GOVERNMENT/RESEARCH COUNCILS INITIATIVE ON RISK ASSESSMENT AND TOXICOLOGY

Exposure assessment in the evaluation of risk to human health

Report of a workshop organised by the Risk Assessment and Toxicology Steering Committee

The Risk Assessment and Toxicology Steering Committee aims to stimulate the development of new, improved approaches to the assessment of risks to human health from chemicals.

The Committee takes forward the work of the Government/Research Councils Initiative on Risk Assessment and Toxicology. The Initiative was established in response to a statement in the 1995 UK Government *'Forward Look of Government Funded Science, Engineering and Technology'*, which recognised the inherent limitations of current procedures and committed the Government to pursuing opportunities presented by scientific advances.

The Steering Committee comprises participants from the Department of the Environment, Transport and the Regions, the Department of Health, the Department of Trade and Industry, the Home Office, the Ministry of Agriculture, Fisheries and Food, the Environment Agency, the Health and Safety Executive, the Medicines Control Agency, the Pesticides Safety Directorate, the Veterinary Medicines Directorate, the Biotechnology and Biological Sciences Research Council, the Medical Research Council, the Natural Environment Research Council and the Institute for Environment and Health.

The secretariat is based at the Medical Research Council's Institute for Environment and Health.

The Risk Assessment and Toxicology Steering Committee operates as a subgroup of the Interdepartmental Liaison Group on Risk Assessment.

The Interdepartmental Liaison Group on Risk Assessment is an informal committee of officials responsible for policy development and practical application of risk assessment in UK Government departments. The group reports periodically to Ministers on a co-ordinated programme to promote consistency and coherence in risk assessment practices across Government.

This document is a report of a workshop held in Leicester on 23–24 September 1998. Opinions and recommendations expressed are those of the participants. The Government/Research Councils Initiative on Risk Assessment and Toxicology's Steering Committee will consider the recommendations further before making its own proposals for future work.

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Contents

Executive summary

A workshop was convened by the Risk Assessment and Toxicology Steering Committee to explore issues associated with exposure assessment in the evaluation of risk to human health. The aims of the workshop were to:

- identify and compare current approaches to exposure assessment;
- identify and explore key issues of concern; and
- identify possible areas where research should be undertaken in order to improve exposure assessment.

To facilitate a debate of these issues, background papers were presented at the workshop on current and potential new approaches for exposure assessment of chemicals in food and consumer products, water, soil and air, and the occupational environment.

A number of specific questions were discussed, resulting in the conclusions and recommendations summarised below.

- Generic exposure models should be developed for screening purposes, directed both at chemicals and at pathways of exposure. The value of personal exposure measurement rather than generic measurement should be considered.
- Probabilistic methods, such as Bayesian, fuzzy arithmetic and simulation of the entire population, should be evaluated and developed to investigate whether these might have advantages over Monte Carlo approaches to risk assessment, either generally or in particular circumstances.
- Exposure data should be collected on susceptible groups in the population and a survey of data sources should be conducted.
- Models are needed for dealing with total exposures to particular chemicals and mechanisms should be developed for addressing mixtures, both in terms of evaluating their toxic effects and in terms of exposure estimation.
- Models for dealing with uncertainty in exposure estimates and guidance on their interpretation should be developed; models are also needed for dealing with bioaccumulation in estimating exposure and in risk assessment.
- Communication with the general public, including susceptible groups within the population, should be improved. Presentational aspects, for example visual displays, should be considered.

Throughout the exposure assessment process there is a need for a more harmonised approach and better pooling of expertise, and for improved clarity and transparency regarding both the choice of procedures, models and other factors to be used in the assessment and the communication of the outcome. To this end it is recommended that Government departments establish a specific forum to address issues common to all departments. Suggested issues for such a forum include:

- harmonisation of approaches where feasible;
- development of guidelines;
- ensuring that total exposure to a chemical being examined is considered;
- the establishment of multidisciplinary groups, both in terms of media being addressed (e.g., food, occupational, environmental — water, air, soil), and the expertise involved (e.g., toxicology, epidemiology, chemistry, regulatory);
- common approaches to the use of expert judgement; and
- shared methods for communicating with the general public.

1 General introduction

UK Government/Research Councils Initiative on Risk Assessment and Toxicology

A number of UK Government departments have a responsibility for assessing risk to human health from potentially toxic substances that may be found in food, household products, human medicines, the environment or the workplace. Since reliable data from human populations exposed to known levels of a substance are rarely available, except in the case of human medicines, the assessment is generally based on animal data. Such an approach has to accommodate the uncertainties inherent in extrapolating from animals to humans, from high to low dose and from one population to another. The uncertainties in the risk assessment process necessitate the adoption of appropriate uncertainty factors to ensure protection. It is clearly desirable to reduce the uncertainties as far a possible and to secure optimal use of resources.

The uncertainties inherent in current methodologies are widely recognised, as is the absence of scientific knowledge to define them more precisely. Recent advances in scientific techniques, such as use of novel biomarkers, *in vitro* toxicology, molecular modelling and computer simulations, may offer new possibilities. Furthermore, the use of such techniques should contribute to the reduction of animal use and the refinement and replacement of animal tests, a principle to which Government departments and agencies are committed. Government departments, together with the relevant research councils, have decided to make a co-ordinated drive to pursue these important opportunities. Their commitment was set out in the 1995 UK Government *'Forward Look of Government Funded Science, Engineering and Technology'* (HMSO, 1995) and resulted in the establishment of the Government/Research Councils Initiative on Risk Assessment and Toxicology in 1996.

The work of the Initiative is being taken forward by the Risk Assessment and Toxicology Steering Committee, which comprises participants from relevant Government departments and research councils and is co-ordinated from the Medical Research Council's Institute for Environment and Health. The Initiative aims to stimulate research so that new, improved approaches to chemicals risk assessment can be developed. It does not have its own research funds, but provides a focus, co-ordination and positive encouragement for research financed by individual Government departments or research councils (or consortia of these bodies).

The Steering Committee has organised a series of workshops on different aspects of risk assessment, with the aim of bringing together regulatory toxicologists, policy-makers from government and experts from academic institutions and industry to develop research specifications.

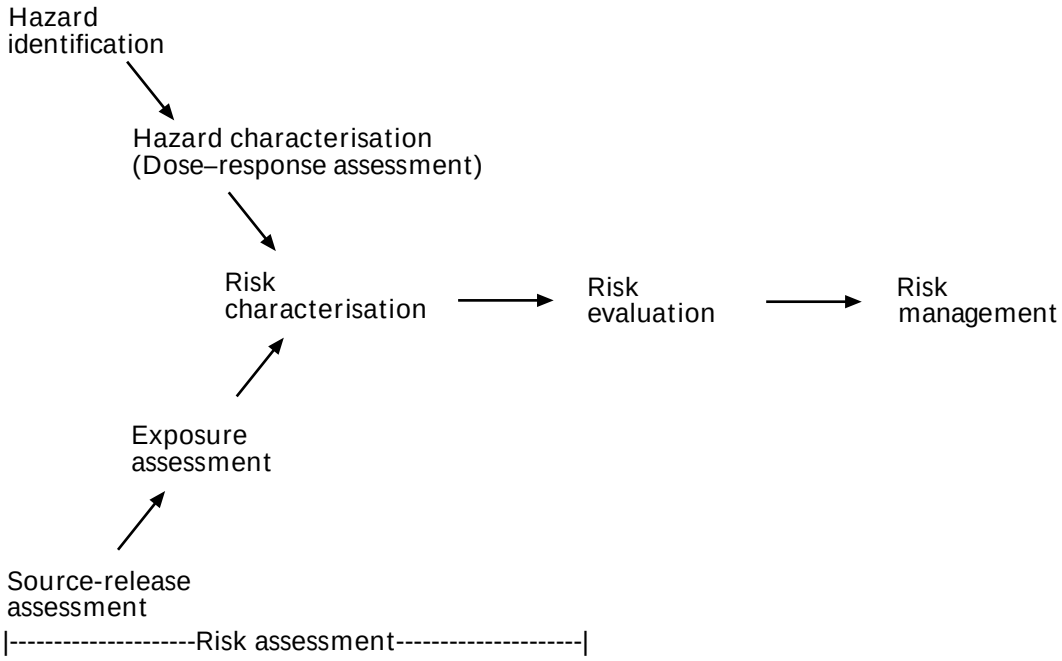
This report is based on a workshop, held in Leicester, UK in September 1998, to examine issues associated with exposure assessment in the evaluation of risk to human health.

