research for man and environment

RIJKSINSTITUUT VOOR VOLKSGEZONDHEID EN MILIEU
NATIONAL INSTITUTE OF PUBLIC HEALTH AND THE ENVIRONMENT

RIVM report 679102 049

Probabilistic risk assessment for new and existing chemicals: Sample calculations

T. Jager, H.A. den Hollander, G.B. Janssen, P. van der Poel, M.G.J. Rikken, T.G. Vermeire

January 2000

This investigation has been performed by order and for the account of the Directorate-General for Environmental Protection, Directorate of Chemicals, External Safety and Radiation Protection of the Ministry of Housing, Spatial planning and the Environment, within the framework of project 679102 "Risk assessment methodology".

RIVM, P.O. Box 1, 3720 BA Bilthoven, telephone: 31 - 30 - 274 91 11; telefax: 31 - 30 - 274 29 71

Abstract

In the risk assessment methods for new and existing chemicals in the EU, "risk" is characterised by the deterministic quotient of exposure and effects (PEC/PNEC or Margin of Safety). From a scientific viewpoint, the uncertainty in the risk quotient should be accounted for explicitly in the decision making. The advantages and disadvantages of probabilistic risk assessment in this legal framework have been extensively discussed in earlier work. To demonstrate the benefits of a probabilistic risk framework, sample assessments for two substances, an existing chemical (dibutylphthalate, DBP) and a new chemical notification (anonymous), are presented in this report. The two examples worked out here show a probabilistic risk framework to be feasible with relatively little extra effort; such a framework also provides more relevant information. The deterministic risk quotients turned out to be worst cases at generally higher than the 95^{th} percentile of the probability distributions. Sensitivity analysis has proven to be a powerful tool in identifying the main sources of uncertainty and thus will be effective for efficient further testing.

Contents

Summary

Risk assessment of new and existing chemicals in the EU is performed according to a harmonised methodology, laid down in technical guidance documents (TGDs), and implemented in the decision support system EUSES. In this framework, “risk” is characterised by the deterministic quotient of exposure and effects (PEC/PNEC or Margin of Safety). As the data basis of these risk assessments is usually narrow, a considerable degree of uncertainty accompanies these calculations. From a scientific viewpoint, this uncertainty should be accounted for explicitly in the decision making. The advantages and disadvantages of probabilistic risk assessment in this legal framework have been extensively discussed in earlier work. Nevertheless, the people involved in risk assessment and risk management in the EU are hesitant to support these developments. To demonstrate the benefits of a probabilistic risk framework, sample assessments for two substances are presented in this report: an existing chemical (dibutylphthalate, DBP) and a new chemical notification (anonymous).

In uncertainty analysis, the choice for a certain parameter distribution is quite important. As this is not a trivial matter, there is a clear need for agreed default parameter distributions for the purpose of risk assessment. For this study, probability distributions were assigned to “chemical-specific” parameters (e.g. emissions, partition coefficients) and not to “environmental” or “scenario-dependent” parameters (e.g. organic matter content in soil, wind speed, dilution factors in surface water). The reason for the omission of this source of uncertainty is that it is virtually impossible to transparently capture this variability in a probability distribution. For these calculations, it was judged more appropriate to tackle this source by using alternative plausible scenarios (e.g. a real worst case and a best case) to provide a feel for the impact of these uncertainties. The examples demonstrate that environmental variability may well dominate the total uncertainty in a risk assessment and should be explicitly addressed. This is especially true for the local aquatic system, caused by the large range of the dilution factor in surface water. It should, however, be noted that the models in the TGD do not always allow for alternative scenarios. The flexibility of the models should therefore be considered in the update of the TGD.

The worked-out examples for DBP and the new chemical demonstrate that a probabilistic risk assessment is feasible with relatively little extra effort and provides more relevant information. The width of the risk quotient distribution (5^{th}-95^{th} percentile) varied between chemicals and endpoints from 1 to 5 orders of magnitude in extreme cases (usually, less than 3 orders). The deterministic risk quotient of EUSES turned out to be worst case (generally higher than the 95th percentile) although this is not necessarily a general rule for all chemicals and depends on our particular choices for input distributions. The use of a sensitivity analysis to identify the main sources of uncertainty proves to be a powerful tool to decide where further testing is most efficient. The distributions assigned to the assessment factors (derivation of the PNEC) proved to dominate the total uncertainty in the risk assessment of these sample chemicals. Uncertainties in the release estimates come second. The effects assessment remains a critical stage when we want a probabilistic risk framework that is scientifically justifiable; the uncertainties in this part need to be addressed but the concept of the PNEC forms a problem in itself. A PNEC is not a measure of ecosystem damage but a conservative trigger value. Furthermore, the exceedance of the PNEC is not a risk level, in fact, the absolute value of the PEC/PNEC ratio cannot be interpreted as the shape of the (theoretical) relationship between exposure level and ecosystem damage is unknown.

Risk assessment is a process where we use limited information to predict the potential of chemicals to cause some toxic effect on different kinds of biotic endpoints. Large uncertainties are an inherent part of this process that we have to deal with. If we want a more realistic and defensible risk assessment, we have to get rid of protective and worst-case thinking in the risk assessment itself. Risk assessment should be as scientific and realistic as possible and that implies that we must admit what we don't know. Attempting to quantify uncertainties is a good step in that direction; we believe that even a rough quantification of uncertainties is better than giving a false sense of accuracy. Further work is necessary in the following areas:

- Guidelines how to perform an uncertainty analysis.
- Agreed default distributions for basic parameters, especially in the release estimation and effects assessment.
- Serious revision of the effects assessment (attempt to quantify real impacts).
- Choice of alternative scenarios or other ways to address variability.
- Thoughts on how to implement uncertainty analysis in risk characterisation and in risk management in the (near) future (e.g. which percentiles to take).

It is the intention to present this report as contribution to the update programme of the EU-Technical Guidance Documents in 2000.

Samenvatting

De risicobeoordeling van nieuwe en bestaande stoffen wordt in de EU gedaan met een geharmoniseerde methodologie, vastgelegd in technische leidraden (TGDs) en geïmplementeerd in het beslissings-ondersteunende systeem EUSES. In dit kader wordt "risico" gekarakteriseerd door het deterministische quotiënt van blootstelling en effect (PEC/PNEC of een Margin Of Safety). Een aanzienlijke hoeveelheid onzekerheid begeleidt deze berekeningen omdat de databasis gewoonlijk beperkt is. Vanuit wetenschappelijk oogpunt is het aan te bevelen deze onzekerheid expliciet in de besluitvorming mee te nemen. De voor- en nadelen van een probabilistische risicobeoordeling in dit wettelijke kader zijn in eerder werk uitgebreid besproken. Desondanks zijn de mensen betrokken in risicobeoordeling en risicomanagement weinig enthousiast over deze ontwikkelingen. In dit rapport zijn daarom twee voorbeeldstoffen doorgerekend om de voordelen van een probabilistisch risicokader te demonstreren: een bestaande stof (dibutylftalaat, DBP) en een notificatie van een nieuwe stof.

De keuze voor parameterverdelingen is enorm belangrijk in onzekerheidsanalyse. Omdat dit geen triviale zaak is, is er een duidelijke behoefte aan geaccepteerde defaultverdelingen voor risicobeoordeling. Voor deze studie is de keuze gemaakt om verdelingen toe te wijzen aan "stof-specifieke" parameters (bijv. emissies, partitiecoëfficiënten) en niet aan "milieu" of "scenario-afhankelijke" parameters (bijv. organisch stofgehalte van de bodem, windsnelheid, verdunningsfactoren in oppervlaktewater). De reden voor deze omissie is dat deze bron van onzekerheid vrijwel onmogelijk op een transparante manier in een verdeling kan worden beschreven. Voor deze berekeningen is gekozen voor het laten zien van alternatieve plausibele scenario's (bijv. een echte worst-case en een best-case) om een idee te krijgen van de invloed van deze onzekerheden. De voorbeeldberekeningen tonen aan dat natuurlijke variabiliteit heel goed de totale onzekerheid kan domineren en dus meegenomen moet worden. Dit is speciaal het geval voor het lokale aquatische systeem door de grote spreiding in de verdunning in oppervlaktewater. De modellen in de TGD laten het gebruik van alternatieve scenario's echter niet altijd toe. De flexibiliteit van de modellen moet dus worden meegenomen in de update van de TGD.

De uitgewerkte voorbeelden voor DBP en de nieuwe stof laten zien dat een probabilistische risicobeoordeling met weinig extra moeite haalbaar is en meer relevante informatie geeft. De breedte van de risicoverdeling (5^e-95^e percentiel) verschilt tussen stoffen van 1 tot 5 ordegroottes in extreme gevallen (meestal minder dan 3 ordes). Het deterministische risicoquotiënt van EUSES blijkt behoorlijk worst-case te zijn (i.h.a. groter dan het 95^e percentiel) hoewel dit afhangt van onze specifieke keuze van invoerverdelingen. Het gebruik van gevoeligheidsanalyse voor het identificeren van de belangrijkste bronnen van onzekerheid is een krachtig instrument om te besluiten waar verder testen het meest efficiënt is. De verdelingen toegewezen aan de "assessment" factoren (in de afleiding van de PNEC) blijken de totale onzekerheid te domineren in de risicoschatting van deze voorbeeldstoffen. Onzekerheden in de emissieschatting komen op de tweede plaats. De effectbeoordeling blijft een kritische stap als we een wetenschappelijk verantwoord probabilistisch risicokader willen; niet alleen moeten de onzekerheden worden gekwantificeerd, het concept van de PNEC vormt zelf een probleem. Een PNEC is slechts een conservatieve limietwaarde, geen maat voor schade aan ecosystemen. Verder is de mate van overschrijding van de PNEC geen risicomaat; in feite kan de absolute waarde van het PEC/PNEC quotiënt niet geïnterpreteerd worden omdat de vorm van de (theoretische) relatie tussen blootstelling en ecosysteemschade

onbekend is.

Risicobeoordeling is een proces waarbij we beperkte informatie gebruiken om de potentie van een stof in te schatten om toxische effecten te bewerkstelligen op allerlei organismen. Grote onzekerheden zijn een inherent deel van dit proces waar we rekening mee moeten houden. Als we een meer realistische en verdedigbare risicobeoordeling willen moeten we af van het beschermende worst-case denken in de risicobeoordeling zelf. Risicobeoordeling moet zo wetenschappelijk en realistisch mogelijk zijn en dat houdt in dat we moeten toegeven wat we niet weten. Volgens ons is zelfs een ruwe inschatting van de onzekerheid beter dan het geven van een vals gevoel van nauwkeurigheid. Proberen de onzekerheden te kwantificeren is een stap in de goede richting, maar vervolgonderzoek is nodig op de volgende gebieden:

- Richtlijnen hoe onzekerheidsanalyse uit te voeren.
- Geaccepteerde defaultverdelingen voor basale parameters, speciaal voor de emissieschattingen en de effectbeoordeling.
- Ingrijpende revisie van de effectbeoordeling (pogen echte schade te kwantificeren).
- Keuze voor alternatieve scenario's (of andere manier om variabiliteit te behandelen).
- Overweging hoe onzekerheidsanalyse kan worden geimplementeerd in de risico-karakterisering en risicomanagament in de (nabije) toekomst (bijv. welke percentielen te nemen).

Het is de bedoeling om dit rapport in te brengen bij de revisie van de EU-technische richtlijnen (TGD) in 2000.

1. Introduction

Risk assessment of new and existing chemicals in the EU is performed according to a harmonised methodology which is laid down in so-called technical guidance documents (TGDs) (EC, 1996b). These TGDs are implemented in the decision support system EUSES (EC, 1996a). In this framework, it is agreed to characterise the level of "risk" by means of the deterministic quotient of exposure and effects (PEC/PNEC or Margin of Safety). As the data basis of these risk assessments is usually narrow, a considerable degree of uncertainty accompanies these calculations. From a scientific viewpoint, this uncertainty should be accounted for explicitly in the decision making. The advantages and disadvantages of probabilistic risk assessment in this legal framework have been extensively discussed (Slob & De Nijs, 1989; Jager & Slob, 1995; Jager, 1995; Jager *et al.*, 1997) Nevertheless, the people involved in risk assessment and risk management in the EU are hesitant to support these developments. A series of interviews was conducted with ten representatives from Member States and chemical industry to learn about their viewpoints on uncertainty analysis and probabilistic risk assessment (Jager, 1998). These interviews were especially important to investigate whether a probabilistic framework is feasible and what types of further studies are necessary in this respect. Summarising, there seemed to be a guarded interest in uncertainty analysis among most of the people interviewed although it does not receive high priority at this moment.

These interviews made clear that there is a gap between the scientist and the risk managers. In the scientific community, it is broadly accepted a necessity to provide confidence intervals when presenting secondary data. As a logical consequence, uncertainty analysis is broadly accepted as a necessity when presenting model results in a scientific manner. The risk manager, however, has to deal with the legal aspects and a decision must be reached within a certain time constraint. A series of probability distributions, although very scientific, does not seem to be an obvious help in this process. The best way to proceed with the work on uncertainty analysis is to try to bring together these two fields: it must be demonstrated how risk management can benefit from the extra work needed in performing and understanding probabilities. In our opinion, the best way to demonstrate this is by performing a few probabilistic risk assessments as examples and compare the results to the current TGD approach. At this moment, it is clear from the interviews that the uncertainty analysis must be kept as simple and transparent as possible to allow interpretation by non-statisticians.

The first chapters of this report expand on the introduction by giving the framework for the uncertainty analysis (Chapter 2), discussing the use of alternative scenarios to tackle environmental variability (Chapter 3), and a short explanation on probability distributions (Chapter 4). Further in the report, sample risk assessments for two substances are presented. The first is dibutylphthalate (DBP, Chapter 5), an existing chemical for which a draft risk assessment has been prepared by the Netherlands in the existing chemicals programme of the EU. The second is a new chemical notification (name withheld, Chapter 6). The difference between the two data sets is large: for DBP, a large and evaluated data set is available whereas for the new chemical the data set is limited to the EU base set. This also means that the uncertainty in the final model results can be different. As much as possible, the parameter distributions were based on the data available for the compound, in other cases, general rules had to be used (Jager *et al.*, 1997). Finally, Chapter 7 gives the general conclusions.

It is the intention to present this report as contribution to the update programme of the EU-Technical Guidance Documents in 2000.

2. Method for uncertainty analysis

Before an uncertainty analysis can be done a choice must be made which uncertainties to represent in the analysis and in what way (the underlying assumptions). This is a crucial step as the interpretation of the resulting probabilistic risk measure will depend on it. For the purpose of these calculations, probability distributions were assigned to “chemical-specific” parameters (e.g. emissions, partition coefficients) and not to “environmental” or “scenario-dependent” parameters (e.g. organic matter content in soil, wind speed, dilution factors in surface water) (Jager *et al.*, 1997). This distinction is not always straightforward; e.g. degradation rates depend on the chemical properties but also on the environmental temperature and bacterial populations.

The use of “chemical-specific” uncertainties only, implies that environmental variability is not covered in the probability distributions. The reason for the omission of this source of uncertainty is that it is virtually impossible to capture this variability in a probability distribution in a transparent manner (Jager *et al.*, 1997). Furthermore, several models in the TGD (and thus in EUSES) are not suited for including variability as they are tailored to a specific scenario (especially the local air model). Nevertheless, variability may be an important source of uncertainty. For these calculations, it was judged more appropriate to tackle this source by using alternative plausible scenarios (e.g. a real worst case and a best case) to provide a feel for the impact of these uncertainties (see Chapter 3).

A source of uncertainty that is not addressed is the fundamental uncertainty in the model concepts (e.g. the assumption of well-mixed compartments in SimpleBox) and the choices for scenarios (e.g. exposure to air at 100 m from the source). It should be acknowledged that these uncertainties may well compromise the accuracy and precision of a risk assessment.

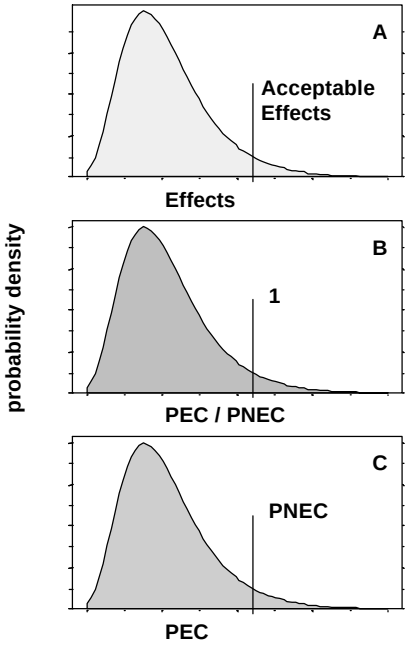


Figure 1 Options for probabilistic risk assessment.

From the interviews (Jager, 1998), it became clear that there is currently little support for quantifying the uncertainties in the effects assessment. The scientific understanding of this part of the assessment was judged insufficient to warrant even a limited quantification. The uncertainties in the effects assessment may, however, well dominate the assessment (Jager *et al.*, 1997). Therefore, two options for probabilistic risk assessment will be worked out in this report:

1. Probabilistic risk estimate where the PEC is uncertain and the PNEC, or the NOAEL for humans, fixed (option C in Figure 1). The result is a probability distribution of the PEC and “risk” is interpreted as the position of the curve in relation to the vertical line, the PNEC.
2. Probabilistic risk estimate where both PEC and PNEC are uncertain (option B in Figure 1). Uncertainty in the PNEC results from uncertainty in the extrapolation steps (assessment factors). For humans, a comparable extrapolation to a

PNEL[1] is performed. The result is a probability distribution of the PEC/PNEC quotient. “Risk” is interpreted as the position of the curve in relation to the vertical line PEC/PNEC=1.

The effects assessment remains the critical stage when we want a probabilistic risk framework that is scientifically justifiable (Jager *et al.*, 1997). The uncertainties in this part need to be addressed but the concept of the PNEC forms a problem in itself. A PNEC is not a measure of ecosystem damage but a conservative trigger value and the exceedance of the PNEC is not a risk level[2]. In fact, the absolute value of the PEC/PNEC ratio is difficult to interpret as the shape of the (theoretical) relationship between exposure level and ecosystem damage is unknown. A further limitation of the PNEC derivation is that only a part of the available toxicological information is used: only the lowest LC50 or NOEC. Unfortunately, our options to revise this stage are limited as the current state of knowledge is insufficient to estimate dose-response relationships of ecosystems or human populations with any degree of realism. The PAF approach as worked out earlier (option A in Figure 1) is a step in that direction but the support for this approach in the EU is currently limited. Further study in this area is however desirable.

Uncertainty analysis was performed with the EUSES 1.00 equations programmed in Microsoft Excel™. This version was programmed for the purpose of testing the development of the official version of EUSES and includes the SimpleBox and SimpleTreat spreadsheets. Uncertainty analysis was performed using Crystal Ball™ version 4.0c, an add-in for Excel. Sampling was performed according to the Latin-Hypercube option, 2000 runs were sufficient to obtain smooth distributions. Crystal Ball contains a large gallery of distributions including lognormal, triangular and uniform (the assumed distributions for the sample calculations).

[1] Predicted No-Effect Level. This parameter is called a level as it is usually given as a dose (mg/kg BW/d) and not as a concentration. This approach differs from that in the TGD as in the TGD, no explicit extrapolation to a “safe” level is performed.

[2] “Risk” is generally defined in the scientific community as an “impact” times the probability or frequency that this impact will actually occur. A clear example is the risk associated with flying in an airplane: risk is the expected number of casualties times the frequency of a plane crash (e.g. expressed as expected number of casualties per kilometer of air travel). In risk assessment we have two problems: probabilities are not routinely quantified and impacts are poorly defined (exceeding a PNEC says nothing about the impact on ecosystems).

3. Alternative scenarios

For some parameters, the uncertainty caused by environmental variability is relatively straightforward to quantify. Examples are human consumption rates where distributions can be fitted on results of consumer surveys. Other sources of variability are much more difficult to capture in distributions. As an example, the fish for human consumption is caught in fresh surface water at the point of complete mixing of the effluent with the receiving water body. In reality, the fish moves around and fish may be caught at different distances from an STP. When considering one river it may be possible to capture this variability in an acceptable distribution but since most chemicals have more sources from which they enter the environment, the situation becomes complicated. One has to assume a distribution for the distance between the catch and the STP and a distribution for the probability that a fish is caught from a water where a certain source is located. Clearly, we enter in a web of interconnecting uncertainties which is extremely complicated to resolve.

In the earlier calculations (Jager, 1995; Jager *et al.*, 1997), we ignored this source of uncertainty entirely. For this report, we chose to handle variability by calculating alternative plausible scenarios for several endpoints. Although this is a poor way to represent the total influence of variability it provides some clues as to whether variability plays a role in the risk assessment.

