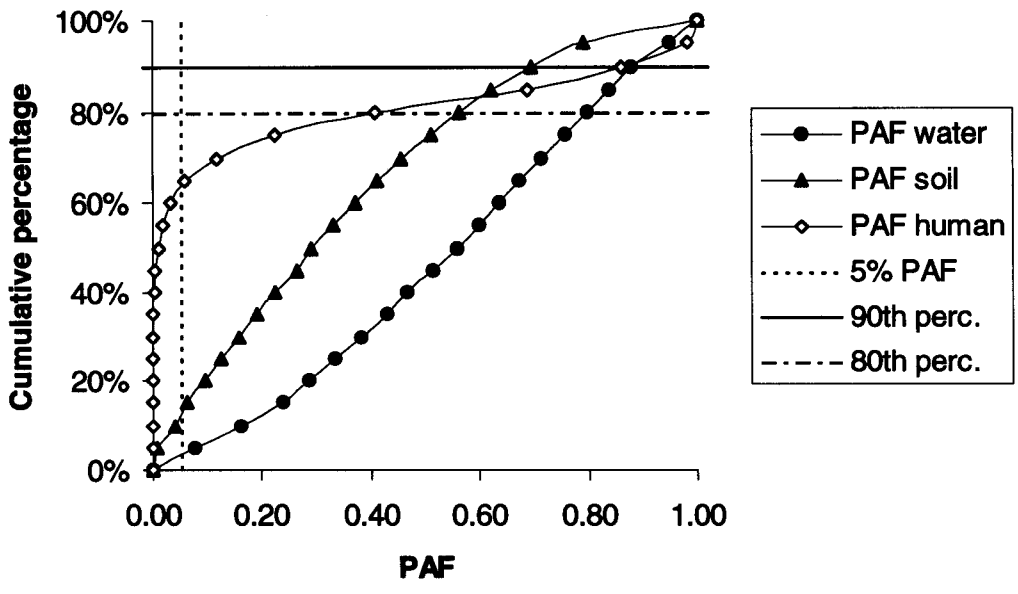



***Figure 12** Cumulative probability distribution for the PAF. The PAF for water and soil includes the NOEC for predators.*

## 5.4. Example risk distributions when PEC/PNEC of EUSES is 1

An additional calculation was performed with the same chemical to illustrate the probabilistic risk estimates for a safer situation. For this purpose, all releases were divided by a fixed factor to yield an EUSES RCR for the aquatic ecosystem of exactly one. In this way, the aquatic RCR is exactly at the cut-off value used to indicate "concern". The RCRs for the other endpoints are lower than one. Although this indicates a relatively "safe" situation, the probability that the fixed PNEC is exceeded for the aquatic ecosystem is still 24% (Table 16), for the uncertain PNEC 12% (Table 17) and the probability that a PAF of 5% is exceed is still 15% (Table 18).

*Table 16 Summarised results of uncertainty analysis with a fixed PNEC.*

| | Water | Fish-eater | MOS |
|---|---|---|---|
| **EUSES** | 1 | 0.00283 | 9623 |
| **Fixed PNEC** | | | |
| 50% | 0.50 | 0.00 | 57715 |
| 80% | 1.1 | 0.02 | 22285 |
| 90% | 1.7 | 0.04 | 14154 |
| 95% | 2.4 | 0.07 | 8840 |
| Prob RCR>1 | 24 | 0 | - |
| Prob MOS<100 | - | - | 0 |
| Prob MOS<1000 | - | - | 0 |

*Table 17 Summarised results of uncertainty analysis with uncertain PEC and PNEC.*

| | Water | Fish-eater | Sens. human | MOS |
|---|---|---|---|---|
| **EUSES** | 1 | 0.00283 | - | 9623 |
| **Uncertainty** | | | | |
| 50% | 0.09 | 0.01 | 0.001 | 58168 |
| 80% | 0.46 | 0.14 | 0.009 | 17655 |
| 90% | 1.3 | 0.42 | 0.02 | 9638 |
| 95% | 2.8 | 1.0 | 0.08 | 5039 |
| Prob RCR>1 | 12 | 5.2 | 0.70 | - |
| Prob MOS<100 | - | - | - | 0 |
| Prob MOS<1000 | - | - | - | 0.10 |

*Table 18 Summarised results of uncertainty analysis with the dose-effect approach (PAF).*

| | Water | Soil | Sens. human |
|---|---|---|---|
| **EUSES** | 1 | 0.692 | - |
| **PAF** | | | |
| 50% | 0.01 | 0.00 | 0.00 |
| 80% | 0.04 | 0.01 | 0.00 |
| 90% | 0.07 | 0.02 | 0.00 |
| 95% | 0.10 | 0.04 | 0.00 |
| Prob PAF>5% | 15 | 3.1 | 0.70 |

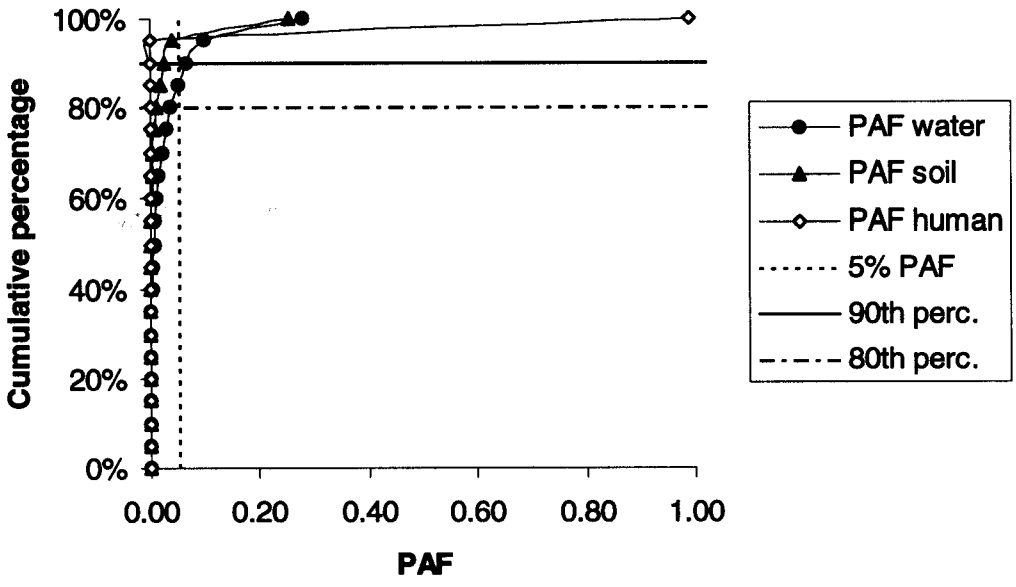



*Figure 13 Cumulative probability distribution for the PAF. The PAF for water and soil include the NOEC for predators.*

# 6. CONCLUSION

From a scientific point of view, there is sufficient argumentation to strive for a probabilistic framework in chemical risk assessment (see Chapter 1 and the summary in Table 19). The uncertainties in risk assessment should preferably be taken into account in the risk management decisions. This requires a high degree of transparency in the methods to facilitate interpretation of the results. The decision maker needs to understand which uncertainties are represented in the risk distribution and which not (see Chapter 2). Three approaches to incorporate uncertainties in a probabilistic risk estimate are discussed: the probability that PEC exceeds a fixed PNEC, the probability that PEC exceeds an uncertain PNEC, and a dose-effect approach (see Chapter 3). Each approach has merits and disadvantages (see Table 19). Clearly, the effects assessment is the critical stage in the probabilistic framework and needs further consideration. Especially in the field of human toxicology, much remains to be done as even extrapolation to "safe levels" is not broadly accepted.

Uncertainty analysis requires probability distributions for selected input parameters (see Chapter 4). For the purpose of example calculations, a preliminary quantification of the chemical-specific model parameters is presented in Appendix I. This is not a worked-out proposal but merely presents the way to approach the problems of defining distributions. Clearly, more work in this area is needed before an uncertainty analysis can be made operational in chemical risk assessment.

***Table 19*** *Summary of the advantages and disadvantages of the quotient method and of probabilistic risk assessment.*

| | **Advantage** | **Disadvantage** |
|---|---|---|
| Quotient method | • Rapid<br>• criterion is easy to interpret for risk manager (quotient>1)<br>• Well established | • Little information about true risk<br>• Unknown degree of conservatism<br>• no quantitative value (no comparison between chemicals possible) |
| Probabilistic risk assessment | • Lot of information<br>• True risk estimates possible<br>• Better comparison between chemicals<br>• Identify main sources of uncertainty | • Relatively time and computer resources consuming<br>• Less easy to interpret (probability distribution) |
| **Approaches to incorporate uncertainty analysis in risk characterisation** | | |
| Only uncertain PEC | • Maintains current agreed procedure for PNEC<br>• Sense of "safety" | • Ignores important uncertainties<br>• Danger of conservatism<br>• No "impact" assessed |
| Uncertain PEC and PNEC | • Less conservatism in assessment factors<br>• Sticks to well-accepted quotient approach | • No risk assessment for ecosystem but only for most sensitive species<br>• No "impact" assessed |
| Dose-effect approach | • Quantitative "impact" assessed<br>• Chemicals can be compared<br>• Work currently in progress to underpin the approach | • Limited theoretical background<br>• Ecological relevance of "PAF" unknown |

This report is meant as a discussion document. Its main aim is to demonstrate the advantages of probabilistic risk assessment and present some alternatives for the current quotient approach. These are illustrated with an example risk assessment of a new chemical in Chapter 5. More information is presented to the risk managers to base decisions on which is both powerful as well as potentially confusing. Note that an important contribution of uncertainty and variability is ignored in these examples: the exposure scenario. This scenario is currently

worst case and thus influences the representation of the risk distribution. This needs to be kept in mind when interpreting risk distributions as in Chapter 5. Furthermore, only the chemical-specific uncertainties were quantified. The parameters with variability were taken as part of the exposure scenario and the uncertainty was ignored (e.g. the human consumption rates of food products).

## 6.1. Amending the risk assessment scheme

Quotient methods can be used to narrow the scope, focus limited resources, or set priorities in an assessment challenged by many contaminants and many potential risks (Bartell, 1996). The current deterministic approach of using "reasonable worst-case" defaults may thus provide an efficient first screening. The results of a quotient method can, however, only be semi-quantitative at best and strict interpretation of quotient values could lead to serious mismanagement of risks (Moore & Elliott, 1996). The interpretation of the PEC/PNEC thresholds of 10, 100 and 1000 in the decision scheme for new chemicals may therefore need reconsideration. Risk characterisation in the framework of EU risk assessments of new and existing chemicals requires that one of the following conclusions is reached:

1. There is need for further information and/or testing.
2. There is at present no need for further information, testing or risk reduction measures.
3. There is need for limiting the risk.

The risk assessments are carried out in an iterative (tiered) approach until conclusion 2 or 3 can be drawn. The deterministic quotient approach may serve in the first tier to determine a need for further information or testing (decide between conclusion 1 or 2). It seems questionable to use this approach to reach conclusion 3 (as indicated by the TGD decision scheme when PEC/PNEC>1000). In subsequent tiers of risk assessment, probabilistic approaches may be preferred as they are closer to the "truth". Figure 14 gives an impression of how both approaches may be combined in a decision scheme although the definition of "acceptable risk" requires further discussion. The degree of confidence which is needed will depend on the scope of the analysis and the conservatism in the exposure scenario.

