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**SCIENTIFIC COMMITTEE ON
TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE)**

Final report on:

**EXPOSURE DATA IN RISK ASSESSMENTS OF
ORGANIC CHEMICALS**

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EXPOSURE DATA IN RISK ASSESSMENTS OF ORGANIC CHEMICALS

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EXECUTIVE SUMMARY

The Technical Guidance Document (TGD) describes a procedure for the risk assessment of new and existing chemicals in the EU. The document suggests methods to estimate the exposure to and the effects of the assessed substance, but the assessor is free to follow other procedures. The Scientific Committee on Toxicity, Ecotoxicity and Environment (CSTEE) has been asked to review the risk assessment reports produced over a number of years. These assessments have mainly been carried out according to the guidance in the TGD, and the CSTEE has noticed some problems connected with the present process. This report is a summary of such problems observed in the exposure assessments, and presents suggestions for improvement. Some of this advice may be useful for those now revising the TGD.

The potential environmental risk of a substance is calculated as the ratio of the predicted environmental concentration (PEC) to the predicted no-effect concentration (PNEC). The potential risk to human health is calculated as the ratio of PEC to observed no-adverse-effect level (NOAEL). The exposure (PEC) can be measured and/or predicted with models. A number of parameters need to be known for this prediction, but if these are not available default values can be used. The default values are in most cases conservative and thus tend to overestimate the exposure, which may lead to unnecessary and expensive action against the use of the substance. Underestimated exposure estimates will, on the other hand, not be protective enough. It is thus important to reduce the uncertainty in PEC as far as possible.

The exposure assessment is probably the most critical part of the risk assessment procedure. The combined use of predicted and measured data is an art, and the assessor often has significant difficulties in judging the available data.

Further work on Industry Category Documents is needed, and here the importance of contributions from industry is obvious, e.g. through the LRI project. Emissions of a chemical throughout the whole life cycle have to be considered, including releases from unintentional point and diffuse sources. Good information on downstream use is essential. There is a need for improved knowledge regarding the emission of chemicals from products, and chemicals in imported goods also have to be taken into account. The importance of these points should be stressed in the new version of the TGD, but obviously more research is needed in this field.

Sources of a substance other than its production and use as a chemical have to be taken into account in the exposure assessment. The present TGD food basket does not include sea fish or meat other than beef, nor does it contain any imported food. The currently used human environmental exposure scenario does not take into account dermal exposure or soil ingestion. All these things could be improved in the TGD.

Differences in environmental conditions between the European regions have to be taken into account. Instead of the present "standard environmental characteristics" in the TGD, European environmental variability could be better covered by choosing parameter values for e.g. three scenarios: a Central European, a Nordic and a Mediterranean situation. For higher-tier assessments, uncertainty analysis using probabilistic techniques could be considered. With regard to degradation, further research is needed into the prediction of environmental degradation rates from laboratory tests. Anaerobic degradation of some classes of compounds has to be taken into account, and this should be included in the new TGD. The possible risk of groundwater contamination has also to be considered in the risk assessments.

The models used in any risk assessment must be properly documented. Validation of assumptions, choices and theories is essential, as is a functional validation by comparing model results with the results of other models and measurements. Model software should be thoroughly tested as well. Specifically, consumer exposure models are in need of such validation. It is also obvious that the analogue exposure model for workers needs updating. Uncertainty analysis should reveal the main sources of variability and uncertainty as well as the sensitivity of the model to input.

Models should be applied on the appropriate time and spatial scale. Consumer exposure models currently lack databases with consensus default values for data on product use, contact and concentrations in products. The development of such databases is strongly recommended.

Furthermore, the application range of the model and other limitations must be complied with. Ideally, the model software should provide a warning when it is used outside its valid range. The importance of these factors should be pointed out in all risk-assessment guidance documents. More guidance is needed on the risk assessment of the so-called difficult substances such as highly polar, lipophilic, dissociated or surface-active substances and organometals.

There are a lot of monitoring activities being carried out, but the use of the resulting data is often limited to the respective programmes. There is a need for better harmonisation, and new substances should be included to a greater extent. A more targeted approach is recommended. A consequence of this may be that some of the ongoing measurements have to be reduced or terminated. The need for good communications between the risk assessment and monitoring communities is obvious.

There is a need to know the quality of measured data, and the development of a "representativeness index" for the sample and a "quality index" for the measurement is suggested. It is not within the scope of this report to suggest how this could be done, but a dialogue between the stakeholders is essential in this development. Ideally, this should be held in a global context (UNEP/WHO/ILO), but the responsible organisation within the EU would be the European Environment Agency (EEA).

To improve the possibilities for retrieving measured data, they should be made accessible via the Internet and the databases should be better harmonised. A global meta-database for measured data should be developed, for which the OECD database EXICHEM could provide a starting point. Again, the EEA would be the natural focal point within the EU.

To make the risk assessment as transparent as possible, it is important that there is support for the assumptions made and for the values of the default parameters used, and as few data as possible (if any) should remain confidential.

A weakness in the present TGD is the limited attention paid to vulnerable subgroups, such as people with particular diets (e.g. vegetarian, high proportion of fish). Children need special attention, and dermal contact and ingestion e.g. of soil should be included in the new version of the TGD.

Predicted and measured data should always be compared, and disagreements discussed. This is already stated in the TGD, but not always done in practice. The scope for improving our knowledge from all the efforts spent on assessments should not be underestimated.

The use of probabilistic risk assessment should be considered. A comparison of deterministic and probabilistic risk assessments should be carried out for a few chemicals to demonstrate the advantages of the two methods.

INTRODUCTION

A large number of chemicals are used in society today. In the EU, the handling of these are dealt with in several directives and regulations. One of the first was Council Directive 67/548/EEC, which deals with the classification and labelling of hazardous chemical products. In 1981, the producer and importers of chemicals were asked to declare the substances they were bringing onto the European market. The response was more than 100 000 compounds. These were listed in the European inventory of existing commercial chemical substances (EINECS), since then known as 'existing substances'. If anyone wants to introduce another substance onto the market, they have to show that the "new" substance fulfils a number of criteria before it is allowed to be marketed within the EU.

The knowledge of the properties of many of the existing substances is less well developed. It was thus decided (Council Regulation (EEC) 793/93) that "in order to ensure the protection of man, including workers and consumers, and of the environment, it is necessary to carry out at Community level a systematic evaluation of the risks involving existing substances appearing in the EINECS". Priority lists of the substances to be dealt with first were established and the work started. As a basis for this work, a "Technical Guidance Document (TGD)" (European Chemicals Bureau, 1996) was published outlining the procedures to follow for both new and existing chemicals. The work is shared between the Member States. The TGD has proven very valuable in this respect and also ensures that the risk assessments (RAs) are uniform.

The RA process is rather complicated with each assessment being discussed at several meetings between the competent authorities. So far, the output has thus been rather limited and critics argue that the process is too slow and will take a very long time if all existing substances are to be assessed.

The Scientific Committee for Toxicology, Ecotoxicology and Environment (CSTEE) is called upon to give an opinion on the RA document in its final form. The committee has now looked at some 20 reports and has observed several difficulties encountered by assessors. The present document points to some of the problems found in exposure assessments, and hopefully provides some ideas on how to improve the situation. It is the intention of the CSTEE to feed this report into the revision of the TGD currently under way.

This report will focus on external environmental and human exposure (to some extent also occupational exposure), but will not review the difficulties in estimating the internal and target organ dose. The report will not look at effects, but it has to be remembered that the effects of a chemical may make certain exposure routes more important than others (e.g. inhalation for effects in the respiratory tract). The exposure to chemicals via food, pharmaceuticals and cosmetics is dealt with in other scientific committees and will be touched upon only briefly in this report.

EXPOSURE ASSESSMENT IN THE EU RISK ASSESSMENT PROCEDURE

This section will review the distribution and fate of chemicals in different media and possible routes of exposure. The assessment of exposure will be discussed with the particular focus on the methods suggested in the present TGD.

Environmental Exposure

Environmental exposure can be assessed by means of experimental methods (measurements) and/or theoretical approaches (predictive models). Both approaches have advantages and disadvantages and need to be appropriately used with procedures carefully evaluated on a case by case basis.

Planning a measurement programme raises a series of questions, such as what parameters should be included, where and when should they be measured? Moreover, without knowledge of the distribution and transport patterns of a chemical, monitoring data represent only single points in space and time, providing little opportunity for extrapolation in order to reconstruct a territorial distribution. Finally, environmental monitoring is an *a posteriori* approach, without any possibility for prevention.

Modelling is an *a priori* approach and represents the only possibility of obtaining data for preventive purposes and for estimating potential exposure before a new chemical is used. On the other hand, models cannot be calibrated and validated without experimental data. In order to avoid mistakes in applying predictive models, the proper model for the specific environmental situation must be carefully selected.

Recently, Mackay et al. (1996a) proposed a five-stage procedure for using environmental fate models. Schematically, the procedure is as follows:

1. Classification of the substance: selection of a suitable model as a function of molecular properties and selection of data needed.
2. Identification of uses and use patterns: collection of data on production, uses, emissions and background concentrations.
3. Application of evaluative models: determination of general patterns of environmental behaviour (distribution and fate) in a standard environment.
4. Application of regional models: evaluation of the environmental behaviour within a large region (e.g. 10^5 to 10^6 km²) and identification of the local situation of concern.
5. Application of site-specific models: evaluation of environmental behaviour in particularly interesting local situations.

Taking into account the relative value and limitations of experimental and theoretical approaches, the best solution, where possible, could be a combined application of both methods, using models to ensure the proper planning of monitoring and better interpretation of experimental data and using monitoring data in order to avoid possible mistakes due to the improper use of models.

Concentration in the atmosphere

Chemicals may reach the atmosphere via direct emissions from several kind of sources (industrial emissions, urban emissions, etc) or as a result of volatilisation after discharge to water or application upon soil.

Air is the most mobile of the environmental compartments and is the major medium responsible for the long-range transport of chemicals. In particular, the atmosphere is responsible for global pollution by POPs (Persistent Organic Pollutants). Atmospheric transport pathways for semi-volatile organic chemicals have been intensively studied in the last few years (Wania and Mackay, 1996, Bidleman, 1999).

Monitoring the atmosphere presents some difficulties, mainly due to the variability and mobility of the compartment. Wind speed and direction may strongly affect chemical concentrations in air. Therefore, air monitoring data must be interpreted very carefully. For this reason, it can be helpful to use living organisms as biomonitors and indicators of air contamination (as it is also done for other media). Lichens, mosses, pine needles or other plant leaf are often successfully utilised (Ockenden et al., 1998).