Basis for the workshop

Current risk assessment and management practices

A generic approach to current risk assessment and risk management practices in the UK is outlined in Figure 1.1. It can be seen that *exposure assessment* is an integral part of the risk assessment process. In the first stage, *hazard identification*, the known or potential health effects associated with a particular agent are identified. In the second stage, that is the dose–response assessment or *hazard*

Figure 1.1 Generic approach to risk assessment and management



characterisation, information (from laboratory studies, controlled studies on humans and epidemiological studies) on which effects occur at which levels of exposure is used to define the dose–response relationship for the agent in question and to determine levels of exposure that are deemed to be without appreciable risks. This hazard information is integrated with the exposure assessment, that is information on current or predicted exposures within the population, to characterise the risks to the exposed population. The *risk characterisation* is, therefore, a synthesis of the hazard identification and characterisation and the exposure assessment. Source–release assessment is sometimes considered to be part of the exposure assessment.

The next stage, *risk evaluation*, is often considered to be part of risk management. At this stage the outcome of the risk assessment is considered. Other stages in risk management are the *risk management option assessment*, where available management options are identified and the preferred option chosen, the *implementation* stage and, finally, the *monitoring and review* stage, where the effectiveness of the risk management action is checked. Risk management includes economic and social considerations and at this stage a decision is made on whether it is necessary to manage the risks. The risk management options may take a number of forms; for example, a chemical may be banned, permitted for use only under certain conditions or in specified circumstances, or standards may be established either for the sources of exposure (e.g. emission standards or maximum residue limits) or as limits or guidelines on exposure itself (e.g. acceptable daily intakes, environmental quality objectives and occupational exposure limits).

Exposure information

From the description above it can be seen that exposure information is considered at two stages. The first of these is at the exposure/dose–response assessment stage; it is here that information on exposures causing particular effects is examined and the dose–response relationship established. Epidemiological data considered here will include information on exposure. The second point at which exposure information feeds into the process is at the exposure assessment stage, and this is the focus of this report.

The European Commission (EC) Guidance on Risk Assessment for New and Existing Substances (EU, 1996) states that the objective of the exposure assessment is to predict the concentration profile or dose of a substance to which the receptor will be exposed. For human health exposure assessment this involves evaluating occupational, consumer and environmental exposure. For environmental exposure, the assessment should, in principle, consider all stages of the life cycle of a substance, from production, through use, to disposal and recovery.

Exposure to a chemical may be a result of topical administration (e.g. of a cosmetic or toiletry), through the food chain or drinking water or through the environment. Chemicals may enter the

food chain or drinking water supply as deliberate additives, as residues from pesticides or veterinary products, as migrants from packaging materials, or as contaminants. Undesirable chemicals in food include natural toxicants and degradation or pyrolytic products formed during the cooking process. Chemicals may enter the environment from identifiable point sources, such as industrial plant, or from diffuse sources, and may be transported within the environment. In addition, exposure to chemicals may occur in the workplace. Normally, humans are exposed to mixtures of chemicals. For example, a varied diet is made up of range of foods which may contain a number of different additives. Emissions from motor vehicles consist of a large range of different chemicals, and occupational exposure may be to a 'cocktail' of chemicals being used in the workplace.

The hazard identification and hazard characterisation stages provide information on the pattern and frequency of exposure, for example whether exposure is to intermittent peak concentrations or over a lifetime. These stages will also provide information on whether there are particular periods of raised susceptibility, for example during childhood or pregnancy.

Exposure estimates may be obtained by direct measurement or from modelling. Direct measurements may be made in the medium through which exposure occurs, (e.g. concentrations in food, drinking water, air) or may be measurements of personal exposure, (e.g. intake, personal exposure sampling in the workplace or ambient air). Measurements of personal exposure using biological samples, for example lead in blood, can be useful for assessing total uptake of a chemical where exposure can occur through a number of routes.

In the absence of relevant direct measurements, models can be used to predict likely exposure. These may be simple or complex and may include models that predict exposure based on information on the sources from which the exposures arise. The various ways of assessing exposure have different merits and degrees of uncertainty.

Whether exposure is measured directly or modelled, predictions are made about the exposure of the population in general or of specific subgroups, either as 'average' or 'worst case' exposures. Such predictions may be based on, for example, for dietary exposure:

- an assumption that the maximum permitted exposure occurs from all components of diet;
- an assumption that a subgroup consists of high consumers for a particular component of diet; or
- assumptions concerning frequencies of achieving certain residue levels after a given withdrawal time (e.g. for a veterinary medicine).

Some of these assumptions will be included in the ways in which the exposure information is incorporated into models, for example including high rather than average values, while some may relate to the structure of the model. Clearly there is a potential for multiple conservatism in an overall exposure estimation or risk characterisation and this needs to be addressed.

Aims of the workshop

The purpose of the workshop was to explore issues associated with exposure assessment with the following aims:

- to identify and compare current approaches to exposure assessment;
- to identify and explore key issues of concern; and
- to identify possible areas where research should be undertaken in order to improve exposure assessment.

The workshop addressed the following questions.

- Are current exposure estimates satisfactory? How can measured or modelled exposure estimates be improved? Is there a role for probabilistic modelling?
- Should 'average' or 'worst case' assumptions be used at each stage of an exposure estimation? What are the implications for the final exposure estimate?
- Are there groups (e.g. children, elderly, asthmatics, individuals with unusual diets (vegetarian, fish based, different ethnic diets)) whose exposure is sufficiently different to justify separate exposure estimates? Should these groups be examined separately? How effectively do current default values cover these groups?
- Should there be consistency between media (e.g. air, water, soil, food additives, plant protection products, veterinary medicines) in the ways in which exposure data are collected and analysed? If so, how might this be achieved?

- How should exposure in other media be taken into account when setting standards for a single medium? How can this be co-ordinated?

- How can uncertainty and sparse data be dealt with in estimating exposure?

- How can the ways in which exposure assessment is incorporated into the risk characterisation process be improved?

Workshop report

To provide a background to the discussions at the workshop a number of independent experts made presentations on current and potential new approaches to exposure assessment. These are summarised in Section 2.

The questions listed above were then considered, in whole or in part, by four working groups, each dealing with one of the following areas:

- multiple pathways of exposure;

- exposure assessment and risk characterisation;

- sensitive subgroups in the population; and

- probabilistic modelling.

The conclusions and recommendations arising from a synthesis of the working group discussions are presented in Section 3. The participants in the workshop are listed at the end of the report.

Reference

EU (1996) *Technical Guidance Document in support of the Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and the Commission Regulation (EC) 1488/94 on Risk Assessment for Existing Substances* (CR-48-96-000-EC-C), Directorate-General Environment, Nuclear Safety and Civil Protection

2 Approaches to exposure assessment

2.1 Risk assessment approaches in the UK: A review of exposure issues

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An exercise to look at approaches in the UK to the management of risks from toxic chemicals, undertaken as part of the Government/Research Councils Initiative on Risk Assessment and Toxicology, identified licensing and standard setting as two such activities undertaken by government (Risk Assessment and Toxicology Steering Committee, 1999). For each of these activities one of two main approaches is employed.

In one approach, consideration is given to whether exposed individuals are adequately protected from harm. The aim is to ensure that actual or intended exposures of individuals are lower than some maximum acceptable level (an 'intake' standard). The setting of a standard requires a toxicological risk assessment that identifies hazards and their dose–response relationships, determines an exposure amount (level and duration) that represents a maximum acceptable ('safe'*) exposure and, if necessary, allocates this exposure between its possible sources. The setting of such a standard requires no knowledge of actual or anticipated exposure. The standard is then compared with actual or anticipated exposures, to ascertain whether individuals or subgroups in the population are adequately protected.