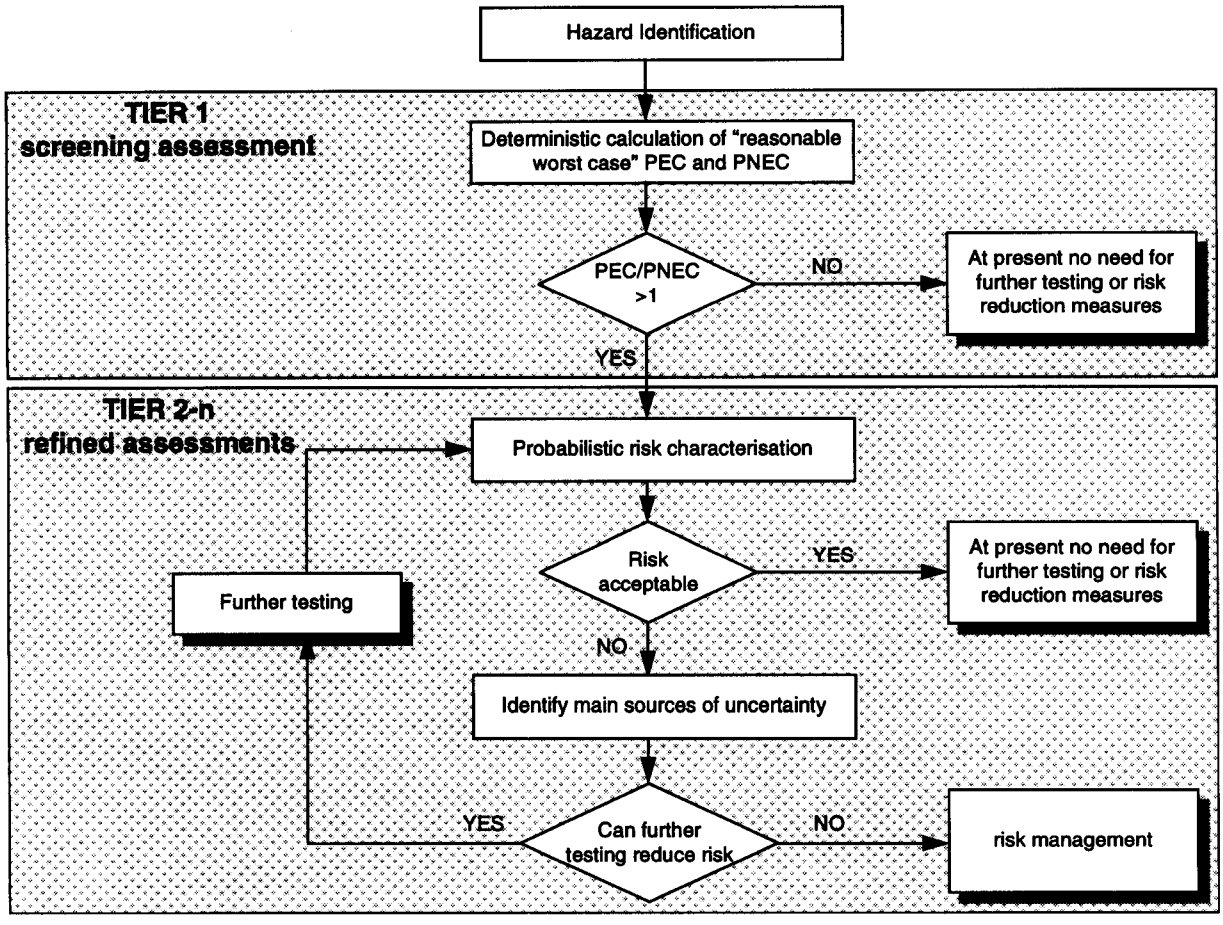



*Figure 14 Example of a possible decision scheme incorporating both deterministic and probabilistic elements.*

## 6.2. Future discussion

This report is meant as a discussion document and leaves several points for future discussion in a European framework. In summary:

1. Do we want to make the transition from deterministic to probabilistic risk assessment?
2. If we adopt a probabilistic approach, what scope is most appropriate? Which uncertainties must be included and how can we deal with variability?
3. What measure of risk is most appropriate in this framework and how can we represent it to facilitate interpretation?
4. How can we base decisions on risk distributions. What is an acceptable risk level?
5. Parameter distributions must be defined. Distributions in this report must be seen as very preliminary but may provide starting point.

It is our opinion that probabilistic risk assessment is better suited to address the complex problems of chemical risk assessment and risk management. Nevertheless, it takes time to change the conventional and well-accepted deterministic approaches and risk managers as well as risk assessors need to familiarise themselves with probabilistic methods. We hope that this report provides a step in this direction. Perhaps it is possible to use a deterministic and a probabilistic approach side-by-side in a decision-support system to compare them and to allow users to appreciate risk distributions.

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# APPENDIX I: PARAMETER DISTRIBUTIONS

This appendix describes the derivation of the parameter distributions that were used for the example calculations. The quantification is only preliminary but may provide a starting point for future activities. In the summary tables, the following symbols are used to characterise the type of distribution:

L Lognormal. Defined by a median (the median value is usually clear, otherwise it is denoted by M) and an uncertainty factor k (95% of the parameter values is within a factor *k* from the median)

U Uniform. Defined by an upper and lower limit.

T Triangular. Defined by an upper and lower limit and a mode. Not that this mode can differ extremely from the median or the average in case the triangular distribution is skewed.

## I.1. Physico-chemical properties

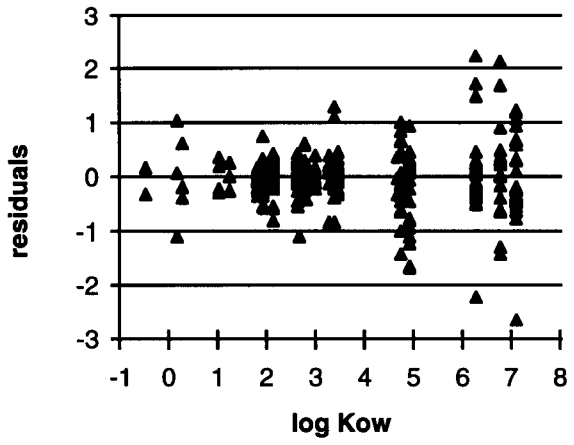
Uncertainty in the physico-chemical properties results from measurement errors. Several "representative" chemicals were selected and for these, properties were collected from literature sources. All the compounds used for the uncertainty analysis of each parameter are listed. The underlying data are derived from several sources (Etienne, 1996; Howard, 1990; Mackay, 1995; Verschueren, 1983; Weast *et al.*, 1985).

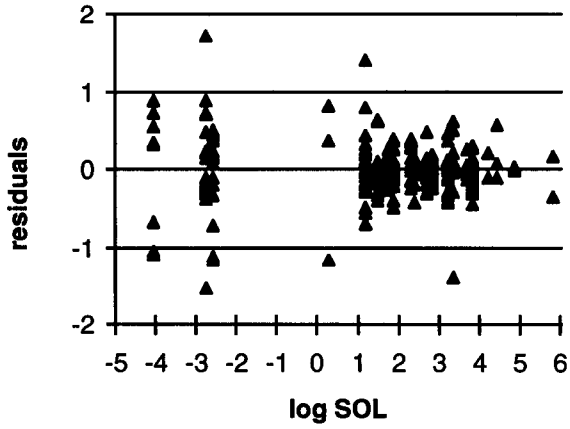
Uncertainty in physico-chemical properties may depend upon the absolute value of the parameter. For very hydrophobic chemicals, the uncertainty in *Kow* will be higher than for more hydrophilic chemicals. A different uncertainty is therefore attached to different parts of the parameter range. The choice for cut-off values was mainly based on visual judgement from the residual plots of the log-linear regression against the geometric mean values of a parameter. Correlations between *Kow*, solubility and vapour pressure were calculated from the average values on log scale. Relationships between *Kow* and solubility are well known but the correlation of *Kow* with vapour pressure is also plausible as both parameters are affected by molecular weight of the chemical (W. Peijnenburg, pers. comm.).

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Octanol-water partition coefficient | Kow<br>log Kow≤4<br>log Kow 4-5.5<br>log Kow>5.5 | <br>L (k=2.8)<br>L (k=12)<br>L (k=24) | Different uncertainty for low, medium and high *Kow* values |
| Water solubility | SOL<br>SOL≤1 mg/L<br>SOL>1 mg/L | <br>L (k=12)<br>L (k=2.4) | Different uncertainty for low and high solubility. Correlated to uncertainty in *Kow*, (corr. coeff.= -0.96 on log scale) |
| Vapour pressure | VP<br>VP≤1 Pa<br>VP>1 Pa | <br>L (k=60)<br>L (k=1.9) | Different uncertainty for low and high vapour pressure. Correlated to *Kow* (corr. coeff.= -0.87 on log scale) |
| Melting point | TEMPmelt | U (+- 3°) | Judged from residuals |

**Remarks**

- Because of the high accuracy of the molecular weight, the uncertainty for this parameter is not relevant.
- The boiling point is not studied in detail as it is only used for some release estimates.
- The correlation coefficients were calculated on log-transformed data. In Monte Carlo sampling this is implemented by drawing log *SOL* and log *VP* from normal distributions, correlated to a normal distribution of log *Kow*. After sampling, the parameter values are transformed to the original scale and used in the calculations.



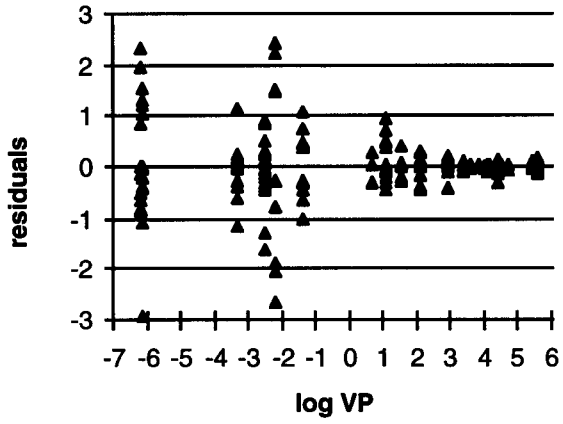



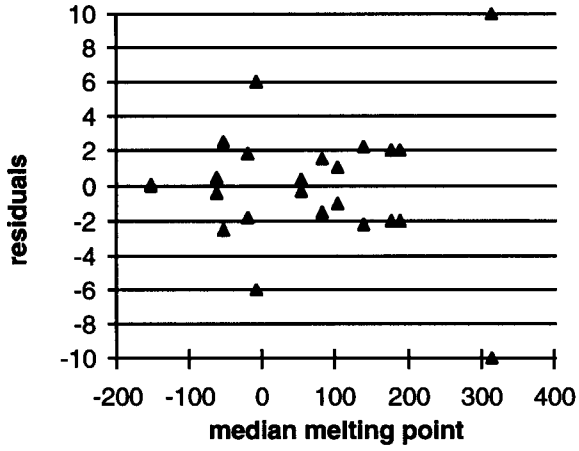

| | Log Kow <4 | Log Kow 4-5.5 | Log Kow >5.5 |
|---|---|---|---|
| Source | (Etienne, 1996; Howard, 1990; Mackay, 1995; Verschueren, 1983; Weast *et al.*, 1985) | | |
| n | 524 | 99 | 119 |
| sd (log) | 0.232 | 0.545 | 0.705 |
| k | 2.8 | 12 | 24 |

| | Log SOL < 0 | Log SOL > 0 |
|---|---|---|
| Source | (Etienne, 1996; Howard, 1990; Mackay, 1995; Verschueren, 1983; Weast *et al.*, 1985) | |
| n | 72 | 581 |
| sd (log) | 0.544 | 0.193 |
| k | 12 | 2.4 |

Compounds

| **Log Kow** | **CAS no.** | **Solubility** | **CAS no.** |
|---|---|---|---|
| 1,1-Dichloroethane | 75-34-3 | 1,1-Dichloroethane | 75-34-3 |
| 1,2-Dichloropropane | 78-87-5 | 1,2-Dichloropropane | 78-87-5 |
| 1,2,3,4-Tetraclorobenzene | 634-66-2 | 1,2,3,4-Tetraclorobenzene | 634-66-2 |
| 1,3-Butadiene | 106-99-0 | 1,3-Butadiene | 106-99-0 |
| 1,4-Dichlorobenzene | 106-46-7 | 1,4-Dichlorobenzene | 106-46-7 |
| 2,3,7,8-TCDD | 1746-01-6 | 2,3,7,8-TCDD | 1746-01-6 |
| 2,4-D | 94-75-7 | 2,4-D | 94-75-7 |
| 2-Chloroaniline | 95-51-2 | 2-Chloroaniline | 95-51-2 |
| Acrolein | 107-02-8 | Acrolein | 107-02-8 |
| Acrylonitrile | 107-13-1 | Acrylonitrile | 107-13-1 |
| B(a)P | 50-32-8 | B(a)P | 50-32-8 |
| Benzene | 71-43-2 | Benzene | 71-43-2 |
| Chloroform | 67-66-3 | Chloroform | 67-66-3 |
| Cyclohexane | 110-82-7 | Cyclohexane | 110-82-7 |
| DEHP | 117-81-7 | DEHP | 117-81-7 |
| Dichloromethane | 75-09-2 | Dichloromethane | 75-09-2 |
| Ethylene oxide | 75-21-8 | Ethylene oxide | 75-21-8 |
| Naphtalene | 91-20-3 | Naphtalene | 91-20-3 |
| PCB153 | 35065-27-1 | PCB153 | 35065-27-1 |
| Pentachlorophenol | 87-86-5 | Pentachlorophenol | 87-86-5 |
| Styrene | 100-42-5 | Styrene | 100-42-5 |
| Tetrachloroethylene | 127-18-4 | Tetrachloroethylene | 127-18-4 |
| Toluene | 108-88-3 | Toluene | 108-88-3 |
| Trichloroethylene | 79-01-6 | Vinylchloride | 75-01-4 |
| Vinylchloride | 75-01-4 | | |




| | Log VP < 0 | Log VP > 0 | TEMPmelt |
|---|---|---|---|
| Source | (Etienne, 1996; Howard, 1990; Mackay, 1995; Verschueren, 1983; Weast *et al.*, 1985) | | |
| n | 97 | 209 | 24 |
| sd (log) | 0.907 | 0.146 | |
| k | 60 | 1.9 | |