For the same reason, the development and validation of models capable of predicting chemical concentrations in the atmosphere are not comparable with those used for the aquatic and terrestrial environments. At present, relatively reliable results can be obtained with large-scale predictive approaches at the global or regional scale, whereas the reliability of local and site-specific models needs to be carefully checked.

TGD procedures for calculating a predicted environmental concentration (PEC) in air are based on more or less "realistic" scenarios, but can hardly ever be verified by experimental data. A substantial improvement is difficult to envisage, at least for the local level.

Concentration in the aquatic environment

Chemicals may reach surface water bodies by direct discharge, by surface and subsurface transport through runoff or drainage and by atmospheric drift and deposition. Chemicals enter groundwater usually by leaching through the ground and occasionally by direct contamination of wells.

In comparison to the atmosphere, water monitoring is less affected by environmental factors. Nevertheless, here too, monitoring must be carefully planned in order to take account of space and time variability due to the mobility of the compartment. For rivers, a relationship has been developed between the minimum recommended sampling frequency and the flow variability. As a general rule, big rivers are more stable and need fewer samples for a reliable characterisation.

For lakes, the annual cycle must be taken into account. Sampling during the spring overturn and the summer stratification periods can take account of this annual variability, for both the water and sediment compartments. For the aquatic environment too, the use of biomonitors may be very helpful.

The European Directive establishing a framework for Community action in the field of water policy highlights the need for suitable protocols for water monitoring at European level.

Several models, often based on the fugacity concept, have been developed for predicting runoff and leaching. Extensive work on the selection of more reliable and validated models for regulatory use in EU has been carried out by the FOCUS (FORum for the Co-ordination of pesticide fate models and their USE) Working Group (FOCUS, 1995). Distribution among compartments within water bodies may also be predicted by means of fugacity-based models (Mackay et al., 1983a, 1983b).

TGD approaches have been developed for calculating PEC in surface water and groundwater at local and regional level. At present, these approaches do not take into account the differences in environmental conditions among European countries. There is therefore a need for suitable scenarios to take account of these differences. Here too, useful suggestions have been proposed by the FOCUS group (FOCUS, 2000).

Coastal waters may be very variable on account of tides and currents. At present, however, no standard protocols are available for the prediction of concentrations in the marine coastal environment.

Concentration in soil

Potentially dangerous chemicals may be intentionally or unintentionally applied onto soil. The first kind of application involves pesticides, nutrients and chemicals present in sludge disposed onto soil.

Pesticides are applied in known amounts according to agricultural practices, thus the load for the soil compartment can be easily estimated. Nevertheless, depending on application practices, different situations may occur:

1. Chemicals directly applied onto soil (herbicides, insecticides, nematocides or other active ingredients used for disinfecting soil);
2. Chemicals applied to the crop (mainly insecticides and fungicides);
3. Chemicals reaching soil by drift. Quantitative attempts to estimate drift losses are found in the literature (Ganzelmeier et al. 1995).

Sludge from sewage treatment plants may be applied to soil as organic fertilisers. Moreover, soil can be used as a medium for the disposal of waste sludge. To quantify the load of contaminants in soil, detailed knowledge of sludge composition is needed. Additional information is also needed in order to assess the bioavailability of contaminants. The same applies to animal manure applied as organic fertiliser, as this often contains significant amounts of contaminants (metals, medicinal products, etc.).

Unintentional emissions of chemicals may occur as a consequence of accidents in human productive activity (industry, transport of chemicals, mining, etc.). In an intensive industrial area, chemical spillages on soil may occur as a more or less regular consequence of production. Soil pollution may also occur as a result of leakage from inadequately protected solid-waste disposal sites. An additional source of soil pollution may be the use of contaminated water (e.g. domestic sewage) for agricultural soil irrigation. Finally, chemicals may enter the soil may as a result of atmospheric (wet and dry) deposition.

Soil is a non-mobile compartment, but it has a more heterogeneous structure and composition compared with other compartments (air, water). Therefore, soil monitoring needs to be planned to take into account the spatial variability of soil characteristics.

The fate of a chemical applied to soil depends on its physical and chemical properties, taking into account the partitioning among soil phases (air, water, organic and inorganic solid matrices), and on degradation patterns.

Chemicals may be lost through water transport by leaching or runoff. Leaching and runoff potential may be estimated as a function of the water solubility and, for non-polar chemicals, the organic-carbon sorption coefficient (K_{oc}). For polar compounds (anionic or cationic), the affinity for the solid matrix of soil must be estimated through the soil sorption coefficient (K_p), including the interactions with the inorganic soil component.

Several simple indices have been developed in order to qualitatively estimate the leaching potential of a chemical, such as the GUS (Groundwater Ubiquity Score) index based on K_{oc} and degradation half-life (Gustafson, 1989). Vighi and Di Guardo (1995) review these indices.

A quantitative assessment of the distribution of a chemical among soil phases and a prediction of losses through leaching and runoff can be made with suitable multimedia models (Cowan et al., 1995). As soil is not a well-mixed compartment, soil modelling needs approaches quite different from models developed for describing distribution in the aquatic environment.

For soil, as well as for water, standard procedures for calculating exposure in soil proposed by the TGD, at the local and regional level, do not take into account European environmental variability. There is therefore a need for suitable scenarios.

Concentration in biota

Uptake of chemicals by living organisms may occur through bioconcentration, bioaccumulation and biomagnification processes. Moreover, direct deposition of chemicals on living organisms may occur in the area where a chemical is intentionally applied or unintentionally emitted.

Bioconcentration is a simple physical-chemical process based on equilibrium partitioning among different phases, and can be predicted on the basis of the properties of the chemical (K_{ow} , K_{oa}).

The prediction of bioaccumulation and biomagnification is more complex. Examples of food chain models have been developed (Campfens and Mackay, 1997) but reliable standard procedures are not yet available.

As described above, living organisms may be used as biomonitors for assessing contamination in water and air. This is possible only if bioconcentration is the only (or at least the major) uptake pattern. As complex and largely unpredictable metabolic processes are often involved in bioaccumulation and biomagnification processes, mainly plants or lower animals are used for biomonitoring.

Standard procedures have been developed, in particular for pesticides, in order to calculate the deposition on plants and animals as a function of application or emission rates, emission patterns, etc. (Hoerger and Kenaga, 1972; EPPO, 1994).

Human exposure

In the TGD, a distinction is made between exposure to workers (depending on their past and present occupational environment), consumers exposed through substances in consumer products and the general population exposed through the environment (see Fig. 1).

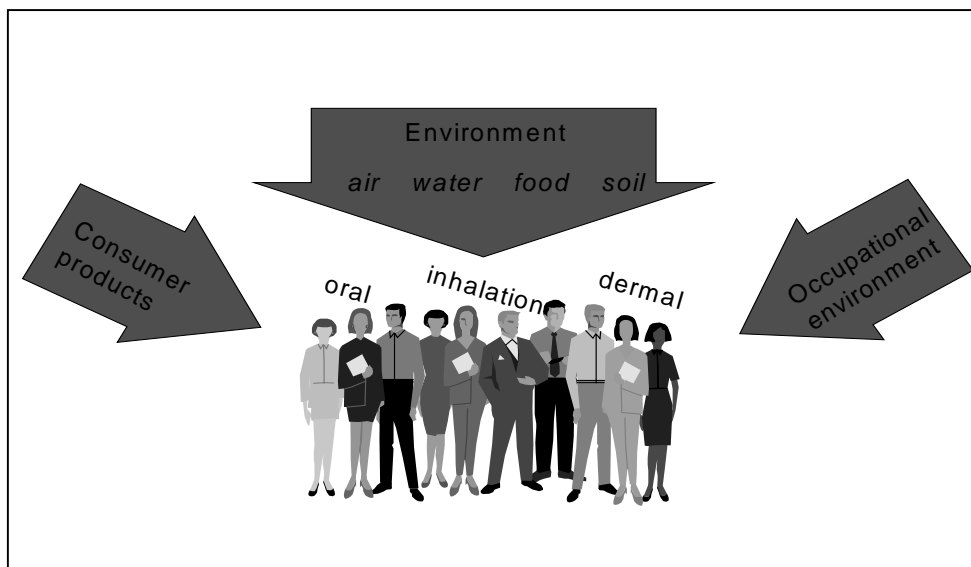


Fig. 1: Exposure routes of human beings in the TGD

The risk assessment for humans in the TGD aims for a level of protection, expressed as the 'Margin of Safety', such that the likelihood of adverse effects occurring is 'of no concern', taking into account the nature of the potentially exposed population, including sensitive subgroups, and the severity of the effects. The interpretation of this strongly depends on expert judgment.

The exposure assessment should cover human risks during the whole life cycle of substances, i.e. from production to application and then on to recycling and waste treatment. Representative exposure levels for each potentially exposed population need to be derived. The spatial scale of the exposure (e.g. personal, local, regional) has to be taken into account. In some cases, aggregate exposure from different sources needs to be considered, e.g. exposure to a substance via food and air following its use as a pesticide and as a biocide, respectively. Exposure as a result of accidents or abuse is not addressed in this document.

The human exposure assessment should be based on both representative monitoring data and model calculations. Relevant monitoring data for substances with analogous uses and exposure patterns or analogous properties should be considered.

As a general rule, the best and most realistic information available should be given preference. However, it may often be useful to conduct a risk assessment initially using exposure estimates based on worst-case assumptions. Subsequently, in an iterative process, the risk assessment can be refined, if necessary using a worst-case scenario where the substance is 'of concern'.

The exposure assessment should aim for 'reasonable worst-case' results. A reasonable worst case is defined as a 'reasonable unfavourable but not unrealistic situation: covering normal use patterns, including cases where populations are exposed to the same substance in more

than one scenario, e.g. consumers or workers may use several products containing the same substance. The reasonable worst-case prediction should also consider upper estimates of extreme use and reasonably foreseeable misuse'. Exposure as a result of accidents or abuse is not addressed here.

Workplace exposure

The workplace exposure assessment is based on modelling, preferably using the general-purpose predictive model for exposure assessment EASE (Estimation and Assessment of Substances Exposure, currently under review), and the use of representative and reliable monitoring data, for which a number of requirements have been specified. The workplace assessment does not consider the use of personal protective equipment (PPE).