In the other approach, the risk considered is that posed by the emission, discharge or leaching of a chemical into an environmental medium, or the presence of a chemical as a residue in a foodstuff. A (sometimes limited) toxicological assessment may have been undertaken to determine the maximum acceptable intake and hence the maximum total amount that can be accommodated in the environmental medium or diet. An 'input' standard (based, for example, on the emission limit, discharge limit, maximum residue limit etc.) may then be developed for the source of the pollutant and compared with measured values. Models are required for describing the movement of chemicals from input source, through the environment or food supply chain, to intake by humans. The mapping exercise conducted by the Risk Assessment and Toxicology Steering Committee indicated that there is scope for improvement in this modelling and for sharing of experience across Government departments and agencies.

Another major discussion area to emerge from the mapping exercise was the degree of conservatism that should be employed in making exposure assessments and, in particular, the appropriate use of 'worst case' and 'best' estimates of exposure. Worst case estimates are not generated for all chemical exposure situations. They tend to be used most where exposure of the general public is involved or where there is scope for an initial worst case estimate to be refined if exposures exceed a specified 'standard'. Where they are used, there is a diversity of scenarios employed by different UK Government departments and agencies.

Many exposure estimates use default assumptions about the anatomy and physiology of the human

* Although the word 'safe' has been used in the context of risk assessment, its use has been avoided, as far as possible, in this document. Similarly, although the term 'safety factor' is commonly used, the term 'uncertainty factor' has been used in this document.

body to estimate intakes. The mapping exercise indicated that default values used vary across Government and internationally.

Individuals may be exposed to a particular chemical from different sources and via different routes. Risk assessments on common pollutants or commonly used chemicals are undertaken piecemeal by different UK Government departments and agencies; in such cases it may be appropriate to consider conducting overall risk assessments for total human exposure.

Reference

Risk Assessment and Toxicology Steering Committee (1999) *Risk Assessment Approaches used by UK Government for Evaluating Human Health Effects of Chemicals*. Leicester, UK, Institute for Environment and Health

2.2 Dietary exposure assessments

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2.2.1 Introduction

Exposure assessment has been defined as:

> The qualitative and/or quantitative evaluation of the likely intake of biological, chemical, and physical agents via food as well as exposures from other sources if relevant (FAO/WHO, 1995).

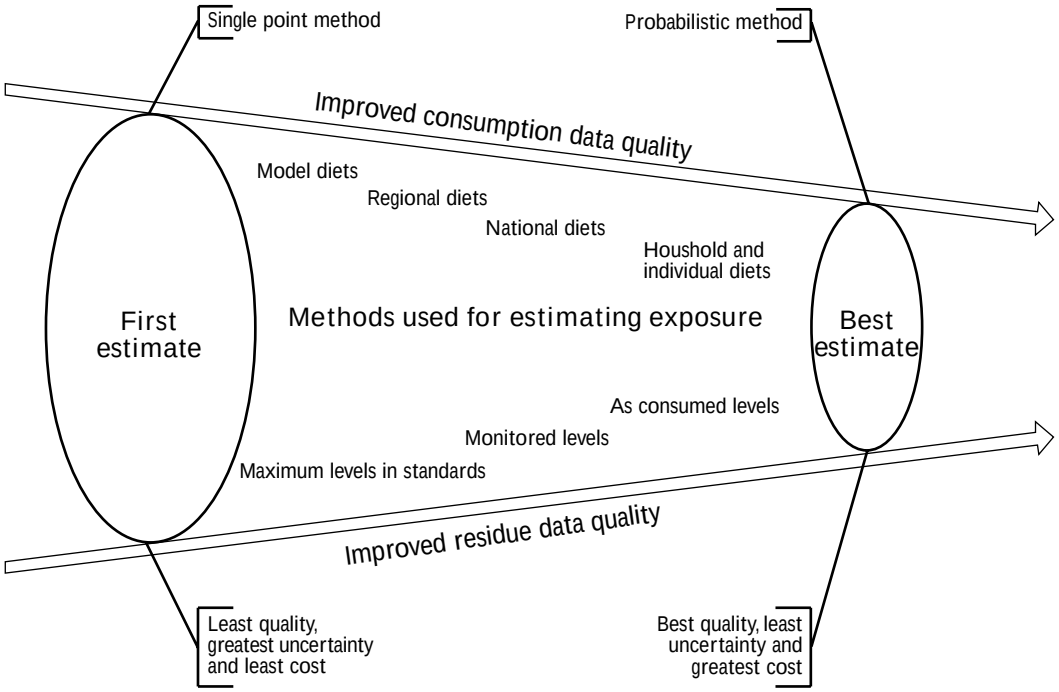
The overall approach for estimating dietary exposure to a chemical is a stepwise progression from relatively simple methods to very sophisticated modelling, distribution or probabilistic techniques. The method selected depends on the quality of information available, the urgency with which the assessment is required, its value to policy development and the availability of expertise to perform such analysis (Rees & Tennant, 1993, 1994).

There are three pieces of information that must be considered, regardless of chemical type, when estimating dietary exposure; namely, the amount of food consumed, the concentration of the chemical in the food and the method used to combine the information. There is a relationship between this information and the quality, uncertainty, and cost of the resulting dietary exposure assessment (Figure 2.1). The first assessment of dietary exposure to a specific food chemical is usually made to ensure that underestimation does not occur. Refinements made in subsequent assessments allow a better estimate of actual dietary exposure with decreased uncertainty in the data, but with extra cost and resource implications (FAO/WHO, 1998).

2.2.2 Expression of dietary exposure estimates

Dietary exposure estimates can be expressed in several different ways depending on how the data are collected, the population group and time frame used. The five most common approaches in assessments of dietary exposure are summarised in Box 2.1.

Figure 2.1 Relationship between sources of data used and quality of the dietary exposure assessment



From: FAO/WHO (1998) Consultation on Food Consumption and Exposure Assessment of Chemicals

* The author is grateful for the statistical assistance of Mr Day and Mr Gay in exploring these techniques

Box 2.1 Approaches in assessments of dietary exposure

'Per capita' approach The dietary exposure estimate reflects the average amount of a substance available to a member of the population usually over an average year. This approach has limited use in risk assessment because 'high consumers' can have an exposure several times greater than the average.

Total-Diet survey approach The dietary exposure estimate is based on an 'average' diet derived from studies of households. It does not describe the possible distribution of exposures by individual consumers.

Critical group approach The dietary exposure estimate is based on a group of individuals assumed to have the highest exposure. Subgroups of the population may be classed as being a 'critical' group due to their geographical location, higher susceptibility or consumption, or greater exposure to other, non-food sources.

High-level approach The dietary exposure estimate is based on the top end of the distribution of a representative sample of consumers. The underlying assumption is that dietary habits giving rise to dietary exposure higher than the 97.5th percentile are unlikely to be maintained over a significant part of the individual's lifetime.

Worst-case approach The exposure is estimated using worst case assumptions; for example, all relevant food in the diet contains the chemical at the maximum level. If such an estimate falls below the level of concern then it usually means that further work is not required. Resources may then be focused on more complex or urgent issues.

2.2.3 Methods for estimating dietary exposure

The basic methodology for estimating dietary exposure is fairly well established in the UK (Rees & Tennant, 1993, 1994). Distribution analysis techniques are increasingly used to make more realistic estimates of dietary exposure (Petersen & Barraj, 1996; Parmar *et al.*, 1997; FAO/WHO, 1998). This section describes an example of how such techniques could be developed further.

There are several reasons why more sophisticated methods such as modelling, distribution or probabilistic analysis are being considered for estimating dietary exposure.

- Increasingly more detailed questions are being asked by UK expert committees. Knowledge of the distribution of exposure may facilitate characterisation of those consumers who are at a greater risk of exceeding acceptable limits.

- Exposure may need to be assessed over short periods of time. Existing approaches do not take into account the probability that a high concentration will be found in the food eaten by the high-level consumer within a day or meal.

- There is increased need to consider ranges found from surveillance activities, rather than the average level, in order to support any regulatory action.

There are advantages and disadvantages in using such sophisticated methods to estimate dietary exposure, and these are summarised in Table 2.1.

2.2.4 Modelling approaches

Two modelling approaches are currently being developed. The 'distribution data model' estimates exposure by taking into account the distribution of consumption with the distribution of chemical concentration found in the relevant foods. The 'duration data model' estimates exposure over shorter or longer periods of time than the original dietary survey. It should be noted however that it is not always appropriate to use these techniques.