Compounds

| **Vapour pressure** | **CAS no.** | **Melting point** | **CAS no.** |
|---|---|---|---|
| 1,1-Dichloroethane | 75-34-3 | 1,4-Dichlorobenzene | 106-46-7 |
| 1,2-Dichloropropane | 78-87-5 | 2,3,7,8-TCDD | 1746-01-6 |
| 1,2,3,4-Tetraclorobenzene | 634-66-2 | 2,4-D | 94-75-7 |
| 1,3-Butadiene | 106-99-0 | 2-Chloroaniline | 95-51-2 |
| 1,4-Dichlorobenzene | 106-46-7 | B(a)P | 50-32-8 |
| 2,3,7,8-TCDD | 1746-01-6 | Chloroform | 67-66-3 |
| 2,4-D | 94-75-7 | DEHP | 117-81-7 |
| 2-Chloroaniline | 95-51-2 | Naphtalene | 91-20-3 |
| Acrolein | 107-02-8 | PCB153 | 35065-27-1 |
| Acrylonitrile | 107-13-1 | Pentachlorophenol | 87-86-5 |
| B(a)P | 50-32-8 | Tetrachloroethylene | 127-18-4 |
| Benzene | 71-43-2 | Vinylchloride | 75-01-4 |
| Chloroform | 67-66-3 | | |
| Cyclohexane | 110-82-7 | | |
| DEHP | 117-81-7 | | |
| Dichloromethane | 75-09-2 | | |
| Naphtalene | 91-20-3 | | |
| PCB153 | 35065-27-1 | | |
| Pentachlorophenol | 87-86-5 | | |
| Styrene | 100-42-5 | | |
| Tetrachloroethylene | 127-18-4 | | |
| Toluene | 108-88-3 | | |
| Trichloroethylene | 79-01-6 | | |
| Vinylchloride | 75-01-4 | | |

## I.2. Release estimates

The release tables of EUSES contain the fraction of the tonnage released to the environmental compartments and the number of emission days, based on the use pattern of the chemical. These fractions are limited between 0 and 1, the number of emission days between 1 and 365. This makes triangular or beta distributions most appropriate. Triangular distributions were selected here for their simplicity and transparency. Due to the large amount of tables in EUSES, only a selection has been investigated. It should be pointed out that because of the lack of "hard" data on minimum and maximum values, figures were based on expert judgement (P. van der Poel, pers. comm.).

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Release fraction | $F_{air}$ / $F_{water}$ | Triangular | Several tables |
| Fraction of the local main source | Fmainsource | Triangular | Several tables |
| Number of emission days | Temission | Triangular | Several tables |

**Remarks**

- The production volume can be seen as a scenario property.
- The same goes for the fraction of the production volume for the region, import and export, the fraction of tonnage for separate applications, and the fraction of chemical in a formulation. These parameters are ignored for now.
- Triangular distributions are not very useful when the distributions are highly skewed. The mode may be much lower than the median or average in those cases.

The following emission estimation tables have been examined:

| | | |
|---|---|---|
| | A TABLES | |
| 1. | Production, general emission factors | Table A1.1 |
| 2. | Production, emission factors for intermediates (UC = 33), MC = 1a for air | Table A1.2 |
| 3. | Processing, metal extraction, refining and processing industry (IC=8) | Table A3.7 |
| 4. | Formulation, photographic industry (IC=10, UC=42) | Table A2.3 |
| 5. | Processing, photographic industry (IC=10) | Table A3.9 |
| | B TABLES | |
| 6. | Production, fr. main source and no. days for general purpose | Table B1.1-B1.4 |
| 7. | Production, fr. main source and no. Days for IC10, NSEC | Table B1.12 |
| 8. | Processing, fr. main source and no. days for IC=8 | Table B3.5/3.6 |
| 9. | Formulation, fr. main source and no. days for IC=10 | Table B2.8/2.3 |
| 10. | Processing, fr. main source and no. days for IC=10 | Table B3.8 |

# A-TABLES

Table A1.1 and Table A1.2 for MC=1a

Emissions to the air in the production process will be dependent on e.g. the apparatus used (closed, open, dedicated equipment, multi-purpose equipment, only open at dosage of reagents or for sampling, etc.) and the vapour pressure at the working temperatures). In the tables of EUSES, estimates are presented for four main categories.

| | solubility (mg/l) | vapour pr.(Pa) | Lower limit | Release | Upper limit |
|---|---|---|---|---|---|
| AIR | | <1 | 3.33E-06 | 0.00001 | 0.00003 |
| MC=3 | | 1-10 | 3.33E-05 | 0.0001 | 0.0003 |
| | | 10 - 100 | 0.000333 | 0.001 | 0.003 |
| | | 100 - 1,000 | 0.003333 | 0.01 | 0.03 |
| | | 1,000 - $10^4$ | 0.0125 | 0.025 | 0.05 |
| | | >=10,000 | 0.025 | 0.05 | 0.1 |
| MC=1a | | <100 | 0 | 0 | 0 |
| (A1.2) | | 100 - 1,000 | 3.33E-06 | 0.00001 | 0.00003 |
| (UC=33) | | 1,000 - $10^4$ | 3.33E-05 | 0.0001 | 0.0003 |
| | | >=10,000 | 0.0005 | 0.001 | 0.002 |
| MC=1b | | <10 | 0 | 0 | 0 |
| | | 10 - 100 | 3.33E-06 | 0.00001 | 0.00003 |
| | | 100 - 1,000 | 3.33E-05 | 0.0001 | 0.0003 |
| | | 1,000 - $10^4$ | 0.0005 | 0.001 | 0.002 |
| | | >=10,000 | 0.0025 | 0.005 | 0.01 |
| MC=1c | | <1 | 0 | 0 | 0 |
| | | 1-10 | 3.33E-06 | 0.00001 | 0.00003 |
| | | 10 - 100 | 3.33E-05 | 0.0001 | 0.0003 |
| | | 100 - 1,000 | 0.000333 | 0.001 | 0.003 |
| | | 1,000 - $10^4$ | 0.0025 | 0.005 | 0.01 |
| | | >=10,000 | 0.005 | 0.01 | 0.02 |
| | production volume | | Lower limit | Release | Upper limit |
| WASTE | <1000 tonnes/year | | 0.0005 | 0.01 | 0.15 |
| WATER | >=1000 tonnes/year | | 0.00015 | 0.0025 | 0.035 |
| | solubility (mg/l) | vapour pr.(Pa) | Lower limit | Release | Upper limit |
| SOIL | | | 0 | 0.00005 | 0.00025 |

Tabel A3.7 IC=8 Metal extraction, refining and processing industry for the stage of processing

| Compartment | Remarks | Conditions/solubility | Lower limit | Release estimate | Upper limit |
|---|---|---|---|---|---|
| Air | Main category III (default) | | 0.05 | 0.15 | 0.4 |
| | Main category II | | 0 | 0.0001 | 0.001 |
| | UC = 29 & 35 [1)] | log H < 2 | 0.00004 | 0.0002 | 0.001 |
| | | log H ≥ 2 | 0.0004 | 0.002 | 0.001 |
| Waste water | Main category III (default) | | 0.1 | 0.3 | 0.75 |
| | Main category II | <100 | 0 | 0.001 | 0.005 |
| | | 100 - 1,000 | 0 | 0.025 | 0.15 |
| | | ≥1,000 | 0.01 | 0.075 | 0.3 |
| | UC = 29 & 35 [1)] | pure oils | 0.15 | 0.185 | 0.2 |
| | | water based + unknown | 0.25 | 0.316 | 0.4 |
| Soil | Main category III (default) | | 0.01 | 0.025 | 0.1 |
| | Main category II | | 0 | 0.00005 | 0.0005 |
| | UC = 29 & 35 [1)] | | 0.00001 | 0.0001 | 0.001 |

[1)] UC 29 = heat transferring agents and UC 35 = lubricants and additives (both used in metalworking fluids)

Tabel A2.3 IC=10 Photographic industry for the stage of formulation for UC=42 (photochemicals), and other UCs in the manufacture of solid materials (films, photgraphic paper)

| Compartment | Conditions | Lower limit | Release | Upper limit |
|---|---|---|---|---|
| Air | Control of crystal growth | 0 | 0 | 0 |
| | Other functions, vapour pr.(Pa): | | | |
| | <1 | 0.00001 | 0.00005 | 0.00025 |
| | 1-10 | 0.0001 | 0.0005 | 0.0025 |
| | 10 - 100 | 0.01 | 0.05 | 0.4 |
| | 100 - 1,000 | 0.05 | 0.2 | 0.9 |
| | ≥1,000 | 0.2 | 0.8 | 1 |
| Waste water | Control of crystal growth | 0.95 | 0.99 | 1 |
| | Other functions | 0.0004 | 0.002 | 0.01 |
| Soil | | 0.00001 | 0.0001 | 0.001 |

Table A3.9 IC=10 Photographic industry for the stage of processing

| Compartment | Remarks | Lower limit | Release etimate | Upper limit |
|---|---|---|---|---|
| Air | solid materials (e.g. films)/Main category II | 0 | 0 | 0 |
| | Else, vapour pr.(Pa): | | | |
| | <1 | 0.00001 | 0.000035 | 0.0001 |
| | 1-10 | 0.0001 | 0.00025 | 0.0005 |
| | 10 - 100 | 0.005 | 0.0075 | 0.01 |
| | 100 - 1,000 | 0.005 | 0.025 | 0.15 |
| | >=1,000 | 0.01 | 0.075 | 0.5 |
| Waste water | aqueous solutions: | | | |
| | coupler of dye | 0.125 | 0.15 | 0.2 |
| | else | 0.5 | 0.8 | 0.95 |
| | solid materials (e.g. films)/Main category II | 0 | 0 | 0 |
| Soil | solid materials (e.g. films)/Main category II | 0.00005 | 0.00025 | 0.001 |

## B-TABLES

In the example calculations, the number of days is rounded to whole days maximising the range (lower limit rounded down, upper limit rounded up, estimate rounded). T indicates the production volume or tonnage for the region.

Table B1.1 Non-HPVC for UC ≠ 38 & 41

| Tonnes/year | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| <1000 | 0.5 | 0.8 | 1 | 1 or 0.017T [1] | 1 or 0.08T [2] | 1 or 0.3T [3] |
| 1000-2000 | 0.4 | 0.65 | 1 | 0.013T | 0.065T | 0.1T |
| 2000-4000 | 0.3 | 0.5 | 1 | 0.01T | 0.05T | 0.1T or 350 [4] |
| >=4000 | 0.25 | 0.4 | 1 | 0.008T [4] | 0.004T [4] | 0.1T or 350 [4] |

[1] T>117 [2] T>=25 [3] T>7 [4] Maximum = 350

Table B1.2 Non-HPVC for UC = 38 & 41

| Tonnes /year | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| <10 | 0.6 | 0.95 | 1 | 1 or 0.3T [1] | 1 or 3T [2] | 1 or 20T [3] |
| 10-50 | 0.5 | 0.9 | 1 | 0.75T | 2T | 15T |
| 50-100 | 0.4 | 0.8 | 1 | 0.4T | 0.5T [4] | 350 |
| 100-1000 | 0.3 | 0.6 | 1 | 0.3T | 0.3T | 350 |
| 1000-2500 | 0.25 | 0.5 | 1 | 0.2T | 0.1T | 350 |
| >=2500 | 0.2 | 0.4 | 1 | 200 | 300 | 350 |

[1] T>6.5 [2] T>2 [3] T>0.667 [4] Maximum = 350

Table B1.3 HPVC for UC ≠ 38 & 41

| Tonnes/year | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| <25000 | 0.7 | 0.9 | 1 | 200 | 300 | 350 |
| 25000-$10^5$ | 0.6 | 0.75 | 1 | 250 | 300 | 350 |
| >=100000 | 0.4 | 0.6 | 0.85 | 300 | 300 | 350 |

Table B1.4 HPVC for UC = 38 & 41

| Tonnes/year | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| <5000 | 0.6 | 0.8 | 1 | 175 | 300 | 350 |
| 5000-25000 | 0.5 | 0.65 | 0.9 | 200 | 300 | 350 |
| 25000-$10^5$ | 0.35 | 0.5 | 0.8 | 250 | 300 | 350 |
| >=100000 | 0.25 | 0.3 | 0.65 | 275 | 300 | 350 |