The EASE model is not a predictive, deterministic model, but an analogue model, i.e. based on measured data, all 8-hour time-weighted averages, which are assigned to 160 specific dermal and inhalation scenarios. The user can build these scenarios by choosing from three categories of input information: physical process properties, use pattern and pattern of control. The measured data have been derived from the UK National Exposure Database for inhalation exposure and from experimental data and expert judgment for dermal exposure. The results are expressed as ranges.

Consumer exposure

The consumer exposure assessment is based on modelling and the use of reliable and representative monitoring data. Since the latter are almost never available, assessment has to rely heavily on modelling.

Gathering information on the number and type of substances in consumer products is of special concern. The product register may provide this information but the use of these registers may be restricted by confidentiality issues and by their national/regional focus. It has, however, to be kept in mind that the quality of the data in these registers may be variable. The chemical industry often claims to be unaware of all downstream uses of their products and European legislation does not require industry to gather this information actively.

The TGD offers simple algorithms for a series of common exposure scenarios to be used in first-tier exposure assessments. A number of computerised models are presented, but the TGD does not recommend a particular model above any other. It is noted that one of the models, CONSEXPO 1.0, includes, besides more refined deterministic and stochastic models, the TGD screening models also available in EUSES 1.00.

Modelling heavily depends on the availability of data on product use (e.g. intended and actual use, amount, physical form of use), contact (e.g. frequency and duration of use, air exchange rate, site of product use) and concentrations (e.g. weight fractions, concentration in product). The result of the exposure assessment depends on the choice of such parameter values, which are currently based on different sources of information and expert judgment. There are no databases of generally agreed (distributions of) default values, though work on such databases is in progress in the US (THERdbASE) and in the EU (CONSEXPO).

Validation of consumer exposure models is generally lacking. Since measured data are scarce, validation of consumer exposure models should include both analytical work and modelling.

Exposure through the environment

The total exposure of human beings through the environment (Fig. 2) can be assessed on the basis of measured data, on the basis of modelling, or a combination thereof. Complete and representative measured data on levels in food, drinking water and air will be scarce for most substances, though in some cases market basket surveys will be available. The estimated exposure can be based on measured data for one or more environmental compartments and subsequent modelling.

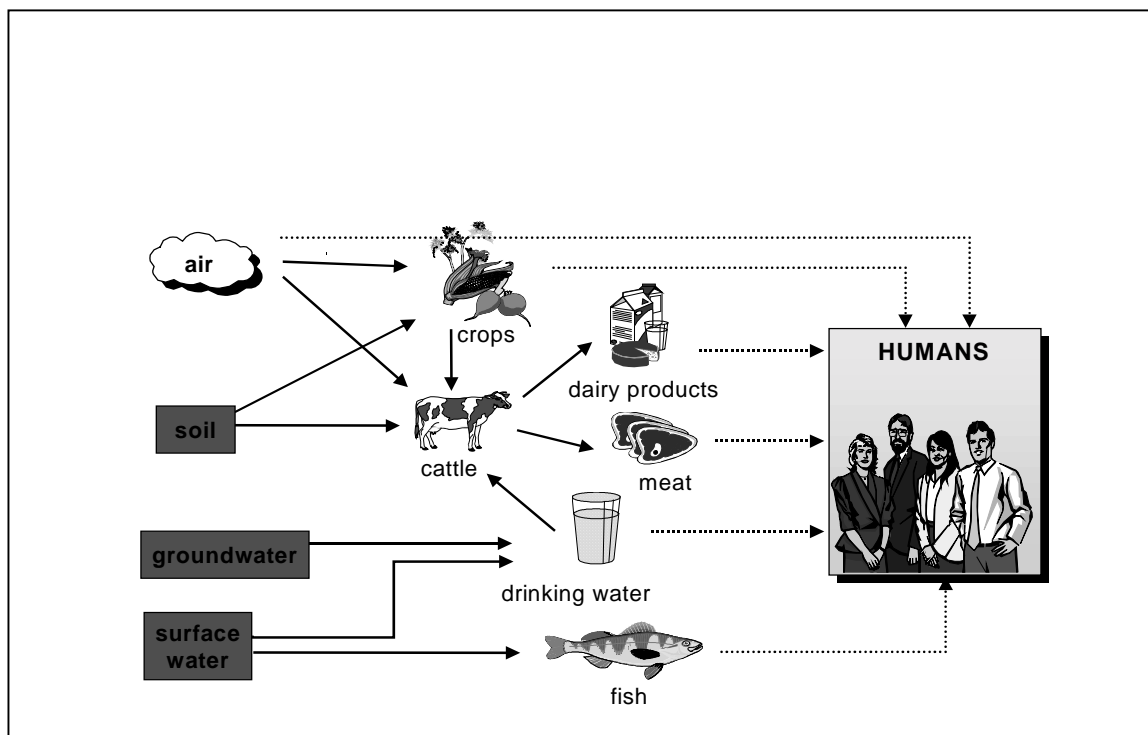


Fig. 2: TGD environmental exposure scenario for human beings. This simplified figure does not include biomagnification.

The exposure scenario as shown in Fig.2 is used for an assessment at local and regional level. Dermal exposure and soil ingestion are not taken into account. The food basket does not include wild or farmed sea fish, nor meat other than beef. Imports are not included in the assessment. Only adults are considered, though it is possible to adapt body weights and consumption patterns in the model. In the local assessment, all food products are conservatively assumed to be derived from the vicinity of one point source, while in the regional assessment all food products are taken from the model regional environment. The worst-case character of this assessment is reinforced by the standard consumption pattern defined: to take account of the variability in intake rates across EU countries, for each food product the rate for the EU country with the highest average consumption is used.

Validation work has been reported for the bioconcentration and biotransfer factors in the model as well as for the total dose (summarised by Jager, 1998a and, with regard to uptake by plants, by Rikken et al., 2000).

Population subgroups

According to the TGD, the following human populations are to be taken into account: workers, consumers, and humans exposed indirectly via the environment. In some cases, all three types of exposure estimates or, within one type, exposure through various scenarios/products may be combined to produce an overall exposure value. Specific subpopulations such as pregnant women (and foetus), children or elderly are not mentioned and consideration of these groups is apparently left to the judgment of the risk assessor. This is a field where more research is needed.

DIFFICULTIES IN ASSESSING EXPOSURE

The risk assessor encounters a number of difficulties in the assessment process, not least in assessing exposure. This section will give some examples of such problems, some of which have been observed in the EU risk assessments so far performed.

Basic data availability

The provision of data for the risk assessment (RA) of a chemical is the responsibility of the companies that produce and process it. Where the volumes produced, imported, exported and processed are not completely accounted for, the local, regional and continental estimates of environmental concentrations are understated. In such instances, some RAs appropriately use maximum estimated production and/or processing volumes; a worst-case scenario approach. It would be of interest to know why the data are incomplete so that the reader can consider whether this approach is reasonable. For example, did industry simply not provide the data within a certain time period, or were hundreds of companies involved so that a complete reply could not be expected in the time available? To assist with the RA, it may be helpful to agree a maximum time limit by which industry should provide adequate data (e.g. two months). If no data are forthcoming by this deadline, the RA should be based on a worst-case scenario.

Some chemicals may be contained in materials and end products (e.g. textiles, plastics) imported into the EU. The industry in the EU may have very incomplete or no information on the volumes and concentrations of the chemical in these products. Where the use and/or disposal of these products could pose a risk to humans or the environment, this must be clearly stated in the RA. Another problem can be to get information on impurities in a chemical.

The RA typically includes a description of the methods of production of a chemical, how it is processed, and what the end products are. The concentration in the final product can be compared to the amounts discharged to air and water to support estimates and measurements of environmental concentrations. Information on the physical and chemical properties of a substance may be found in publications and reports. It is important that the primary literature is checked to confirm these data, especially to help clarify how different values may have arisen. These data are fundamental to the EUSES models and must be as accurate as possible. A worst-case scenario approach is not appropriate in this instance because erroneous values will result in a different predicted distribution of the chemical between environmental compartments.

The octanol-water partition coefficient (P_{ow}) is the ratio of the solubility of a chemical in octanol and water, respectively. If the P_{ow} is higher than 3, it is often used to produce a "Bioconcentration Factor". A higher BCF (i.e. more octanol-soluble) predicts greater concentrations in biota. Measured concentrations in biota (e.g. plants, invertebrates, vertebrates), freshwater, seawater, soil and sediments are seldom available. The calculated BCF can be a useful indicator of the risk to animal and plant life and the potential bioaccumulation of a chemical in the food chain. However, its use is limited and not applicable to some types of substances, including polar or very lipophilic substances and metals. Where the P_{ow} is derived from only one study, or varies between studies, a worst-case scenario (high BCF) approach may be adopted. Measured data on bioconcentration is very desirable to assess the accuracy of predictions from BCF.

Measured concentrations

Every year, a large number of concentration measurements are carried out for various purposes at local, national and international levels. To assess exposure in order to characterise the risk of chemicals, there is a need for relevant high-quality measured concentration data. However, the production of such data requires considerable resources. A more cost-effective approach would therefore be to facilitate the wider use of these measurements than just for their original purpose (e.g. monitoring, surveillance, research and development). Important issues in this context will of course be the accessibility, representativeness and accuracy of the data.

Data accessibility for the environmental assessment

In particular, measured exposure data may be available for some of the existing substances, veterinary drugs, pesticides, food additives and contaminants. The data may come from multiple sources. Thus, for existing substances, monitoring programmes in industry, particularly for occupational exposure, or other monitoring studies may provide data. However, measured data provided by industry may be confidential, which, even if these data are available to the assessor, makes the risk assessment less transparent. For pesticide and contaminant residues in food, potential data sources at national level may include supervised trial data (residues), government monitoring and surveillance data and surveys funded by industry. Furthermore, both on the local and more global scales, a large number of measurements are carried out of chemicals in the environment. Large-scale monitoring programmes continue over long periods of time to study temporal and spatial trends, but there are also smaller surveys to study specific chemicals in selected areas. These programmes are quite often financed under what are more or less research and development schemes. The results of such measurements could in many cases be used more widely than for the original purpose if they were easier to access. A large proportion of the results of research projects are published in peer-reviewed journals, which ensures a good quality control. This is, however, a slow process, and it is often impossible to obtain the individual data used for the conclusions in the final article.