In the theoretical example below the consumption pattern data are taken from the 1986 dietary survey of infants aged 6–12 months (Mills & Tyler, 1992). This survey involved recording, over seven days, all food eaten by 258 infants aged 6–9 months and 230 infants aged 9–12 months. Of the 488 infants, 410 were recorded as having eaten manufactured baby food. The chemical concentration data were derived from a survey of baby food purchased from retail outlets according to market share.

Table 2.2 summarises the factors considered when developing these modelling techniques.

Distribution data model

The distribution data model considers the distribution of consumption values with a distribution of chemical concentration values in order to make a more realistic estimate of dietary exposure (Petersen & Barraj, 1996; Parmar *et al.*, 1997).

Table 2.1 Advantages and disadvantages of using modelling techniques for estimating dietary exposure to chemicals

Advantages	Disadvantages
Acknowledged as useful tools for addressing more complex problems	Require a considerable amount of time and expertise and are reliant on large quantities of reliable data
Can be based on, or mimic, what actually happens 'in real life'	Decision managers are not usually familiar with probabilistic concepts
Facilitate identification of effective risk management options	Can be difficult to formulate risk management options if the uncertainty in the estimates is high
Can provide additional assurance about food 'safety', particularly for subgroups of the population	Methods of communicating these more complex analyses to the general public need to be developed
Have advantages for making more realistic estimates of exposure and supporting risk communication and risk management activities	Detailed information is required from a range of disciplines, e.g. consumer behaviour, toxicology, statistics etc., and any deficiency in one area can effect the quality of the overall assessment

Table 2.2 Summary of factors considered

Factor	Comment
Distribution	Distributions of consumption or chemical concentration data can be expressed in different ways and the method selected can affect the outcome. The raw (empirical) data can be used or the data can be expressed as a probability distribution.
Selection	Sampling from the consumption and residue distribution can be structured or random. Random sampling can require longer computing times. Care also needs to be taken when deciding how to structure sampling.
Cut-off	Distributions can, potentially, have unrealistic 'tails'. These outliers need to be considered. An option may be to limit the distribution to the observed data set.
Sampling	The method used for collecting consumption or chemical concentration data may be biased and this should be considered.
Sample unit	If the amount of food sampled for analysis is much greater than the amounts regularly consumed it may be necessary to correct the chemical concentration distribution to take this into account.

For this preliminary work each infant was considered in turn. The amount of baby food eaten in a day (g/person/day) was multiplied by a chemical concentration value (randomly drawn from a log normal continuous probability distribution having a mean of 8.0 mg/kg and a standard deviation of 15.0 mg/kg), to give the infant's dietary exposure for that day (mg/person/day). This was repeated for the seven days of the study and averaged to give a daily exposure for each infant. This value was divided by the infant's bodyweight in order to express exposure in mg/kg bodyweight/day. Figure 2.2 shows the consumption pattern of the 410 infants in the study expressed as g/person/day. Figure 2.3 shows the distribution of the chemical concentration in these foods expressed as mg/kg. Figure 2.4 shows the dietary exposure to the chemical expressed as mg/kg bodyweight/day.

In this model the distribution of chemical concentration values is described by their mean and standard deviation. Two additional pieces of information are used, a maximum chemical concentration value and the typical weights of samples from which the chemical was determined.

Duration data model

The duration data model estimates dietary exposure over shorter periods of time than the original data set. This is useful for assessing the exposure to chemicals which are acutely toxic (where exposure from a meal or day is important).

The dietary survey information used to estimate dietary exposure is usually collected over 4 or 7 days. It is also possible to model exposure for periods greater than those in the original survey. This can be a useful technique if it is known how

Figure 2.2 Consumption of baby food by 410 infants (g/person/day)

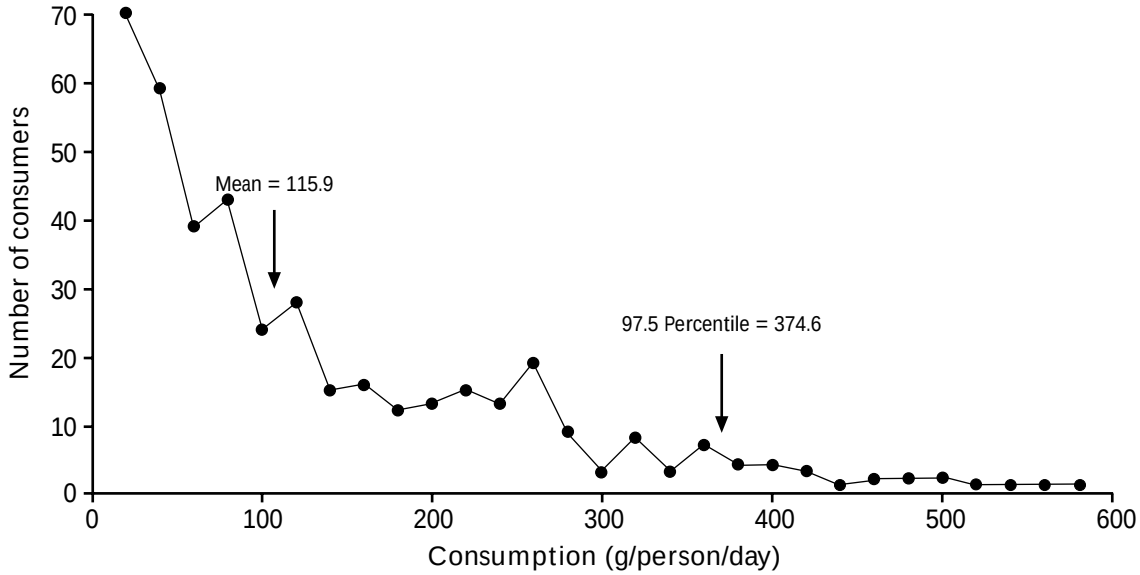


Figure 2.3 Distribution of a chemical in baby foods (mg/kg)

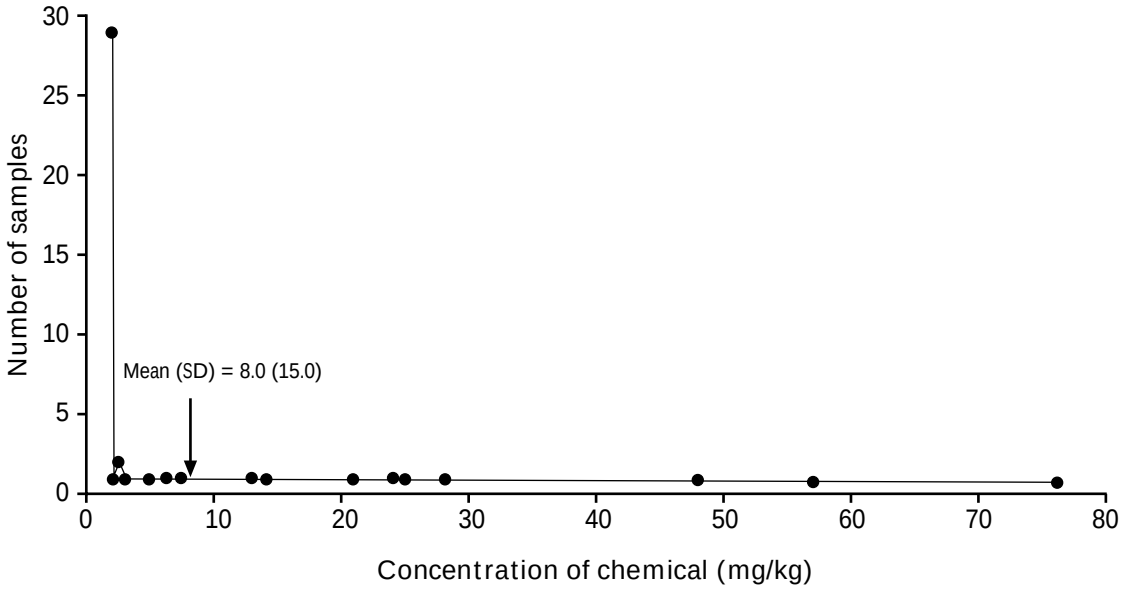
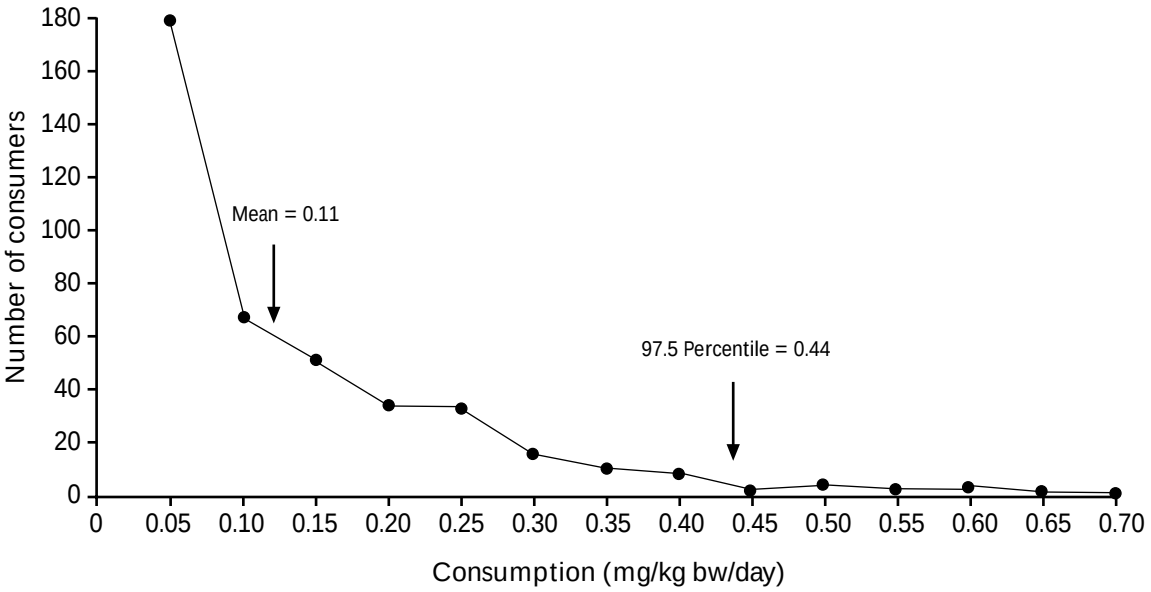