The following scenarios were selected:

Surface water (local)	STP discharging on a large river (dilution factor=10000)
	STP discharging on a small ditch (dilution factor=2)
	Releases to waste water discharged directly to surface water: in this case also a small ditch (dilution factor=2).
Soil (local)	High fraction organic carbon in soil (30%), high rain rate (4 times normal)
	Low fraction organic carbon in soil (0.1%), low rain rate (1/4 times normal)
	Normal organic carbon content but no sludge applied as fertiliser
Regional	Spain vs. Finland (see Appendix 2.5)

For the aquatic endpoints, we changed the dilution factor as most important scenario property: ranging from 2 (a small ditch) to 10,000 (a large river). Furthermore, a scenario is presented were the effluent is discharged directly into the surface water without STP. The connection percentage in the EU-Member States ranges from 45 to 100% which makes this scenario not unrealistic.

Changing the organic carbon fraction in soil has several effects. A higher sorption coefficient in soil leads to lower degradation rates. This is incorporated in the TGD in the form of degradation classes; here, a linear relationship is assumed. A second effect is that terrestrial ecotoxicity data should be normalised to a standard soil. Here, we also assumed a linear relationship between the fraction organic carbon (*Foc*) and PNEC. The percentage of sludge used as fertiliser in agriculture ranges between 10 and 80%, therefore, also a scenario were no sludge is applied will be shown.

Due to the way that the air module in EUSES is implemented, it was not possible to make different scenarios for deposition or atmospheric concentrations.

For the regional scenarios, the differences in temperature between the model countries Spain and Finland were accounted for. This required the implementation of temperature dependencies of degradation rates and physico-chemical properties (Brandes *et al.*, 1996) which is not part of EUSES.

4. Interpretation of probability distributions

Risk managers are not usually experienced statisticians, which may be a reason for the lack of enthusiasm for uncertainty analysis. The interpretation of distributions requires some knowledge of statistics and probability calculus. Therefore, we provide a short introduction in this chapter.

Most people will be familiar with probability distributions for discrete stochastic variables. In the example of Figure 2: the sum of one throw with a pair of dice. The height of a bar means the probability of a certain outcome and the sum of all bars equals a probability of 1 or 100%. The probability of a sum of 2 is 1/36 (of the 36 possible outcomes, only one will yield a sum of 2; i.e. 1 and 1), the probability of 7 is highest: 6/36 or 1/6 (6 possible outcomes with a sum of 7). The right part of Figure 2 shows the same distribution in a cumulative form. Over the range of possible outcomes, the cumulative function rises from 0 to 1. At an x value of 8, the cumulative probability is 0.72. This means that when throwing a pair of dice, the probability of obtaining a sum *lower or equal* to 8 is 72%. The probability of getting a value higher than 8 is the reciproque value: 28%.

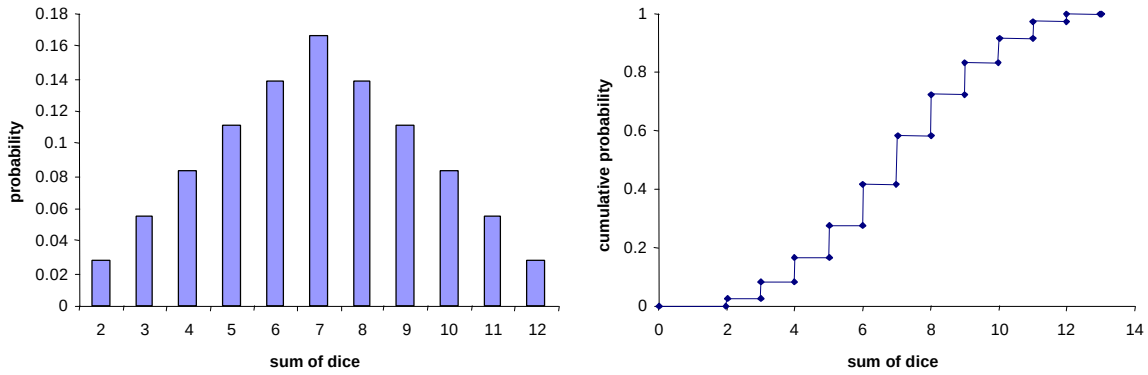


Figure 2 Probability distribution of a discrete variable (the sum of one throw with a pair of dice) shown left; the cumulative function shown on the right.

For a continuous variable like our RCR[1], the cumulative distribution (the right part of Figure 3) allows a similar interpretation although the cumulative is now a smooth curve. The probability function is, however, a different situation. Other than in the dice example, there are an infinite number of possible RCRs and the probability of any single RCR is infinitesimally small. A useful analogue for continuous functions is the probability density function (left part of Figure 3) which is the derivative (slope) of the cumulative function just as the probability distribution for the sum of the dice is defined by the "jumps" in the cumulative function in Figure 2. In contrast with probabilities, the probability density can take values larger than one but the area under the total curve is always one (or 100%). Probabilities are found by taking the area under a part of the density curve (as shown with the area in the left Figure 3).

[1] The term RCR (Risk Characterisation Ratio) is used in the context of the TGD and EUSES to cover all the quotients of exposure and effects, thus including both PEC/PNEC as well as the Margin Of Safety for human health assessments.

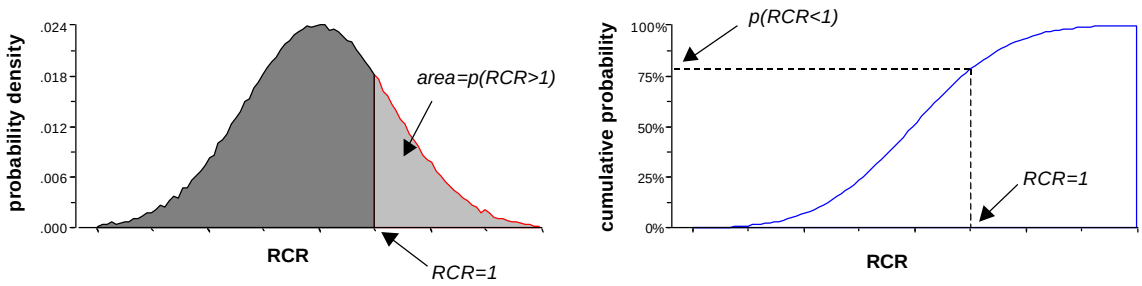


Figure 3 Probability density function and its cumulative for a continuous variable (in this case the risk characterisation ratio – RCR).

The resulting probability distributions in this exercise will be presented as cumulative functions. An example is shown in Figure 4. The probability that RCR is lower than 1 can be read from the value found on the y-axis. A more obvious parameter to focus on is the probability that RCR exceeds one, which is 100% minus this value. The different steps of the life cycle and the regional results will be shown as separate distributions in the same graph and three lines are shown as reference to facilitate interpretation:

1. The line RCR=1 allows to quickly assess the part of the curve which exceeds this risk limit. In the case of only uncertainty in the PEC, the vertical reference line will be the PNEC (see also Figure 1C).
2. The 90% probability line. Of course, this cut-off value is an arbitrary choice but given the fact that the curve represents the uncertainty originating from input parameters only and given the worst-case scenario, this seems more appropriate than a 95% or 99% level[1].
3. A small vertical line on the x-axis shows the location of the deterministic point estimate of RCR or PEC as derived from EUSES for the worst step of the life cycle. This allows assessing the degree of conservatism in the deterministic values.

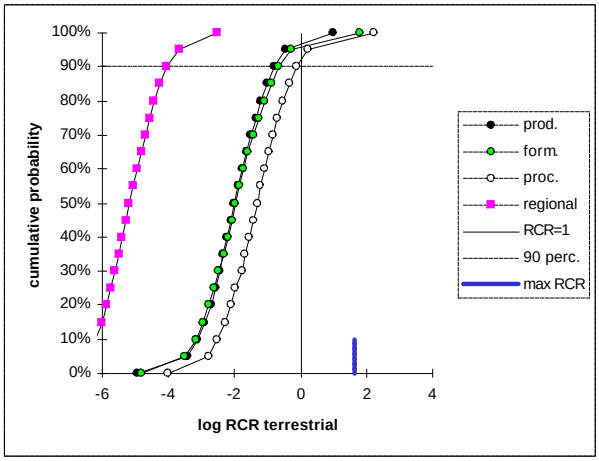


Figure 4 Example of a cumulative probability density function.

[1] The choice of cut-off value should be inspired by the conservatism in the fixed scenarios, the gravity of the expected impacts, and perhaps also socio-economical considerations. This is the responsibility of the risk manager, not the risk assessor. As the local scenarios are far more worst-case than the regional one, a stricter cut off seems appropriate for the latter.

5. Probabilistic assessment of DBP

5.1 Introduction to DBP

DBP is a high-production volume chemical that is used mainly as plasticiser in resins and polymers such as polyvinyl chloride. Other usages include the use in printing inks, adhesives, sealants, nitrocellulose paints, film coatings and glass fibres. Furthermore, DBP is ubiquitous in cosmetic consumer products. This chemical was selected as it is currently discussed in the existing chemicals framework and because it does not pose too many problems for EUSES (it is a neutral organic chemical).

The analysis presented in Section 5.2 to 5.4 is based on the draft risk assessment report (RAR) of November 1998. In this draft, the emission data for 1997 were used. Our calculations, however, were made with the production and use figures from 1994 (as these were more complete at the time). To allow for a comparison between probabilistic and deterministic risk assessments, we recalculated the deterministic data with EUSES. The values in Table 1 therefore differ from the values given in the draft RAR. In Sections 5.5-5.6, a new risk assessment is made using the latest available data (RAR of 3 May 1999) was used with the emission data for 1998.

More information on the probability distributions that were used can be found in Appendix 2.

5.2 Conclusions of the dossier and EUSES

In Table 1 the highest risk ratios and lowest MOS values for DBP are shown as calculated with 1994 production data. Clearly, on the basis of this data set, there is reason for concern for all endpoints except fish-eating predators. Especially effects on plants through the atmosphere is a crucial endpoint.

Table 1 Deterministic risk characterisation ratios (RCR) from EUSES for DBP calculated with 1994 data from RAR 17 November 1998.

Environmental	***PEC***	***PNEC***	***PEC/ PNEC***	***Scenario****
Aquatic system	0.38 mg/L	10 µg/L	38	III-b2 processing adhesive
Terrestrial	86 mg/kg	2 mg/kg_{dw}	43	III-b2 processing adhesive
STP	3.8 mg/L	220 ug/L	17	III-b2 processing adhesive
Predator fish	6.5 mg/kg	104 mg/kg_{food}	0.063	III-b2 processing adhesive
Predator worm	484 mg/kg	104 mg/kg_{food}	4.7	III-b2 processing adhesive
Plant (air)	21 $\mu g/m^3$	0.01 $\mu g/m^3$	2100	III-a softener processing
Human exposure	***PEC or DOSE***	***NOAEL***	***MOS***	**Scenario**
Via environment, inhal.	21 $\mu g/m^3$	0.5 mg/m^3	24	III-a softener processing
Via environment, total.	1.2 mg/kg/d	52 mg/kg/d	44	III-b2 processing adhesive
Consumer Exposure, inhal.	1.26 mg/m^3	0.5 mg/m^3	0.4	Hairspray

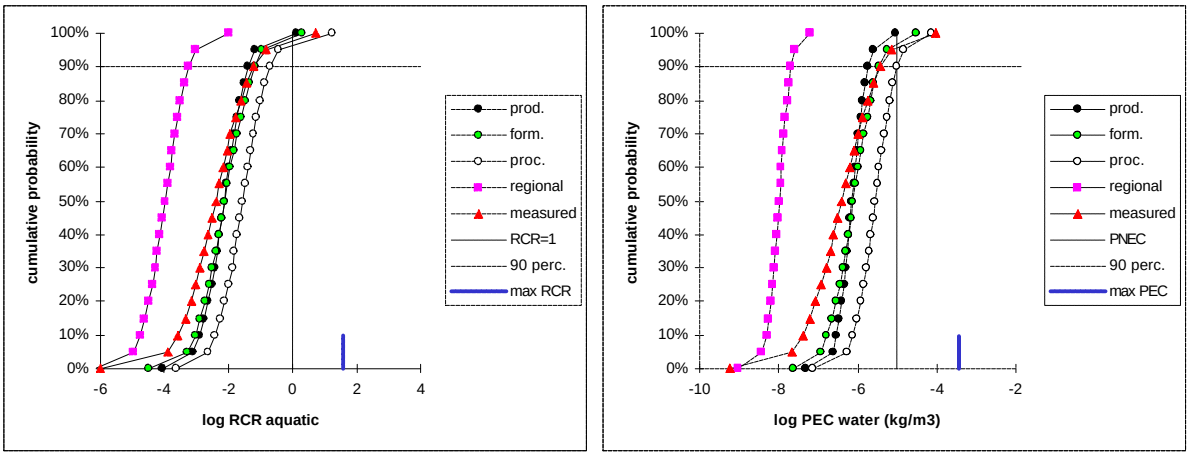
* The scenario code is the one that is used in the RAR.

5.3 Probabilistic risk assessment

Separate probability distributions are made for the local risk assessments (for each step of the life-cycle) and the regional assessment. Furthermore, where appropriate, the RCR on the basis of the available measured data is also shown in the same figure. The distribution of the measured values was taken as the best fitting log-normal distribution through all available data as given in the RAR. This distribution must be interpreted with care as the geographical relation between sources and sample sites was not clear. In the risk assessment report they were considered as "regional" concentrations.

For each endpoint, a sensitivity analysis is given for the standard local scenario with the worst step of the life cycle (in this case processing). The sensitivities are presented as contribution of an input parameter's uncertainty to the total uncertainty. Calculation is done by Crystal Ball by calculating the correlations between input sampling and the corresponding output. The parameters contributing at least 1% to the total variation of the RCR or PEC are shown.

5.3.1 Aquatic ecosystem



Sensitivities

Assessment factor lab-eco	57.3%	Local emission to water	86.8%
Local emission to water	35.2%	Biodegradation in STP	9.9%
Biodegradation in STP	4.7%	Koc	1.0%

The probability distributions of the RCR are for the most part to the left of the vertical line RCR=1 (left figure). This means that it is unlikely (p < 5%) that the RCR will exceed unity[1]. Processing is the most critical life-cycle stage (this distribution is most to the right of the graph) and the regional model leads to the lowest RCRs. The main source of uncertainty in the RCR for the processing step is the assessment factor on the data used to extrapolate from the NOEC of the most sensitive species to an ecosystem in the field. Second important, and dominating uncertainty in the PEC, is the uncertainty in the emission to water.

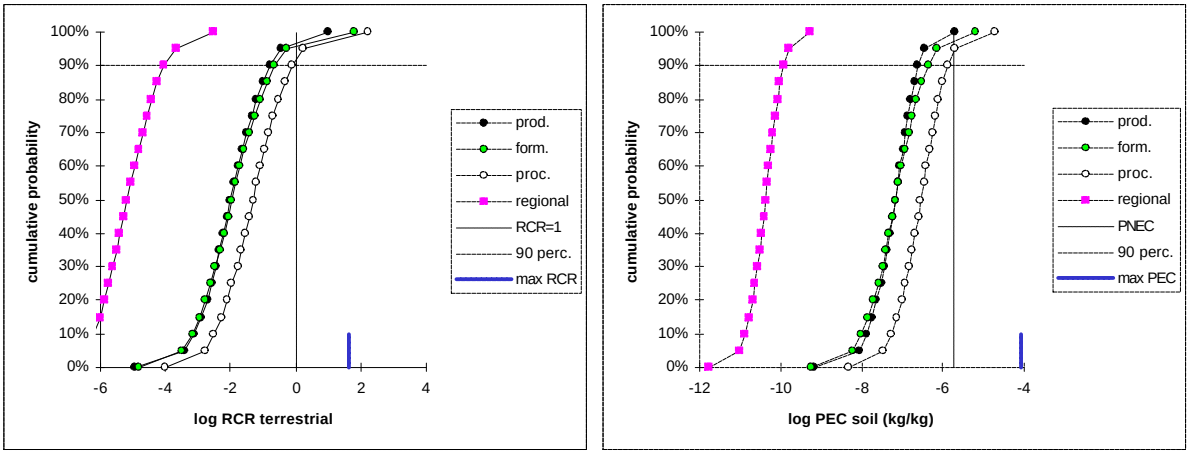
The PEC distribution seems to be a bit more critical (closer to the vertical PNEC line; right figure)) than the RCR distribution. This is a response to the fact that the deterministic PNEC is quite conservative (at the lower end of its assumed distribution). For the stage of processing,

[1] One has to realise that this interpretation must be made *given* the realism of the scenario and *given* the appropriateness of the model assumptions. In case a processing facility is located on a river that runs dry each summer, the probability of RCR exceeding 1 is no longer negligible. These limitations must be kept in mind when interpreting these distributions.

the probability that PEC exceeds this PNEC is approximately 10%. The measured PEC is more or less comparable to the local assessments although the risk assessment report claims them to be not point-source related. This implies that the local scenarios are not extreme worst cases.

In conclusion, there seems to be little reason for concern for the aquatic system considering that the applied scenario is a conservative one. For the standard exposure scenario, the processing step indicates borderline risk when the assessment is based on uncertainties in the PEC only. The RCR and the PEC calculated with EUSES (the short lines in the figures) are above the highest percentile of the distributions. This indicates that the degree of compounded conservatism in the EUSES estimate is high.

5.3.2 Terrestrial ecosystem



Sensitivities

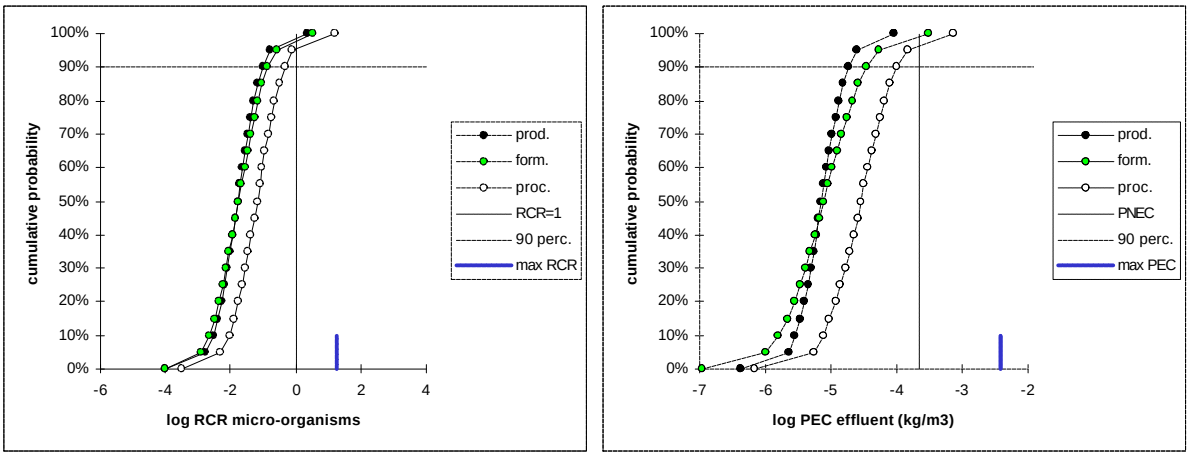
Assessment factor inter-species	35.9%	Local emission to water	48.1%
Assessment factor lab-eco	29.8%	Koc	44.8%
Koc	15.1%	Biodegradation in soil	3.9%
Local emission to water	14.3%		
Biodegradation in soil	2.0%		

The situation with regard to the terrestrial ecosystem is largely similar to the aquatic: little reason for concern although the processing step is borderline. The 90th percentile of the processing distribution is close to the risk limit in both graphs: the probability of RCR>1 (left figure) and PEC>PNEC (right figure) are both slightly less than 10%. The regional results are far below the critical levels.

Uncertainties in the effects assessment dominate the total uncertainty. Of the uncertain parameters in the exposure assessment for processing, the local emission to water and *Koc* are most important. This implies that the uncertainty in the route via sludge is more important than via deposition from air.

Again, EUSES estimates are conservative (close to, or exceeding the 100th percentile of the Monte Carlo samples generated by Crystal Ball).

5.3.3 Micro organisms in the STP

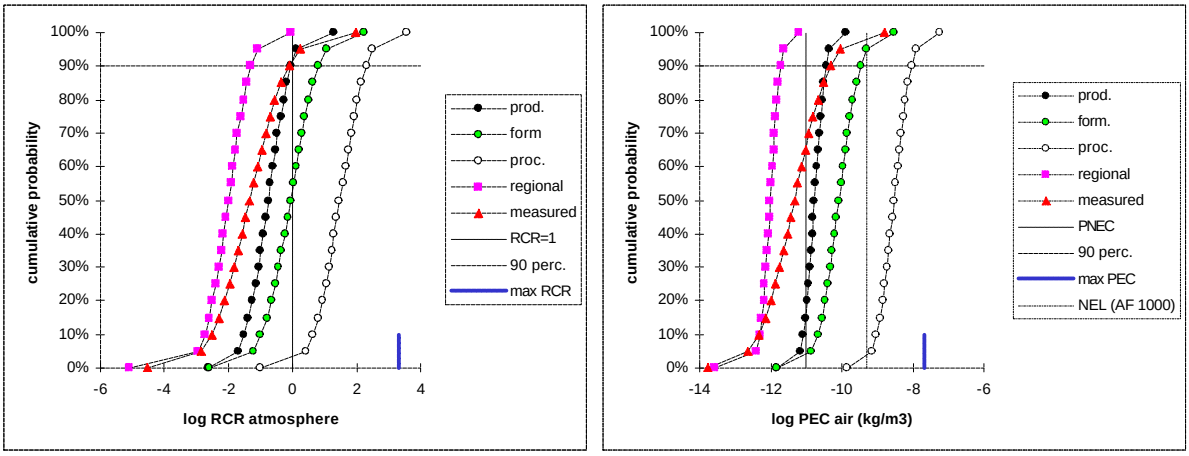


Sensitivities

Assessment factor acute-chronic	57.1%	Local emission to water	86.9%
Local emission to water	35.6%	Biodegradation in STP	9.9%
Biodegradation in STP	4.0%		

The estimated risk for micro-organisms is rather low. The probability that RCR>1 (left figure) or PEC>PNEC (right figure) is less than 5%. Nevertheless, the EUSES estimates indicate more reason for concern. Major uncertainties are in the effects assessment and the emission to water.