The Arctic Monitoring Programme (AMAP) is an example of an international effort to use measured data from various sources for a special purpose. AMAP was established in 1991 to implement components of the Arctic Environmental Protection Strategy (AEPS) adopted by the Ministers of 8 Arctic countries. Specifically, AMAP was charged with monitoring the levels and assessing the effects of a few well-known anthropogenic pollutants in all compartments of the Arctic. This task was carried out largely by adapting ongoing national and international activities, while new monitoring and research work was initiated only where necessary. Aiming to use all relevant measured data produced in the various countries for various purposes, AMAP faced considerable challenges in overcoming the problems of the availability, representativeness and accuracy of data. To obtain results from scientists in the relevant field, the programme had to undertake not to release the data to any third party, making it impossible for anyone outside the programme to use the original data. The very comprehensive results of this work are published in the AMAP Assessment Report (AMAP 1998), where the recommendations for future work include the need to improve the basis for the intercomparability of measurements.

In general, there is a need to improve the comparability of the data to be used in exposure assessment, and data sets should be homogenous in the sense that their comparability has been

established. The data provided should be harmonised at least to the extent that they follow a similar format and provide minimum information for the requested purpose. It is thus recommended that future monitoring programmes, to ensure improved intercomparability, should continue to address the issue of improved quality assurance/quality control protocols for sampling and analysis, including inter-laboratory comparison, the storage and archiving of samples, and the handling, reporting and analysis of data.

In order to increase the availability and use of measured data, the existence of the data must be widely known. The most effective way to make data available is via the Internet and via the increasing number of databases for monitoring results. The only centrally coordinated reference databases for food chemicals are the ones on contaminant and pesticide residue data collated from the Member States by GEMS/Food data (CSTEE/99/10 Add 2). The data in AMAP went into the ICES (International Council for the Exploration of the Seas) database. Unfortunately, the structures of these databases are often not compatible, so efforts to harmonise them would be most welcome. Standardisation of information on sampling, analysis and reporting procedures, together with standardised information on the accuracy of measurements, is required. The use of consistent procedures is particularly important at international level, where data from several countries may be compared or combined.

Data accessibility for the consumer exposure assessment

A number of data sources summarise existing data from multiple sources of exposure. An important source of residential exposure data focussing on Germany are the *Standards zur Expositionsabschätzung* prepared by the *Arbeitsgemeinschaft der Leitenden Medizinalbeamtinnen und -beamten der Länder* (BAGS, 1995). These Standards summarise anthropometric data, time budgets, food consumption, drinking water consumption, and oral soil intake.

Essentially, exposure to compounds in food can be determined by two main methods. Firstly, intake can be calculated by comparing the concentration of a compound in every possible food item with the composition of the diet. Slob (1993a; 1993b; Slob and Krajnc, 1994; van Veen et al., 1995) has developed a statistical method to calculate food exposure from concentration data and diet composition, which also reveals intra- and inter-individual variations. To apply this method, data on food consumption and data on concentrations are needed. Dietary composition has been investigated in a number of countries (WVC and LNV, 1990, Adolf et al. 1994a and b, and Combris et al., 1995, MAFF, 1995). An overview containing average food consumption data for all EU Member States is also published by ECETOC (1994), using data from Euromonitor (1992).

There are several national programmes for monitoring food concentrations. A second and more direct method of obtaining the intake of a compound is to perform a duplicate diet study, as e.g. reported by Vaessen et al. (1995), Vahter et al. (1990) and Sherlock et al. (1983).

Indoor air quality is determined by sources inside and outside the house. Compounds emitted by sources outside the house into the outdoor air may be carried into the house by ventilation (Ekberg, 1994; Ekberg 1996; Hoffman et al., 1996; Leuret, 1985). A second outside source comprises compounds that evaporate from contaminated soil and enter the house from below. This source has been modelled by Waitz et al. (1996). Many sources of pollution may exist indoors (see Bieva, 1989). Seifert and Ullrich (1987) provide methodologies for measuring and classifying these indoor sources. Examples include carpets (e.g. Clausen et al., 1993),

paints, and lacquers (Clausen et al., 1991; Hansen et al., 1991), which emit volatile organic compounds, or sprays that release chlorodifluoromethane (Hartop and Adams, 1996). Many other consumer products may also emit volatile compounds into indoor air (see e.g. Seifert and Ullrich, 1987; Brown et al., 1993; Crump et al., 1996). The European Collaborative Action on indoor air quality and its impact on humans has produced two main reports on the testing of emissions from products and materials (2; EUR 12196 EN and 13; EUR 15054 EN).

Concentrations in indoor air are not the only factors important for exposure: the contact duration also determines exposure and possible health effects. Time activity patterns, or time budgets, have been investigated to determine the time spent indoors in various environments, e.g. school, work and home. Time activity patterns for the Netherlands are reported by Freijer et al. (1997), and for Croatia by the Croatia Radiation Protection Association (<http://mimi.ini.hr:80/~ksega/index.html>). Hoffman et al. (1996) used personal sampling in combination with recorded activity patterns to search for behaviours that correlate with large exposures to VOCs. For example, reading a newspaper or a magazine correlates with exposure to ethylbenzene, xylene, propylbenzene, and ethyltoluene.

Consumer products vary widely in composition, packaging, usage, etc. This diversity implies that exposure to compounds in or from consumer products may follow any route of exposure, or any combination of routes. Essentially, assessing exposure to compounds in or from consumer products requires knowledge of i) product composition, ii) the concentrations that occur in any medium that consumers can come into contact with (which will depend on product usage), iii) contact patterns with the product and all media containing compounds from the product and iv) the intake and uptake of compounds (van Veen, 1996).

Product composition data can be gathered from a number of sources, the main ones being product labels, poison information centres (e.g. Hofstee et al., 1990; Velvart, 1993; Flyvholm and Andersen, 1993 — many countries have a poison information centre), and product registers (e.g. at the Swedish Chemicals Inspectorate). Environmental health groups may also provide information on product composition.

To estimate the concentrations in media receiving compounds from the product, models and measurements are used. Screening models are provided by the TGD, Vermeire et al. (1993), ECETOC (1994), and van de Meent et al. (1995). Mechanistic exposure models are provided by van Veen (1995; 1997), using CONSEXPO, a program combining contact, exposure and uptake models for the inhalatory, dermal and oral routes of exposure for a single compound. Measurements of exposure concentrations are reported by e.g. Clausen et al. (1991), Hansen et al. (1991), Hartop and Adams (1996), Seifert and Ullrich (1987), Brown et al. (1993), and Crump et al. (1996). Other sources are mentioned above.

A problem area in assessing exposure to consumer products is product usage and contact with the product. Some information is presented in appendix 6 of the TGD. Data on extreme uses can be gathered from poison information centres (e.g. Velvart, 1993), but these data often represent accidents. Weegels (1997) investigated consumer product use and concluded that questionnaires tend to overestimate use. For variables measured such as the amount used and duration of use, it was concluded that they exhibit a large variation (a coefficient of variation of 1 is commonly encountered) and hardly ever correlate with one other. For example, the amount of dishwashing fluid used does not correlate with the amount of water used. If no data on the consumer exposure are available, a worst-case scenario has to be applied.

Representativeness

In the planning of monitoring surveys, consideration needs to be given to the suitability of the sampling plan in both qualitative and quantitative terms for obtaining representative samples for the specific use to which they are to be put. The selection of chemicals to be monitored is often based on criteria not related to the actual probability of environmental distribution. Public concern and the availability of analytical methods may quite often determine the choice of chemicals to be measured. Heterogeneity in the production and use of a chemical, together with variation in the environment, may result in considerable variations in the concentration of a chemical in the environment and in food. Thus, in selecting the site and nature of sample to be monitored, hot spots, ground conditions, homogeneity of sample, residue variability etc. must be evaluated against the aims of monitoring. Furthermore, the design of the survey must consider the final quality of the data. In the report of a FAO/WHO consultation exercise in Geneva (Food consumption and exposure assessment of chemicals, 1997), data quality is defined to include the suitability of the sampling plan for obtaining representative samples, the appropriateness of sampling handling procedures, the selection and validation of the analytical methodology, the use of an analytical quality programme, and the number of samples determined on the basis of the statistical characteristics of each data set. Likewise, there needs to be careful evaluation of the applicability of existing measurements as estimates of exposure concentrations.

In order to make critical decisions on the representativeness of available data for a specific use, it is recommended that specific evaluation criteria be developed to assist in the evaluation of data quality. Indicators of data quality need to be clearly defined and available to users. It would be welcomed if relevant committees could take on the task of developing criteria for the representativeness of measured environmental concentrations.

Accuracy

The characterisation of uncertainty in measured data is an integral component in the evaluation of data quality. Extensive monitoring surveys should therefore include an assurance programme for analytical quality with mandatory participation in inter-laboratory comparisons, where such exercises are available for the chemicals and matrices in question. Participation in quality assurance programmes should be possible at both national and international levels. Laboratories submitting analytical results for use in exposure assessment should ideally have participated satisfactorily in inter-laboratory comparisons. Measurements must be accompanied by information on analytical quality. Thus, information on accuracy (how close is a measured value to the true value), precision (how close will repeated measurements be to each other), selectivity (how large is the risk that other compounds will interfere with the measurement), linearity (is the response a linear function of the amount), detection limits (the lowest amount of the compound that can be observed), quantification limits (the lowest amount of the compound that can be measured quantitatively), concentration range and sensitivity should ideally be available to permit an adequate evaluation of the measurement quality. It is important to keep in mind that data do not have to be of the highest quality to be useful in different applications. However, it would be very useful if at least the accuracy could be estimated in order to avoid improper use of measured data.

Predicted data

Emissions and emission factors

From the experiences of users of the emission estimation method set out in the TGD, it is clear that most of the difficulties in environmental exposure assessment are encountered in the emission estimation.

Since emission monitoring data are often lacking, emission estimation provides the basis for environmental exposure estimation. Specific information from producers, product registers or open literature is preferred. If such information is lacking, the second choice is Industry Category Documents. A last option is to rely on default emission factors. Emission factors are expressed as fractions of the total tonnage of a substance. A default emission factor is an expert judgment based on Industry Category Documents or best guesses. Current experience shows that, except for production, specific release information is difficult to obtain. Industry Category Documents are available for only a limited number of Industry/Use Category combinations. In addition, these documents often deal with only one compartment, one or two life stages and either the local or the regional situation. Therefore, one often has to rely on default emission factors.

The default emission factors in the TGD are only partly based on Industry Category Documents, while the other factors are heavily based on expert judgments. Some studies used to derive emission factors are over 10 years old. Large inaccuracies may also occur because the estimations within an Industry Category/Use Category combination are generic; i.e. have to cover all possible applications in all different branches of industry.