Table B1.12 Fraction of main source and number of days for IC10, production, NSEC

| Tonnes/year | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| <5 | 0.6 | 0.95 | 1 | 1 or 0.3T | 1 or 3T | 1 or 30T |
| 5-50 | 0.5 | 0.9 | 1 | 0.75T | 2T | 7T |
| 50-250 | 0.4 | 0.8 | 1 | 0.4T | T | 350 |
| 250-3000 | 0.3 | 0.6 | 1 | 0.25T | 0.1T | 350 |
| >=3000 | 0.2 | 0.4 | 1 | 200 | 300 | 350 |

Tabel B3.5/3.6 Fraction of main source and number of days for IC8, processing

| Tonnes/year | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| UC <> 29/35 | | | | | | |
| <10 | 0.6 | 0.8 | 1 | 5 | 50 | 100 |
| 10-50 | 0.5 | 0.7 | 1 | 15 | 75 | 150 |
| 50-500 | 0.35 | 0.6 | 0.9 | 20 | 100 | 250 |
| 500-2000 | 0.25 | 0.5 | 0.8 | 75 | 150 | 300 |
| 2000-10000 | 0.2 | 0.4 | 0.7 | 100 | 250 | 300 |
| 10000-50000 | 0.15 | 0.3 | 0.6 | 150 | 275 | 325 |
| >=50000 | 0.1 | 0.25 | 0.5 | 200 | 300 | 350 |
| UC 29/35: Primary steelw. | | | | | | |
| <1000 | 0.85 | 0.95 | 1 | 150 | 250 | 350 |
| 1000-5000 | 0.7 | 0.9 | 1 | 200 | 275 | 350 |
| 5000-50000 | 0.6 | 0.8 | 1 | 250 | 300 | 350 |
| >=50000 | 0.5 | 0.7 | 1 | 300 | 325 | 350 |
| Else | | | | | | |
| <1000 | 0.5 | 0.8 | 1 | 175 | 250 | 350 |
| 1000-5000 | 0.3 | 0.6 | 0.9 | 250 | 300 | 350 |
| 5000-50000 | 0.2 | 0.4 | 0.75 | 275 | 325 | 350 |
| >=50000 | 0.1 | 0.3 | 0.6 | 300 | 325 | 350 |

Tabel B2.8 Fraction of main source and number of days for IC10 (non-HPVC)

| Tonnes/year | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| <5 | 0.9 | 1 | 1 | 10 | 50 | 150 |
| 5-50 | 0.8 | 0.95 | 1 | 50 | 100 | 200 |
| 50-100 | 0.7 | 0.9 | 1 | 100 | 150 | 250 |
| 100-500 | 0.5 | 0.7 | 0.9 | 150 | 200 | 300 |
| 200-1000 | 0.25 | 0.5 | 0.75 | 200 | 250 | 325 |
| >=1000 | 0.1 | 0.3 | 0.6 | 250 | 300 | 350 |

Tabel B2.3 Fraction of main source and number of days for IC10 (HPVC)

| Tonnes/year | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| <3500 | 0.6 | 0.9 | 1 | 150 | 250 | 350 |
| 3500-10000 | 0.4 | 0.7 | 1 | 200 | 275 | 350 |
| 10000-25000 | 0.3 | 0.6 | 0.9 | 250 | 300 | 350 |
| 25000-50000 | 0.2 | 0.5 | 0.8 | 275 | 300 | 350 |
| >=50000 | 0.1 | 0.3 | 0.7 | 300 | 325 | 350 |

Tabel B3.8 Processing. Fraction of main source and number of days for IC10

| Company size | fraction of main source | | | Number of days | | |
|---|---|---|---|---|---|---|
| | Lower limit | Estimate | Upper limit | Lower limit | Estimate | Upper limit |
| one company | 1 | 1 | 1 | 300 | 325 | 350 |
| large companies | 0.1 | 0.333 | 1 | 300 | 325 | 350 |
| small companies | 0.005 | 0.05 | 0.5 | 250 | 300 | 350 |

## I.3. Partition coefficients

In EUSES, the organic-carbon normalised partition coefficient (*Koc*) can be estimated from *Kow* with a log-linear regression. The original data (training set) were used to quantify the uncertainty in the estimate from the residuals. The uncertainty increases with increasing *Kow* and therefore a distinction is made between the uncertainty for log *Kow* less than 4 and more than 4.

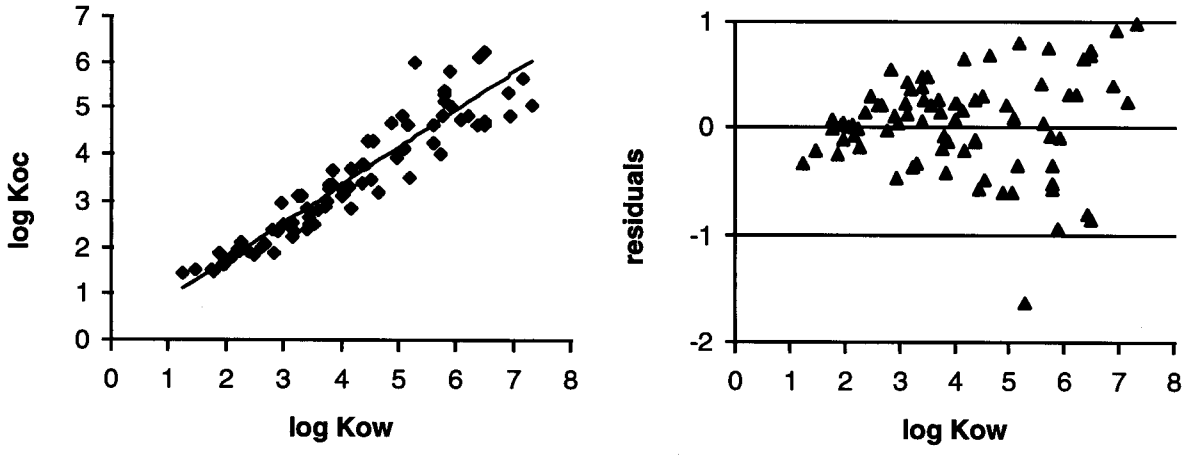
The fraction of the chemical associated with aerosol is estimated from the chemical's vapour pressure, a "constant" (*CONjunge*), and the surface area of aerosol particles. The product of the constant and the surface area is set to a fixed $1.10^{-4}$ in EUSES. Since the constant is actually chemical-specific and the surface area an environmental property, they must be treated separately. The constant is generally between 0.13 - 1.3 Pa.m and typically 0.2 Pa.m (Noordijk & De Leeuw, 1991). This range can be described by a lognormal distribution with a median of 0.4 and an uncertainty factor *k* of 3.3. The surface area of aerosol particles ranges between $1.1.10^{-3}$ (city) - $3.5.10^{-4}$ (rural) $m^2/m^3$. Since this range describes environmental variability, it is at this moment not included in the analysis. The geometric mean of this range is approximately $6.10^{-4}$ (consequence of using this value is that the product of these parameters is now larger than the standard value in EUSES).

Henry's law constant is generally calculated from vapour pressure and solubility. No additional uncertainty for this parameter is assumed. Only when a measured value is given, an uncertainty needs to be attached to this parameter. The distribution is calculated from reported data in the literature.

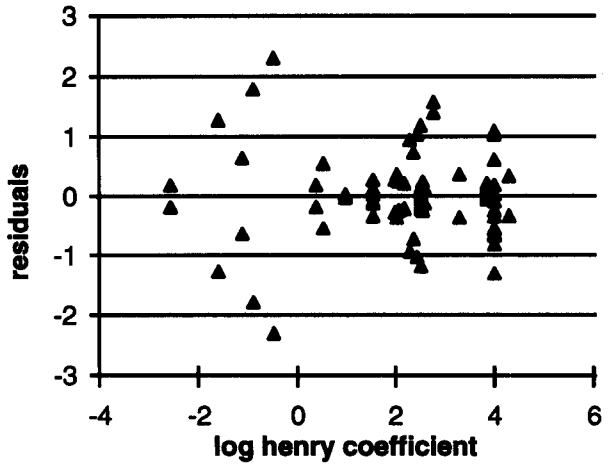
| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Organic-carbon normalised partition coefficient | Koc<br>log Kow 1-4<br>log Kow 4-7 | <br>L (k=3.2)<br>L (k=14) | Calculated from original data |
| Henry's law constant | HENRY | L (k=16) | Only when measured |
| Constant of Junge equation | CONjunge | L (M=0.4, k=3.3) | Derived from observations (Noordijk & De Leeuw, 1991) |

**Remarks**

- For other partition coefficients the uncertainty follows from the calculations.



| | Log Kow 1-4 | Log Kow 4-7 |
|---|---|---|
| Source | (Sabljic *et al.*, 1995) | |
| n | 42 | 39 |
| Sum of squares (log) | 2.70 | 13.2 |
| sd (log) | 0.256 | 0.590 |
| k | 3.2 | 14 |




| | HENRY |
|---|---|
| Source | (Etienne, 1996; Howard, 1990; Mackay, 1995; Verschueren, 1983; Weast *et al.*, 1985) |
| n | 108 |
| sd (log) | 0.612 |
| k | 16 |

Compounds

| Henry's law constant | CAS no. |
|---|---|
| 1,1-Dichloroethane | 75-34-3 |
| 1,2-Dichloropropane | 78-87-5 |
| 1,2,3,4-Tetraclorobenzene | 634-66-2 |
| 1,3-Butadiene | 106-99-0 |
| 2,3,7,8-TCDD | 1746-01-6 |
| 2,4-D | 94-75-7 |
| 2-Chloroaniline | 95-51-2 |
| Acrylonitrile | 107-13-1 |
| Benzene | 71-43-2 |
| Chloroform | 67-66-3 |
| Cyclohexane | 110-82-7 |
| DEHP | 117-81-7 |
| Dichloromethane | 75-09-2 |
| Naphtalene | 91-20-3 |
| PCB153 | 35065-27-1 |
| Pentachlorophenol | 87-86-5 |
| Styrene | 100-42-5 |
| Tetrachloroethylene | 127-18-4 |
| Toluene | 108-88-3 |
| Trichloroethylene | 79-01-6 |
| Vinylchloride | 75-01-4 |

# I.4. Degradation rates

Rate constants for biodegradation are attached to the results of screening tests for biodegradability. In the TGD, the rate constants are set to relatively worst-case values, owing to the limited relevance of these standard tests to environmental situations. Instead of these values, more median values are selected together with an uncertainty factor for the purpose of this study. Furthermore, new categories are added which give an additional degree of information. For example, a chemical which is judged as "non biodegradable" may have received this judgement on the basis of failing a ready test, failing an inherent test, or because no information whatsoever was available. These categories all have different uncertainties. Distributions are quantified very preliminary (J. Struijs, pers. comm.) to clarify the type of approach to be followed.

| Parameter | Values in TGD | Type of distribution |
|---|---|---|
| **$DT50bio_{stp}$** | **Rate constant ($hr^{-1}$)** | |
| Readily biodegradable | 1 | L (M=3, k=2) |
| Readily, but failing 10 day window | 0.3 | L (M=3, k=3) |
| Inherently, fulfilling criteria | 0.1 | L (M=1, k=3) |
| Inherently, failing criteria | 0 | 0 |
| Not biodegradable, failing ready test | 0 | L (M=0.1, k=10) |
| Not biodegradable, failing inherent test | 0 | 0 |
| No information | 0 | L (M=0.03, k=100) |
| **$DT50bio_{water}$** | **DT 50 (days)** | |
| Readily biodegradable | 15 | L (M=4, k=4) |
| Readily, but failing 10 day window | 50 | L (M=9, k=2) |
| Inherently | 150 | L (M=30, k=3) |
| Not biodegradable, failing ready test | ∞ | L (M=100, k=10) |
| Not biodegradable, failing inherent test | ∞ | L (M=3000, k=10) |
| Not biodegradable, no information | ∞ | L (M=1000, k=30) |
| **$DT50bio_{soil\ \&\ sed}$ Kp <=100 l/kg** | **DT 50 (days)** | |
| Readily biodegradable | 30 | L (M=10, k=3) |
| Readily, but failing 10 day window | 90 | L (M=10, k=3) |
| Inherently | 300 | L (M=100, k=3) |
| Not biodegradable, failing ready test | ∞ | L (M=100, k=10) |
| Not biodegradable, failing inherent test | ∞ | L (M=10000, k=3) |
| Not biodegradable, no information | ∞ | L (M=1000, k=10) |
| **DT50 bio soil & sed 100 < Kp <= 1000 l/kg** | **DT 50 (days)** | |
| Readily biodegradable | 300 | L (M=100, k=3) |
| Readily, but failing 10 day window | 900 | L (M=100, k=3) |
| Inherently | 3000 | L (M=1000, k=3) |
| Not biodegradable, failing ready test | ∞ | L (M=1000, k=10) |
| Not biodegradable, failing inherent test | ∞ | L (M=30000, k=3) |
| Not biodegradable, no information | ∞ | L (M=10000, k=10) |
| **DT50 bio soil & sed 1000 < Kp <= 10000 l/kg** | **DT 50 (days)** | |
| Readily biodegradable | 3000 | L (M=300, k=3) |
| Readily, but failing 10 day window | 9000 | L (M=300, k=3) |
| Inherently | 30000 | L (M=3000, k=3) |
| Not biodegradable, failing ready test | ∞ | L (M=30000, k=30) |
| Not biodegradable, failing inherent test | ∞ | L (M=100000, k=3) |
| Not biodegradable, no information | ∞ | L (M=30000, k=100) |

**Remarks**

- It was not investigated whether a median estimate and uncertainties could be attached to the rate constants for abiotic degradation, hydrolysis and photolysis.