5.3.4 Atmospheric exposure of plants



Sensitivities

Assessment factor lab-eco	61.7%	Local emission to air	97.6%
Local emission to air	35.3%		

This endpoint is where the highest risks are, as indicated by EUSES (see Table 1). For the stage of processing, the probability that RCR>1 is more than 95% (left figure), the probability of PEC>PNEC is essentially 100% (right figure). Also the formulation stage is important: p(RCR>1)≈50%, and possibly the production stage: p(RCR>1)≈10%. These percentages are even higher when the exceedance of the deterministic PNEC are considered.

This reason for concern is not an artefact of the exposure scenario: when the measured data are considered, the 90th percentile of the RCR is close to 1 and the probability that PEC>PNEC is 30%. The measured data are largely intermediate between the local and the

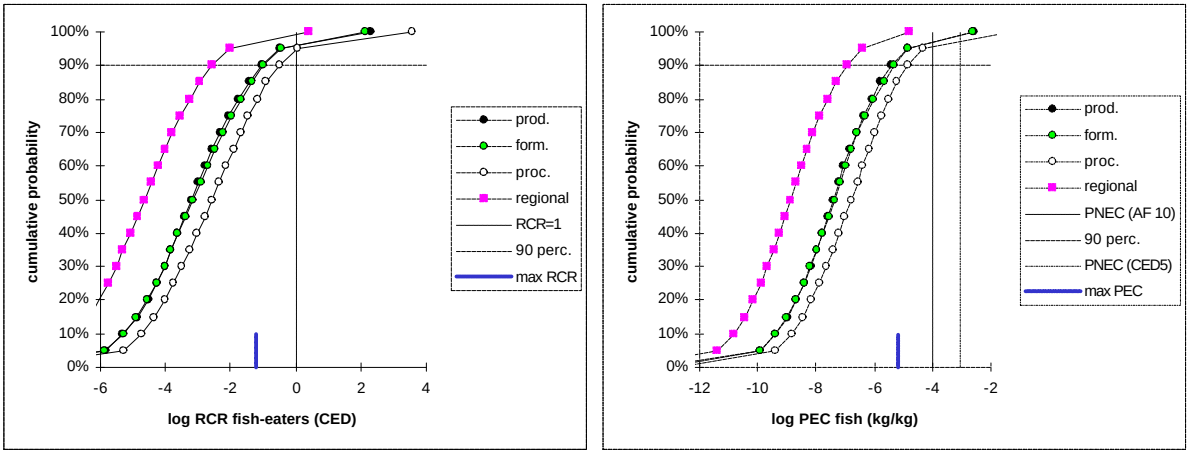
regional estimates. Since the scenario for these measurements is not necessarily worst case, a 95th percentile may be more suitable than a 90th percentile[1].

The most important source of uncertainty lies with the assessment factor from laboratory data to the field situation. In the exposure assessment, the uncertainty in the local emissions to air dominates.

Also shown in the right figure is a human NEL (the inhalatory NOAEL divided by 1000). Humans exposed via inhalation seems to be a less critical endpoint than toxic effects in plants. Nevertheless, the PEC distribution for processing exceeds this NEL for 95%. Even an assessment factor of 100 would lead to unacceptable RCRs.

In conclusion, this endpoint can clearly be considered at risk and since the risk estimate is so high, refinement will be difficult. Most useful in refinement seems to be more detailed toxicity testing with plants to lower the uncertainty about the no-effect level. Second important, and dominating the exposure assessment is the emission to air.

5.3.5 Fish-eating predators



Sensitivities fish-eater

BCF fish	80.6%	BCF fish	90.5%
Assessment factor inter-species	8.9%	Local emission to waste water	6.1%
Local emission to waste water	5.2%	Biodegradation in STP	1.0%
Assessment factor lab-field	1.8%		

For the predating birds and mammals, the exposure scenario is such that half of the diet is sourced from the local environment and the other half from the region[2]. The distributions in the figures representing steps of the life cycle therefore include 50% from the region. An additional calculation shows the contribution from the region only.

Although the distributions are very broad (owing mainly to a high uncertainty in the BCF)

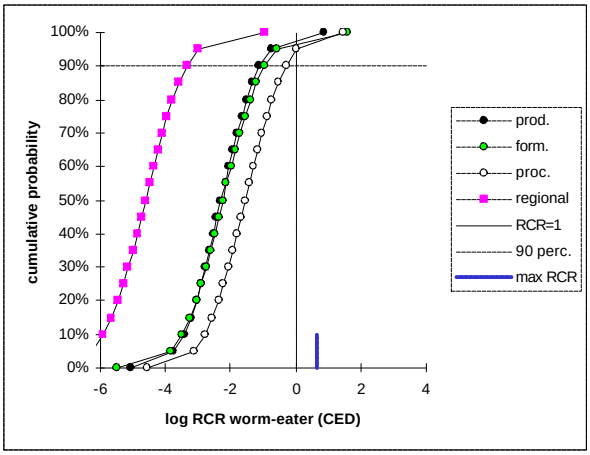
[1] The interpretation of the percentiles hinges on the underlying uncertainties and scenarios. The local estimates represent a hypothetical worst case situation (100 m from the main point source). Measured data represent a more realistic scenario and one may want to have more certainty that this does not lead to exceedance of the PNEC. For the rather optimistic, highly averaged, scenario of the regional model a much higher percentile (e.g. 95 or 99%) should be considered. Please note that the distribution of the measured PEC represents mostly spatial and temporal variability whereas the uncertainty in the estimates represents operational uncertainty from the input parameters.

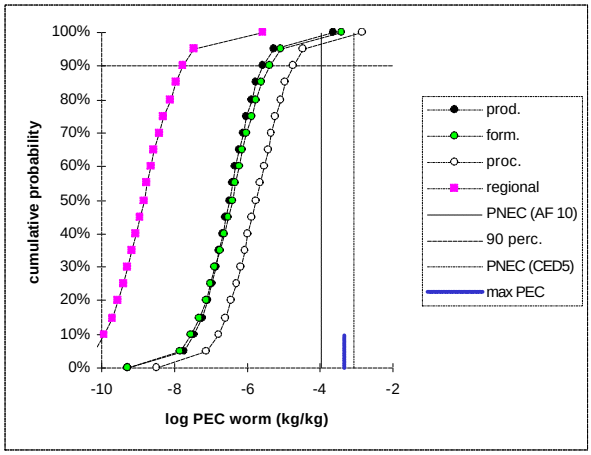
[2] This was done to accommodate the fact that the feeding range of many species will exceed the boundaries of the local scale. The 50-50 division is quite arbitrary.

the probability of RCR>1 (left figure) or PEC>PNEC (right figure) is 5% or less[1]. This means that there is little reason for concern for these endpoints. Interestingly, the EUSES estimate for fish-eating predators is not very conservative. This is mainly due to the fact that we took all the available BCFs in a distribution whereas the dossier selects a very low one as most appropriate (see Appendix 2.2).

The BCF distribution is the main source of uncertainty. This is not surprising as reported BCFs range from 10 to 7000 L/kg.

5.3.6 Worm-eating predators





Sensitivities worm-eater

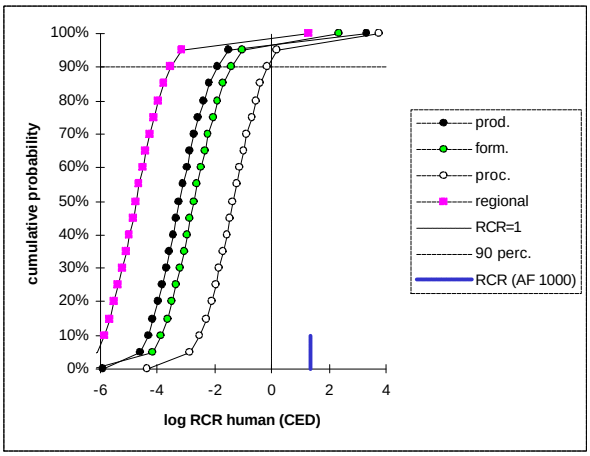
BCF worm	44.5%	BCF worm	66.1%
Assessment factor inter-species	27.1%	Local emission to water	15.0%
Local emission to water	10.1%	Biodegradation in soil	8.2%
Biodegradation in soil	5.6%	Koc	6.6%
Koc	4.4%		
Assessment factor lab-field	3.2%		

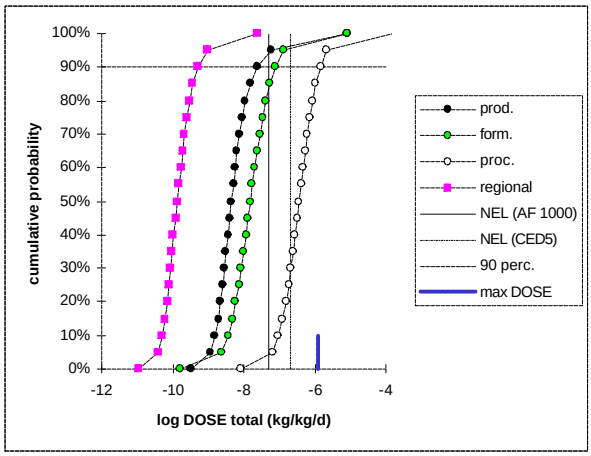
For this endpoint, the local scenarios include 50% of the diet sourced from the region. The contribution of the region is also shown as a separate distribution. The probabilities for RCR>1, PEC>PNEC are 5% or less, indicating little reason for concern. The EUSES estimate is quite conservative and is located between the 95th and 100th percentile. The same PNECs are used as for the fish eating predators.

These distributions are narrower than those for the fish-eating predators but are still quite broad (three orders of magnitude between 5th and 95th percentile). Main source of uncertainty is the BCF for earthworms which is derived from the QSAR training set.

[1] CED5 is the lower 5th percentile of the critical effects dose as estimated from the toxicological data. The PNEC (CED5) is based on this value with an assessment factor of 10. In this case, the difference between the PNEC and the CED5 is only a factor of four. The probabilistic RCR is based on the entire distribution of the CED and assessment factors for inter-species and lab-field differences. More information can be found in Appendix 2.3/2.4.

5.3.7 Humans via the environment





Sensitivities

Assessment factor time-scale	44.4%	Local emission to air	70.3%
Assessment factor inter-species	25.8%	Leaf conductance	22.0%
Local emission to air	15.4%	BCF fish	2.4%
Assessment factor intra-species	6.5%	BAF meat	1.0%
Leaf conductance	4.4%		

The distribution of the RCR reveals a borderline situation for the step of processing. The 90th percentile of the RCR is just below 1 (left figure), but the distribution has a long tail that extends all the way up to 2600[1]. This means that there is a 10% probability that the (uncertain) critical effect dose (see Appendix 2.4) is exceeded in an adult person of 70 kg, consuming 1.2 kg of leaf crops per day, all derived from the soils at 100m from the processing facility (the main route of exposure is through leaf crops which in turn are mainly exposed through air). This is not a highly unlikely scenario when there are vegetable gardens in the neighbourhood. When there are no agricultural areas or gardens in the vicinity of this source, a 90% protection level can be considered acceptable. The deterministic MOS is in this case 44, indicating insufficient protection (see Table 1).

Based on a fixed NEL (either using an AF of 1000 as used in the RAR or the lower 5% confidence level of the critical effects dose) the situation is worse, in particular for the stage of processing (right figure). The 5th percentile of the CED crosses the curve for processing at the 30th percentile. This means that there is a 70% probability that this level is exceeded in our hypothetical adult. If we adhere to the NOAEL and use an assessment factor of 1000, the probability of exceeding this NEL is more than 95%.

The main sources of uncertainty are formed by the assessment factors to extrapolate from the experimental study to the human situation. In the exposure assessment, the main uncertainty is the local emission to air followed by the conductance of the leaf crops.

In conclusion, whether there is a high risk depends on whether or not uncertainties in the effects assessment are accounted for as these dominate the total uncertainty. Nevertheless, because of the extreme right tail of the distribution, caution is required and more information seems desirable.

[1] This a-symmetric shape after log-transformation is probably related to the fact that human exposure via the environment sums the contributions from several food sources. Summing of (nearly) log-normal distributions could lead to such strangely skewed distributions.

5.4 Conclusions for DBP

Especially the risk assessment for the atmosphere (i.e. toxicity for plants via gas-phase exposure) and, to a lesser extent, exposure of humans via leaf crops are leading to serious concerns. Main possibilities for refinement can be found in the effects assessment for plants and humans and the local emissions to air at processing. Given the extent of risk observed for the atmospheric compartment, refinement must be quite extensive in order to achieve an acceptable risk. For the other endpoints, the probability that RCR exceeds 1 is less than 10%. In view of the conservatism of the exposure scenario, this seems acceptable.

The EUSES estimates are quite worst case, (far) above the 95th percentile. This does not immediately imply that EUSES is too conservative. It depends on the uncertainties that we accounted for and the selected distributions. Nevertheless, the present results indicate that the TGD may be too protective, or at least, it must be considered that the results are certainly on the safe side.

5.5 New data for DBP

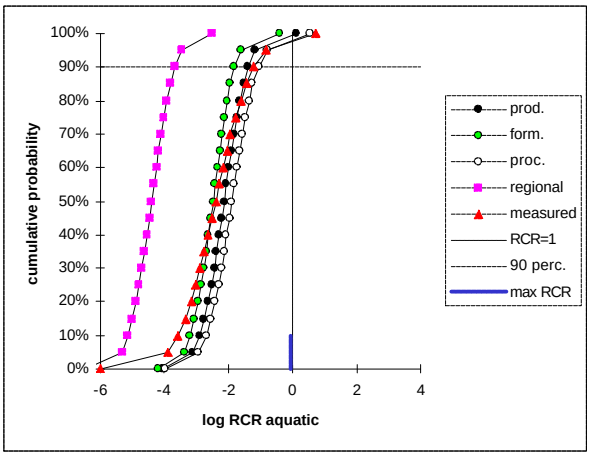
The production and use of DBP has declined over the past years. In this section, the latest available data (RAR of 3 May 1999) was used and the emission data for 1998. Human effects data is currently being revised, therefore, no new data for this endpoint are used. For most of the endpoints, the RCRs could be pushed back below zero. Only the atmospheric exposure of plants remains a serious problem. Whereas in the previous Risk Assessment Report, processing was most important, now formulation has become the stage in the life cycle of highest concern. Only for plants, the processing step still dominates.

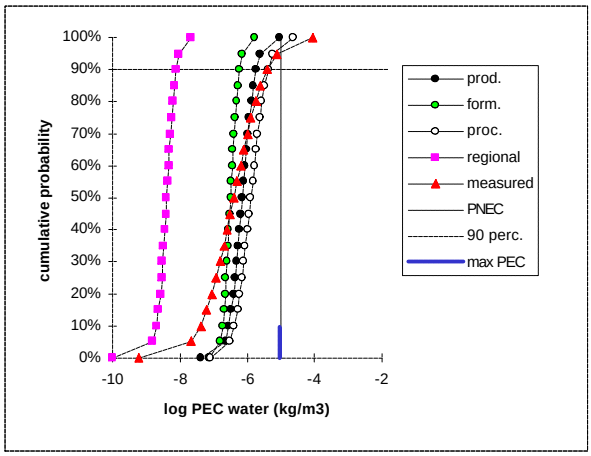
In this section, the distributions will not be discussed in detail again as this was already done in the previous section. Here, the focus will be on the changes due to the newer data.

Table 2 Deterministic risk characterisation ratios (RCR) from EUSES for DBP calculated with 1998 emission data (RAR version 3 May 1999).

Environmental	***PEC***	***PNEC***	***PEC/ PNEC***	***Scenario***
Aquatic system	8.9 ug/L	10 μg/L	0.9	III-b1 formulation adhesive
Terrestrial	1.8 mg/kg	2 mg/kg$_{dw}$	0.9	III-b1 formulation adhesive
STP	0.08 mg/L	220 ug/L	0.4	III-b1 formulation adhesive
Predator fish	8 ug/kg	104 mg/kg$_{food}$	7.3e-5	III-b1 formulation adhesive
Predator worm	10.2 mg/kg	104 mg/kg$_{food}$	0.1	III-b1 formulation adhesive
Plant (air)	2.4 μg/m^3	0.01 μg/m^3	236	III-a softener processing
Human exposure	***PEC or DOSE***	***NOAEL***	***MOS***	**Scenario**
Via environment, inhal.	2.4 μg/m^3	0.5 mg/m^3	212	III-a softener processing
Via environment, total.	93 ug/kg/d	52 mg/kg/d	562	III-a softener processing

5.5.1 Aquatic ecosystem



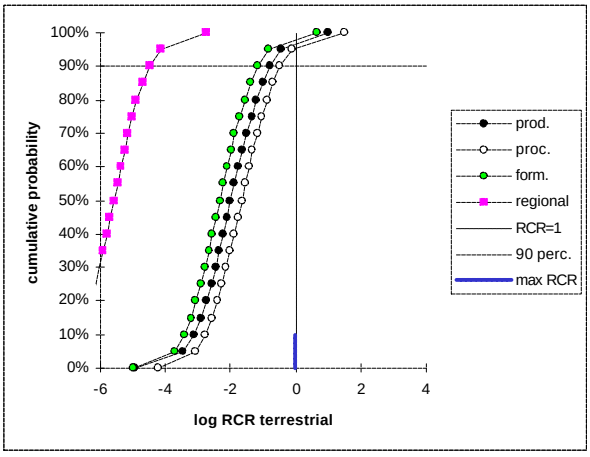


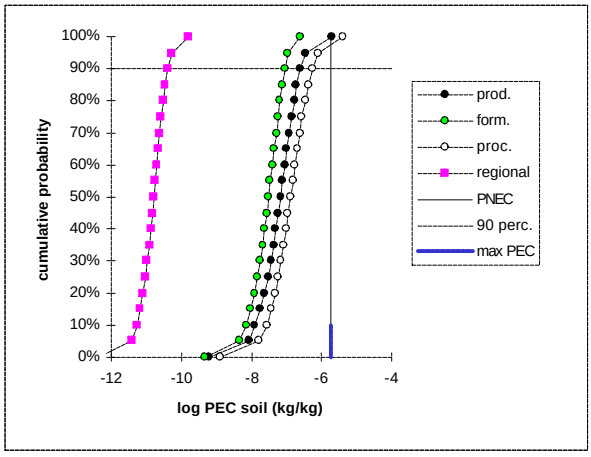
Sensitivities

Assessment factor lab-eco	62.6%	Local emission to water	84.3%
Local emission to water	28.7%	Biodegradation in STP	11.7%
Biodegradation in STP	4.6%	Koc	1.4%
Koc	1.5%		

Risk is limited as the probability of RCR>1 and the probability that PEC>PNEC are less than 5%. The distributions have only been very slightly shifted to the left.

5.5.2 Terrestrial ecosystem



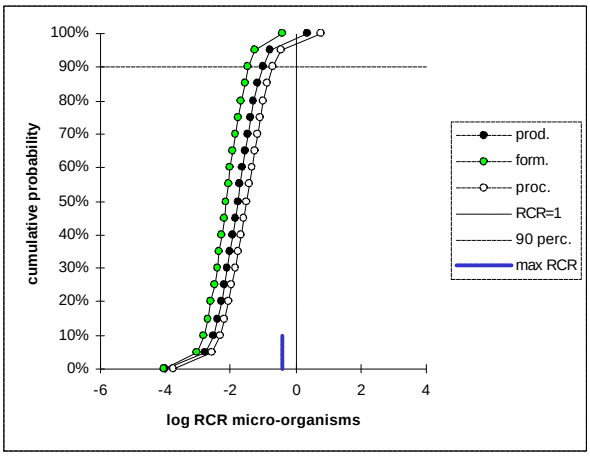


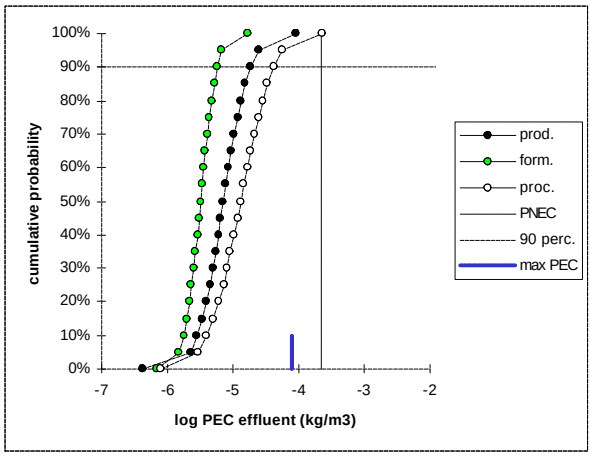
Sensitivities

Assessment factor inter-species	35.9%	Koc	49.0%
Assessment factor lab-eco	32.4%	Local emission to water	41.8%
Koc	13.7%	Biodegradation in soil	6.1%
Local emission to water	12.2%		
Biodegradation in soil	2.4%		

These distributions have also moved slightly to the left. The maximum exceedance of RCR=1 or the PNEC is less than 5%, which can be interpreted as “no reason for concern”.