The validation status of the TGD emission factors has been discussed in Jager (1998a). Comparing specific release factors for production and processing with the defaults leads to the conclusion that the defaults are conservative and are sometimes more than 3-4 orders of magnitude higher than measured values (Fig. 3).

Further work on Industry Category Documents is critical in order to reduce the uncertainty in exposure assessment. In view of the amount and scope of work involved, international co-operation and prioritisation is essential. Industry has an important role here. Several EU Member States have recently developed or are developing new Industry Category Documents, which should be incorporated in a future version of the TGD as soon as possible. In addition, industry is undertaking related work under the Long-Range Research Initiative (LRI) of the European Chemical Industry Council (CEFIC) as part of the project entitled "Identification and Evaluation of Emission Databases in Europe". The overall aim of the project is to improve the data basis for release estimation methods for the risk assessment of chemicals in the environment.

Information on downstream uses, and therefore information on emissions from these uses, is often lacking, along with the legal instruments for obtaining such information from industry.

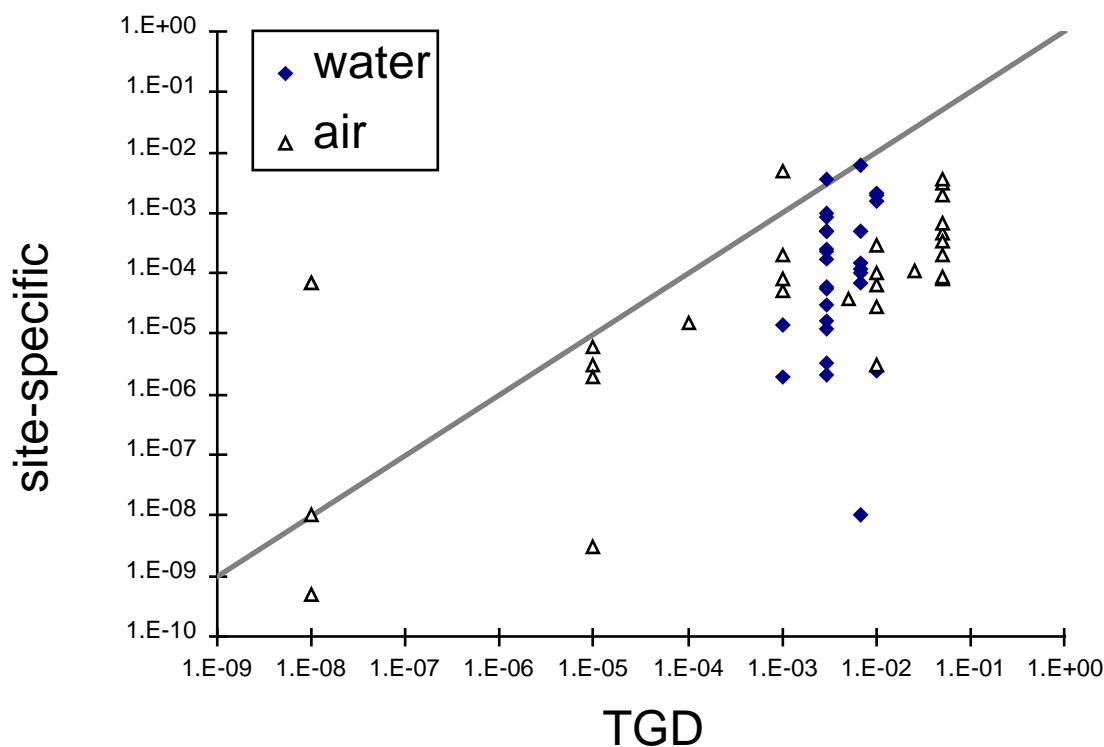


Fig.

Fig. 3: Local emission factors vs. TGD defaults for production and processing of 20 substances from EU risk assessment reports on existing substances. The 1:1 line reflects the situation where the estimated factors (x-axis) are equal to the measured factors (y-axis) (from Jager et al., 1998a).

Emissions of existing substances may include emissions from unintentional point and diffuse sources (e.g. as by-products from an industrial point source, emissions from traffic and waste). Such emissions may turn out to be more important in terms of risk than the intentional emissions. There is no guidance in the TGD on how to approach this problem.

Degradation rates

The following degradation processes are discussed in the TGD: aerobic biodegradation in a sewage treatment plant (STP) and in soil, sediment and air, and abiotic degradation in water (hydrolysis, photolysis) and air (photodegradation). Anaerobic degradation is ignored. The latter may be a problem for substances such as highly halogenated aromatics. These substances are known to be resistant to aerobic biodegradation, but degrade more rapidly anaerobically. The local assessment takes into account only biodegradation in the STP, probably assuming that the retention times in the environmental compartments are short and degradation therefore negligible. Degradation in the STP, soil and sediment is inversely related to sorption and aerobic degradation in sediment is assumed to be restricted to the upper 10% of the sediment layer.

Degradation rates measured in the environment are often not available. Rates are estimated on the basis of standardised laboratory tests. Partly validated quantitative structure-activity relationships (QSARs) are described in the TGD as well. The default estimates from standard laboratory tests are expert judgment values. The validity of these estimates for the real world is a constant subject of debate. For example, the rate constants very much depend on environmental pH, seasonal and geographic conditions, the presence of suspended matter or particulates etc., which may differ considerably from the testing environment.

Validation work has been carried out for biodegradation rates and is summarised by Jager (1998a). Measured half-lives have been compared to the default rates. It was concluded that in general the default emission estimates are worst-case. The deviation may be up to a factor of 100, indicating the low predictive power of the standard tests for the situation in the real world.

QSARs have been applied to predict biodegradability (see TGD, Part III). It was concluded in the TGD that QSARs could be applied in a conservative and confirmative way for negative indications of biodegradability.

QSARs for photodegradation are also available (see TGD, Part III). It was concluded in the TGD that the most promising models, the Atkinson models, predict rate constants for photodegradation in the atmosphere within a factor of 3 from those measured for over 90% of 370 substances. Valid models for photolysis in water have not been identified.

Degradation patterns in the atmosphere are often largely uncertain. Literature data on chemical persistence often relate to experimental conditions where chemicals are maintained in the gas phase. Therefore, well-known persistent chemicals are often reported to have an astonishingly short half-life in air. In the real environment, chemicals are mainly associated with solid particles (hydrophobic POPs) or aerosols (more water-soluble chemicals), which strongly reduces reactivity and degradation rate.

Model limitations for some types of compounds

The environmental exposure assessment in the TGD has been developed primarily for apolar organic substances and cannot be performed without modifications for the following types of compounds: inorganic substances, including metals and their compounds, organic and inorganic ionic, surface-active and polar substances and organometals. The octanol-water partition coefficient (K_{ow}) for these substances, if measurable at all, is not a good predictor for estimating environmental partition coefficients, biotransfer and bioconcentration factors. Trapp and Schwartz (2000) investigated the boundaries of the four K_{ow} -dependent regressions used in estimating the indirect exposure of humans: i.e. the regressions for the transpiration stream concentration factor, the bioconcentration factor for fish, and the biotransfer factors for beef and milk. Although most of these regressions have quite a broad regression range, the common range is only between K_{ow} 3.0 and 4.6. This means that for polar and very lipophilic substances the use of these regressions gives uncertain results. For some chemical classes, 'extra' processes may occur, e.g. active uptake by plants and micelle formation by surfactants. In general, little guidance is given on how to approach these difficult substances. The assessment of metals is possible, as shown by the current endeavours in the EU to assess zinc, chromium and cadmium, but requires a lot of effort and additional assumptions.

The external exposure assessment for consumers is a first-tier assessment independent of substance properties and therefore no limitations exist with regard to substance properties. However, the application of more advanced models may present difficulties.

It is not clear what the domain of the worker exposure assessment with EASE is: the composition of the underlying database is not reported. The limited validation work carried out indicates that EASE provides a conservative estimate of workplace exposure, though the observed variation between measured data and estimates is considerable (measured data may deviate by up to a factor of 1000 or more from the EASE estimate (summarised by Jager,

1998a)). The underlying database and exposure scenarios have not been updated since the publication of the TGD and therefore may not reflect current knowledge of exposure.

Validation status of the models and uncertainty analysis

The principle aim in the validation of risk assessment systems as described in the TGD and implemented in EUSES should be to prove their reliability, accuracy and usefulness within the specified field of use. The validation should consist of a conceptual validation – are assumptions, choices and theories correct? – an algorithm and software validation and evaluation, and a functional validation. In the latter validation, the accuracy of the model or submodels is tested by comparing model results with independent measurements or the results of other models. Uncertainty and sensitivity analysis can form part of this analysis. It is up to decision-makers to judge whether or not the accuracy is sufficient to justify (the absence of) risk reduction measures. Explicit validation criteria are not specified in the TGD.

The validation status of EUSES was investigated by Jager (1998a). Important conclusions were:

1. The validation status of EUSES leaves much to be desired. Validation activities for individual models have been performed, but are seldom directly applicable to EUSES. However, the system represents the ‘state-of-the-art’ in generic risk assessment and a consensus has been reached on its contents.
2. The degree of deviation from reality may be substantial for the results: see Table 1.
3. An important limitation is the use of a fixed, standard environmental exposure scenario. The model results represent this standard situation, but the influence of these scenario assumptions on the risk estimates remains unclear. This may be one of the most important sources of uncertainty. Perhaps it is possible to allow for alternative standard EU-scenarios (see the discussion of uncertainty analysis below).

Table 1: Summary of the validation status of the EUSES sub-modules (Jager, 1998a)

Module	Conservatism*	Indication of possible deviation from measured values
Release estimation	worst case	1-1000
Environmental distribution		
<i>partition coefficients</i>	median estimate	up to factor of 15 for high Kow
<i>biodegradation rates</i>	generally worst case	0.1-100
<i>sewage treatment</i>	median case	within factor of 10
<i>local distribution</i>	largely unknown, worst-case scenario	unknown
<i>regional distribution</i>	optimistic case	0.001-10
Environmental exposure		
<i>BCFs</i>	usually median case	within a factor of 10
<i>drinking water</i>	worst case	unknown
<i>total dose</i>	worst case	unknown
Consumer exposure	worst-case scenario	unknown
Workplace exposure	generally worst case	0.1-1000

* Qualitative classification ranging from worst case (overestimation), through median case (around the average) to optimistic case (underestimation)

The accuracy of the models in the strict sense is not essential as long as the uncertainty in the results is quantified and taken into account in decision-making. Due to the generic nature of

the exposure assessment, the models used have a low degree of detail. Uncertainty analysis can reveal the main sources of variability and uncertainty and indicate whether and where further refinement in models or data is required. An uncertainty analysis not only can reveal the overall uncertainty due to variability and uncertainty in substance-specific parameters, but can also include an analysis of 'environmental variability', i.e. the variability in exposure scenarios. Probabilistic uncertainty analysis for the exposure assessment according to the TGD has been demonstrated to be feasible (Jager, 1995; Jager and Slob, 1995; Jager et al., 1997; Jager et al., 2000; van Veen, 1997; Huijbregts et al., 2000). This approach still meets with a lot of scepticism in the EU (Jager, 1998b). An example of the output of an uncertainty analysis for an existing substance (DBP) is shown in Figure 4.