Figure 2.4 Dietary exposure to a chemical (mg/kg bodyweight/day)



the chemical accumulates. For example, there may be concern about the accumulation of a chemical over a period of three months by young children. The duration data model estimates exposure by assuming that the daily dietary habits of each child repeat randomly over several months.

2.2.5 Conclusions

The main difficulty in modelling dietary exposure is the lack of sufficient information. More research is needed to assess the uncertainty in the calculations and the impact of the underlying assumptions on the final result. Modelling takes time and expertise and this may not always be available. Decision managers are not usually familiar with probabilistic concepts; thus greater emphasis needs to be placed on presenting findings in an understandable way so they can be used more effectively to support policy development. Methods for communicating these more complex analyses to the general public also need to be developed.

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2.3 Assessment of exposure to chemicals in consumer products

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For a thorough risk assessment of consumer products to be carried out it is essential to have information on likely or known exposures to the products and the substances they contain. Consideration of human exposure to substances forms part of the hazard assessment process and also part of the risk characterisation phase (see Figure 1.1). It is important to distinguish between the defined exposure in animal studies at the hazard assessment phase and the sometimes less well defined understanding of consumer exposure which is also established during this phase.

In its guidance document on the assessment of consumer exposure to notified new substances, the European Union (EU; 1996) has defined a consumer as a member of the general public who may be of any age, either sex and in any state of health. Thus any estimation of consumer exposure has to consider whether all sectors of the population will come into contact with the substance in a product, to what extent and with what degree of control. A consumer product is one which can be purchased from a retail outlet by members of the general public; it may be the substance itself, a preparation (formulation) containing the substance or an article containing the substance. Estimation of use of a substance should include normal or intended use and reasonably foreseeable misuse.

Approaches to obtaining information on external human exposure to consumer products may include direct assessment, diary recall and modelling.

For assessment of internal human exposure to, for example, a washing powder or a dish wash liquid, more information is required, including knowledge of the intended matrix (formulation) where the substance is present, the intended purpose (e.g. is the formulation designed for hand or automatic machine use), the concentration of the substance in the formulation and the duration of exposure and frequency of use of the product. Furthermore, where indirect exposure is possible, for example from residues of the substance left on food crockery, or where the substance is a leave-on product, the dermal penetration characteristics and half life of the substance and its decay products are of particular importance.

Different approaches and algorithms can be used for different exposure scenarios. For example, dermal uptake can be calculated using the following equation.

$$U_{derm} = \frac{K_p C_{derm} S_{derm} t}{BW}$$

K_p = skin permeability coefficient of substance

C_{derm} = concentration of substance in solution (mg/cm^3)

S_{derm} = area of skin exposed (cm^2)

t = exposure time (h)

BW = body weight (kg)

Exposure estimation models use formal procedures to enable estimations of direct chemical contact to be made by using a variety of default assumptions, which can generally be changed as and when required. The main advantage of such models is that they provide a reasonably logical series of questions, the answers to which enable the process of consumer exposure estimation to be completed. Their strength is that worst case, reasonably foreseeable worst case and general misuse scenarios can be investigated. However, exposure estimation models have some important limitations. In particular, allowance for skin absorption is limited and the internal dose cannot be derived. A consequence of this is that the targeted body dose at the site of toxicological interest cannot be determined using these models.

Reference

EU (1996) *Technical Guidance Document in support of the Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and the Commission Regulation (EC) 1488/94 on Risk Assessment for Existing Substances* (CR-48-96-000-EC-C), Directorate-General Environment, Nuclear Safety and Civil Protection

2.4 Environmental exposure assessment in the Environment Agency

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2.4.1 Background

The Environment Agency of England and Wales (hereafter the 'Agency') was established as a non-departmental Government body on 1 April 1996. It has specific statutory responsibilities for water resources, pollution prevention and control, flood defence, fisheries, conservation, navigation and recreation across England and Wales*. Given this broad remit, any framework for environmental risk assessment must be sufficiently generic to encompass a wide variety of situations, thus facilitating a harmonised approach. Such a framework must also allow the component stages of risk assessment, such as exposure assessment, to retain a discrete focus representative of their position within the accepted process as a whole. Critically, the exposure assessment stage harbours substantial uncertainties for environmental risk assessment, perhaps second only to those associated with dose–response assessment. There is a clear need, therefore, to establish approaches to exposure assessment at different tiers of scientific sophistication. Above all, the need, at the outset, for a conceptual model of exposure to support any exposure assessment associated with a specific issue is recognised as a critical first step.

Environmental exposure assessment involves evaluating the mechanisms, probability, duration and magnitude of exposure to a hazard. It is principally concerned with 'pathways' via which exposure may take place. Hazard sources of interest may be physical (e.g. flood waters), chemical (e.g. oestrogenic substances) or biological (e.g. algal blooms) in nature, and the receptors of interest may include humans, buildings and infrastructure, ecosystems or environmental capital (air quality, aquifers). The study boundaries for environmental exposure assessment extend from the initiation of the hazard (whether intentional or accidental, natural or anthropogenic) to the point where harm is manifest. Ultimately included therefore are:

- direct release of a pollutant or source of a hazard to the recipient environmental medium (e.g. stack emissions to the atmospheric environment);
- advective transport and distribution within a recipient medium to an exposure point (e.g. transport of a point-source discharge via surface water flow);
- multimedia fate processes between recipient media and other, indirect media (e.g. partitioning of pesticides between soil and groundwater);
- transport mechanisms to points of exposure; and
- 'dose' estimation (via direct and indirect pathways), with reference to factors influencing exposure to the hazard, ultimately as the 'effective' dose.

In practice, the detail of dose estimation, other than consideration of an exposure point concentration (for example, as an actual or predicted environmental concentration), is encapsulated within the derivation of an environmental quality standard.