5.5.3 Micro-organisms in STP



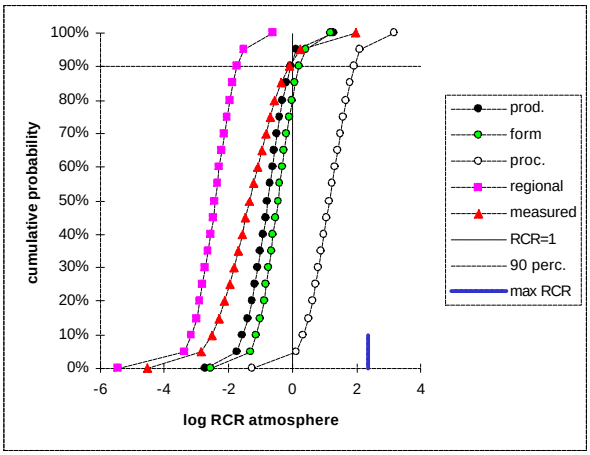


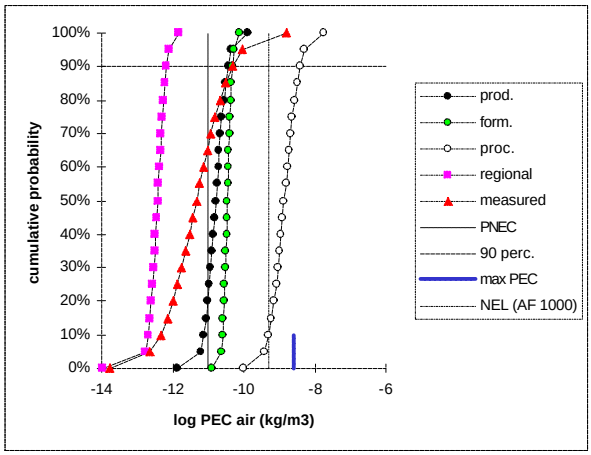
Sensitivities

Assessment factor acute-chronic	62.7%	Local emission to water	84.5%
Local emission to water	30.0%	Biodegradation in STP	11.7%
Biodegradation in STP	4.3%	Koc	1.2%

Again, slightly shifted distributions which sets the maximum risk levels at less than 5%.

5.5.4 Atmospheric exposure of plants





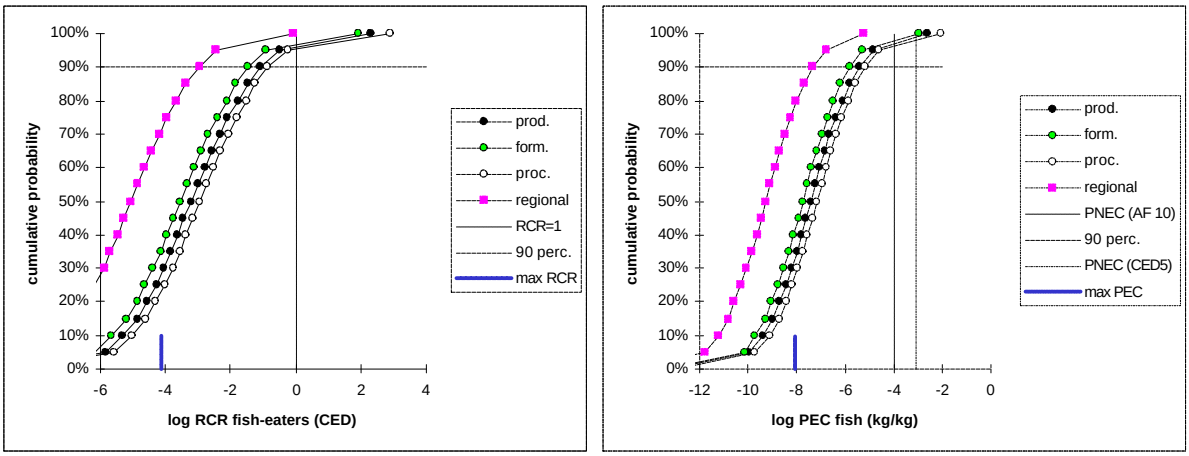
Sensitivities

Assessment factor lab-eco	67.4%	Local emission to air	97.6%
Local emission to air	29.7%		

Analysis of the new data improves the situation only marginally. This endpoint is still of highest concern, especially for the stage of processing (although the other stages, as well as the measured data, do not provide an entirely safe situation). For processing, the probability of RCR>1 is approximately 95%, the probability that PEC>PNEC is effectively 100%. Clearly, there is a need for further study on this endpoint. The main uncertainty is in the lab-eco assessment factor and the emission to air but it should be noted that the total uncertainty is not very large. In fact, an acceptable risk can only be achieved when further studies yield parameter values beyond the range of the probability distributions currently applied. One should note that the PEC for this endpoint is not very conservative (at the 75th percentile).

Also shown is a human NEL (the inhalatory NOAEL divided by 1000), which is less stringent than the plant PNEC, but is also exceeded at the stage of processing.

5.5.5 Fish-eating predators

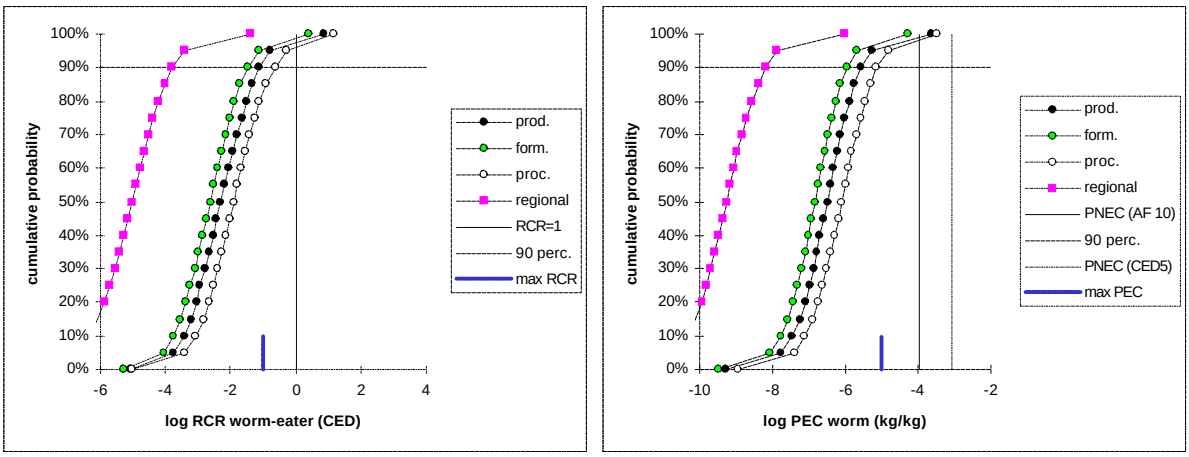


Sensitivities

BCF fish	82.4%	BCF fish	92.2%
Assessment factor inter-species	9.3%	Local emission to water	4.9%
Local emission to water	4.4%	Biodegradation in STP	1.0%
Assessment factor lab-field	1.3%		

Again, we see the distributions shifted slightly to the left. The distributions are very broad but the probability of RCR>1 and PEC>PNEC are <5%. In this assessment, EUSES is definitely not conservative, as the deterministic quotient lies at the 25th percentile. This is caused by the fact that a very low BCF was selected in the update of the dossier (1.8 instead of 41.8 L/kg). The reasons for this choice are not entirely clear from the RAR.

5.5.6 Worm-eating predators

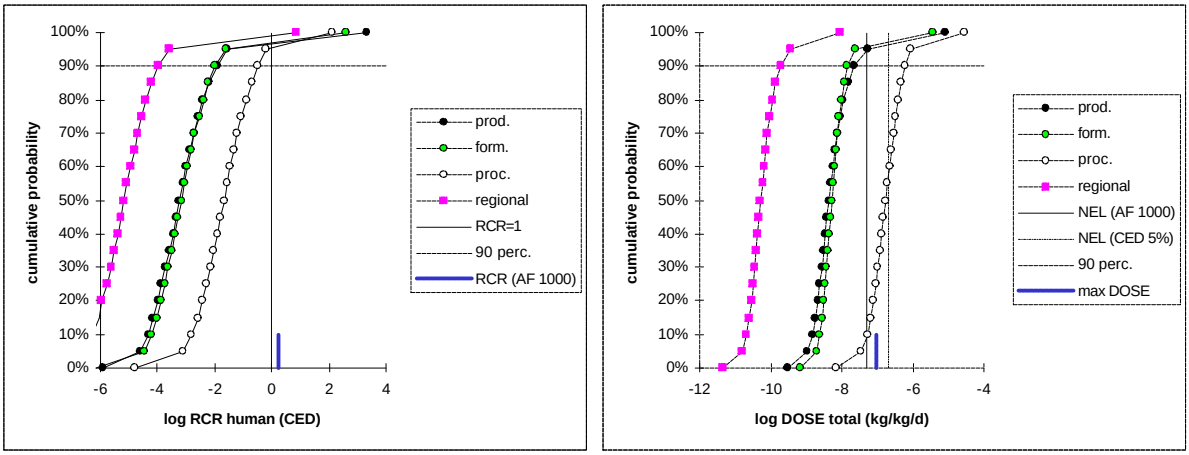


Sensitivities

BCF worm	44.5%	BCF worm	65.3%
Assessment factor inter-species	27.7%	Local emission to water	13.2%
Local emission to water	9.9%	Koc	8.4%
Biodegradation in soil	5.1%	Biodegradation in soil	6.7%
Koc	4.7%	Deposition rate gas phase	1.9%
Assessment factor lab-field	2.9%		
Deposition rate gas phase	1.0%		

The distributions are very broad but the probability of RCR>1 and PEC>PNEC are <5%.

5.5.7 Humans



Sensitivities

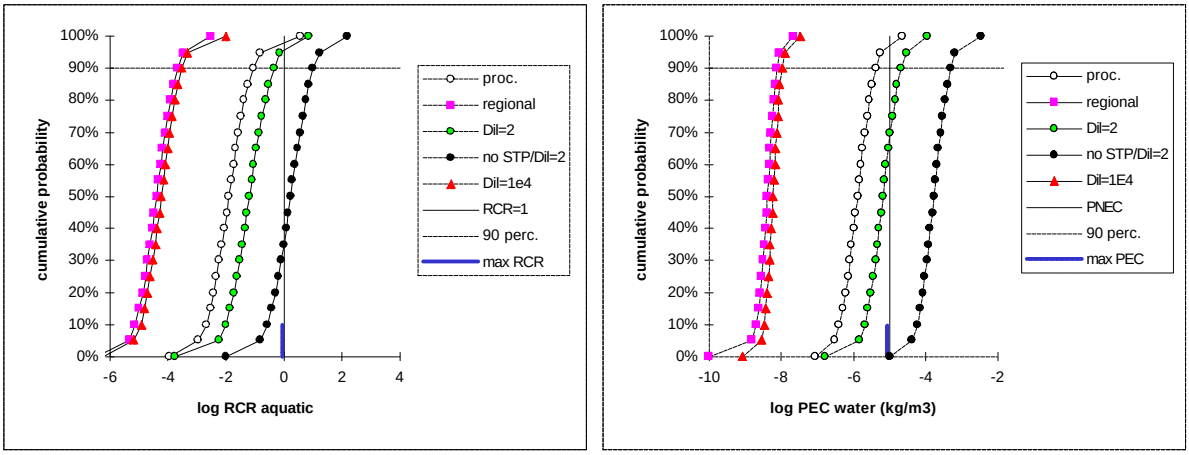
Assessment factor time scale	47.2%	Local emission to air	61.9%
Assessment factor inter-species	26.8%	Leaf conductance	29.8%
Local emission to air	11.1%	BCF fish	2.1%
Assessment factor intra-species	6.0%	BAF meat	1.5%
Leaf conductance	5.1%		

The situation for humans has improved slightly. For the processing stage, the probability of RCR>1 has gone below 5% although the tail extends up to an RCR of 130. When adhering to the fixed NELs, there is still an obvious risk situation for this chemical for processing (the probability that the CED5 is exceeded is approximately 40%). The reason for this diverging conclusions is the large uncertainty in the effects assessment. The other stages give little reason for concern.

The deterministic PEC is very optimistic at 25th percentile of the distribution. Air is the main exposure of plant, which is the main source for human exposure, but the PEC for air was at the 75th percentile. The reason for this discrepancy is that we selected distributions for water solubility and vapour pressure. The medians of these parameters differ from those in the dossier in such a way that we got a much lower air-water partition coefficient (more than a factor of 10 with the median parameters values). This is a very important parameter for the air-plant partitioning, leading to higher values in plants than the value in the dossier. It should be noted that the median value of our plant-water partition coefficient is very high (at the top of the experimental range reported in a validation study (Polder *et al.*, 1997) and may be unrealistic as it is extremely dependent on small changes in physico-chemical properties. Nevertheless, this stresses the importance of uncertainty analysis since the choice of vapour pressure and water solubility is so important!

5.6 Alternative scenarios for DBP (new data)

5.6.1 Aquatic ecosystem



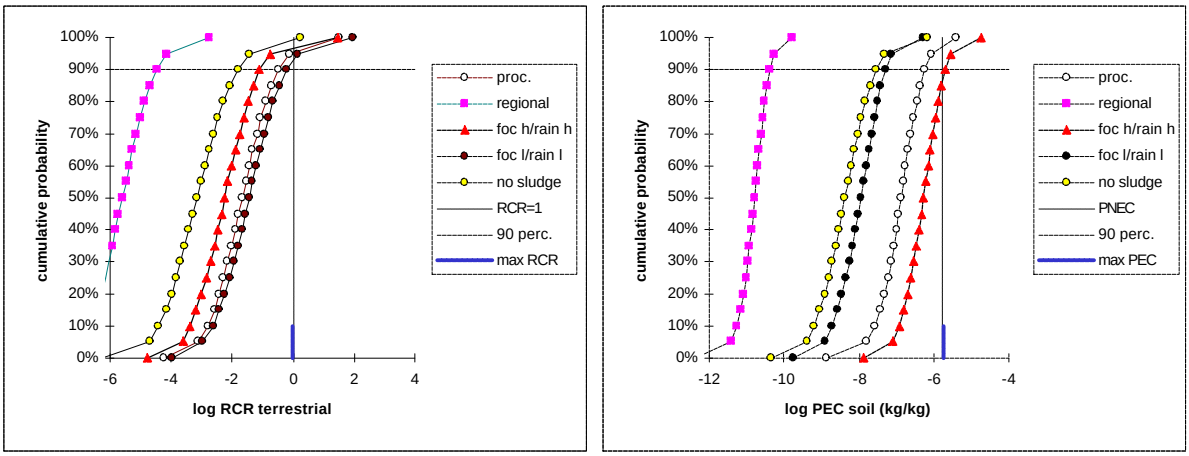
Alternative scenarios are:

Dil=2	dilution factor set to 2; indicating a very small stream
no STP/Dil=2	dilution factor set to 2 and no sewage treatment; absolute worst case
Dil=1e4	dilution factor set to 10000; indicating a large river

Only the stage of processing is used for the alternative scenarios; the regional values are shown as reference. The choice of a dilution factor is quite important. The absolute worst-case scenario without STP is a definite risk situation. This means that we may have a problem when a processing site (or probably the also a formulation or production site) would discharge his effluent directly on such a small stream. With an STP, however, the RCR will stay below one but there is still a 30% probability that PEC exceeds the fixed PNEC.

Interestingly, the width of the probability distributions is approximately two orders of magnitude (5-95%) but the difference between the best and worst-case scenarios is four orders of magnitude. This implies that the choice for an exposure scenario is potentially more important than the operational uncertainty in the input parameters.

5.6.2 Terrestrial ecosystem



Alternative scenarios are:

foc h/rain h	high fraction organic carbon in soil (30%), high rain rate (4 times normal)
foc l/rain l	low fraction organic carbon in soil (0.1%), low rain rate (1/4 times normal)
no sludge	normal *Foc* content but no sludge applied as fertiliser

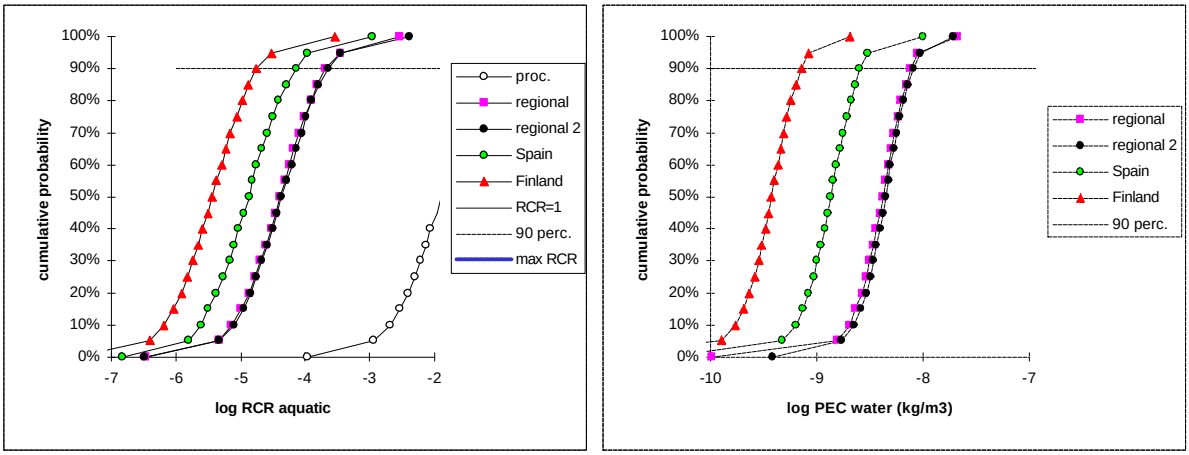
Changing the rain rate had no influence on the model results whatsoever as degradation was the primary removal process in soil. The scenario with high rain rate is combined with high organic carbon content (*Foc*) as these both tended to work to decrease the RCR. Changing *Foc* changes the soil sorption and hence the bioavailability of the compound. In the assessment, we assumed that *Foc* effects biodegradation and the PNEC linearly. A high *Foc* therefore leads to higher PECs (lower degradation) but high *Foc* leads to lower RCRs as the PNEC is lowered. In this way, the effects nearly cancel each other out in the RCR, but not in the PEC (in this graph, the vertical line representing the PNEC should shift with *Foc* which is not shown). The different scenarios affect the distributions less than for the aquatic environment.