Schwarz (2000) and Berding (2000) have performed validation studies of the human indirect exposure models and the regional distribution model in EUSES, respectively.

With regard to the human exposure models (Schwarz, 2000), important conclusions are:

1. the models strongly depend on the lipophilicity of the substance;
2. the underlying assumptions drastically limit applicability;
3. realistic concentrations are seldom to be expected;

With regard to the regional distribution model (Berding, 2000), important conclusions are:

1. the model complies with its designated purpose of calculating regional background concentrations;
2. the highest deviations occur if the preliminary estimations of emissions, degradation rates and partition coefficients deliver unrealistic values;
3. the parameter uncertainty is relatively low, but using default values can lead to high uncertainties.

Both studies conclude that EUSES is generally a good compromise between complexity and practicability with restrictions for the difficult substances already identified above.

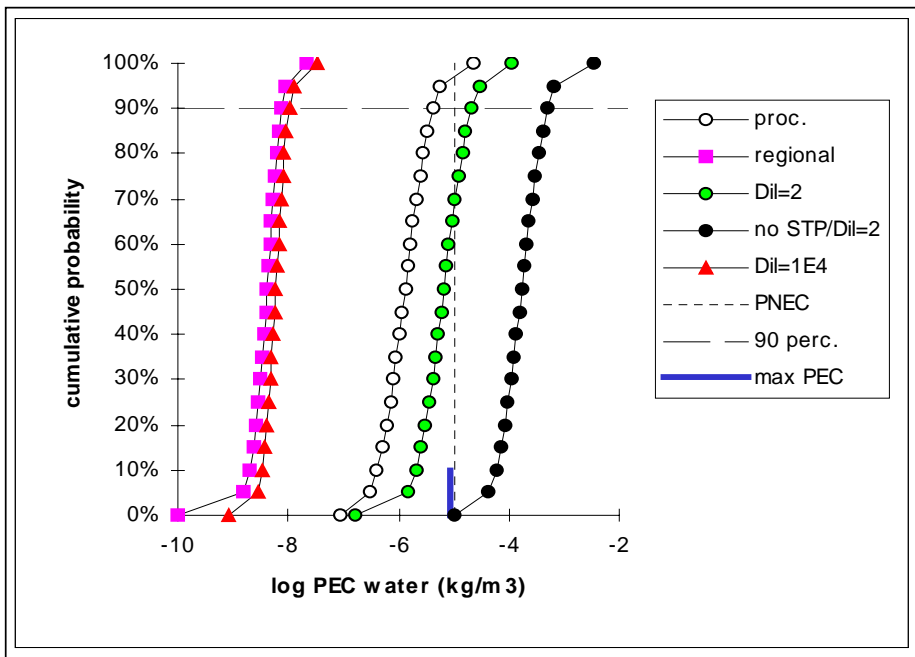
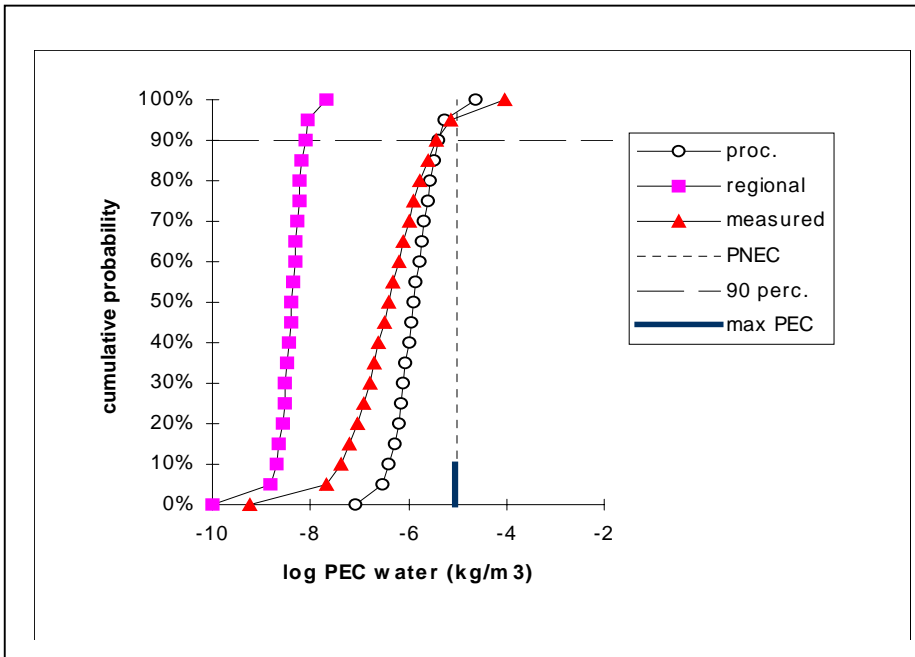


Fig. 4: Cumulative probability plots of Predicted Environmental Concentrations (PEC) for aquatic organisms for DBP, based on the EU RAR, using the TGD/EUSES standard scenario (top diagram) and applying alternative scenarios (lower diagram). Both diagrams show the distributions of the local PEC in surface water for processing (proc.) and the distribution of the regional background PEC for all life cycle stages together (regional) in the standard scenario. The top diagram in addition shows the distribution of the available measured data (measured). In the lower diagram, the distribution of the local PEC-processing in surface water for alternative scenarios is shown: applying a dilution factor of 2 instead of 10 (Dil=2), applying a dilution factor of 2 and leaving out the sewage treatment plant (no STP/Dil=2), and applying a dilution factor of 10000 instead of the TGD default of 10 (Dil=1E4). The line 'max PEC' shows the deterministic PEC estimated according to the TGD/EUSES. The distributions are based on uncertainty in substance-dependent parameters and not in environmental or scenario-dependent parameters (from Jager et al., 2000)

Complex mixtures

Cumulative exposure can be defined as the total exposure, whether or not aggregated, to two or more substances with the same mechanism of action, e.g. organophosphorous pesticides. This is not addressed in the TGD except in a discussion of the environmental risk assessment of fractions of petroleum substances (Hydrocarbon Block Method), which has also been implemented in EUSES.

Classical examples are PCBs and dioxins. As far as we know today, the most toxic dioxins act through the same mechanism and their relative activities have been determined. This means that the sum effect of a complex dioxin mixture can be estimated by applying these factors to the concentrations of the individual compounds. Some of the PCB congeners act through the same mechanism as the dioxins, and equivalent factors have been determined for these as well. There are, however, other effects connected to other PCB congeners and the evaluation of the effects of PCBs becomes quite complicated.

If it is difficult to judge the risks associated with one pure substance, it becomes more difficult if it contains impurities and even worse if the product to be assessed is a complex mixture of a number of different compounds. General problems with mixtures are that they may have different compositions from different producers and may even vary over time from the same producer. When environmental levels are to be assessed, the composition can again be quite different due to the varying fate of the components in the mixture. The implication of this is that it is difficult to compare lab analyses of the commercial mixture and the compositions found in the environment.

One of the prioritised "substances" for a EU RA was short chain chloroparaffins, which comprise a mixture of probably thousands of compounds. The chain length of the compounds in this group normally varies between 10 and 13 carbons and their chlorination degree varies over a very wide range. Little is known of these substances as very few (if any) are prepared in pure form. Different products with different chlorine content have been shown to behave differently in the environment and to give rise to different biological effects. The resulting ratio of the predicted environmental concentration to the predicted no-effect level (PEC/PNEC) may therefore not be comparing like with like.

Procedures and criteria for developing protocols for risk assessment of chemicals in combination and to assess the environmental exposure to complex mixtures are at present under development (Vighi et al., 2001; Grimme et al., 2000)

Aggregate exposure

The TGD states that in some cases all three types of human exposure estimates (i.e. consumer/worker/environmental) may contribute to an overall value, which will then be considered in the risk characterisation. Aggregate exposure assessment can be defined as a process for developing an estimate of the extent of exposure of a defined population to a given substance by all relevant routes and from all relevant sources (Olin, 1998). An important issue here is the varying levels of exposures over certain time periods and at different stages of the life cycle of a chemical. No guidance on how to conduct an aggregate exposure assessment is given in the TGD except for limited guidance on the calculation of the total human dose from several sources and by inhalatory and oral routes in the estimation of exposure through the

environment. The consumer exposure assessment in EUSES allows for the calculation of an aggregated dose for the oral, dermal and inhalatory routes on an acute or (sub)chronic time scale. Aggregate exposure can also be relevant for organisms in the environment, e.g. food chain exposure of predators in addition to direct exposure to pesticides.

Formation and degradation

The environmental levels of a given substance depend on emissions and on the formation and degradation of the compound in the environment. Precursors may degrade to form the substance of interest, so the levels of the precursor and its transformation rate become of interest. An example of this can be seen in the RA report on nonylphenol. The major source of this compound in the environment is the degradation of nonylphenol-ethoxylates, and this transformation was appropriately taken into account in the report.

The degradation of the investigated substance is measured in specific test systems and the results permit a comparison of the relative stability of different substances in these systems. However, conditions in the environment may differ greatly from those in the test systems and processes other than microbial degradation may be more important.

The problem of metabolites has been taken into account for plant protection products in the implementation of EU Directive 91/414/EEC concerning the placing of plant protection products on the market. Guidelines for assessing the risk to humans and the environment from major metabolites of pesticides have been proposed (EC 2000a, EC 2000b).

A serious limitation in Regulation 793/93 is that substances are defined as "chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the product and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition". Thus, there is no mention of degradation products, which can be a problem for some compounds. There are a number of situations where e.g. a metabolite is the biologically active component, and if this is formed to a high degree the risk may be higher than indicated by the presence of the assessed substance. The metabolism of DDT to DDE is a classic example of this. In the TGD it is, however, mentioned that "if stable degradation products are formed, these should be assessed as well".