The above interpretation of exposure assessment is sufficiently broad to cover the analysis of situations as diverse as coastal flooding, accidental point releases from chemical plant, ecological risks from over-abstraction of surface and groundwaters and the long-term and diffuse releases from landfill facilities. The approach adopted may be qualitative, semi-quantitative or quantitative in nature, in line with a 'tiered' approach to risk assessment as a whole. Qualitative exposure assessment focuses, then, on the existence of source (of a hazard), pathway and receptor components of a risk, and on establishing actual or potential *connectivity* between these components. Semi-quantitative approaches consider ranking the relative *availability* of exposure pathways, and quantitative approaches focus on formally estimating intakes on the basis of modelled or monitored exposure point concentrations, usually invoking some distribution modelling in their support.

Agency activity in exposure assessment ranges from the formalised requirements of regulatory risk assessment under Council Regulation 793/93, which

* Environment Agency (1998) *Corporate Plan 1999–2000: Our Forward Look to 2002*, available from Rio House, Waterside Drive, Aztec West, Almondsbury, Bristol, BS12 4UD

outlines the procedure for the evaluation of risks posed by 'existing substances' (EEA, 1998) to the critical review and independent evaluation of risk assessments submitted to the Agency in support of authorisations for discharge (Halfacree, 1998).

2.4.2 Current practice

For chemical exposure, environmental concentrations in the source term may be estimated through monitoring or modelling. At present, environmental modelling efforts focus largely on the use of environmental distribution models concerned with the transport, degradation or multiphase partitioning of contaminants in the environment in space and time. In practice, dose determination modelling for the evaluation of exposure intakes is not widely applied at present across the Agency's functions, with the exception of product licensing and radioactive waste disposal. In the future this type of evaluation will become a wider feature of the Agency's new duties and powers on contaminated land, for example. Pharmacokinetic modelling for the determination of effective doses from exposure point 'intakes' is not in routine practical use. Most environmental standards apply to particular receptors and are routinely expressed as simple pollutant loadings (e.g. mass concentrations per unit mass or volume of media) rather than as risk criteria, although there are regulatory dose constraints and risk targets in radioactive substance regulation that require more sophisticated assessments of environmental exposure. Although standards in many cases have been derived using toxicologically-based risk assessment (e.g. the environmental quality standards derived under the framework 'Dangerous Substances' Directive 76/464/EEC), the general user of models in the Agency is not particularly aware of these assessments, and tends to view exposure modelling in terms of obtaining a model result which is on one side or the other of the environmental quality standard. A comprehensive review of the role and setting of standards in environmental policy has been published by the Royal Commission on Environmental Pollution (RCEP, 1998).

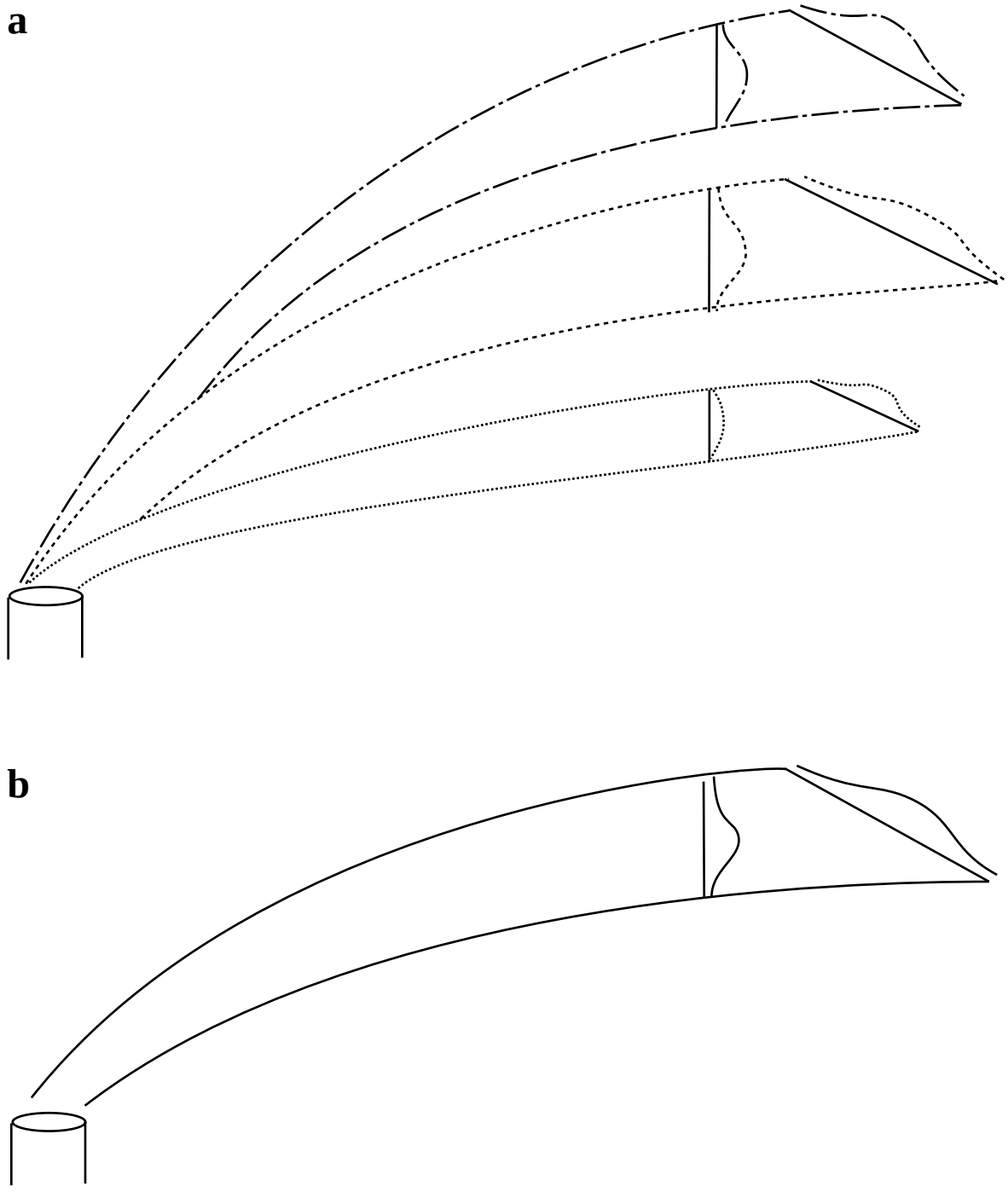
2.4.3 Capabilities of exposure assessment models

Increasingly, environmental distribution models can incorporate contaminant removal processes such as biotransformation, decay or hydrolysis-processes that might themselves be incorporated within bulk transport (advection, diffusion, dispersion) models. For rivers, groundwater and air, finite element dispersion modelling is used to determine concentration distributions within a medium, usually as a function of space and time or both. Many models of pollution dispersion in environmental media are based on simplified parameterisations of ensemble-average conditions. This is particularly true of air dispersion models, for example, which for many years have focused on ensemble-mean dispersion rather than on trying to include the detailed (in time and space) fluctuations occurring around the ensemble mean on specific occasions (i.e. realisations). The advent of shorter-term and higher-percentile air quality standards has made it necessary to develop models that can predict the probability of such fluctuations, as illustrated and explained in Figure 2.5. Using such models, the risk of concentrations above the ensemble mean prediction occurring occasionally can be properly appreciated and taken into account in regulatory decisions.

Generic multiphase partitioning models (e.g. USES and EUSES) are applied in chemical product licensing for predicting equilibrium distributions of contaminants across air, water, soil and biota, and invoke Mackay fugacity modelling for these purposes (see, for example, van Leeuwen, 1995).

The conversion of exposure point concentrations to exposure intakes is performed using dose determination models in limited circumstances and where statutory requirements dictate. A dose determination is made for human health under Council Regulation 793/93 on 'existing substances', whereby various distribution models are used to model soil and groundwater concentrations from water and air emissions; these are then translated to concentrations in plant, fish, mammals and milk for the purposes of aggregating an overall environmental 'intake', which itself then forms part of a 'total human exposure intake'. In the requirements of dose assessments for operating land disposal facilities taking radioactive wastes, exposed groups are often identified from habit surveys and the derived radiological doses are compared with internationally accepted dose constraints. Under the requirements of Part IIA of the Environmental Protection Act, 1990, Contaminated Land, a risk-based approach to regulating contaminated sites will require polluters to undertake exposure assessments for review against risk-based guideline values derived using a generic exposure assessment model. For the vast majority of contaminants this contaminated land exposure assessment (CLEA) model stops short of any toxicokinetic or toxicodynamic considerations (see Section 2.6).