5.6.3 Regional systems

Alternative scenarios are (see Appendix 2.5):

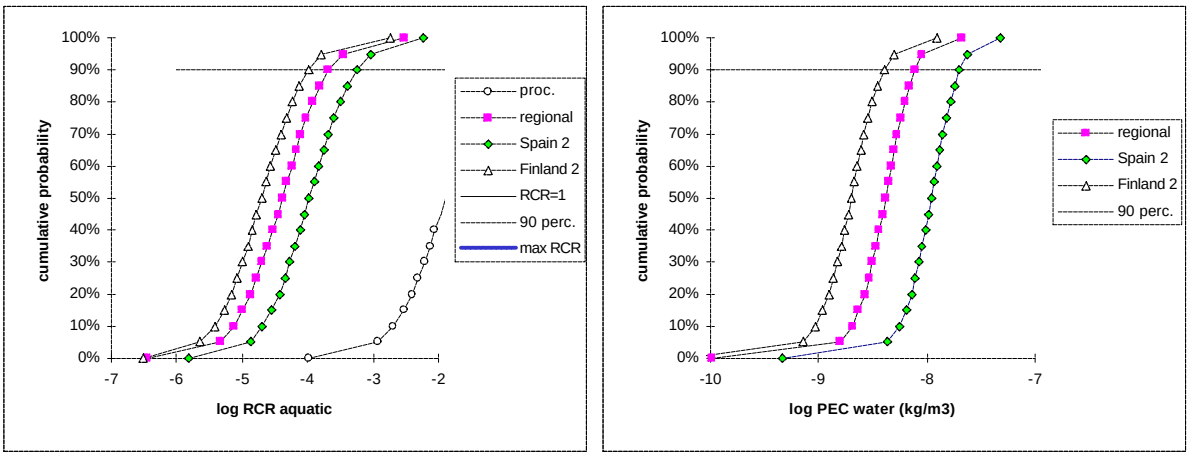
regional 2	same as regional but with temperature correction
Spain	Spanish country definition
Finland	Finnish country definition

Aquatic ecosystem



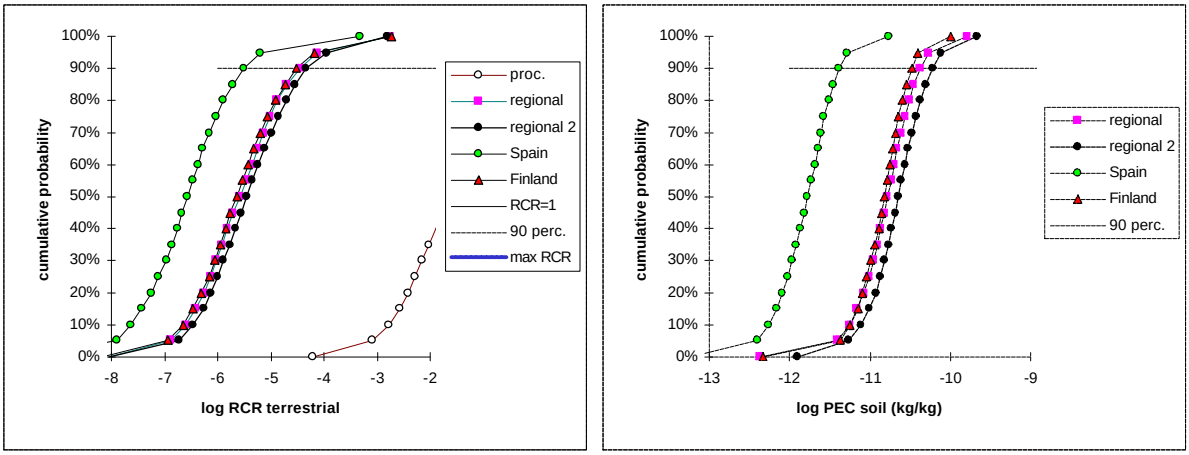
The result of the regional 2 scenario are virtually the same as the standard regional scenario. This implies that the temperature correction for vapour pressure and water solubility do not affect the fate of this chemical significantly.

The difference between the countries is not very large. Finland is the most optimistic, a factor of 10 less than the standard regional system. Spain is somewhat worse than Finland which can be caused by the lower connection percentage to STPs, but still better than the standard region. Playing with the system settings revealed that the standard regional scenario is a kind of worst case because the emission is relocated to such a small area. This implies that size of the system needs to be carefully considered. Country borders may not be the most ideal choice, as national borders do not hamper the distribution of the chemical. To allow for a better comparison, another assessment was made with these extreme countries but with the same size as the standard region (Spain 2 and Finland 2 in the figures below).

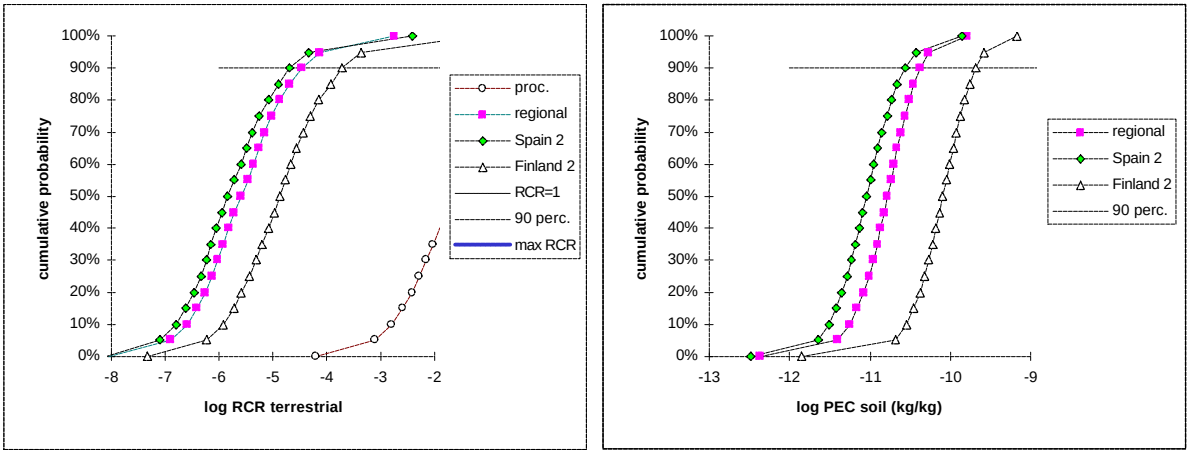


From these figures it is clear that the Spanish system is more at risk because of the low connection percentage to STPs. The Finnish system has lower concentrations because of the slightly higher connection percentage and probably because the water is much deeper. Still, the difference between the average concentrations in these systems is only a factor of 5.5.

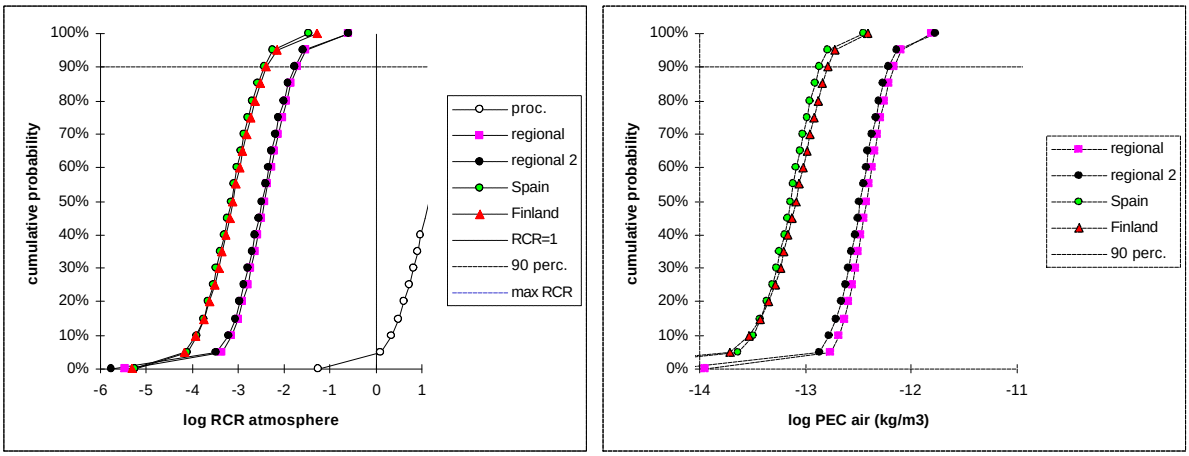
Terrestrial ecosystem



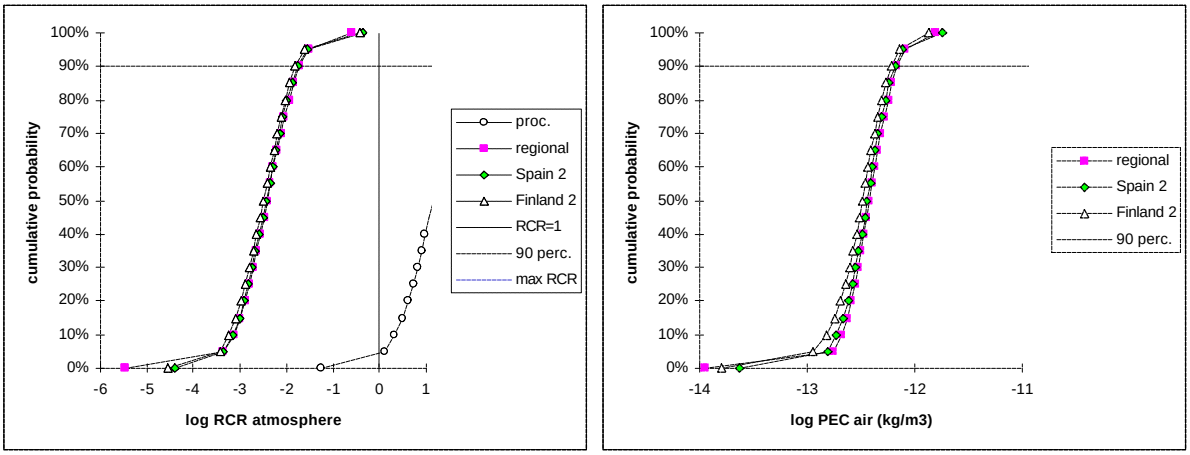
Again, the differences are not very large. The standard regional system is similar to Finland with respect to the distributions, Spain is a factor of 10 lower. This is probably caused by fact that degradation is more rapid and because there are less STPs and thus less sludge can be applied to soil as fertiliser. Again, these results are confounded with the different size of the system. When the standard regional size is used for the two countries (see Figure below), Spain has only slightly lower concentrations, but Finland is somewhat higher (due to the slower degradation rates). The difference in average PEC between the countries is a factor of 8.8.



Atmosphere



Here, Finland and Spain give similar results but the standard region is a factor of 5 worse. The main cause of this difference is probably that the regional system is smaller than the others. This is supported by the figures below where the all countries are the same size (figures below): since wind is the only removal mechanism and as the wind speeds are set equal in all countries, the concentrations in air are not affected.



5.7 Conclusions new data

With the new data, the situation for most endpoints has improved to an acceptable level of risk. However, for plants via the atmosphere, the situation still gives serious reason for concern. The probability of RCR>1 is very large (approximately 95%) which implies that serious study is required to see whether a reduction is possible by refining parameters. When the selected parameter distributions are a fair representation of the uncertainty, further studies will not get the RCR below one and emission reduction should be considered. However, when a more reliable study with plants can yield a toxicity value that is less stringent than the lower bounds of the current distribution, refinement of the assessment is possible.

For humans, there may also be a problem when looking at the fixed no-effect levels and refinement is desirable.

Additional scenarios provide insight in the role of variability, which turned out to be especially relevant for the aquatic system. For the aquatic ecosystem, an unacceptable risk will occur when a processing facility is discharging its effluent directly on a small water body. It depends

on the realism of this scenario whether this gives reason for concern. For this endpoint, the scenario choice is dominating the total uncertainty. For the terrestrial ecosystem, the RCR distribution is not influenced much by the different scenarios since PEC and PNEC are affected in different directions by a change in organic matter content. Non of the scenarios leads to an unacceptable risk in this preliminary assessment. The differences between the standard region and two extreme countries (Spain and Finland) remain within a factor of 10. The standard region is worse than the other countries due to its small size. When the sizes are set equal, the regional system is between the others. Spain is the worst case for water, Finland for soil, for the air compartment, the differences are negligible. It must, however, be noted that not all country-specific defaults were adjusted in this assessment (see Appendix 2.5).

6. Probabilistic assessment of a new chemical

6.1 Introduction to the new chemical

The selected chemical has recently been notified in the Netherlands. The chemical is used in the production of fragrances for soaps, cleaners and air fresheners. Apart from production and formulation, private use is a relevant life-cycle step. For production and formulation, 1 source is considered, for private use the 10% rule is applied (assuming 10% of the tonnage is used in the region and 90% in the continent).

6.2 Conclusions of the dossier and EUSES

The exposure levels and the no-effect levels for this chemical are summarised in Table 3. For environment, conclusion ii was drawn (reason for concern, further information required at next tonnage threshold) because of the RCRs for the aquatic ecosystem and sediment[1] at production but especially at formulation. With regard to consumer exposure, immediate further information was required.

Table 3 Deterministic risk characterisation ratios (RCR) from EUSES for the new chemical.

Environmental	***PEC***	***PNEC***	***PEC/PNEC***	***Scenario****
Aquatic system	98 µg/L	35 µg/L	2.8	Formulation 2
Terrestrial	27 µg/kg$_{wwt}$	38 µg/kg$_{wwt}$	0.71	Formulation 2
Predator fish	110 µg/kg	5 mg/kg$_{food}$	0.023	Formulation 2
Predator worm	29 µg/kg	5 mg/kg$_{food}$	5.8e-3	Formulation 2
Human exposure	***PEC or DOSE***	***NOAEL***	***MOS***	**Scenario**
Via environment, inhal.	0.077 µg/m^3	233 mg/m^3	3.0e6	Production
Via environment, total.	1.2 µg/kg/d	50 mg/kg/d	4.4e4	Formulation 2
Consumer Exposure	mg/m^3	mg/m^3	19	Skin cream

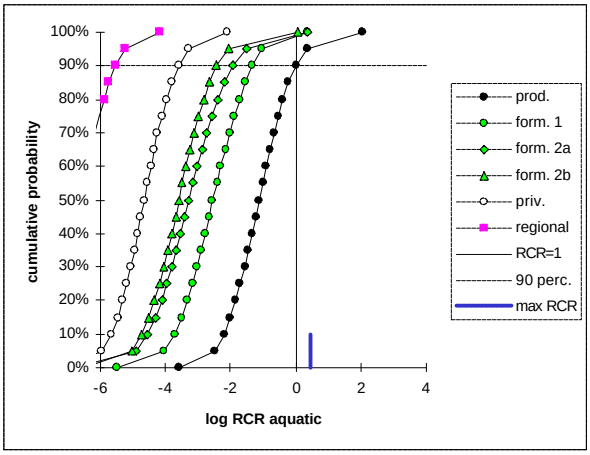
* For this chemical three formulation steps were identified. More information in Appendix 2.1.

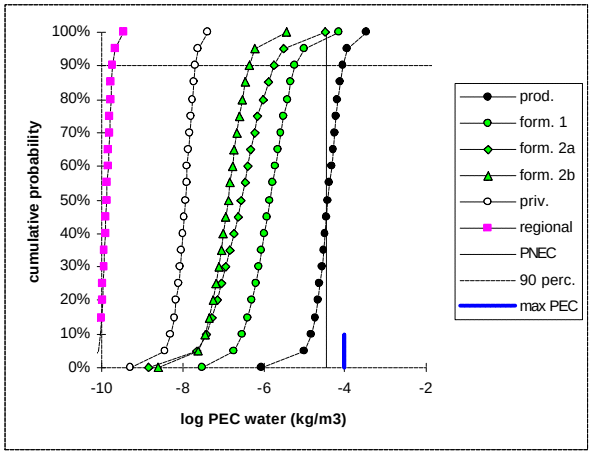
Please note that the EUSES calculation is based on a production volume of 10 tons per year whereas the probabilistic assessment applies the current production volume.

[1] The sediment RCR is not shown in the table as it provides no extra information: both the concentration in sediment as well as the PNEC are derived by equilibrium partitioning from the water compartment. The reason that the RCRs for the aquatic and sediment are not entirely equal is that the PNEC is calculated with sediment properties whereas the PEC is calculated with the properties of suspended matter (i.e. freshly deposited matter).

6.3 Probabilistic risk assessment

6.3.1 Aquatic ecosystem





Sensitivities

Assessment factor lab-eco	46.9%	Biodegradation in STP	42.5%
Assessment factor inter-species 1	11.0%	Number of emission days	34.2%
Assessment factor inter-species 2	8.8%	Local emission to water	20.7%
Assessment factor acute-chronic 1	6.4%		
Assessment factor acute-chronic 2	6.2%		
Biodegradation in STP	5.0%		
Local emission to water	4.9%		
Number of emission days	4.7%		
Assessment factor inter-species 3	3.0%		

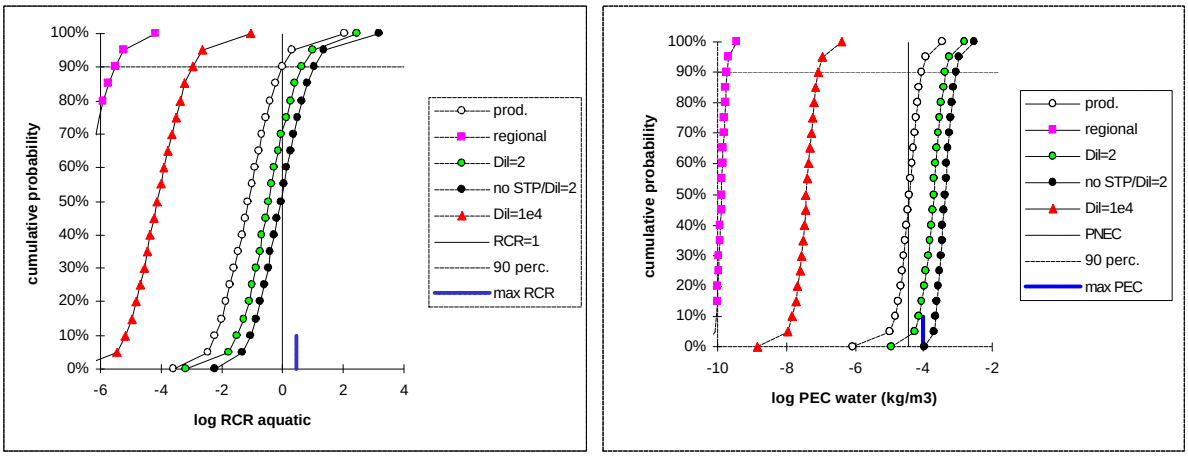
As was indicated by the RCRs in Table 3, there is reason for concern for this endpoint. At production, the probability that RCR exceeds one is 10%; the probability that PEC exceeds the fixed PNEC is approximately 55%. Interestingly, the uncertainty analysis reveals production as the most important life cycle stage whereas the deterministic assessment selected the second formulation stage. This illustrates that reconsidering the release estimation according to expert judgement can give different results than the EUSES tables. The formulation stages and private use do not lead to appreciable risk in the uncertainty analysis. The regional assessment is even more to the left, as may be expected from the low production volume of this chemical.

The deterministic estimate of the RCR and the PEC are at high percentiles of the distribution (especially considering the fact that these come from the formulation 2 step). This is partly caused by the fact that a lower tonnage was used in the calculations.

The assessment factors are the most important sources of uncertainty[1]. In the exposure assessment, biodegradation in the STP and emission parameters are the most important. On the basis of this assessment, further toxicity testing could be proposed (and would be desirable before the 10 ton threshold is reached!).

[1] The specification 1-3 in the sensitivities table originates from the fact that these factors are applied on all three available taxonomic groups independently. As the toxicity values from groups 1 and 2 were comparable, this resulted in the fact that the fish are the most sensitive group in some samples and the Daphnia in others.

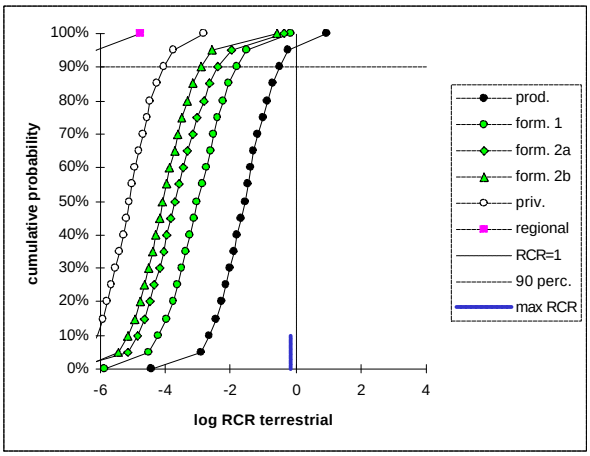
6.3.2 Aquatic ecosystem alternative scenarios

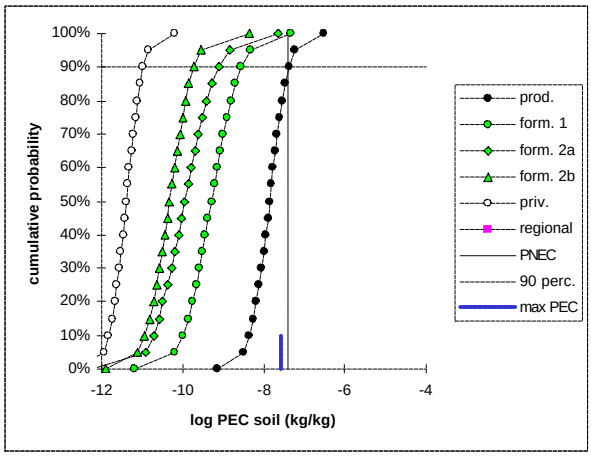


Changing the scenario has a profound impact on the risk assessment. When the production facility is located on a large river (Dil=1e4), the risk is negligible. Using a small stream (Dil=2) increases the RCR by a factor of 5, excluding the STP (no STP/Dil=2) adds another factor of 2. In those cases, the *p*(RCR>1) is 30% and 50%, respectively. The *p*(PEC>PNEC) is much more critical as a large part of the distribution exceeds the PNEC.

Based on these data, the risk assessment can be efficiently refined by choosing a more realistic scenario for the production site.