## I.5. Distribution models

The uncertainty in the standard concentration in air is low and depends mainly on characteristics of the source and not those of the chemical (A. van Pul, pers. comm.). Since source and environmental characteristics are part of the scenario, they are not further investigated.

For a certain range the deposition flux can be calculated as the product of the deposition velocity and the standard concentration in air. For gaseous substances the effect of deposition on the air concentration at a local scale is negligible. In this case the uncertainty of the deposition flux is only determined by the uncertainty in the deposition velocity. This uncertainty depends on for instance physico-chemical properties and environmental factors. The estimated uncertainty for the standard deposition flux of gaseous compounds can be up to a factor of 10 (A. van Pul, pers. comm.). It was not possible to distinguish between uncertainty caused by physico-chemical properties and environmental factors.

For aerosols the effect of deposition on air concentrations at a local scale is very small. Only in special cases (low source, low atmospheric mixture, particles > 20 μm), the influence can be a factor of 2. The estimated uncertainty for the standard deposition flux of aerosol-bound compounds is about a factor of 5. This uncertainty depends on the composition of the aerosol mixture and further on the height of the source and the atmospheric conditions (A. van Pul, pers. comm.).

Partial mass transfer coefficients are used to determine the gaseous exchange between soil and air. The uncertainty in these parameters is mainly caused by uncertainty in the environment (e.g. roughness of the surface) and uncertainty in using this molecular diffusion model concept for soil (e.g. with respect to stagnant boundary layers). Therefore, these parameters are hardly chemical dependent and uncertainty can therefore be neglected (D. van de Meent, pers. comm.).

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Standard deposition flux of gaseous compounds | $DEPstd_{gas}$ | L (k=10) | (Toet & De Leeuw, 1992) and A. van Pul (pers.comm.) |
| Standard deposition flux of aerosol-bound compounds | $DEPstd_{aer}$ | L (k=5) | (Toet & De Leeuw, 1992) and A. van Pul (pers.comm.) |

**Remarks**

- Since these distributions include variability in source and environmental characteristics, they are probably too conservative. In the future, additional work is required.

## I.6. Bioconcentration factors

Most estimation routines for BCFs are regressions on log-transformed experimental data and therefore result in median estimates. The uncertainty can be quantified from the experimental data points of the training set. The plant-water partition and plant-air partition coefficients are not regressions but are calculated from physico-chemical properties. No additional model uncertainty is attached.

For bioconcentration in fish, a large data set from the literature was taken (Devillers *et al.*, 1996). Multiple BCFs for the same compound were averaged as it was assumed that this variability resulted from differences between species or between individual fish. This uncertainty tends to average out as predators consume more than one fish and usually from several species. Uncertainty is especially high for compounds with log *Kow*>6. For this part of the range, a separate uncertainty factor is defined.

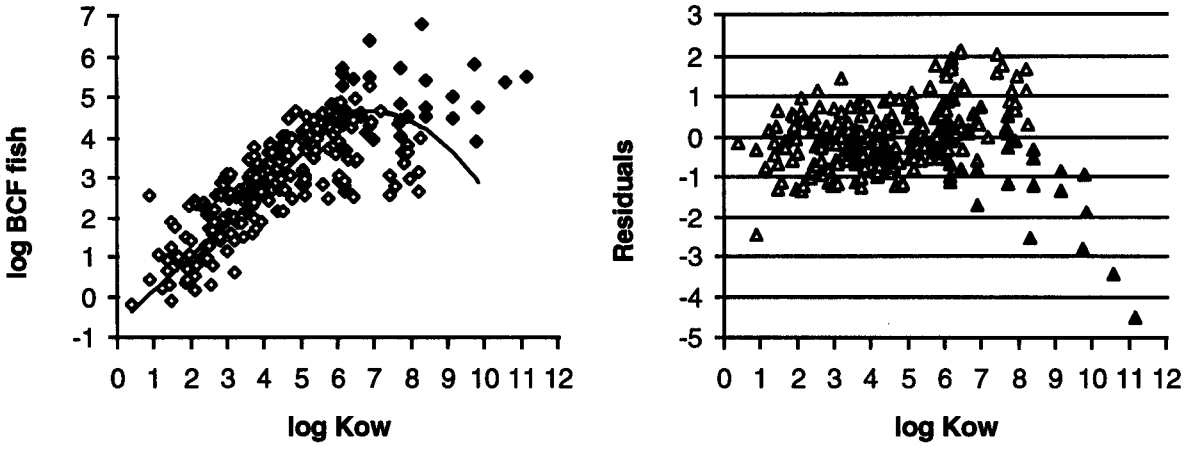
The transpiration stream concentration factor (TSCF) shows little relation with *Kow* although there seems to be a trend for lower values at high and low *Kow*. Due to the bad fit of the regression to the experimental data, no further quantification of uncertainty is attempted. At this moment, a triangular distribution is taken between 0 and 1 where the estimate is used as the mode.

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| BCF for fish | $BCF_{fish}$<br>log Kow 1-6<br>log Kow 6-10 | <br>L (k=20)<br>L (k=185) | From experimental data |
| Worm-porewater partition coeff. | $K_{worm\text{-}porew}$ | L (k=17) | From experimental data |
| Transpiration stream conc. Fact. | TSCF | T (0-1) | Estimate taken as mode |
| Conductance | $g_{plant}$ | L (k=4.1) | From experimental data |
| Biotranfer factor for meat | $BAF_{meat}$ | L (k=64) | From experimental data |
| Biotranfer factor for milk | $BAF_{milk}$ | L (k=36) | From experimental data |

**Remarks**

- Uncertainty in the degradation rates in plant tissues (metabolism and photodegradation) were not investigated. Although the potential influence on concentrations is very high, there are no estimation routines available.

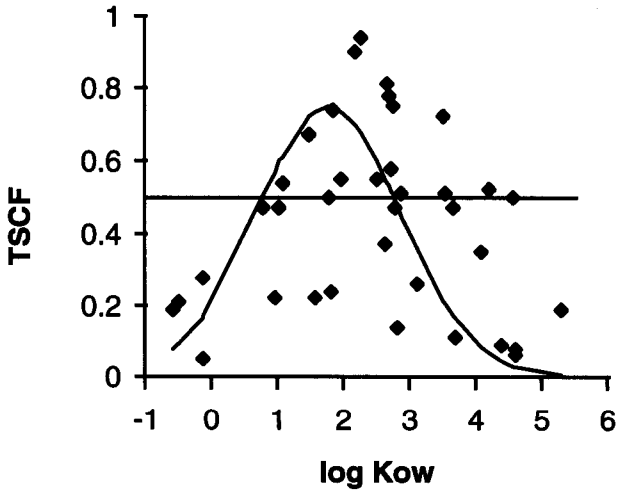
*Bioconcentration factor fish*




| | Log Kow 1-6 | Log Kow 6-10 |
|---|---|---|
| Source | (Devillers *et al.*, 1996) | (Devillers *et al.*, 1996)<br>(Nendza, 1991) * |
| n | 190 | 64 |
| Sum of squares (log) | 83.0 | 84.3 |
| sd (log) | 0.663 | 1.16 |
| k | 19.9 | 185 |

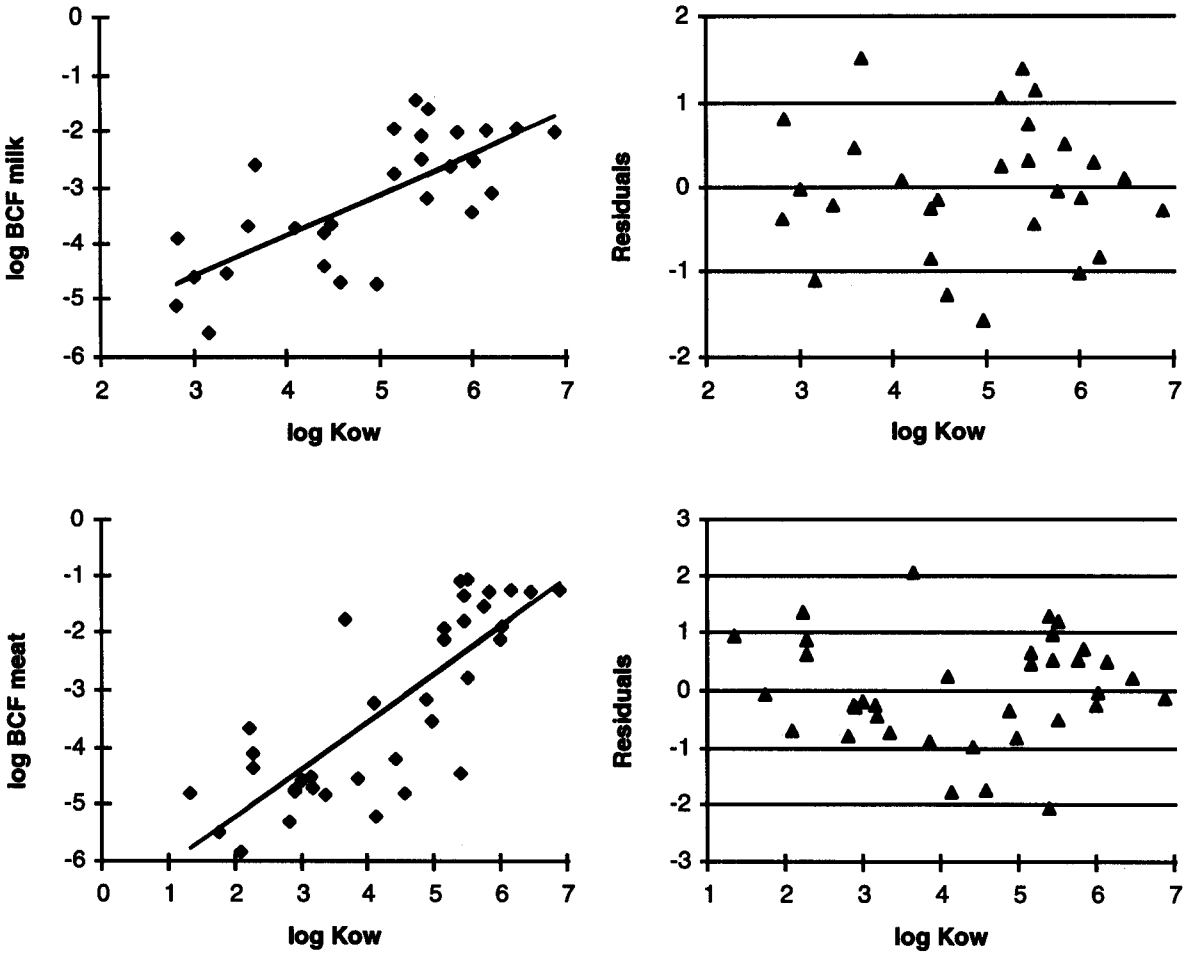
* The data of Nendza used in this study are shown as filled symbols in the graphs.