Another example is the organophosphate Trichlorfon (active ingredient trichlorvos), which was used in solution in sea cages to control sea lice on farmed Atlantic salmon in Norway. Its degradation product, dichlorvos (trade name Nuvan), was later and more widely used directly for lice control. Trichlorvos was typically dosed at 300 mg/l and dichlorvos at 1 mg/l. Because trichlorvos degrades rapidly (within minutes) in open water in warm sunny summer conditions to its 100 times more toxic degradation product, several mass mortalities of farmed salmon occurred (reviewed by Costello 1993).

Another problem is when there are other sources for the assessed substance than its use as a chemical. This situation has been described in the RA report on acrolein, where motor vehicle exhausts represent a larger source than the intentional use of the substance. In such cases, an aggregated approach is necessary and all exposure routes have to be taken into account.

Sinks

Some environmental compartments may be temporary or permanent sinks for some classes of chemicals. Cationic organic compounds (e.g. paraquat or other cationic herbicides) are strongly bound to clay and are practically immobile in soil. Highly hydrophobic chemicals are also strongly bound to soil, even if, for volatile or semivolatile organic compounds, transport may occur through a series of volatilisation and re-condensation processes, the so-called "grasshopper effect", reaching sites very far from emissions (Wania and Mackay, 1996).

The real sink, for the global distribution of hydrophobic chemicals, is represented by deep, mainly oceanic, sediments, where cycling and remobilisation through physical, chemical and biological processes may be assumed to be negligible. Freshwater lakes and estuarine sediments represent more temporary sinks for persistent chemicals.

Even the atmosphere may be a sink for very volatile persistent chemicals if the condensation temperature is very low. In these cases, chemicals may be trapped in the higher atmospheric layers without further condensation at the surface of the earth. It is worth noting that the trapping of chemicals in the high atmosphere does not necessarily exclude environmental problems. The case of CFC reactions with stratospheric ozone is the most significant example.

A reliable quantification of temporary and permanent sinks may be a problem for the mass balance of chemicals. It must be taken into account, particularly for highly persistent compounds.

Population subgroups

Specific subpopulations such as children, people on special diets, teenagers or the elderly are not mentioned in the TGD and consideration of these groups is apparently left to the judgment of the risk assessor. Oral exposure, particularly pica behaviour, and the dermal exposure of children should be considered.

A major source of variability arises from the differences between individuals and the uncertainty associated with the delivery of the chemical to the target (toxicokinetics) or the inherent tissue response to the presence of the chemical (toxicodynamics). Great inter-individual differences particularly in the potential and capacity for metabolising xenobiotic compounds should be taken into consideration in the risk assessment. This is a field where more research is needed.

POSSIBILITIES FOR REFINING CRITICAL EXPOSURE DATA

Data quality

In general, the TGD approach advocates a tiered assessment procedure, starting with a screening risk assessment and, depending on the availability of input data and the outcome of the risk assessments, proceeding to risk management either directly or via one or more refined risk assessment stages. Further refinement should normally lead to a reduced PEC/PNEC ratio or an increased Margin of Safety. If the outcome of the overall assessment is that the substance is "of no concern", the risk assessment can be stopped. If, in contrast, the substance is "of concern", the assessment should be further refined or, where this is not possible, risk reduction strategies should be developed.

The quality of the data used in the exposure assessment may be different at different levels of this procedure. In the first (screening) tier, a worst-case situation is examined, using the highest exposure ever measured or predicted. If there is still no reason for concern, and the database covers the possible routes of exposure, there is no need for refinement if the data are expected to be "reasonably" accurate.

The proper use of exposure data would thus be facilitated if they were accompanied by a quality parameter. Many of the monitoring programmes incorporate extended quality control programmes, including intercalibrations between laboratories. This will not apply to most of the data used in risk assessments and a more pragmatic approach or protocol would be welcome.

For measured data, the quality depends on both the sample and the accuracy of the measurement. The sample quality is difficult to describe, but the critical information is what the sample represents. What is the variability in time (over age, time, seasons etc), in space (character and homogeneity of matrix, homogenates, distance to sources etc.)? This is difficult to describe with a limited number of parameters, but given that the proper use of measured data depends on such information on the sample, these descriptors would still be very useful. CSTEEN encourages experts in this field to try to develop such simplified sample descriptors, which would be very useful not only in the risk assessment field.

The quality of the measurements is easier to describe and, as already mentioned, there are well-developed schemes for this purpose. These are, however, in most cases expensive and can be applied only to long series of measurements, e.g. monitoring programmes. Most of the measured data used in exposure assessments come from shorter series with no provision for advanced quality control. In this case, there are several factors that can be used to rank quality and this information should be attached to the results. These factors may include whether the laboratory has an accreditation for the measurement, whether recovery experiments are given, whether the method used has a built-in quality measure, whether the method has been intercalibrated and so on. It may be possible to weight such factors in an index providing a rough estimate of the quality of the results. This index should then accompany the data (also in databases), thus improving the prospects for their proper use. Any initiative in this field would be encouraged by the CSTEEN.

The quality of model-predicted exposure data depends on the quality of the input data, which exposure assessors have to judge themselves. The model itself has probably been validated for

chemicals within certain ranges of properties. If the program could warn users if they were applying the model in non-validated ranges, this would indicate that the result might be of a lower quality.

Monitoring and survey strategies

There are monitoring activities on different geographic scales ranging from global to local, and sometimes, but not always, data from the smaller scale are also fed into the larger-scale programmes. Lack of coordination is one of the reasons why local data cannot always be used in larger-scale data sets. In most cases, the restrictions are due to differences between the samples used, but sometimes the measurements may not be comparable. In the design of any measurements, it is thus very important to have a wide view of where the results can be used. This may influence the sampling strategy and a small adjustment may significantly increase the use of the results. It also has to be pointed out that for many of the classical persistent substances there may be little need for local measurements.

The measurements in monitoring programmes often focus on single substances or rather narrow groups of substances. These choices are governed by several factors, scientific knowledge being just one. The political (=public) awareness of a potential problem is probably the most powerful factor. A broader view would in most cases allow for more parameters to be included in a programme. The techniques used for the measurements will very often be able to measure several other chemicals as well, at little extra cost. In the planning of monitoring activities, it is therefore recommended that compounds with a high RA priority are included as far as possible.

In order to increase the use of the data produced in a monitoring programme, the existence of the data must be widely known. The most effective way to make data available is via the Internet, and the number of Internet databases with monitoring results is increasing. Unfortunately, the structures of these databases are very different and it is not easy to compile data from more than one of them. Efforts to harmonise these structures would therefore be most welcome. The importance of information on the sample and on the accuracy of the measurement has already been discussed above. It is important to remember that data do not have to be of the highest precision to be of use in different applications. It would, however, be very useful if at least the accuracy could be estimated in order to avoid improper use of the results.

Initiatives to ensure compatible database structures probably have to come from the larger-scale levels. A dialogue with regional and local levels may lead to improvements, but it may be a slow process. It is difficult, and perhaps not useful, to change the structure of established databases. The solution may be to build another database with a structure that is more compatible with other databases, or it may be possible to transfer information to another existing database. An agreement on general structure would at least improve the prospects for greater compatibility between new databases. An activity recently launched under the United Nations Environment Programme (UNEP), called "Global Network for Monitoring of chemicals in the environment", may provide a good platform for discussing the harmonisation of monitoring databases.

There is also a need for a meta-database describing sources of data. Several such databases exist already, but to our knowledge none of them cover a broad range of sources. One of these could be developed into a "universal" data node, or a new database could be established. The

Organisation for Economic Co-operation and Development (OECD) is currently building a database describing environmental monitoring programmes, which provides a starting point for a meta-database. Another OECD project, which has been running for several years, is EXICHEM. This database contains information on all kinds of activities involving chemicals in the Member States, including monitoring and risk assessments. Although this very useful information source is available on the Internet, surprisingly limited use seems to be made of it.

In spite of the efforts to publish data on the Internet, a large proportion of the results end up in grey reports. Often only few people read or know about them and the data are not available for others who may have use for them. If, for some reason, the data do not fit into a widely available database, the report itself should be put on the Internet. As most of the documents produced today are at some point in an electronic format, this is not very difficult. The EU RA reports should also be made freely available on the Internet, considering the amount of work required and the often unique nature of these documents.

Refinement of models

In the tiered approach, exposure estimations can be improved by the generation of more representative monitoring data or through refined modelling. Such refinements include:

1. More appropriate, sometimes measured, default parameter values. Care should be taken to bear in mind the generic nature of many exposure assessments: the application of very specific default values may leave out relevant exposure scenarios or populations at risk.
2. More appropriate QSARs or measurements, e.g. for the estimation of partition coefficients, bioconcentration factors and degradation rate constants;
3. Exposure models more adapted to the relevant exposure scenarios and the type of substance. Any model proposed should fulfil a number of criteria (adapted from Jager, 1998a):
 - the model must be properly documented and analysed,
 - the model should have the appropriate time and spatial scale,
 - the application range of the model and other limitations must be complied with,
 - the mathematical relations and the conceptual and theoretical background must be known,
 - the expected degree of uncertainty and the sensitivity of the model to input must be known,
 - there should be support for the assumptions made and for the values of the default parameters used.

Recently, some approaches have been developed to apply fugacity-based multimedia models to ionisable organic chemicals (Shiu et al., 1994). These approaches use the pK_a of the chemicals and the environmental pH to assess the fraction of the ionised chemical and to apply different partitioning schemes to the dissociated and undissociated fractions. These methods seem promising but need to be experimentally validated. A modified fugacity-based approach (fugacity/equivalence) has also been developed by Mackay and co-workers to predict the environmental distribution and fate of inorganic chemicals (Mackay and Diamond, 1989; Diamond et al., 1992; Mackay et al., 1996b).

Probabilistic models versus worst case

In the TGD and the underlying legal framework, the level of "risk" is characterised as the deterministic quotient of exposure and effects (PEC/PNEC or Margin of Safety). This quotient is considered to be the 'reasonable worst case'. As the data set for these risk assessments is usually narrow, a considerable degree of uncertainty accompanies these calculations. From a scientific viewpoint, this uncertainty should be taken into account explicitly in decision-making. If the aim is a more realistic and defensible risk assessment, the assessment should not be limited to a worst-case approach. Of course, we need to be protective when dealing with the environment and human health but these considerations belong to the risk management stage, where the discussion should take place on what level of risk is still acceptable (e.g. by selecting a high percentile from the risk distribution). If we wish to remain on the safe side because the chemical may have impacts we have not considered (such as suspected endocrine effects, based on structural similarities), this is part of risk management and should be dealt with there, e.g. by applying the precautionary principle. Risks cannot be estimated for an impact for which no relevant data exist (Jager et al., 2001).