6.3.3 Terrestrial ecosystem





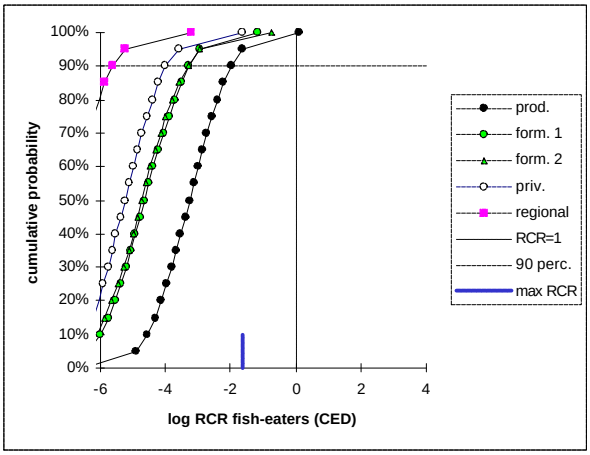
Sensitivities

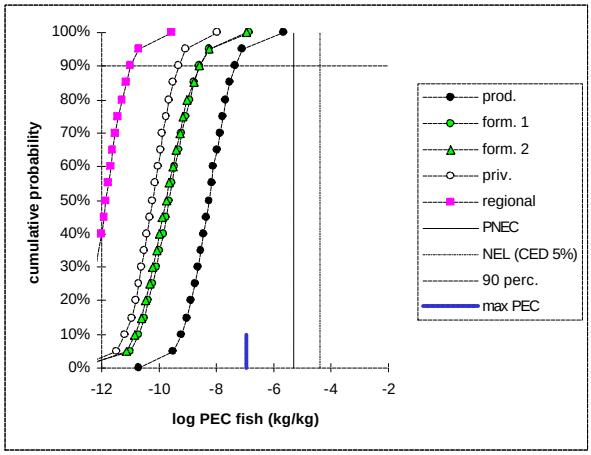
Assessment factor lab-eco	49.7%	Koc	61.1%
Assessment factor inter-species 1	11.3%	Number of emission days	16.6%
Assessment factor inter-species 2	9.7%	Local emission to water	14.3%
Assessment factor acute-chronic 1	6.6%	Biodegradation in soil	4.9%
Assessment factor acute-chronic 2	6.1%		
Local emission to water	5.4%		
Number of emission days	4.2%		
Assessment factor inter-species 3	2.9%		

The EUSES risk estimate indicated that there was no reason for concern as the RCR was just below one. This is confirmed by the probabilistic assessment as the *p*(RCR>1) is less than 5%. However, the 90th percentile of the PEC distribution slightly exceeds the deterministic PNEC.

It is interesting to note that *Koc* is very important in the PEC but not in the RCR distribution. This results from the fact that PNEC is calculated with equilibrium partitioning as terrestrial toxicity data are lacking. A random sample with a high *Koc* increases accumulation in soil and thus the PEC. At the same time, it also decreases the PNEC (expressed on total soil basis) due to a lower availability of the compound to the organism. In the RCR, these processes cancel out the uncertainty in *Koc* while it remains dominant in the PEC distribution.

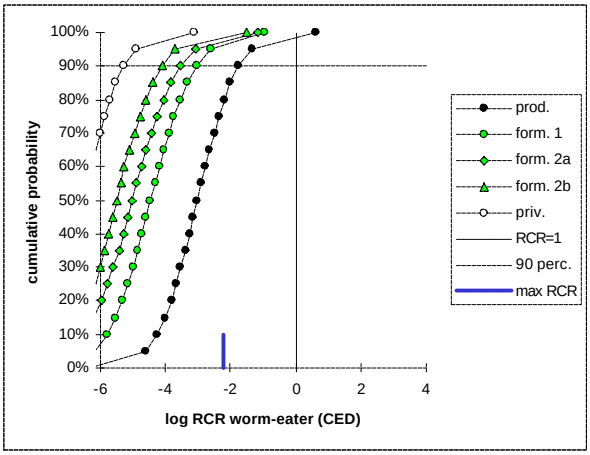
6.3.4 Fish-eating and worm-eating predators

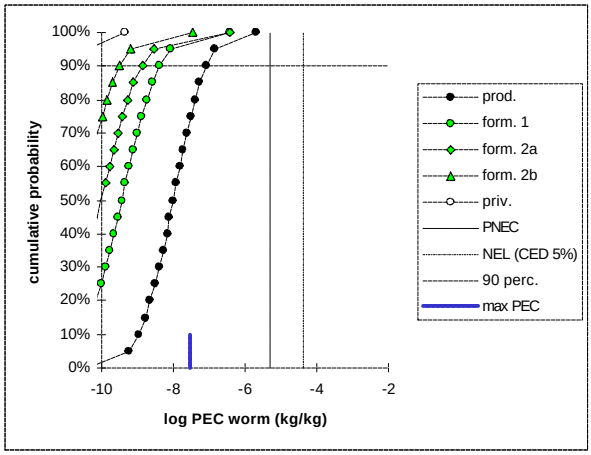




Sensitivities

BCF fish	45.9%	BCF fish	86.6%
Assessment factor inter-species	22.3%	Biodegradation in STP	6.3%
CED animal	19.7%	Local emission to water	2.9%
Assessment factor lab-field	3.8%		
Biodegradation in STP	3.6%		
Local emission to water	2.3%		



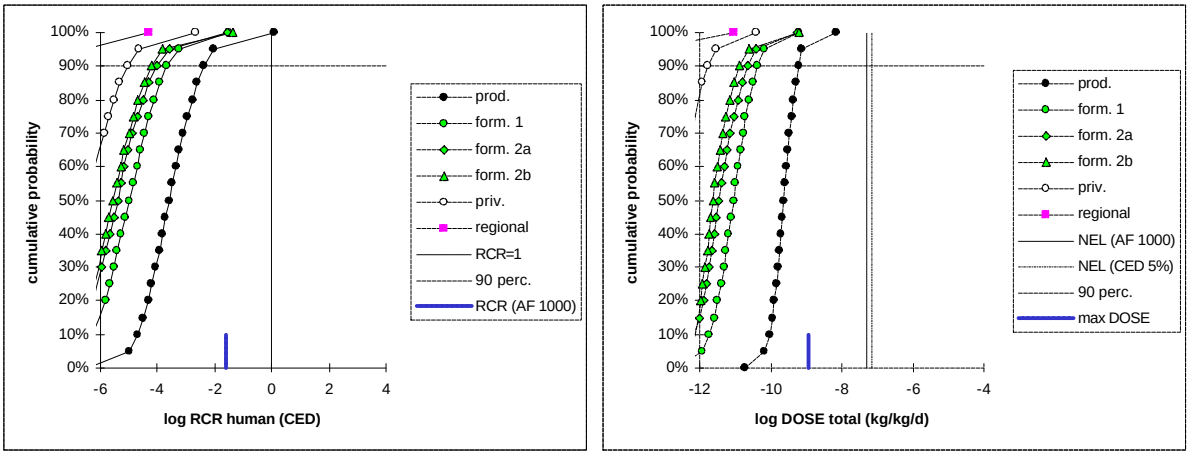


Sensitivities

BCF worm	40.2%	BCF worm	77.4%
Assessment factor inter-species	23.3%	Biodegradation in soil	7.4%
CED animal	18.0%	Number of emission days	5.0%
Biodegradation in soil	4.1%	Local emission to water	4.5%
Number of emission days	4.1%	Koc	3.2%
Assessment factor lab-field	3.2%		
Local emission to water	2.0%		
Koc	1.9%		

The risk for these two endpoints is very low, as also indicated by the deterministic quotients in Table 3. The main uncertainty is in the BCFs, with the effects assessment on the second place.

6.3.5 Human



Sensitivities

Assessment factor time scale	34.2%	Biodegradation in soil	28.6%
Assessment factor inter-species	29.7%	Local emission to water	21.3%
CED animal	17.3%	Number of emission days	20.2%
Assessment factor intra-species	4.2%	Koc	13.9%
Local emission to water	3.5%	BCF fish	9.2%
Biodegradation in soil	3.5%	Biodegradation in STP	2.7%
BCF fish	2.6%		
Number of emission days	2.1%		

As indicated by the high MOS in Table 3, the risk for humans is low. The distributions are well below the critical lines of RCR=1 and NEL (interestingly, the NEL using an assessment factor of 1000 is nearly equal to the CED5).

Uncertainty in the effects assessment dominates the RCR distribution. The uncertainty in the PEC is dominated by biodegradation although the emission parameters combined (emission to water and number of days) have a larger contribution. The main exposure routes are through drinking water and fish consumption. Root crops also play a role which could explain the importance of biodegradation in soil.

6.4 Conclusions for the new chemical

For most endpoints, the distributions are sufficiently below the critical values to warrant the conclusion of acceptable risks. Contrary to the deterministic assessment, the stage of production was found to be the worst step of the life cycle. The aquatic ecosystem is the most sensitive endpoint as was already indicated by the EUSES calculations (see Table 3). The probability that RCR>1 was estimated at 10% and could be worse in case the production facility is located on a small river and/or is without STP. Even though the deterministic RCR was 2.8, the conclusion was reached that further testing could wait to the next tonnage threshold. The situation for the terrestrial ecosystem is less worrying as the *p*(RCR>1) is less than 5%. However, the *p*(PEC>PNEC) is 10%, indicating a borderline risk situation.

As was observed in the DBP assessment, the deterministic RCR from EUSES was quite conservative although part of this conservatism was caused by the fact that a lower production volume was used in the probabilistic assessment. Main uncertainties are again the effects assessment and, for predators, the BCF QSARs.

7. Conclusions

The worked-out examples for DBP and the new chemical demonstrate that a probabilistic risk assessment is feasible with relatively little extra effort and provides more relevant information. The uncertainty analysis clearly shows the effect of our lack of knowledge about the input data on the risk assessment and allows for more straightforward decision making on the basis of the entire risk distribution. The width of the resulting distributions (5-95th percentile) ranges from one to five orders of magnitude (in extreme cases), but is usually less than three orders. A major point of criticism about deterministic risk quotients is that the *degree* of conservatism is unknown. In other words, it is not clear whether the quotient represents a reasonable worst case or an unrealistic situation. The probabilistic risk assessments do not usually identify different endpoints of concern than the deterministic risk estimates as shown in the tables. However, the present report shows that the deterministic risk quotient is quite worst case (generally higher than the 95th percentile of the probability distribution) although this is not necessarily a general rule for all chemicals and depends on our particular choices for input distributions. Nevertheless, it indicates a compounding of uncertainties in the assessment and possibly an unnecessary high level of protection.

As we are unaware of the degree of conservatism of the deterministic RCR, it is strange that the absolute value of the risk quotient is currently used with so much confidence. A value of 0.9 or even 0.99 is considered acceptable and there are RCR thresholds of 10, 100 and 1000 in the decision scheme for new chemicals to make the choice whether to ask for further testing immediately or wait till the next tonnage level. Without knowing the shape of the relation between RCR and toxicological impacts, these figures have no meaning. Furthermore, this scheme proves that the designers were aware of the worst-case nature of the assessment and judged that even at PEC/PNEC between 1-10 (and in some cases also between 10-100) no immediate further actions are required. For chemicals with a very steep dose-effect relation, an exceedance of the PNEC by a factor of 10 may have important consequences whereas for a chemical with a very flat dose-response this can still be acceptable. It is important to note that an RCR, even a probabilistic one, is not a risk level. The relationship between the RCR and (eco)toxicological impacts is unknown and the slope of this relationship will differ between chemicals. This implies that the absolute value of the RCR cannot be interpreted. For a proper assessment of true risks, uncertainties have to be quantified but also the effects assessment needs to be addressed. We must attempt to move away from conservative no-effect levels towards quantifying (eco)toxicological impacts. For ecotoxicological risk assessment, the use of species sensitivity distributions is a step in the right direction (Klepper & Van de Meent, 1997; Klepper *et al.*, 1998; Van de Meent, 1999; see also discussion in Jager *et al.*, 1997).

Uncertainty analysis is more difficult for an existing chemical than a new chemical. For the latter, few data are available and thus, general rules can be applied in a straightforward manner. For DBP more data and knowledge is available which should all be combined and evaluated to provide realistic parameter distributions[1]. This is especially notable in the emission estimation because of the more complicated life-cycle of the chemical and as measured data are available for some life-cycle steps but not for others. This implies that for DBP, more case-specific choices were required.

[1] This is were Bayesian updating would be an excellent solution: the default distribution can be “updated” based on given experimental data, resulting in a new distribution.

The use of a sensitivity analysis to identify the main sources of uncertainty proves to be a powerful tool for efficient further testing. The analysis identifies the parameters where a reduction in uncertainty will be most effective in reducing the overall uncertainty which is usually not obvious beforehand. Risk assessors usually consider release estimation as the most uncertain part of the risk assessment. Contrary to these expectations, the distributions assigned to the assessment factors proved to dominate the total uncertainty in the risk assessment of these sample chemicals for most endpoints. Uncertainties in the release estimates come second. It should however be noted that this conclusion hinges on distributions that were based on limited data. Nevertheless, it underlines the need for a further investigation of the uncertainties in the effects assessment (e.g. by rigorous statistical analysis of toxicological data, available in existing databases).

As stated earlier, the conclusions reached from the sample risk assessments are based on our particular choice for parameter distributions. The choice for a distribution is quite important in uncertainty analysis, which could be considered a disadvantage. For release estimation, the distributions were solely based on expert judgement, which is a serious weakness. There is a clear need for agreed default parameter distributions for the purpose of risk assessment. This could include different distributions for different types of chemicals (e.g. broader distributions for "difficult" chemicals like organo-metals). In this example study, only the operational uncertainty in the input parameters is captured in distributions. Environmental variability is investigated by making calculations for alternative plausible scenarios. For the aquatic ecosystem, variability has a larger impact than the operational uncertainties (four orders of magnitude versus two orders), caused by the large range in dilution factors. For the terrestrial ecosystem, the effect of variability and uncertainty is similar (two orders of magnitude). These examples demonstrate that environmental variability may well dominate the total uncertainty in a risk assessment and should be addressed. For the regional model, changing the system settings to mimic two extreme countries (Spain and Finland) resulted in differences within a factor of 10. In fact, the standard TGD settings could be considered a worst case because of the small surface area of the system. When the sizes are set equal, Spain is the worst case for water and Finland for soil (for air, the differences are negligible) but again, the differences stay within a factor of 10.

The use of alternative scenarios proved a quite transparent approach. However, although it increases the realism of the assessment, it will complicate decision-making as the relevance of each scenario has to be discussed. A further problem is that operational uncertainty and variability are sometimes difficult to treat separately. As example, degradation rates in soil also depend on the properties of the soil (e.g. organic matter content). Representing these uncertainties in a transparent way requires further investigation, also because the current models in EUSES do not always allow these kinds of exercises (the air model, for instance, is simplified in such a way that alternative scenarios cannot be run). This implies that in updating the TGD and EUSES, attention should be paid to the flexibility of the models.

Risk assessment is a process where we use limited information to predict the potential of chemicals to cause some toxic effect on different kinds of biotic endpoints. Large uncertainties are an inherent part of this process that we have to deal with. If we want a more realistic and defensible risk assessment, we have to get rid of protective and worst-case thinking in the risk assessment itself. Of course, we need to be protective when dealing with the environment and human health but these considerations belong in the risk management stage where it should be discussed what level of risk is still acceptable (e.g. by selecting a high percentile from the risk

distribution). If we like to be on the safe side because the chemical may have impacts we have not considered (like suspicions of endocrine effects, based on structural similarities), this is part of risk management. We cannot estimate risks for an impact where we have no relevant data. It would be unwise to pollute our risk assessments by asking for additional safety factors. Risk assessment should be as scientific and realistic as possible and that implies that we must admit what we don't know. Even though it may be complicated, attempting to quantify uncertainties is a good step in that direction. Changing the well-accepted procedures takes time but it would be a good idea to address these issues in the TGD in the near future.

Critics may say that even a probabilistic risk assessment is based on the same limited data set and therefore cannot give new information (Jager, 1998). Although this is partly true, one should consider the vast body of literature data that is available. It is possible to use data for other chemicals to improve the risk assessment in a statistical way. Although not exhaustive, this was extensively demonstrated earlier (Jager *et al.*, 1997; Vermeire *et al.*, 1999). Furthermore, uncertainty analysis is an excellent way to use *all* available data, instead of taking one value (e.g. only the lowest experimental LC50 or a worst case BCF) thus providing an incentive for the notifier to submit more data. Finally, we believe that even a rough quantification of uncertainties is better than giving a false sense of accuracy.

As summary, further work is necessary in the following areas:

- Guidelines how to perform an uncertainty analysis.
- Agreed default distributions for basic parameters, especially for the release estimation and effects assessment.
- Serious revision of the effects assessment (attempt to quantify real impacts).
- Choice of alternative scenarios or other ways to address variability.
- Thoughts on how to implement uncertainty analysis in risk characterisation and in risk management in the (near) future (e.g. which percentiles to take). This probably means reopening the discussion on "what do we want to protect and how certain do we need to be?"

References

Brandes, L.J., H. Den Hollander, and D. Van de Meent (1996). SimpleBox 2.0: A nested multimedia fate model for evaluating the environmental fate of chemicals. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 719101 029.

EC (1996a). EUSES, the European Union System for the Evaluation of Substances. National Institute of Public Health and the Environment (RIVM), the Netherlands. Available From European Chemicals Bureau (EC/DGXI), Ispra, Italy.

EC (1996b). Technical Guidance Documents in support of Directive 93/67/EEC on risk assessment of new notified substances and Regulation (EC) No. 1488/94 on risk assessment of existing substances (Parts I, II, III and IV). EC Catalogue Numbers CR-48-96-001, 002, 003, 004-EN-C. Office for Official Publications of the European Community, 2 Rue Mercier, L-2965 Luxembourg.

Jager, D.T. (1995). Uncertainty Analysis of the Uniform System for the Evaluation of Substances (USES): Example Calculations. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 679102 032.

Jager, D.T., and W. Slob (1995). Uncertainty Analysis of the Uniform System for the Evaluation of Substances (USES). Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 679102 027.

Jager, T. (1998). Uncertainty analysis of EUSES: interviews with representatives from Member States and industry. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 679102 047.

Jager, T., M. Rikken, and P. Van der Poel (1997). Uncertainty analysis of EUSES: Improving risk management by probabilistic risk assessment. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 679102 039.

Klepper, O., J. Bakker, T.P. Traas, and D. Van de Meent (1998). Mapping the potentially affected fraction (PAF) of species as a basis for comparison of ecotoxicological risks between substances and regions. Journal of Hazardous Materials **61**: 337-344.

Klepper, O., and D. Van de Meent (1997). Mapping the Potentially Affected Fraction (PAF) of species as an indicator of generic toxic stress. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 607504 001.

Polder, M.D., E.M. Hulzebos, and D.T. Jager (1997). Bioconcentration of gaseous organic chemicals in plant leaves: comparison of experimental data with model predictions (revised version). Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 679102 034.

Slob, W., and A.C.M. De Nijs (1989). Risk Assessment of New Chemical Substances; Quantification of uncertainty in estimated PEC-values of aquatic ecosystems. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 958804 001.

Van de Meent, D. (1999). Potentieel Aangetaste Fractie als maatlat voor toxische druk op ecosystemen. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 607504 007.

Vermeire, T.G., H. Stevenson, M.N. Pieters, M. Rennen, W. Slob, and B.C. Hakkert (1999). Assessment factors for human health risk assessment: a discussion paper. Crit. Rev. Toxicol. **29**(5): 439-490.

Appendix 1 Mailing list

1 Directie RIVM
2 Dr. H. Merkus, DGM/SVS, SG UBS
3 Drs. A.W. van der Wielen, DGM/SVS, SG UBS
4 Dr. S. Schwartz (Univ. Osnabrück, Germany)
5 Dr. B. Hansen (JRC/ECB, Italy)
6 Dr. J.S. Jaworska (Procter & Gamble, ECETOC, Belgie)
7 Drs. M.A.J. Huijbregts (Universiteit van Amsterdam, The Netherlands)
8 Drs. A. Ragas (Katholieke Universiteit Nijmegen, The Netherlands)
9 Dr. F.M. Carpanini (ECETOC, Brussels, Belgium)
10 Depot van Nederlandse publikaties en Nederlandse bibliografie
11 Sectordirecteur Stoffen en Risico's, dr. G. de Mik, SG UBS
12 Sectordirecteur Milieuonderzoek
13 Sectordirecteur Volksgezondheidsonderzoek
14 - 18 Projectleider UBS, RIVM-Taakgroep UBS, d.t.v. drs.T.G.Vermeire
19 - 21 Centrum voor Stoffen en Risicobeoordeling
22 Dr. J.H.M. de Bruijn, CSR
23 Ir. M. Hof, CSR, SG UBS
24 Prof.dr. C.J. van Leeuwen, CSR, SG UBS
25 Drs. T. Aldenberg, LWD
26 - 31 Auteurs
32 SBD/Voorlichting & Public Relations
33 Bureau Rapportenregistratie
34 Bibliotheek RIVM
35 - 37 Reserve-exemplaren auteur (d.t.v. drs. D.T. Jager)
38 - 50 Bureau Rapportenbeheer

Appendix 2 Parameter distributions

In this appendix, more information on the applied distributions is provided. Literature references are given at the end of each section.