*Leaf conductivity and TSCF*



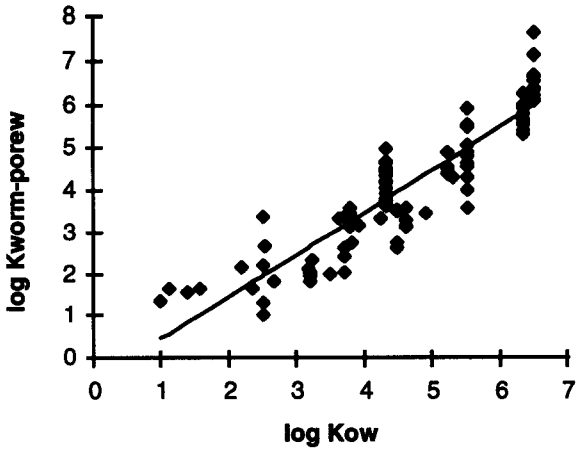

| | TSCF | g |
|---|---|---|
| Source | (Polder *et al.*, 1995)<br>(Briggs *et al.*, 1982) | (Riederer, 1995) |
| n | 37 | 10 |
| Sum of squares (log) | | 0.883 |
| sd (log) | | 0.313 |
| k | | 4.1 |

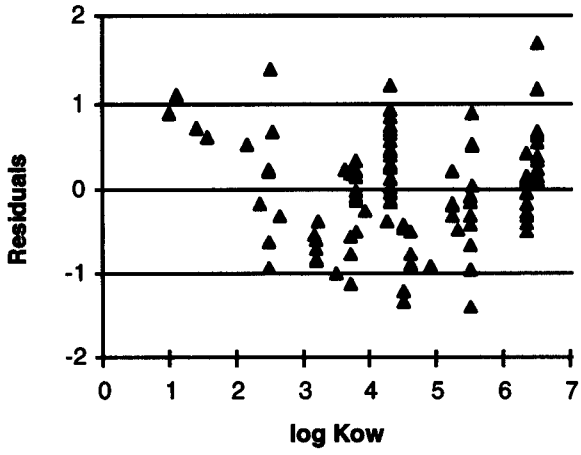
*Biotransfer factors to milk and meat*




| | BCF milk | BCF meat |
|---|---|---|
| Source | (Travis & Arms, 1988) | |
| n | 28 | 36 |
| Sum of squares (log) | 16.9 | 29.6 |
| sd (log) | 0.792 | 0.920 |
| k | 36 | 64 |

*Partition coefficient worm-porewater*




| | $K_{worm-porew}$ |
|---|---|
| Source | (Connell & Markwell, 1990) |
| n | 100 |
| Sum of squares (log) | 39.6 |
| sd (log) | 0.632 |
| k | 17 |

## I.7. Purification of drinking water

The uncertainty in the purification factors for drinking water is based on measured removal percentages of 8 organic compounds, mainly pesticides (F. van Gaalen, pers. comm.). These data reflect a worst-case situation; for each compound and purification step the lowest available removal percentage was chosen. With the removal percentages of each purification step, purification factors were calculated for the treatment systems dune recharge and storage in open reservoirs (as applied in EUSES). For dune recharge the purification step with powdered activated carbon was left out. The removal percentages for the purification by slow sand filtration are not used for storage in open reservoirs. The uncertainty was determined by interpreting the overall distribution of the purification factors for all compound and both treatment systems. Because of the limited data set, and the limited predictive ability of physico-chemical properties, an overall triangular distribution was chosen.

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Purification factor drinking water | Fpur | T (M 0.15, range 0-0.65) | Based on F. van Gaalen (pers. comm.) |

## I.8. Bioavailability for humans

The standard default for the respirable fraction of the inhaled substance is 1 within EUSES. For gaseous compounds the respirable fraction depends on the water solubility. For insoluble compounds, the respirable fraction is 0 and for soluble compounds the absorption via inhalation is linearly related to water solubility, with a range of 0-1 (T. Vermeire, pers. comm.). For aerosols the respirable fraction depends on the particle size. For particle sizes of 0.1 µm to 5 µm the respirable fraction varies from 0.2 to 0.6. For particles of 5 µm to 10 µm the respirable fraction decreases to a value of 0 (T. Vermeire, pers. comm.). As an initial assumption a uniform distribution is chosen between 0 and 1.

The standard defaults within EUSES for the bioavailability for inhalation and for oral uptake are 0.75 and 1, respectively. The bioavailability for inhalation and for oral uptake depends on compound properties. For organic compounds and for metals the uptake ranges from 0.5 to 1 and from 0.05 to 1, respectively (T. Vermeire, pers. comm.). Considering all compounds, an initial assumption was made that the distribution of the bioavailability for oral uptake is uniform between 0 and 1, for inhalation between 0 and 0.75.

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Respirable fraction of the inhaled substance | Fresp | U (range 0-1) | T. Vermeire (pers. comm.) |
| Bioavailability for inhalation | BIOinh | U (range 0-0.75) | T. Vermeire (pers. comm.) |
| Bioavailability for oral uptake | BIOoral | U (range 0-1) | T. Vermeire (pers. comm.) |

## I.9. Environmental effects assessment

Three approaches will be tested for probabilistic risk characterisation:

1. No uncertainty in PNEC, only in PEC. Calculate the probability that PEC exceeds the fixed PNEC. In this case, the effects assessment remains as described in the TGD.
2. Uncertainty in PEC and PNEC. The effects assessment must be changed from worst case factors to medians and distributions. The aim is to extrapolate to a hypothetical "most sensitive species" in the field.
3. Dose-effect approach (PAF). The aim is to extrapolate the given toxicity data to "random field NOECs" from all possible species in the system. From these NOECs, a species-sensitivity distribution is constructed.

These approaches differ in the way in which uncertainties in the effects assessment are quantified. The last two approaches will be described separately.

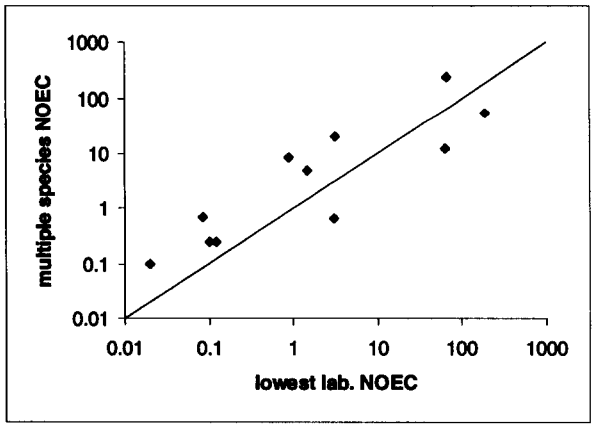
*Assessment factors*

The problem with the assessment factor approach is its lack of transparency. It is not entirely clear what these factors represent and their values seem quite arbitrarily chosen. Here, each factor is assumed to account for an extrapolation step and is derived from available experimental data.

The median acute to chronic ratio is based on experience with a large set of experimental data (Roghair *et al.*, 1997) (see also (Traas *et al.*, 1997).

For inter-species variability, a factor of 10 is routinely applied. This factor should account for the fact that the tested species was not necessarily the most sensitive of its taxonomic group. The objective is to arrive at the most sensitive species. From a data set with toxicity test results (D. de Zwart, pers. comm.) we have calculated the difference between a random NOEC and the lowest NOEC from its taxonomic group. This gives a range from 1 to 440. Values lower than one are not possible and a lognormal distribution therefore cannot be used. As approximation, the assessment factor minus 1 is taken as lognormally distributed (as done by (Slob & Pieters, 1997). This yields a median assessment factor with a $k$ value. There may, however, be more sensitive groups which were not tested. This uncertainty can be combined with the last uncertainty factor: lab to field ecosystems.

An additional lab to field factor may be required to extrapolate from the most sensitive tested NOEC from the three tested groups to an ecosystem threshold. To get an idea of this uncertainty, data of (Emans *et al.*, 1993) were used. NOECs from multiple species experiments were compared to the results of the modified EPA method (largely comparable to the TGD approach). Multiple species experiments which were judged "unreliable" were not used and when several multi-species NOECs were given, the lowest was used. Only data were used for compounds were statistical extrapolation methods could be applied to ensure that at least 4 NOECs were also available for the EPA method. Subsequently, the lowest underlying laboratory NOEC could be derived from the PNEC divided by 10 (this factor is used in the modified EPA method for 3 or more NOECs). Results are shown in the figure at the right. In most cases, the lowest NOEC from the laboratory is actually lower than



the NOEC for the multi-species experiments. The difference is never larger than a factor of 10. Thus as initial guess, the lab-field extrapolation is taken as a factor of 1 with uncertainty factor of 10.

For the PNEC for predators, the TGD applies a factor of 100 on a 28-day study, and 10 on a chronic study. This implies that a factor of 10 is used to extrapolate from sub-chronic to chronic, and an additional 10 to cover inter-species differences and extrapolation from laboratory to the field situation.

The tested species is not necessarily the most sensitive one. An inter-species extrapolation factor is calculated from data of (Romijn *et al.*, 1991). The data set for risk assessment usually includes an NOEC or NOAEL for a mammalian species. The assessment factor is calculated from the difference between a random NOEC for mammals and the most sensitive for all birds and mammals together. This factor ranges from 1 to 88, values lower than one are not possible. As an approximation, the assessment factor minus 1 is taken as lognormally distributed (as done by (Slob & Pieters, 1997). This yields a median factor with a $k$ value.

The factor from sub-chronic to chronic and from sub-acute (e.g. 28 days for rat study) to chronic were taken as proposed by (Vermeire *et al.*, In prep.).

The lab to field factor may include inter-species differences between predators and tested species although there are no indications that predators are more or less sensitive than lab species (Jongbloed *et al.*, 1994). This factor may especially include differences in assimilation efficiency of the feed and differences in metabolic rate between lab and field (although this was ignored in the TGD). According to Jongbloed *et al.* (1994), the most important factors for predators are factors to convert:

- metabolic rate: factor of 2.5-4 (average and extreme conditions);
- caloric content of the feed: factor of 1.7-5.6 (several animal food sources).

The resulting range is 4.25-22.4 which can be covered by a lognormal distribution with a median of 10 and an uncertainty factor of 2.5.

| | Assessment factor-1 for NOEC to most sensitive of group ($AF_{inter}$) | | Uncertainty factor of assessment factor (number of tests) ($k$) | |
|---|---|---|---|---|
| | | **excl. fish TCB** | | **excl. fish TCB** |
| **Algae** | 10 | | 21 (8) | |
| **Crus.** | 6.2 | | 17 (13) | |
| **Fish** | 1.8 | 5.4 | 99 (29) | 30 (23) |
| **All** | 3.3 | 6.3 | 51 (50) | 23 (44) |
| | Data obtained from D. De Zwart (pers. comm.) | | | |
| **Predators** | 7.4 | | 15 (20) | |
| | Data from (Romijn *et al.*, 1991) | | | |

**Remarks**

- TCB data for fish were removed because of inhomogeneous data set. Most NOECs for this compound were nearly identical, but two were highly deviating. This causes extreme variance in the data set.

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Acute LC50 to chronic NOEC | $AF_{ac\text{-}chr}$ | L (M=5, k=10) | (Roghair *et al.*, 1997) and D. de Zwart (pers. comm.) |
| NOEC to most sensitive species | $AF_{inter}$ | 1+L (M=6.3, k=23) | Data set D. de Zwart (pers. comm.) |
| Lab to field systems | $AF_{lab\text{-}eco}$ | L (M=1, k=10) | From data of (Emans *et al.*, 1993) |
| Mammals 28 day to chronic | $AFpred_{subac\text{-}chr}$ | L (M=3.5, k=23) | Proposed by (Vermeire *et al.*, In prep.) |
| Sub-chronic to chronic | $AFpred_{subchr\text{-}chr}$ | L (M=2, k=15) | Proposed by (Vermeire *et al.*, In prep.) |
| Mammals to most sensitive from birds and mammals | $AFpred_{inter}$ | 1+L (M=7.4, k=15) | Data (Romijn *et al.*, 1991) |
| Mammals lab to field | $AFpred_{lab\text{-}fld}$ | L (M=10, k=2.5) | Data (Jongbloed *et al.*, 1994) |

**Remarks**

- The acute to chronic factor for aquatic organisms is an educated guess, based on the work of (Roghair *et al.*, 1997) with a large number of aquatic toxicity data.
- This approach is quite preliminary and more work is needed in this area. Results from only five chemicals are used. There may furthermore be chemical-specific differences in the magnitude of these factors.

*PAF-approach*

This approach assumes a log-logistic distribution of NOECs for the species in the field. The parameters of the log-logistic distribution ($\alpha$ and $\beta$) are uncertain due to uncertainties in the NOECs themselves (due to experimental and statistical procedures). When insufficient NOECs are available, the available LC50s may be converted to NOECs by applying the assessment factor acute-chronic of the previous table. This leads to NOECs with a larger uncertainty than the measured ones. A NOEC distribution can be made when at least three NOECs are present although four or more is advisable (Health Council of the Netherlands, 1988). The use of just three NOECs means that the shape of the distribution is more sensitive to changes in the individual NOECs. For the test calculations, the following approach is used:

1. take all available NOECs;
2. fill missing NOECs with converted LC50s (using $AF_{ac\text{-}chr}$);
3. translate mammalian dietary study to environmental concentrations.