Figure 2.5 Schematic illustration of fluctuations and ensemble mean of pollutant concentrations due to a stack plume



a Shows individual cases, or 'realisations', of observed concentrations averaged over short (e.g. 15-minute) periods under the same overall weather conditions. The trajectories and concentration profiles (vertical and horizontal) vary, or 'fluctuate' between the cases because of the varying nature of atmospheric turbulence and wind meandering between individual short periods.

b Shows an aggregation, or 'ensemble mean', of the observed cases, as commonly used for modelling of plume impacts. The ensemble mean represents the statistically-averaged behaviour of the plume across all realisations, but necessarily omits some of the fluctuating behaviour of individual observed cases.

2.4.4 Future directions

Environmental standards themselves are increasingly being expressed in stochastic terms; this requires a wider appreciation of the probabilistic, temporal and spatial consequences of exposure. For example, the 1997 UK National Air Quality Strategy has a standard for sulphur dioxide which applies to short-term concentrations, namely 15-minute averages, and requires a 99.9% rate of compliance. This type of standard is more sophisticated than the 1983 standards under the EC 'Smoke and SO_2' Directive, which were based on daily means and 98th percentiles. A further future consideration is the need to combine risks from two different sources. For example, in the case of SO_2 there is a need to decide to what extent the 99.9 percentile events from a particular emitter (e.g. a stack) are to likely coincide in time and space with 99.9 percentile events from other (background) sources. These are relatively simple questions to pose, but complicated to answer by simple exposure modelling. Strictly, it would require that a model simulated the detailed (15-minute resolution) impacts from all sources over a climatically representative period (e.g. a year) and all relevant locations.

The timescales and statistical bases of the environmental standards used by the Agency are becoming more sophisticated. This highlights the need for a better appreciation of the toxicological considerations and uncertainties which underpin such standards, and a growing need to understand the interfaces between exposure assessment and the other components of the risk assessment process, specifically with respect to risk estimation. Such conclusions, along with others specifically relating to transparency in environmental decision-making, were expressed by The Royal Commission on Environmental Pollution in their recent review of environmental standards (Box 2.2; RCEP, 1998).

Box 2.2 Selected conclusions of the Royal Commission on Environmental Pollution Report 'Setting Environmental Standards' of relevance to exposure assessment

On procedures

- there should be an audit trail documenting all the considerations taken into account in reaching a decision and how they were taken into account
- all the analyses should also be subject to peer review and scrutiny

On scientific understanding

- in setting an environmental standard, the starting-point must be scientific understanding of the cause of the problem or potential problem under consideration
- all exposure models (indeed all mathematical models used within scientific assessments) should be regarded with caution until they are properly validated
- in a scientific assessment of an environmental issue, there are bound to be limitations and uncertainties associated with the data at every stage … The requirement for sound science as the basis for environmental policy is not a requirement for absolute knowledge or certainty and should not be interpreted as such
- transparency should be the watchword in presenting assessments …

On risk and uncertainty

- the limitations and uncertainties in any estimates of risk must always be made clear in ways which are meaningful to people without particular specialist knowledge
- risk assessments should identify the uncertainties which have the largest implications and the actions that would need to be taken to reduce or resolve them. However, it would be inappropriate and misleading to attempt to incorporate into risk assessments estimated probabilities for the correctness of particular scientific theories or interpretations

From RCEP (1998)

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2.5 Exposure to chemicals through water

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2.5.1 Introduction

Exposure of the populace through water is possible by two routes, drinking water and recreational, or ambient water. However, the more important route for most individuals is drinking water. In the UK over 95% of the population obtains its water through the public supply and the remainder obtain water from small private supplies. Public water supply, in countries such as the UK, can be quite complex and has changed significantly in both source and treatment practice over time. Unlike air, drinking water undergoes processing before delivery to the consumer.

2.5.2 Water sources

Drinking water is obtained from three major sources in the UK. These are groundwater, lowland rivers and reservoirs, and upland reservoirs. Each has different chemical characteristics and sources of chemical contamination, both natural and anthropogenic. While approximately one third of UK drinking water comes from each source, different sources dominate in different areas of the country; for example, chalk groundwater dominates in the south and south-east, and upland sources dominate in the north of England and Scotland. However, there can be quite significant variation in a relatively small area and the source may be remote from the supply, as in parts of the midlands and north-west. Sometimes sources are blended to give a particular water quality, and sources may be abandoned or new sources introduced over time.

2.5.3 Drinking water treatment

All drinking water supplied to the public in the UK receives treatment, but the extent of treatment will depend on the supply and the water quality associated with the source. The primary role of drinking water treatment has been to prevent ingress of pathogenic microorganisms, but recently chemical characteristics have become more important, particularly under the requirements of European drinking water legislation. New treatment techniques have been introduced and many advanced treatment processes are now used routinely. There has been substantial change over the past 10 years and that change is continuing. This can have a significant impact on the contaminants present in final drinking water and will change the nature of the mixture that is drinking water.

2.5.4 Water supply

Water supplies are designated into zones for operational and regulatory purposes. An individual zone comprises a discrete area served by a single treatment works and supplying not more than 50 000 people. Most analytical data refer to water supply zones, but the supply system is being made more flexible to enable water suppliers to react more quickly to emergencies and to respond to water shortages; zones may, therefore, change. The water is supplied through distribution networks of varying length depending on the circumstances. The retention time in distribution will, therefore, also vary and this can have an impact on any contaminants present, particularly by-products of the disinfection process, and the concentrations of residual disinfectants.

2.5.5 Sampling and analysis

Samples are taken for both operational and regulatory purposes. In the latter case, they may be taken both immediately post-treatment or at the tap within a zone. Sampling frequency for each parameter is set out in the legislation, but care is needed in interpreting such data. When the parameter is primarily affected by domestic plumbing, zonal samples may appear to give an average exposure; however, this could be very misleading as where the offending materials are not present, exposure will be zero. It is also the case that where an exceedence of the regulatory prescribed value has occurred, sampling will be at an increased rate until such time as the value has returned to below the standard.

2.5.6 Human exposure

Water from the public supply is not only used for drinking but also for cooking, washing and a range of other activities. Exposure will be oral, dermal and, for some volatile substances, by inhalation. Little water is drunk straight from the tap; water is boiled or heated before use in making various kinds of drinks, and this may change exposure to a particular substance. Such change could be quantitative, or qualitative by changing the bioavailability.

Consumption of water will vary according to the individual, but for regulatory purposes the normal default assumption is 2 l/day for an adult, 1 l/day

for a 10 kg child and 0.75 l/day for a 5 kg bottle-fed infant. In reality these are conservative assumptions based on above average exposures. The true average adult consumption is closer to 1.25 l/day, but will vary significantly as a consequence of individual habits, including consumption of canned drinks and bottled water (Hopkin, 1980). Most consumers will also be exposed to drinking water away from the home and in some cases exposure in the workplace is dominant during the working week (MEL Research, 1996). Work places will often be some distance from the home and may receive water from different sources. Exposure to specific contaminants may therefore be substantially modified.

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2.6 Exposure of children to lead in soil

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2.6.1 Background

Bringing industrially contaminated land back into beneficial use and protecting greenfield sites from development pressure are important aspects of sustainable development. Exposure assessment is recognised as a useful tool in helping to decide on appropriate land uses, on the need for site remediation and on clean-up target levels for contaminated soils (Ferguson *et al.*, 1998).

Most exposure assessments for contaminated soils are based on estimating the contaminant concentration in soil that would give rise to the maximum tolerable intake via ingestion, inhalation and dermal absorption. This is uncontentious when site soil is the only significant contaminant source. However, for many environmental contaminants, such as lead, benzene and polychlorodibenzo-dioxins and furans, people are also exposed via other non-site and non-soil sources, such as traffic emissions, diet and household chemicals.

When non-soil and non-site sources combine to give a background intake that is small relative to the tolerable daily intake, it is straightforward to use the difference between these intakes as the tolerable daily intake from soil. However, as the difference gets smaller, the cost of achieving the target for soil may be grossly disproportional to the contribution that soil makes to total risk.