2.1 Default distributions

When no specific information for the chemical is available, default distribution were applied as summarised in the table below. More information can be found in the original report (Jager *et al.*, 1997).

In the summary table, the following symbols are used to characterise the type of distribution:

L Lognormal. Defined by a median (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 (M). Not that this mode can differ extremely from the median or the average in case the triangular distribution is skewed.

Summary of the parameter distributions for EUSES.

PARAMETER	SYMBOL	TYPE OF DISTRIBUTION
Physico-chemical properties		
Octanol-water partition coefficient	Kow log Kow≤4 log Kow 4-5.5 log Kow>5.5	 L (k=2.8) L (k=12) L (k=24)
Water solubility	SOL SOL≤1 mg/L SOL>1 mg/L	 L (k=12) L (k=2.4)
Vapour pressure	VP VP≤1 Pa VP>1 Pa	 L (k=60) L (k=1.9)
Melting point	TEMPmelt	U (+- 3°)
Emission estimation		
Release fraction	F_{air} / F_{water}	Triangular
Fraction of the local main source	Fmainsource	Triangular
Number of emission days	Temission	Triangular
Partition coefficients		
Organic-carbon normalised partition coefficient	Koc log Kow 1-4 log Kow 4-7	 L (k=3.2) L (k=14)
Henry's law constant	HENRY	L (k=16)
Constant of Junge equation	CONjunge	L (M=0.4, k=3.3)
Biodegradation rates		
Biodegradation rates in STP, surface water, soil and sediment	$DT50bio_{stp}$ $DT50bio_{water}$ $DT50bio_{soil}$ $DT50bio_{sed}$	L (M and k depend on characterisation of biodegradability)
Environmental distribution		
Standard deposition flux of gaseous compounds	$DEPstd_{gas}$	L (k=10)
Standard deposition flux of aerosol-bound compounds	$DEPstd_{aer}$	L (k=5)

PARAMETER	SYMBOL	TYPE OF DISTRIBUTION
Exposure assessment predators/humans		
BCF for fish	BCF_{fish} log Kow 1-6 log Kow 6-10	 L (k=20) L (k=185)
Worm-porewater partition coeff.	$K_{worm\text{-}porew}$	L (k=17)
Transpiration stream conc. fact.	TSCF	T (0-1) M depends on Kow
Conductance	g_{plant}	L (k=4.1)
Biotranfer factor for meat	BAF_{meat}	L (k=64)
Biotranfer factor for milk	BAF_{milk}	L (k=36)
Purification factor drinking water	Fpur	T (M 0.15, range 0-0.65)
Respirable fraction of the inhaled substance	Fresp	U (range 0-1)
Bioavailability for inhalation	BIOinh	U (range 0-0.75)
Bioavailability for oral uptake	BIOoral	U (range 0-1)
Effects assessment		
Acute LC50 to chronic NOEC	$AF_{ac\text{-}chr}$	L (M=5, k=10)
NOEC to most sensitive species	AF_{inter}	1+L (M=6.3, k=23)
Lab to field systems	$AF_{lab\text{-}eco}$	L (M=1, k=10)
Mammals 28 day to chronic	$AFpred_{subac\text{-}chr}$	L (M=3.5, k=23)
Sub-chronic to chronic	$AFpred_{subchr\text{-}chr}$	L (M=2, k=15)
Mammals to most sensitive from birds and mammals	$AFpred_{inter}$	1+L (M=7.4, k=15)
Mammals lab to field	$AFpred_{lab\text{-}fld}$	L (M=10, k=2.5)
Inter-species extrapolation from rat to human	$AFhuman_{inter}$	L (M=4, k=34)
Intra-species extrapolation	$AFhuman_{intra}$	1+L (M=3, k=2.3)
Sub-chronic to chronic	$AFhuman_{subchr\text{-}chr}$	L (M=2, k=15)
Sub-acute to chronic	$AFhuman_{subac\text{-}chr}$	L (M=3.5, k=23)

Reference:

Jager, T., M. Rikken, and P. Van der Poel (1997). Uncertainty analysis of EUSES: Improving risk management by probabilistic risk assessment. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 679102 039.

2.2 Release estimation

Uncertainties in the release estimates were estimated using professional judgement (Paul van der Poel, RIVM), based on the available production data for 1994. For production, the release estimates provided by industry were incorporated in the distribution. Because in this calculations, uncertainties were already combined by multiplying the boundary values of the estimates, the final minimum and maximum estimates were considered to represent 99% of the probability distribution. Lognormal distributions were selected for the emission rates. For the new chemical, the number of days was considered separately with triangular distributions.

Uncertainty analysis DBP for emission estimation

PRODUCTION
The draft Risk Assessment Report (RAR) (RIVM, 1998) gives 5 producers with a production >1000 tonnes, together with the locations. Background information for the RAR on 1994 productions were obtained, together with the 1998 data for update (Bodar, CSR, pers. comm.). For one of the sites it turned out that there is no production at the location in Italy mentioned, but at **two** locations in Belgium. There is a possibility that at one of these locations the production will be 1000 tonnes. It is also possible that production took place in Italy until 1998. CBS (1992-1995) states that in 1995 92 tonnes of dibutylorthophthalates were imported into the Netherlands from Italy. It should therefore be considered that there are several small producers of DBP in the EU! Data on production volumes and tonnages of DBP are confidential and therefore not included in this report.

Remarks concerning uncertainties:
1. The total production volume for the 5 producers with an individual production volume >1000 tonnes is presumably very accurate for the 1998 figures. For 1994, two of the producers have given figures rounded to 100 tonnes and two to 1000 tonnes.
2. The number of producers with an individual production volume <1000 tonnes is unknown. It may be assumed that there are up to 5 smaller producers with a total production volume of 0 – 2500 tonnes per year. This broadens the range.

The fractions of the main source based on the data for the 5 largest producers and the estimated total of all assumed producers are 0.52 and 0.51 respectively.

The RAR (RIVM, 1998) gives several actual site-specific emissions, in two cases for both air and waste water, in two cases for waste water and in one case for air. Using the two ratios for waste water : air emissions the minimum and maximum emission factors were estimated. With the estimated ranges for the production volumes, the emission ranges for the local (main source), regional and continental scale were calculated. The results are presented in the table below. It should be noted that the site-specific data on emissions supplied by the producers have an unknown uncertainty themselves. For the local situation (main source) a large uncertainty of a factor 5 has been assumed. This was done because there is no indication on frequency of measurements, methods of measurement, analysis techniques and precision, etc.

Ranges of emission estimates (kg.day^{-1}) for the main source, the regional and continental scale.

	Minimum	Estimate	Maximum
Local scale (main source)			
Air	0.014	0.07	0.35
Waste water	0.075	0.38	1.89
Regional scale			
Air	0.03	0.07	0.10
Waste water	0.12	0.38	0.55
Continental scale			
Air	0.36	1.03	3.21
Waste water	1.76	3.47	6.83

The RAR (RIVM, 1998) does not mention possible imports into the EU of DBP. It is quite likely however that imports occur (it should be noted that import and export of DBP in end products such as adhesives and plastic objects are not considered at all). From CBS (1992-1995) it turns out that some imports into the Netherlands from outside the EU take place. The figures consist of two possible substances, i.e. di-*n*-butylphthalate and di-*iso*-butylphthalate. As the *iso*-ester is produced in a much smaller volume, it is assumed that it concerns only di-*n*-butylphthalate. From the figures it turns out that the exports to countries outside the EU exceed the imports from countries outside the EU by a factor 2 to 30. So, it may be concluded that the figures do not concern transit of DBP. Other EU countries also may import DBP from countries outside the EU as well. With the assumption that the share of the Netherlands in imports from countries outside the EU is 5%, with a maximum of 10% and a minimum of 1%, the ranges for the imports were calculated. Assuming a) the same range of share for the Netherlands for both import and export of the EU and b) the figures for 1994, the range for the quantity applied in the EU can then be calculated.

FORMULATION

For two applications the stage of formulation applies, i.e. for the application in adhesives and in printing inks. The attention focuses on the main application as an adhesive (IC 0, UC 48 Solvent). As the RAR gives nicely rounded figures for the amounts of DBP applied for every use pattern, a range was assumed. The fraction for the application for each use pattern was then calculated. For the application as a processing aid in the production of glass fibres the data on the quantity applied were stated to be confidential. It is likely that this is very uncertain. So, a large range was applied for this use pattern. For the main use pattern for formulation (solvent in adhesives) the following range for the fraction of the tonnage of DBP used ($F_{application,1}$) was calculated:

	Minimum	Estimate	Maximum
$F_{application,1}$	0.117	0.143	0.163

With the range for the total quantity of DBP used, the range for the quantity used in adhesives can be calculated. Even the minimum of this range lies above the figure for this use pattern stated in the RAR. It should be noted that the production (and the use) of DBP has decreased considerably. It is not known whether the decrease concerns only one use pattern or all use patterns and in what proportion. So, this is an extra uncertainty, which could not be taken into account. For the regional tonnage an uncertainty in the default value of 10% will be present. It is possible that more than 10% is used in a region, but that there is not a single site where adhesive formulation with DBP takes place! These uncertainties could not be established in the time available for this investigation (a market survey would have been necessary to get a good impression of the situation in the EU).

The RAR does not supply any data supplied by the users of DBP, but only calculations based on EUSES. The document states that table B2.2 was used; however, this should have been table B2.3. This table has been applied for the calculations in this chapter. For the fraction of the main source, the RAR states that the number of sources in one EU country is known. However, there is no indication given on

the quantity formulated at the largest site. It should be considered that there is a large uncertainty, where a fraction of the main source of 0.7 or 0.8 seems to be very conservative. The proposed estimates and ranges are:

	Minimum	Estimate	Maximum
fraction of the main source	0.10	0.7	0.8
number of emission days	200	300	365

This leads to the following values for the quantities formulated per working day (the number of emission days have been applied as stated, i.e. 365 for the highest tonnage formulated, instead of 200 days as should be in the worst case situation):

	Minimum	Estimate	Maximum
Quantity (tonnes.day^{-1})	0.21	2.0	2.5

The emission factors that may be applicable depend on the main category used. The RAR has chosen for main category 3, which means that for the emissions into the air the highest emission factor was chosen. This is the correct choice that always should be made when no data are supplied by the notifier. As the production of adhesives is likely to be carried out at specialised firms with dedicated equipment and cleaning hardly will have to be carried out, the choice for main category 1b seems to be justified. As the vapour pressure of DBP is rather low and the formulation can be supposed to occur at ambient temperatures, small emission factors are expected. The proposed ranges for the emission factors are:

	Minimum	Estimate	Maximum
Air	0.0001	0.0005	0.0025
Waste water	0.0001	0.003	0.003

The ranges for the emissions are presented in the table below.

Emissions at the main source (local situation) and for the regional situation for the use pattern of adhesives formulation (kg.day^{-1})

	Minimum	Estimate	Maximum
Local scale			
Air	0.021	1.018	6.204
Waste water	0.021	6.11	7.45
Regional scale			
Air	0.12	1.19	7.76
Waste water	0.12	7.17	9.31
Continental scale			
Air	1.04	10.8	69.8
Waste water	1.04	64.5	83.8

PROCESSING

For processing the use pattern plasticiser (softener) for plastics is the most important one. The following range was calculated:

	Minimum	Estimate	Maximum
$F_{application,2}$	0.732	0.762	0.822

With the range for the total quantity of DBP used, the range for the quantity used as a plasticiser can be calculated. The same remarks as stated for the stage of formulation apply here.

For the number of emission days the RAR states that an assumption of 300 is used in the calculations, while the fraction of the main source was set at 0.1, as the number of sources in one EU country is

known (the document does not mention the number nor the size of the largest source). The estimated ranges are:

	Minimum	Estimate	Maximum
fraction of the main source	0.05	0.25	0.4
number of emission days	250	300	350

This leads to the following values for the quantities processed per working day (the number of emission days have been applied as stated, i.e. 350 for the highest tonnage formulated, instead of 250 days as should be in the worst case situation):

	Minimum	Estimate	Maximum
Quantity processed (tonnes.day^{-1})	0.52	3.88	6.54

The following emission factors are applicable according to the table mentioned with the minimum and maximum proposed for the analysis:

	Minimum	Estimate	Maximum
Air	0.0025	0.01	0.02
Waste water	0.00025	0.001	0.0025

The ranges for the emissions are presented in the table below.

Emissions at the main source (local situation) and for the regional situation for the use pattern of plasticiser for plastics at processing (kg.day^{-1})

	Minimum	Estimate	Maximum
Local scale			
Air	1.31	38.8	131
Waste water	0.13	3.88	16.4
Regional scale			
Air	18.0	127	314
Waste water	1.80	12.7	39.2
Continental scale			
Air	162	1147	2824
Waste water	16	115	363

Revised uncertainty analysis DBP for emission estimation

PRODUCTION

For the first version of this document the data for 1994 were used from the draft risk assessment of 17 November 1998 (RIVM, 1998). The data for 1998 were filled up with production data of the 5 producers with a tonnage >1000 tonnes.year^{-1} (Bodar, CSR). The draft risk assessment of 3 May 1999 (RIVM, 1999) states that there were only three producers in 1998. As both total production figures for 1998 are about the same, this implies that the individual production figures of the three producers may be higher than assumed on account of the extra data (Bodar, CSR). Therefore, the production figure of the largest producer in 1998 has been taken as the minimum for the main source. The estimate has been derived from the quantities of the two companies which have been mentioned to have stopped production by 1998. As the production volume at the main source was much higher in the past (about 2.5 times as high in 1994), the maximum has been adjusted. Within the region (200 x 200 km) where the main source is situated a second producer is present. So, also for the region besides an estimate a minimum and maximum have been specified. It is possible that there are several small producers of DBP in the EU (<1000 tonnes.year^{-1}). It has been assumed here that there are up to 5 smaller producers with a total production volume between 0 and 2500 tonnes.year^{-1}.

With the assumption that the share of the Netherlands in imports from countries outside the EU is 10%, with a maximum of 20 % and that the imports may be zero indeed the range and estimate for the EU can be estimated. The exports from the EU were also adjusted. Data on production volumes and tonnages are confidential and not shown in this report.

Ranges of emission estimates (kg.day^{-1}) for the main source, the regional and continental scales.

	Minimum	Estimate	Maximum
Local scale (main source)			
Air	0.014	0.07	0.35
Waste water	0.075	0.38	1.89
Regional scale			
Air	0.01	0.04	0.31
Waste water	0.032	0.20	1.67
Continental scale			
Air	0.05	0.16	0.27
Waste water	0.08	0.12	0.16

FORMULATION

The proposed estimates and ranges are:

	Minimum	Estimate	Maximum
fraction of the main source	0.07	0.4	0.7
number of emission days	200	250	300

The release fractions stayed the same. The ranges for the emissions are presented in Table 4.

Emissions at the main source (local situation) and for the regional situation for the use pattern of adhesives formulation (kg.day^{-1})

	Minimum	Estimate	Maximum
Local scale			
Air	0.08	0.23	0.29
Waste water	0.08	0.23	0.35
Regional scale			
Air	0.06	0.39	2.4
Waste water	0.06	0.39	2.86
Continental scale			
Air	0.55	3.5	21.5
Waste water	0.55	3.5	25.7

PROCESSING

For the number of emission days RIVM (1998) states that an assumption of 300 is used in the calculations, while the fraction of the main source was set at 0.1. The next draft (RIVM, 1999) states that the UCD (Use Category Document) has been used. The documents state that the number of sources in one EU country is known (the document does not mention the number nor the size of the largest source). The following results are obtained when table B3.9 is applied.

	Minimum	Estimate	Maximum
fraction of the main source	0.05	0.25	0.4
number of emission days	200	300	300

The same emission factors are applicable. The ranges for the emissions are presented below.

Emissions at the main source (local situation) and for the regional situation for the use pattern of plasticiser for plastics at processing (kg.day^{-1})

	Minimum	Estimate	Maximum
Local scale			
Air	0.81	10.1	46
Waste water	0.08	1.01	5.8
Regional scale			
Air	8.9	41	95
Waste water	0.89	4.1	12
Continental scale			
Air	80	373	858
Waste water	8	37	107

References:

Bodar, C.W.M. (1999). Confidential production data for 1998 supplied by industry

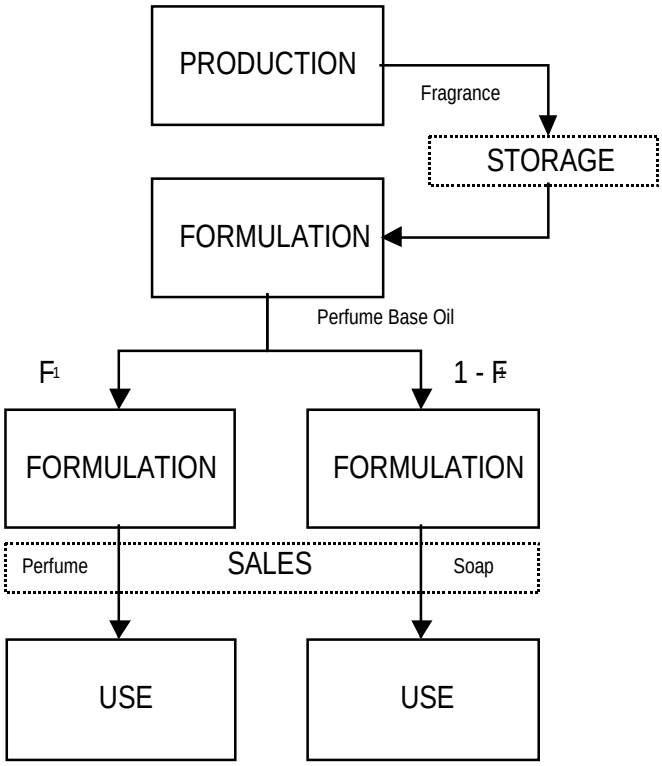
CBS (1992-1995). CBS Jaarstatistiek van de buitenlandse handel 1992, 1993, 1994 and 1995

RIVM (1998). Risk assessment dibutylphthalate. National Institute of Public Health and the Environment (RIVM), Draft, 17 November 1998, Bilthoven, the Netherlands

RIVM (1999). Risk assessment dibutylphthalate. National Institute of Public Health and the Environment (RIVM), Draft, 3 May 1999, Bilthoven, the Netherlands

Uncertainty analysis for emission estimation of the new chemical

The life cycle of this chemical (a fragrance) is presented in Figure 1. There are two formulation stages; the producer sells the fragrance as a 25% perfume base oil. The base oil is used for two types of products for personal/domestic use.



The uncertainty has been introduced for the data according to the SNIF-file and for the EUSES calculations. In Chapter 2 to 5 the choices for parameter values and ranges are discussed. In Chapter 6 the results are presented.

PRODUCTION

Data on production submitted by the notifier:

Tonnage:	1 to 2	tonnes/year (1999)
	1 to 5	tonnes/year (2000)
	2 to 5	tonnes/year (2001)
Tonnes per batch:	1	tonnes/batch
Batches per day:	1	batch/day
Equipment:	no data	

The risk assessment data received do not mention the tonnage notified, but uses the “standard” amount of 10 tonnes/year. This tonnage has been used for the EUSES calculation. The SNIF file contained the data stated above. Based on experience with (this) fragrance industry (P. van der Poel, pers. comm.), it is expected that they will give optimistic sales figures. Often the real production is much lower for new products. This is because of the fact that markets have to be created for new fragrances, and much of the first produced material will go to panels and samples for customer and sales judgement. The notifier claims 0.3% in the end products. With this background the range of 1 (10 batches) to 2 (20 batches) tonnes/year is used.

It has been assumed that production takes place in multi-purpose equipment. This is justified as this

fragrance producer applies this type of equipment. Probably more provisions have been taken to remove vapours of chemicals from the air, as they pose a problem in the surroundings because of the often penetrant odours from the substances they produce.

The release with wastewater according the notifier amounts 0.846%. This seems to be a very exact figure. Probably this percentage has been calculated for the first batch at production scale or as an average for a (small) series of batches at pilot plant scale. Therefore, a range of 0.75 to 2% is suggested (Table A1.1 gives a fraction of 0.02 = 2%). For emission to air no data were available. So, the value of Table A1.1 is used (1%). It is difficult to estimate a reasonable range. It is judged that a range from 0.05 to 1%, with an average of 0.25% is a valid estimation.

FORMULATION I

As described in section 1, there are two stages of formulation. As the first stage takes place at a site in the UK where specific measures are expected (the notifier states “blended into fragrances in a purpose built compounding facility”) formulation takes place in the drum which is used for shipping to the customers. The emissions according to the notifier are 0,01% to waste water. Air emissions are not mentioned, but it may be assumed that they are low. The suggested estimates and ranges for the emission factors (fractions) are:

Compartment	Minimum	Estimate	Maximum
Air	0.000 01	0.000 03	0.000 1
Waste water	0.000 05	0.000 1	0.005

There is one source of emission for the first stage of formulation, where the whole amount of the substance is formulated into a preparation (fraction of substance 0.25 in the preparation). For EUSES the 10 tonnes produced are used, i.e. 10% at the regional scale going to formulation. For the number of days at formulation EUSES chooses 8 (Table B2.4 where T = 1/0.25 = 4). The suggested range (expert judgement) for such a facility is 4 to 20 days, with an estimate of 10.