Even though it may be complicated, attempting to quantify uncertainties is a good step in that direction. Changing the well-established 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. Although this is partly true, one should consider the vast body of literature data available. It is possible to use data for other chemicals to improve the risk assessment in a statistical way. This has already been extensively (though not exhaustively) demonstrated (Jager et al., 1997; Vermeire et al., 1999). Even a rough quantification of uncertainties is better than giving a false sense of accuracy.

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 the chemical industry to learn their views 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. To summarise, there seemed to be a guarded interest in uncertainty analysis among most of the people interviewed although it does not currently have a high priority. These interviews made clear that there is a gap between the scientists and the risk managers. In the scientific community, it is broadly accepted that confidence intervals have to be provided when presenting secondary data. As a logical consequence, uncertainty analysis is broadly accepted as necessary in order to present 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 frame. 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 communities: it must be demonstrated transparently how risk management can benefit from the extra work needed to determine and understand probabilities.

Comparison between predicted and measured data

The TGD calls for a comparison between measured and modelled data. If the differently derived values are not in agreement, analysis is required together with a critical discussion of the approaches used. For a thorough analysis, the following is important:

1. It should be recognised that in many cases the modelled results are partly based on measured emission rates, bioconcentration factors, partition coefficients, concentrations in specific environmental compartments, feed or food, etc. The more measured data are used in place of model results, the more the (representative) measured and final model results should agree.
2. Measured concentrations often vary considerably from place to place and over time due to changing emission and use patterns. Measured data should be representative for the exposure scenario considered. Model results are also affected by uncertainty or variability in substance-specific parameters, scenarios and models (see also Fig.4)
3. Modelled results usually only consider exposure from specific anthropogenic stages in the life cycle of a substance such as production, processing and use. Measured data also take into account unintentional sources, e.g. incineration processes and natural background levels. Background levels may be caused mainly by such unintentional sources, so natural background levels should be taken into account in risk assessment and risk management.
4. For a proper comparison between measured and modelled data, the rapporteur needs to make a thorough analysis of the representativeness and quality of the measured data, the nature of the exposure model scenario and the uncertainty in both the measured and modelled results.

Emissions from the downstream use of chemicals

The production of a specific chemical is today often concentrated among a few large producers. The emissions from these large facilities are in most cases well controlled and measured. There are also numerous models describing emissions from large-scale chemical processes and the estimates of emissions from production can often be relatively realistic.

The use of these primary chemicals to produce other products is more often spread between a large number of companies and locations. These produce a number of different products utilising different processes and a number of emission scenarios have to be taken into account. In the present version of the TGD, there are a number of scenarios available for such processes (use categories). Producers and importers often claim that they have limited knowledge of the downstream use of their chemicals. Contact within the major use categories is therefore an essential part of exposure assessment.

If the chemical is intact in the final product, the emission pattern becomes more and more complex as the products are distributed and used in different applications. This is further accentuated if products containing the investigated chemical are also imported. Information on chemicals in imported goods is very limited. It is, however, the total exposure to a chemical that determines the risk, independently of where it is produced, and therefore the imported amount has to be estimated as well.

The amount (and probably also the number) of chemicals used in our society is continuously increasing, as is therefore the importance of diffuse emission. Not only this year's production but also that of the last couple of years will emit these chemicals, depending on the life cycle of the products. If the chemical has a long half-life in the receiving compartments, part of the dose from previous years will remain and has to be taken into account.

Many of the chemicals used in technical products will be emitted in indoor environments, with humans one of the prime targets. The exposure to volatile organic compounds has been fairly well studied, but data for compounds with higher boiling points are scarce. The role of the dermal and oral exposure routes is also less investigated for substances contained in products. The observations in the assessment of pentabromodiphenyl ether (a flame retardant) that environmental levels seem to decrease while concentrations in human breast milk increase raise questions regarding human exposure routes.

A large number of chemicals have been found in sewage sludge from residential areas, reflecting the wide use of these substances. The inhabitants in the area have most probably been exposed to these chemicals to a more or less greater extent. Part of the sludge is used in agriculture, also exposing the environment and thus humans indirectly.

Products ending up in landfills may be also be a source of chemicals in the environment. If the products start to leak or emit chemicals or if the matrix is broken down faster than the additives, there is a risk of environmental pollution.

Aggregate exposure assessment

All relevant exposure routes have to be taken into account in an exposure assessment for a chemical substance. This is especially important for chemicals with many use patterns and for chemicals that can be formed by other chemicals or natural processes.

Many chemicals have several different use patterns. It is often difficult for the assessors to identify all these, while producers cannot always help as they do not know all the downstream uses of their products. For a high-volume chemical such as diethylhexyl phthalate, there is a risk of focussing exclusively on the major use (98% as a plasticiser in polymers). Its use as a film-forming agent and solvent in cosmetics is a very marginal part of the volume, but may be an important route for human exposure.

There is also a risk that the assessment of chemicals used in cosmetics or medical devices will focus solely on these exposure routes and disregard all other paths. It is important to take the whole picture into account and try to estimate the sum of all exposure components.

The exposure for a certain chemical can be due to sources other than the production or use of the chemical as such. An example from the previous RA reports is the formation of acrolein in combustion processes, especially in car engines. This is probably on a much larger scale than emissions from the use of the compound as a chemical. The total exposure is not dependent on the latter source, so if the risk associated with the use of acrolein as a chemical is to be assessed, the other sources must be taken into account as well.

A similar situation is encountered where there is a natural background level of the investigated compound. It is the sum of the background exposure and the contribution made by the use of the chemical that has to be assessed.

It is also essential that the environmental and human exposure assessments are integrated as far as possible. Information on secondary poisoning in the environment can e.g. often be utilised in the exposure assessment for humans. It is also possible that information on the behaviour of a chemical in laboratory animals can be used in the assessment of environmental fate of the substance.

CONCLUSIONS AND RECOMMENDATIONS

The exposure assessment is probably the most critical part of the risk assessment procedure. The combined use of predicted and measured data is an art, and the assessor often has significant difficulties in judging the available data. The text above has pointed out some weaknesses in the present procedures, and some suggestions for improvement are outlined in this section.

Sources

Further work on Industry Category Documents is needed, and here the importance of contributions from industry is obvious, e.g. through the LRI project. Emissions of a chemical throughout the whole life cycle have to be considered, including releases from unintentional point and diffuse sources. Good information on downstream use is essential. There is a need for improved knowledge regarding the emission of chemicals from products, and chemicals in imported goods also have to be taken into account. The importance of these points should be stressed in the new version of TGD, but obviously more research is needed in this field.

Sources of a substance other than its production and use as a chemical have to be taken into account in the exposure assessment. The present TGD food basket does not include sea fish or meat other than beef, nor does it contain any imported food. The currently used human environmental exposure scenario does not take account of dermal exposure or soil ingestion. All these things could be improved in the TGD.

Environmental fate

Differences in environmental conditions between the European regions have to be taken into account. Instead of the present "standard environmental characteristics" in the TGD, European environmental variability could be better covered by choosing parameter values for e.g. three scenarios: a Central European, a Nordic and a Mediterranean situation. For higher-tier assessments, uncertainty analysis using probabilistic techniques could be considered. With regard to degradation, further research is needed into the prediction of environmental degradation rates from laboratory tests. Anaerobic degradation of some classes of compounds has to be taken into account, and this should be included in the new TGD. The possible risk of groundwater contamination has also to be considered in the risk assessments.

Exposure models

The models used in any risk assessment must be properly documented. Validation of assumptions, choices and theories is essential, as is a functional validation by comparing model results with the results of other models and measurements. Model software should be thoroughly tested as well. Specifically, consumer exposure models are in need of such

validation. It is also obvious that the analogue exposure model for workers needs updating. Uncertainty analysis should reveal the main sources of variability and uncertainty as well as the sensitivity of the model to input.

Models should be applied on the appropriate time and spatial scale. Consumer exposure models currently lack databases with consensus default values for data on product use, contact and concentrations in products. The development of such databases is strongly recommended.

Furthermore, the application range of the model and other limitations must be complied with. Ideally, the model software should provide a warning when it is used outside its valid range. The importance of these factors should be pointed out in all risk-assessment guidance documents. More guidance is needed on the risk assessment of the so-called difficult substances such as highly polar and lipophilic substances, ionics, surface-active substances and organometals.

Measured data

There are a lot of monitoring activities being carried out, but the use of the resulting data is often limited to the respective programmes. There is a need for better harmonisation, and new substances should be included to a greater extent. A more targeted approach is recommended. A consequence of this may be that some of the ongoing measurements have to be reduced or terminated. The need for good communications between the risk assessment and monitoring communities is obvious.

There is a need to know the quality of measured data, and the development of a "representativeness index" for the sample and a "quality index" for the measurement is suggested. It is not within the scope of this report to suggest how this could be done, but a dialogue between the stakeholders is essential in this development. Ideally, this should be held in a global context (UNEP/WHO/ILO), but the responsible organisation within the EU would be the European Environment Agency (EEA).

To improve the possibilities for retrieving measured data, they should be made accessible via the Internet and the databases should be better harmonised. A global meta-database for measured data should be developed, for which the OECD database EXICHEM could provide a starting point. Again, the EEA would be the natural focal point within the EU.

General comments

To make the risk assessment as transparent as possible, it is important that there is support for the assumptions made and for the values of the default parameters used, and as few data as possible (if any) should remain confidential.

A weakness in the present TGD is the limited attention paid to vulnerable subgroups, such as people with particular diets (e.g. vegetarians, people with metabolic diseases, those who eat large amounts of fish). Children need special attention, and dermal contact and ingestion e.g. of soil should be included in the new version of the TGD.

Predicted and measured data should always be compared, and disagreements discussed. This is already stated in the TGD, but not always done in practice. The scope for improving our knowledge from all the efforts spent on assessments should not be underestimated.

The use of probabilistic risk assessment should be considered. A comparison of deterministic and probabilistic risk assessments should be carried out for a few chemicals to demonstrate the advantages of the two methods.

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