In this way, at least 4 NOECs are available. Two approaches are possible to include uncertainty in the PAF value:

1. Uncertainty follows from uncertainty in the NOECs. In Monte Carlo sampling, different NOECs are drawn from their distributions and each time a new species-sensitivity distribution is constructed.
2. Uncertainty is calculated from the fit of the data. In Monte Carlo sampling, values for $\alpha$ and $\beta$ are drawn from their confidence limits. The problem with this approach is that it cannot incorporate the additional uncertainty when LC50s are converted to NOECs.

For the test calculations, the first method is used. The PAF is calculated as follows (Hamers *et al.*, 1996):

$$PAF = \frac{1}{1+\exp\left[\frac{-(\ln[\text{environment}]-\alpha)}{\beta}\right]}$$

$$\alpha = \overline{\ln NOEC}$$

$$\beta = sd_{\ln NOEC}\frac{\sqrt{3}}{\pi}$$

The input toxicity data are chemical-specific parameters. The uncertainty in them is caused by measurement errors but also originates from sensitivity differences between species. If a different species had been tested, the results could lead to a different effects assessment for the ecosystem. Application of the lab to field ecosystem factor is probably not required: there does not seem to be a structural difference in sensitivity in species between lab and field (Emans *et al.*, 1993) and the NOEC distribution also includes the possibility that species exist that are more sensitive than the species tested. The inter-species extrapolation to the lowest NOEC is also not necessary. The PAF approach requires "random" NOECs from the ecosystem. In fact what is needed is the variability in the input data.

The EC/OECD base set requires at least LC50s for an algae, a crustacean and a fish species. For several neutral organic compounds, large amounts of data are available for aquatic organisms. The tested species are grouped in fish, crustacean and algae and a distinction between LC50 and NOEC is made. The sensitivity differences between species are expressed as an uncertainty factor (calculated from the standard deviation on log scale from the experimental data). No specific differences between the organism groups nor between LC50s and NOECs can be distinguished. All data combined yield an uncertainty factor of 28. This is quite large and mainly caused by malathion and partly by lindane. These are pesticides, so for this group of compounds, sensitivity differences may be larger than for other compounds because they are developed to affect (specific) species. Without these compounds, a factor of 13 is calculated. This figure is, however, based on only three chemicals. As initial value, a factor of 15 is taken in view of the variability of the data and the difference between last two columns. Extreme influence can be observed from pesticide data (malathion) and lack of data (NOEC algae).

For mammals, a similar approach is followed using data taken from (Romijn *et al.*, 1991).

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Aquatic toxicity LC50 | LC50 | L (k=15) | Data set De Zwart (pers. comm.) |
| Aquatic toxicity NOEC | NOEC | L (k=15) | Data set De Zwart (pers. comm.) |
| Mammalian toxicity data | NOEC | L (k=6.3) | Data (Romijn *et al.*, 1991) |

Variability in input data as uncertainty factor (number of tests).

| | | 1,2,4-TCB | Benzene | Lindane | Malathion | Napthalene | Non-pest | Incl. pest |
|---|---|---|---|---|---|---|---|---|
| Algae | LC50 | 4.8 (4) | 15 (7) | 57 (2) | | 149 (3) | 16 | 16 |
| | NOEC | 7.8 (3) | 102 (5) | 7.5 (3) | | | 39 | 24 |
| Crus. | LC50 | 13 (15) | 13 (19) | 191 (62) | 656 (23) | 7.0 (28) | 9.6 | 88 |
| | NOEC | 26 (6) | 77 (3) | 11 (7) | | | 29 | 18 |
| Fish | LC50 | 14 (17) | 17 (76) | 12 (174) | 45 (87) | 12 (18) | 15 | 18 |
| | NOEC | 10 (8) | 13 (9) | 34 (12) | | 3.5 (5) | 8.6 | 14 |
| All | | 12 (53) | 17 (119) | 30 (260) | 87 (110) | 9.2 (54) | 13 | 28 |
| Data obtained from D. de Zwart (pers. comm.) | | | | | | | | |

**Remarks**

- The category "All" is calculated from all the deviations from the geometric means per toxicity measure and per chemical.

Variability in input data as uncertainty factor (number of tests).

| | | Lindane | Dieldrin | Cadmium | Inorganic mercury | Methyl mercury | Chemicals combined |
|---|---|---|---|---|---|---|---|
| LD50 | Birds | 7.2 (13) | 11 (15) | | | | |
| | Mammals | 4.1 (5) | 4.3 (12) | | | | |
| | Combined | 6.4 (18) | 7.9 (27) | | | | |
| LC50 | Birds | | 7.7 (5) | 4.4 (4) | 1.5 (3) | | |
| | Mammals | | | | | | |
| | Combined | 8.7 (4) | 6.1 (7) | | | | |
| NOEC | Birds | | 9.2 (9) | 23 (3) | 71 (3) | 8.7 (6) | |
| | Mammals | 5.2 (4) | 8.0 (9) | 8.8 (3) | | 7.6 (4) | 6.3 (20) |
| | Combined | 26 (6) | 8.2 (18) | 11 (6) | 32 (4) | 7.3 (10) | |
| All | | 8.7 (28) | 7.5 (52) | 6.1 (12) | 12 (7) | 7.3 (10) | 7.5 (109) |
| Data from (Romijn *et al.*, 1991) | | | | | | | |

**Remarks**

- The category "All" is calculated from all the deviations from the geometric means (mammals and birds combined) per toxicity measure (LC50, LD50, NOEC) and per chemical. This factor can be used for a random species in the PAF approach.

## I.10. Human effects assessment

As discussed in the main text, two approaches for including uncertainty are possible for human effects assessment:

1. A dose-effect curve as the PAF for ecosystems. The intra-species variation can be used to define a sensitivity distribution. The "PAF" is in this case the percentage of the population exposed above their NOAEL, given the exposure scenario.
2. Make a risk assessment for the "most sensitive individual" by using stochastic assessment factors (as proposed by (Vermeire *et al.*, In prep.) and (Slob & Pieters, 1997).

The TGD avoids any extrapolation from mammalian toxicity data to no-effect levels for humans but for deriving Acceptable or Tolerable Daily Intakes (ADI or TDI), a combination of assessment factors of 10 are used. Factors are used for: inter-species differences (rat to human), intra-species differences (extrapolation to the most sensitive individual), sub-chronic to chronic studies, LOAEL to NOAEL, and other uncertainties in the data.

The inter-species and subchronic-chronic factors are taken from (Vermeire *et al.*, In prep.). These authors based their proposed distributions on data from the literature. For intra-species extrapolation, the authors advice to stick to a fixed factor of 10 because of the limited data. (Slob & Pieters, 1997) propose a shifted lognormal distribution. This shift of the distribution is needed as values lower than one are not possible (the most sensitive individual will always be more sensitive than the average). This distribution is preliminary, it follows from the assumption that a factor of 10 is the 99th percentile of the unknown distribution. An assessment factor from LOAEL to NOAEL was not defined as neither (Vermeire *et al.*, In prep.) nor (Slob & Pieters, 1997) provide a distribution for this parameter. This is not problematic for the example calculations since an NOAEL was provided in the data set.

The proposed approach can be summarised as follows:

1. Take NOAEL from mammalian toxicity study. Extrapolate from LOAEL to NOAEL (not discussed here).
2. Correct for time-scale. Extrapolate from sub-acute or sub-chronic data to chronic values.
3. Extrapolate from the chronic mammalian NOAEL to the average human individual. Since this factor and its distribution were derived from actual data, the uncertainty in the NOAEL itself is probably included.
4. Extrapolate to the most sensitive individual using $AFhuman_{intra}$ (with uncertainty).

| Parameter | Symbol | Type of distribution | Remarks |
|---|---|---|---|
| Inter-species extrapolation from rat to human | $AFhuman_{inter}$ | L (M=4, k=34) | Proposed by (Vermeire *et al.*, In prep.) |
| Intra-species extrapolation | $AFhuman_{intra}$ | 1+L (M=3, k=2.3) | (Slob & Pieters, 1997) |
| Sub-chronic to chronic | $AFhuman_{subchr-chr}$ | L (M=2, k=15) | Proposed by (Vermeire *et al.*, In prep.) |
| Sub-acute to chronic | $AFhuman_{subac-chr}$ | L (M=3.5, k=23) | Proposed by (Vermeire *et al.*, In prep.) |

**Remarks**

- The *k* values for intra-species extrapolation differ from the factors given by Slob and Pieters because they base the uncertainty factor on the 99th percentile whereas here the 95th is used to define a *k* value.

For the "PAF-like" approach, the median or 50th percentile of the NOAEL distribution is the mammalian toxicity data extrapolated to the average human (using assessment factors for inter-species differences and, if needed, other factors to arrive at a chronic NOAEL). The 99th

percentile lies at 10 times this average NOAEL (Slob & Pieters, 1997). A log-logistic distribution is used as there is, in practice, little difference with the lognormal. The parameters of this sensitivity distribution can be calculated as: $\alpha$=ln(NOAEL of the average human) and $\beta$=0.5. For the uncertainty in the NOAEL for the average human, the same approach is used as described for the assessment-factor approach (excluding the extrapolation to most sensitive individual).

# APPENDIX II: EXAMPLE CALCULATIONS

This appendix contains the input data set for the example calculations of Chapter 5 and some additional results, not shown in that chapter.

## II.1. Input data

| Chemical properties | Value | Unit |
|---|---|---|
| Molecular weight | 251.3 | g/mol |
| Vapour pressure | 0.001 | Pa |
| Octanol-water part. coeff. | 2.13 | [-] 10log |
| Water solubility | 607 | mg/L |
| Readily biodegradable | No | |
| Melting point | 61 | °C |
| | | |
| **emission** | | |
| IC/UC | 3/33 | |
| MC processing | Ic | |
| Production volume | 100 | tonnes/year |
| Processed elsewhere? | no | |
| | | |
| **(eco)toxicity** | | |
| L(E)C 50 fish | 25 | mg/L |
| L(E)C 50 algae | 12 | mg/L |
| L(E)C 50 other species | 12 | mg/L |
| NOAEL mammal | 15 | mg/kg/d |
| | | |

Uncertainty in release estimates (tables in Appendix I.2 and P. van der Poel, pers. comm.).

| Stage | | EUSES tables | Uncertain estimates |
|---|---|---|---|
| Prod. | Air | 0 | 0 |
| | Waste water | 0.02 | 0.01 (0.0005 - 0.15) |
| | Fraction main source | n.r. | n.r. |
| | Number of emission days | n.r. | n.r. |
| | | | |
| Proc. | Air | 0 | 0 |
| | Waste water | 0.02 | 0.01 (0.0005 - 0.15) |
| | Fraction main source | 0.5 | 0.6 (0.35-1) |
| | Number of emission days | 20 | 30 (7-200) |

## II.2. Additional results

Uncertainty analysis with a fixed PNEC (results for Section 5.1)

| | Water | Soil | Fish-eater | Worm-eater | Sens. human | MOS |
|---|---|---|---|---|---|---|
| **EUSES** | 413 | 286 | 1.17 | 5.68 | - | 23.3 |
| **Fixed PNEC** | | | | | | |
| 50% | 204 | 75 | 1.7 | 0.79 | - | 140 |
| 80% | 466 | 195 | 7.7 | 4.2 | - | 54 |
| 90% | 719 | 318 | 17 | 8.8 | - | 35 |
| 95% | 982 | 440 | 28 | 17 | - | 21 |
| Prob RCR>1 | 100 | 100 | 62 | 44 | - | - |
| Prob MOS<100 | - | - | - | - | - | 39 |
| Prob MOS<1000 | - | - | - | - | - | 94 |
| EUSES perc. | 77 | 88 | 42 | 84 | - | 94 |
| **Main uncertainties** | | | | | | |
| | No emiss. | No emiss. | $BCF_{fish}$ | $K_{worm-porew}$ | - | No emiss. |
| | $kbio_{stp}$ | Koc | $kbio_{stp}$ | $DT50bio_{soil}$ | - | $DT50bio_{soil}$ |
| | $Femiss_{water}$ | $Femiss_{water}$ | $Femiss_{water}$ | No emiss. | - | $Femiss_{water}$ |
| | $F_{mainsource}$ | $DT50bio_{soil}$ | $F_{mainsource}$ | $Femiss_{water}$ | - | VP |
| | | $F_{mainsource}$ | | $F_{mainsource}$ | - | $BCF_{fish}$ |