FORMULATION II

For the second stage of formulation the following situations occur:

1. According to the SNIF data the preparation with 25% of the fragrance is sold to customers. These customers can be found anywhere in the world. So, for the quantity going to the region considered (the Netherlands) an estimate has to be generated, as well as for the fraction of that quantity formulated at the main source (largest customer in the region). For the EU and continent also quantities have to be estimated (and so, a quantity exported from the EU). For the fraction of the total quantity of the ***substance*** formulated at customers, the following ranges are proposed:

	Minimum	Estimate	Maximum
EU	0.7	0.9	1
Region (fraction of EU)	0.1	0.5	1
Region (fraction of total quantity)	*0.07*	*0.45*	*1*
fraction of the main source (SNIF)	0.25	0.8	1
“ “ “ “ (EUSES) **see 2**			
Local (fraction of total quantity)	*0.0175*	*0.36*	*1*
Continental	0.6	0.4	0

2 It is unclear how many products with different contents of the substance are formulated. The risk assessment considers one product, a perfume which is described in the SNIF-file as an air refresher, with 25% of the fragrance. However, this would mean the use of the undiluted preparation from the first formulation stage. Where the SNIF-file mentions 25% of the fragrance in this product, this should be interpreted as 25% of the preparation I think (= 6.25% of the substance). This, because the SNIF-file gives an estimated maximum content of substance in product of 5%. Furthermore, the notifier assumes 0.3% in the end product and 20% for perfume (air refresher). For the products formulated with the fragrance two products are assumed with the

following range of assumed concentrations:

	Minimum	Estimate	Maximum
Product 1	0.3%	1%	5%
Product 2	6.25%	20%	25%
Share of product 1 (fraction)	0.75	0.95	0.99

For the emission factors and fraction of the main source + number of emission days, the EUSES estimates (Table A2.1) are used as basis:

	Minimum	Estimate	Maximum
waste water	0.001	0.003	0.01
air	0.0025	0.005	0.01

EUSES (Table B2.1)	fraction of the main source	number of emission days
T<100:	1	2f*T
T 100-500:	0.6	f*T
T 500-1000:	0.6	0.5f*T
T=1000:	0.4	300
SNIF	Product 1	Product 2
Minimum	25	1
Estimate	40	5
Maximum	60	10

It is assumed that both products are produced at the same plant at different times in the year. This means that the emissions are summed for the annual average but treated separately for the emissions during an episode.

PRIVATE USE

For this stage it is assumed that all products are sold and used evenly over the EU. This means that 10% of the substance in its products are applied within one region with a small deviation. The suggested range (fractions) is:

Minimum	Estimate	Maximum
0.05	0.1	0.2

The emission factors according to Table A4.1 for odour agents in soaps and cleaning agents (product 1) are:

Waste water	0.8 (vapour pressure <2500)
Air	0.2

The ranges used are (both for SNIF and EUSES) (minimum waste water = maximum air):

	Minimum	Estimate	Maximum
Waste water	0.8	0.98	0.999
Air	0.2	0.02	0.001

For product 2 the emission factor for air = 1 (air refreshener)

2.3 Partition coefficients, degradation, BCFs and environmental exposure

Experimental data for DBP were extracted from handbooks and databases. This data were used to derive parameter distributions for physico-chemical properties, degradation rates in air/water/soil, *Koc* and *BCF* for fish. For the remaining parameters of DBP, and all of the parameters of the new chemical, the default distributions as proposed earlier (Jager *et al.*, 1997) were used. The uncertainty in the physico-chemical properties results from measurement errors and test conditions. Only actual measured data is used for the uncertainty analysis of the physico-chemical parameters of dibutylphtalate (DBP). The measured data were not only collected from the EU existing chemicals framework (RIVM/TNO, 1998; IUCLID, 1995), but also from other literature sources (Mackay, 1998; HSDB, 1998; DOSE, 1998; Verschueren, 1983; Howard, 1989). The physico-chemical properties and the distributions are presented in in the table below. Additionally, the number of experimental values for each parameter are listed in this table. Because of the very few data values, the degradation (DT50) for the different compartments is characterised by a triangular distribution and not by a lognormal distribution. The mode, upper limit and lower limit of the triangular distributions are not calculated, but estimated from the available data. For all other parameters a lognormal distribution is used and the median values and uncertainty factors are calculated from the dataset. Because data was lacking, no distribution could be estimated or calculated for the degradation in sediment and the bioconcentration factor for earthworms.

Parameter distributions for DBP. Third colum gives the value as used in the dossier.

Parameter	Unit	Determin.	Distribution	No values
Melting point	K	204	L k=1.12 M=233	7
Water solubility	mg/l	10	L k=33.7 M=29.6	17
Vapour pressure	Pa	9.7e-3	L k=6.15 M=0.00239	14
Octanol-water partition coefficient	-	4.57	L k=12.5 M=36573 (log=4.56)	19
Organic carbon-water partition coefficient	-	6.34e3	L k=11.4 M=2304	4
Bioconcentration factor for fish	l/kg	1.8*	L k=834 M=131	6
Degradation in air with OH-radicals	Hours	43.2	T M=35 range=5-75	5
(Total) degradation in surface water	Days	15	T M=10 range=1-20	2
(Total) degradation in soil	Days	300	T M=20 range=1-55	4
Measured values surface water	µg/l		L k=32.18 M=0.4	37
Measured values air	ng/m^3		L k=34.60 M=4.74	10

* In the first assessment of DBP this value was 41.8 (used in the deterministic EUSES calculation in Table 1.

References:

DOSE (1998). CD ROM database October 1998; substance dibutyl-phatalate- (84-74-2)

Howard, P.H. (1989). Handbook of Environmental Fate and Exposure Data For Organic Chemicals, Volume I, Large Production and Priority Pollutants, Lewis Publishers

HSDB (1998). HSDB database through October 1998; substance dibutyl-phatalate- (84-74-2); reviewed by SRP on 31-1-1998

IUCLID (1995). IUCLID data sheet of dibutyl phtalate (84-74-2); date of last update 26-OCT-95; producer and substance related part ECB – Existing chemicals

Jager, T., M.G.J. Rikken, P. van der Poel (1997). Uncertainty analysis of EUSES: Improving risk management by probabilistic risk assessment, RIVM Report no. 679102039

Mackay, D. et al (1998). Physical-Chemical Properties and Environmental Fate Handbook, CRC Lewis publishers, CRC net BASE 1999, CD ROM version 18-12-1998

RIVM/TNO (1998). Draft Risk Assessment Dibutylphtalate (84-74-2); EU existing chemicals framework; 17 November 1998; Chemical Substance Bureau, Bilthoven, The Netherlands

Verschueren, K. (1983). Handbook of environmental data on organic chemicals, Second edition, Van Nostrand Reinhold, New York

2.4 Ecological effects assessment

Dibutylphthalate (DBP)
For the distributions of the PNECs for DBP, the same "critical" toxicity study is used as was selected in the risk assessment report. Instead of a fixed assessment factor, distributions are applied to cover the various extrapolation steps (e.g. inter-species and laboratory-field). These distribution were derived from experimental data for other chemicals from a database (Jager *et al.*, 1997).

Compartment	*Data selected in dossier*	*PNEC*	*Distributions (M,k)*
Aquatic	Long term NOEC for fish of 100 ug/L, AF=10 (3 trophic levels)	10 ug/L	100 ug/L AF=L(1,10)
Micro organisms	EC50 for protozoa of 2.2 mg/L, AF=10	220 ug/L	2.2 mg/L AF=L(5,10)
Terrestrial	NOEC for corn of 200 mg/kg dw, AF=100 (not 3 levels)	2 mg/kg dw	200 mg/kg dw AF=1+L(6.3,23) AF=1+L(3.1,1.6) AF=L(1,10)
Atmospheric	NOEC for plants of 0.1 ug/m3, AF=10	0.01 ug/m3	0.1 ug/m3 AF=L(1,10)
Predators	LOAEL of 52 mg/kg BW, conversion=20 (to mg/kg food), AF=10	104 mg/kg food	CED=281 mg/kg BW/d (k=1.26) CV=20 AF=1+L(7.4,15) AF=(10,2.5)

Aquatic compartment The procedure outlined earlier (Jager *et al.*, 1997) proposes an inter-species assessment factor to extrapolate from the given NOEC to the most sensitive NOEC of that taxonomic group. Subsequently, a lab-field system assessment factor to arrive at a PNEC. The dossier refers to "few" long-term studies with fish, 5 NOECs for aquatic invertebrates and 6 NOECs for algae. The reported lowest NOEC for fish may be considered the lowest from that taxonomic group, leaving only the assessment factor from lab to field.
Micro-organisms The protozoan test is considered a specific population, therefore, the NOEC for this species will represent a PNEC. Thus only an acute-chronic AF is required.
Terrestrial compartment Only data for plants were available. That means that an inter- and intra-group and a lab-field extrapolation is required. The report does not specify an intra-group assessment factor as it is assumed that always three taxonomic groups are tested (which is valid for the aquatic assessment). A rapid analyses of aquatic NOEC data for benzene and TCB revealed an assessment factor of 1+L(3.1,1.6) between the lowest NOEC from a taxonomic group and the lowest NOEC over all groups.
Atmospheric compartment An assessment factor of 10 was used as this species was considered a sensitive one in view of the available test data. The atmospheric compartment not only consists of plants (i.e. all other organisms exposed via air) but plants may be considered a specifically sensitive group. Therefore, only a lab to field extrapolation will be used.
Predators The Critical Effects Dose (CED) is taken as the NOAEL for mammals (see human effects assessment, Appendix 2.4), including its uncertainty. The conversion factor to an NOEC (CV=20 kg food/kg BW/d) is considered relatively certain. The earlier report (Jager *et al.*, 1997) proposes an inter-species assessment factor to arrive at the most sensitive species and a lab-field factor accounting for differences in metabolic rate and caloric content of the food. This is generally more stringent than the TGD approach.

New chemical
For the new chemical, default distributions were used as given earlier (Jager *et al.*, 1997).

Aquatic compartment The dossier contains three LC50s and an NOEC for algae only. For the uncertainty analysis, the algae NOEC is used and for the other groups, the LC50s are divided by an acute-chronic extrapolation. From the NOECs, in each sample the lowest is taken on which a lab-field extrapolation is applied.
Terrestrial compartment The dossier contains no toxicity data and therefore, equilibrium partitioning is applied without extra assessment factors.
Micro organisms As no effects were observed in the toxicity test at high concentrations, this endpoint is not considered further.
Predators Same approach as for DBP

Reference:
Jager, T., M. Rikken, and P. Van der Poel (1997). Uncertainty analysis of EUSES: Improving risk management by probabilistic risk assessment. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 679102 039.

2.5 Human health effects assessment

The dose-response data were re-analysed using the "Benchmark approach". We used the software PROAST (possible Risk Obtained from Animal STudies) which has recently been developed at RIVM. With PROAST a dose-response model is fitted to the data, then a Critical Effect Size (CES) is defined, and the associated Critical Effect Dose (CED) is derived from the fitted model. For continuous endpoints, the critical effect size (CES) is defined as a change in average response at any given dose relative to the average response in the controls. For example the CED05 represents the dose associated with a 5% change in the average value of the observed endpoint compared to the average control value. It is difficult to indicate a CES for each parameter as no consensus exists (yet) on this issue. The uncertainty in the estimate of the CED is assessed by a bootstrap method (Slob and Pieters 1998), resulting in an uncertainty distribution from which any desired confidence interval can be derived. In this report the 5% and 95% confidence limits are presented (i.e. 90% confidence intervals). Note that the 5% confidence limit can be considered as the Benchmark dose as originally defined. The dose-response data are described by one of the following models:

model 1: $y = a$
model 2: $y = a \exp(b x$
model 3: $y = a \exp(b x^d))$
model 4: $y = a (c - (c - 1) \exp(b x)$
model 5: $y = a (c - (c - 1) \exp(b x^d)$.

In these models the parameter *a* represents the background level of the particular endpoint. The parameter *b* reflects the 'slope' or the 'strength' of the response. These models are suitable for describing different (sub)populations by the same model. For example, when males and females are equally sensitive to the compound studied with respect to body weight, male and female body weights can be described by the same model, with only parameter *a* differing between males and females, to account for background body weights differing between sexes. When males and females are not equally sensitive, the parameter *b* differs between sexes. The parameters *c* and *d* are assumed to be equal between sexes.

The selection of the model to be used for deriving the CED follows from a procedure of successively fitting the above models, and applying likelihood ratio tests to see if an increase in the number of parameters leads to a significantly better fit to the data. A model with more parameters is considered better only if this leads to a significantly better fit. The selected model is used further analysis of the data to see if the fit can be improved by allowing the parameter *a*, the parameter *b*, or the residual variance (or possibly any combination of these three) to differ between the two sexes. Again, an extension of the number of parameters is only adopted if this results in a significantly better fit. The selected model is also fitted to each of the two sexes separately; the sum of the two associated log-likelihoods may be considered as the maximum achievable log-likelihood value, serving as a reference.

Dibutylphthalate (DBP)

Critical effect The lowest NOAEL was observed in a two-generation reproduction study in rats with a continuous breeding protocol of both male and female animals. At the lowest dose-level of 0.1% in the diet (52 mg/kg bw/d for males and 80 mg/kg bw/d for females) a reduced number of live pups per litter and a decreased pup weights were seen in the absence of maternal toxicity. The effects were reproducible among the litters, however, the greatest effects were observed in litter 3. A NOAEL of 52 mg/kg bw/d has been used in the draft risk assessment of DBP (version November 1998). The MOS for humans should be > 1000 based on assessment factors of 10x10x10 for interspecies, intraspecies and time-scale (semi-chronic to chronic) extrapolations respectively. For the risk assessment for secondairy

poisoning an assessment factor of 10 was used as reproduction studies are regarded as chronic effects.

Benchmark approach With the program PROAST written in S-Plus the whole dose effect curve was analysed by curve-fitting. At the start all litters were included in the model and the best curve was chosen based on the calculated likelihoods, only variations in "a" were included in this phase. As the best fit (highest likelihood) was obtained with model 3 (equation y=a*exp(b*x^c)), subsequently variations between litters, variations in starting level of the litters and variations in slope of the dose-effect relationship between litters were investigated by comparing likelihoods with model 3. It appeared that the greatest likelihood was obtained for individual litters. This means that the best way to analyse the data is separately analyse of each litter instead of combining litters. As litter 3 gave the greatest effects, only this litter was analysed for the best fitting curve. Model 4 (equation y=a*[c-(c-1)exp(bx)]) appeared to fit the data most best based on the likelihoods.

The critical effect size was set at 0.05, meaning an effect of 5% (reduction in live pups per litter). The extrapolation critical effect dose (CED) from the fitted curve was 281.4 mg/kg bw/d. Next 500 bootstraps were performed, which included taking random samples for each dose group based on the mean value, standard deviation and sample number, refitting of the curve and recalculating of the CED. The 500 CED values represent the distribution of CED.animal. The L05 value of the distribution of CED.animal was used in the generation of the CED.human together with the assessment factors for inter-species, intra-species and time scale.

In the uncertainty analysis, the CED_animal distribution is used as starting point for the PNEC for predators (it is used as NOAEL, see Appendix 2.3) and for humans by applying the uncertain assessment factor. The 5th percentile of the CED_human distribution in used as reference NEL in the figures with the distribution of the total dose.

Assessment factors in the generation of a CED.human (geometric mean and geometric standard deviation) (see Vermeire et al., in press).

Assessment factors	**GM**	**GSD**
Interspecies	5 (=1 + 4.0 (rat))	4.5
Intraspecies	3	1.6
Time-scale (semi-chronic to chronic)	2	4

Generated CED.animal and calculated CED.human with 5th ang 95th percentiles.

	CED	**L05**	**L95**
CED.animal	281	224	356
CED.human	5.87	0.210	215

New chemical

Critical effect The human toxicological data included acute toxicity (oral and dermal), irritation (skin and eye), sensitization, repeated dose toxicity (28-days) and mutagenicity (Amex/Salmonella, chromosome aberrations test and a mouse micronucleus test). In the 28-day test with the substance, 4 groups of rats were exposed by gavage to doses of 50, 150 and 1000 mg/kg bw/day. The NOAEL was 50 mg/kg bw based on changes in clinical chemical parameters and decreased liver weights seen at 150 and 1000 mg/kg bw/d. The observed effects are considered as adverse because at 1000 mg/kg bw/d these changes were more pronounced and accompanied by histopathological changes (minimal centrilobular hypertrophy). For the risk assessment for secondary poisoning an assessment factor of 100 was used.

Benchmark approach The dose effect relationship for the effects observed on total protein, cholesterol, albumine/globulin ratio, ALAT and relative liver weights were analysed by curve-fitting with the add of the program PROAST (version v6.7) written in S-Plus (version 4.5). First for each parameter the best

fitted curve (model) was chosen based on the calculated likelihoods, only variations in the starting levels ("a") were included in this phase. Next variations in slope of the dose-effect curve ("b") between sexes and variations in variance ("var") between sexes for each parameter were analysed by comparing likelihoods with the fitted curve (model) with and without any combination of "a", "b" and/or "var". With the final model 500 bootstraps were performed, which included taking random samples for each dose group based on the mean value, standard deviation and sample number, refitting of the curve to establish the doses-effect relationship. With these distributions effect doses and L05 and L95 values at different effect sizes (5%, 10%, 20% and 40%) were calculated for each parameter. Based on the variation of the parameters and on experiences in interpretations of these parameters the critical effect sizes for total protein, cholesterol, albumine/globuline ratio, ALAT and relative liver weights were determined to be 10%, 20%, 10%, 40% and 10% respectively. This choice was approved in personal communications with T. Vermeire (senior-toxicologist) and R. Beems (senior-pathologist). The lowest L05 value of all parameters was the L05 value for cholesterol, which was used in the generation of the CED.human together with the following assessment factors:

Used assessment factors in the generation of a CED.human

Assessment factors	**GM**	**GSD**
Interspecies	5 (=1 + 4.0 (rat))	4.5
Intraspecies	3	1.6
Time-scale (subacute to chronic)	6	3.5

Generated CED.animal and calculated CED.human

	CED	**L05**	**L95**
CED.animal (cholesterol females)	115	20.0	421
CED.human	2.34	0.0692	102

In the uncertainty analysis, the CED_animal distribution is used as starting point for the PNEC for predators (it is used as NOAEL, see Appendix 2.3) and for humans by applying the uncertain assessment factor. The 5th percentile of the CED_human distribution in used as reference NEL in the figures with the distribution of the total dose.

Reference

Slob, W. and Pieters, M.N. (1998). A Probabilistic Approach for Deriving Acceptable Human Intake Limits and Human Health Risks from Toxicological Studies: General Framework. *Risk Analysis*, **Vol 18,** No 6.

Vermeire, T.G., H. Stevenson, M.N. Pieters, M. Rennen, W. Slob, and B.C. Hakkert (in press). Assessment factors for human health risk assessment: a discussion paper. Crit. Rev. Toxicol.

2.6 Parameters for Spain and Finland

For Finland, data were based on Hunter (1992) and on data received from the Finnish Environment Agency during the Development of the TGDs for new and existing substances. For Spain, data were taken from ECETOC (1994); the percentage connection to sewage treatment was taken from data received in the framework of the development of the TGDs; water depth was assumed similar to the standard value. The search for parameters was not exhaustive; the current data were used as example only.

	Standard	**Finland**	**Spain**
Area (km^2)	40000	338145	500000
Inhabitants	20e6	5.1e6	39.7e6
Area frac. water (%)	3	9.9	1.0
Area frac. agric. (%)	27	8.3	63.9
Area frac. natural (%)	60	79	28.9
Area frac. industr. (%)	10	2.8	6.2
Rainfall (mm/yr)	700	618	520
STP connection (%)	70	75	45
Temperature (°C)	12	2	17
Water depth (m)	3	7	3

Temperature corrections were applied to vapour pressure, solubility and degradation rates according to Brandes *et al*. (1998). The standard EUSES calculation do not make a temperature correction and, to allow comparison with the other scenarios, an additional calculation was performed with vapour pressure and solubility corrected from 25°C to 12°C (indicated as regional 2 in the graphs). The degradation rates in EUSES are already valid for this environmental temperature.

References:

Brandes, L.J., H. den Hollander, D. van de Meent (1996). SimpleBox 2.0: a nested multimedia fate model for evaluating the environmental fate of chemicals. Bilthoven, National Institute of Public Health and the Environment (RIVM). Report No. 719101 029.

ECETOC (1994). Environmental exposure assessment. Technical Report 61. ECETOC, Brussels.

Hunter, B (1992). The Stateman's Year-book