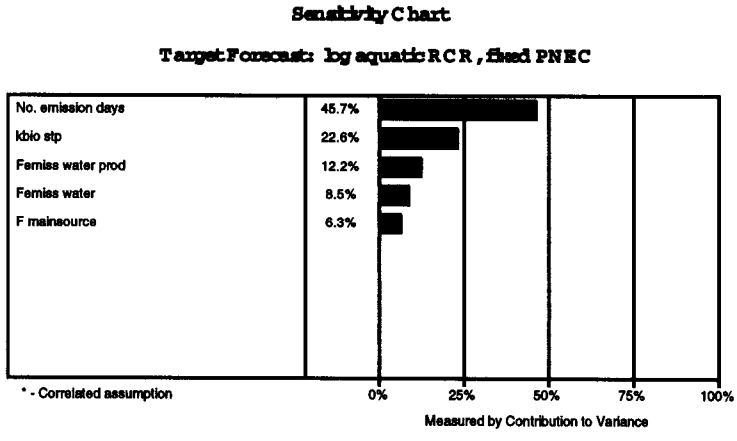



*Figure 15 Example sensitivity output from Crystal Ball for the aquatic RCR.*

Uncertainty analysis with uncertain PEC and PNEC (results for Section 5.2)

| | Water | Soil | Fish-eater | Worm-eater | Sens. human | MOS |
|---|---|---|---|---|---|---|
| **EUSES** | 413 | 286 | 1.17 | 5.68 | - | 23.3 |
| **Uncertainty** | | | | | | |
| 50% | 37 | 15 | 5.2 | 2.5 | 0.39 | 141 |
| 80% | 190 | 73 | 56 | 31 | 3.5 | 43 |
| 90% | 523 | 189 | 176 | 95 | 10 | 23 |
| 95% | 1140 | 401 | 430 | 230 | 32 | 12 |
| Prob RCR>1 | 97 | 92 | 74 | 64 | 36 | - |
| Prob MOS<100 | - | - | - | - | - | 41 |
| Prob MOS<1000 | - | - | - | - | - | 90 |
| EUSES perc | 88 | 93 | 28 | 60 | - | 90 |
| **Main uncertainties** | | | | | | |
| | No emiss. | No emiss. | $AF_{subac-chr}$ | $AF_{subac-chr}$ | $AFhum_{inter}$ | UF NOEC |
| | $AF_{inter}$ | $AF_{inter}$ | $BCF_{fish}$ | $K_{worm-porew}$ | $AF_{subac-chr}$ | No emiss. |
| | $AF_{lab-eco}$ | $AF_{lab-eco}$ | $AFpred_{inter}$ | $AFpred_{inter}$ | No emiss. | $DT50bio_{soil}$ |
| | $AF_{ac-chr}$ | $AF_{ac-chr}$ | $Femiss_{water}$ | $DT50bio_{soil}$ | $DT50bio_{soil}$ | log VP |
| | $kbio_{stp}$ | $DT50bio_{soil}$ | $AF_{lab-field}$ | No emiss. | $Femiss_{water}$ | $Femiss_{water}$ |

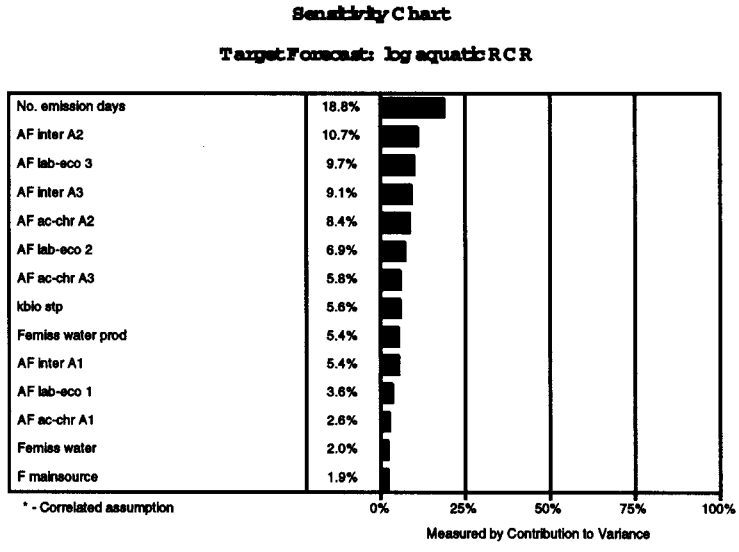



***Figure 16** Example sensitivity output from Crystal Ball for the aquatic RCR.*

Dose-effect approach (results for Section 5.3)

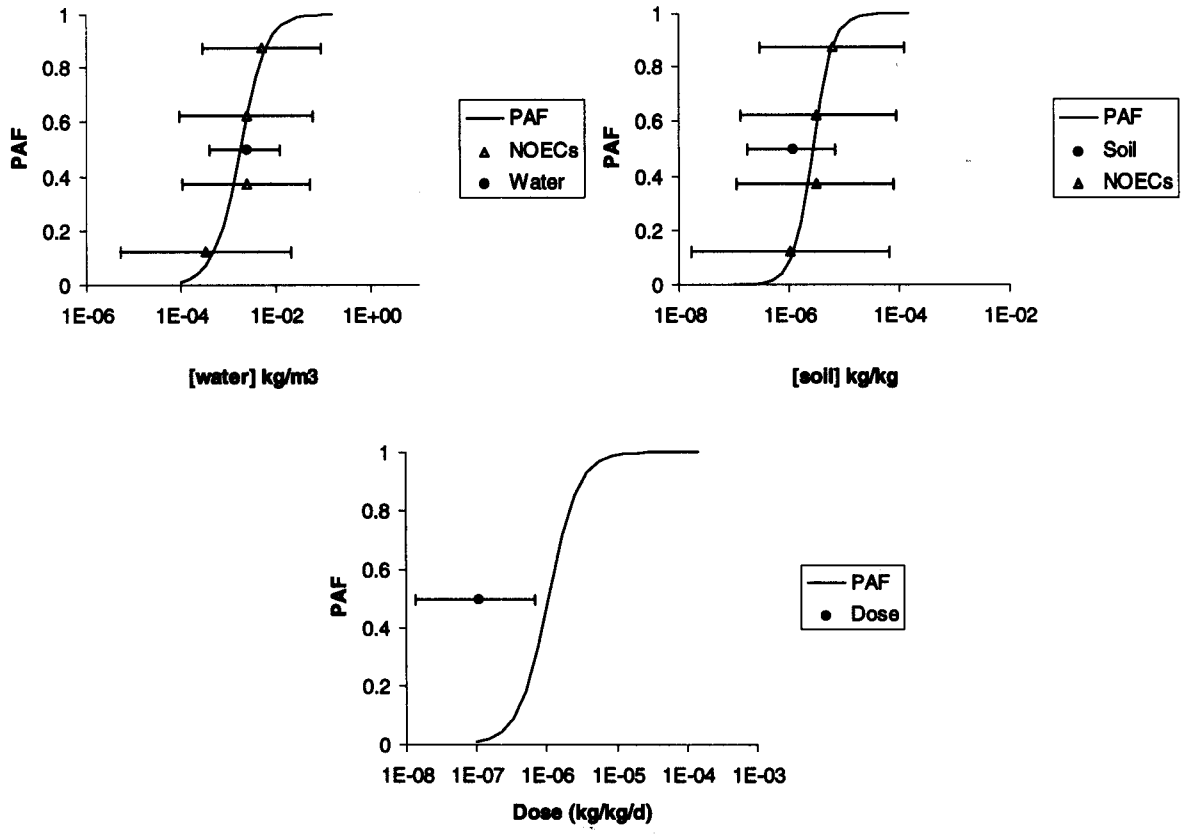



***Figure 17*** *Log-logistic species-sensitivity distributions for aquatic and terrestrial organisms, including predators (shown as black triangles). Environmental concentrations shown as black circles. Ranges indicate 5th and 95th percentiles.*

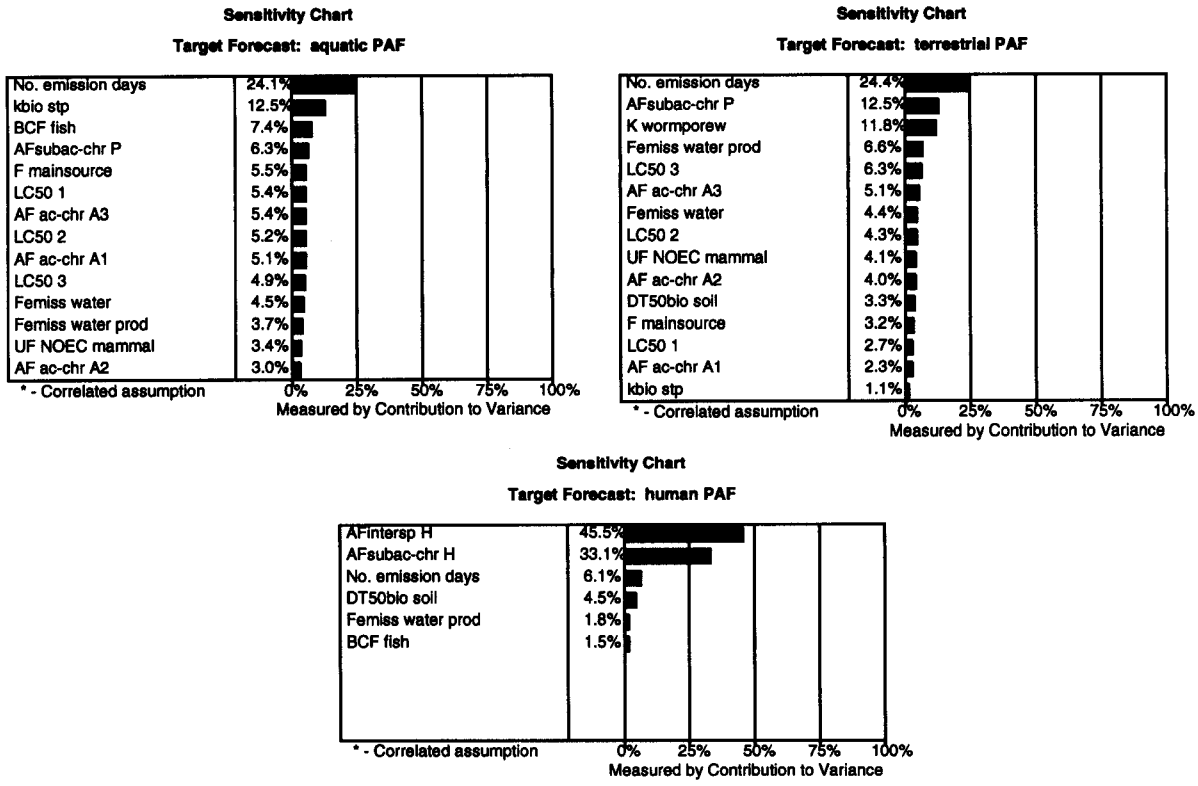



***Figure 18** Sensitivity output from Crystal Ball for the PAFs.*

Risk distributions when PEC/PNEC of EUSES is 1 (results for Section 5.4)

Results of uncertainty analysis with a fixed PNEC:

| | Water | Soil | Fish-eater | Worm-eater | Sens. human | MOS |
|---|---|---|---|---|---|---|
| **EUSES** | 1 | 0.692 | 0.00283 | 0.0138 | - | 9623 |
| **Fixed PNEC** | | | | | | |
| 50% | 0.50 | 0.18 | 0.00 | 0.00 | - | 57715 |
| 80% | 1.1 | 0.47 | 0.02 | 0.01 | - | 22285 |
| 90% | 1.7 | 0.77 | 0.04 | 0.02 | - | 14154 |
| 95% | 2.4 | 1.1 | 0.07 | 0.04 | - | 8840 |
| Prob RCR>1 | 24 | 5.9 | 0 | 0 | - | - |
| Prob MOS<100 | - | - | - | - | - | 0 |
| Prob MOS<1000 | - | - | - | - | - | 0 |
| | | | | | | |

Results of uncertainty analysis with uncertain PEC and PNEC:

| | Water | Soil | Fish-eater | Worm-eater | Sens. human | MOS |
|---|---|---|---|---|---|---|
| **EUSES** | 1 | 0.692 | 0.00283 | 0.0138 | - | 9623 |
| **Uncertainty** | | | | | | |
| 50% | 0.09 | 0.04 | 0.01 | 0.01 | 0.001 | 58168 |
| 80% | 0.46 | 0.18 | 0.14 | 0.07 | 0.009 | 17655 |
| 90% | 1.3 | 0.46 | 0.42 | 0.23 | 0.02 | 9638 |
| 95% | 2.8 | 0.97 | 1.0 | 0.56 | 0.08 | 5039 |
| Prob RCR>1 | 12 | 4.9 | 5.2 | 3 | 0.70 | - |
| Prob MOS<100 | - | - | - | - | - | 0 |
| Prob MOS<1000 | - | - | - | - | - | 0.10 |
| | | | | | | |