2.6.2 Description of the problem

The problem is that there are no established or obvious methods for setting target values that take into account the relative contributions of various sources to total risk. A novel, risk partitioning approach to this problem has been developed for lead in soil, as part of the Department of the Environment, Transport and the Regions (DETR)/Environment Agency Contaminated Land Research Programme (DETR, in press). It builds on a model developed by the Society for Environmental Geochemistry and Health (SEGH, 1993) for deriving guideline values to protect young children from adverse effects of exposure to lead in soil.

The governing equation is given below.

$$S = 1000 ((T/G^n) - B)/\delta$$

S = the soil guideline value, a geometric mean concentration in µg lead per g (soil)

T = the blood lead target concentration in µg lead/d1 whole blood

G = the geometric standard deviation of the blood lead distribution

n = the number of standard deviations corresponding to the degree of protection required for the population at risk

B = the background blood lead concentration in the population from sources other than soil

δ = the slope of the blood lead: soil lead relationship in µg lead/d1 blood per 1000 µg lead/g increment in soil

A major difficulty with the SEGH model is that soil clean-up levels are very strongly influenced by background (non-soil) exposure to lead. For example, using a blood lead intervention limit of T = 10 µg/dl whole blood and typical values of G = 1.4 and n = 1.645 to protect 95% of the hypothetical population at risk, T/G^n would be about 5.75 µg/dl whole blood. Many children in urban environments probably have background blood lead concentrations (from exposure to lead in diet, drinking water, paint and traffic emissions) that approach or exceed 5.75 µg/dl (e.g. Davies *et al.*, 1990). This implies very low (or even zero) soil target values.

2.6.3 The risk partitioning approach

The alternative model developed for the DETR incorporates an additional and fundamental assumption — that in reducing the exposure of human populations to lead, the exposure from contaminated soil should be reduced (if necessary) only in proportion to the contribution that soil lead makes to total lead uptake.

For example, in some parts of the UK the major contribution to excessive lead uptake comes from dissolved lead from lead pipework in domestic water supply systems. Therefore the reduction in uptake should be effected largely by tackling the source of the problem. It makes neither scientific nor economic sense to treat the background exposure as a fixed parameter and then attempt to solve the

problem by setting stringent soil guidelines for lead. The governing equation for the risk partitioning model can be described as follows.

$$S = \Gamma\left[\theta\phi\left(\frac{\theta U_{NS}}{\Gamma} + 1\right)\right]^{-1}$$

Γ = T/G^n and is the reduced blood lead target concentration as above

U_{NS} = the mean uptake of lead from non-soil sources
- In a study of 2-year-old Birmingham children (Davies *et al.*, 1990), dietary intake of lead was estimated at 23 µg/day and intake from ambient air as 1.56 µg/day. Converting to uptake, using absorption factors for the gut and lung, yields an estimated mean daily uptake of about 13 µg/day.

ϕ = the slope of the uptake: lead concentration in soil relationship
- Intake varies as a function of exposure (land use) scenario; for a 2-year old child conversion to uptake uses an absorption factor of 0.25 for lead in soil.

θ = the slope of the equilibrated blood lead: lead uptake relationship

A site-specific or area-specific blood lead: soil lead slope factor, δ, may be available for some sites. There are significant variations in the value of δ between mining, smelter and general urban communities, which probably reflect variations in the bioavailability of soil lead.

The risk partitioning approach therefore allows soil target values for lead to vary depending on the relative contribution to total lead uptake from different sources, and the bioavailability of soil lead. It should be possible to generalise the approach for setting other environmental quality objectives where there are multiple sources of exposure.

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2.7 Assessment of personal exposure to air pollution

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2.7.1 Introduction

Exposure to air pollutants can occur both outdoors and indoors, including occupational situations; the focus of this section is non-occupational exposure. For outdoor air pollution, the UK Government has recently launched a National Air Quality Strategy (DETR, 1997), aimed at reducing effects on human health. This strategy aims, by 2005, to reduce concentrations determined at fixed-site monitoring stations (FSMs) to objectives which are related to air quality standards at which the effect on the health of the population is judged to be negligible. In contrast, Government policy on indoor air quality has no quantified exposure targets, but provides guidance aimed at reducing exposure from indoor sources (DoE, 1995).

However, the real health effects of air pollution depend on the concentrations experienced by people as they move between a range of microenvironments, both indoors and outdoors, rather than on the measurements made at FSMs. The interaction between the spatial and temporal variation in air pollutant concentrations and the time–activity of people means that almost every individual will have a unique exposure to air pollution. Thus, when considering health risk assessment for air pollution over a region, a city or a locality, it is necessary to consider the frequency distribution of exposures within the population of concern. These exposures may differ greatly between individuals, and many studies have shown them to be quite different from those measured at FSMs (Wallace, 1993; Loth & Ashmore, 1994). A major reason for this difference between personal and outdoor exposure is the amount of time people spend indoors; about 90% of people's time on average is spent indoors, where the exposure sources are quite different from those outdoors.

The air pollutants for which ambient air quality standards have been set in the UK can broadly be divided into three categories from an exposure perspective. For ozone and sulphur dioxide, outdoor emissions are the only major exposure source; indoor concentrations of these pollutants are therefore generally lower than those outdoors, leading to personal exposures which are lower than outdoor concentrations. In the case of carbon monoxide and nitrogen dioxide, both indoor and outdoor emissions are important, and indoor concentrations may be significantly greater than those outdoors when there are indoor sources. For particles, both indoor and outdoor sources are important, but the situation is further complicated by the fact that the physical and chemical characteristics of particles found in different indoor and outdoor microenvironments vary significantly. Finally, for lead and benzene, direct inhalation is one of a number of exposure pathways, and an approach which takes account of exposure through other pathways and media is essential. It is also important to note that there are many contaminants which are found in insignificant concentrations outdoors, but for which exposure from indoor sources may be important for health.

2.7.2 Links to health outcomes and policy interventions

Thus, the current approaches to risk assessment and management for air pollution in the UK are not based on quantitative exposure assessment. This situation may lead to pollution control policies that are not well focused or cost-effective. The use of personal exposure assessment may provide a different perspective. For example, there is debate at present about policies to encourage use of transport modes other than the car, and the effectiveness of such alternatives in improving ambient urban air quality. However, the exposure of individuals making the same journey by different forms of transport may be quite different (e.g. Fernandez-Bremauntz & Ashmore, 1995), with travellers by car often experiencing higher pollution concentrations than those using public transport. Consequently use of personal exposure-based assessment may provide a better indication of the value to individuals of a shift to travelling by a different mode. In a different context, Zhang & Smith (1996) estimated that the lifetime cancer risks from exposure to benzene arising from biomass cooking stoves in developing countries were about two orders of magnitude greater than those from outdoor exposures to benzene in the USA; hence these risks can be reduced most effectively by measures targeted at indoor sources.

In linking personal exposure assessment to health risk assessment there is a need to identify the basis of the air quality standard or risk evaluation; this can be illustrated by comparing two pollutants. In the case of sulphur dioxide, the standard set for the UK is based on short-term chamber studies using

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volunteers; it is clear, therefore, that it is individual exposures, rather than concentrations measured at FSMs, that are the proper basis of comparison. For particles, however, the standard is based on epidemiological studies, in which various health outcomes have been shown to be significantly associated with temporal variation in concentrations determined at FSMs. Furthermore, recent studies (e.g. Janssen *et al.*, 1997) have shown good correlations between personal exposures and outdoor concentrations in time, but not in space. Hence the extent of confounding by exposure misclassification in time-series analysis may be low, but this may be a major issue in the interpretation of cross-sectional studies. Even in the case of time-series studies, the extrapolation of findings in US or European cities to other parts of the world may be very misleading, as the exposure patterns in the population may be quite different, even at comparable FSM concentrations.

2.7.3 Methodological approaches

When considering methods of exposure assessment, there is an important distinction to be drawn between direct and indirect methods (Figure 2.7; NRC, 1991). The direct method involves attaching a personal monitor directly to an individual. It can, therefore, provide data on the real exposure of individuals; for some pollutants, personal monitors providing continuous data are available but, in most cases, measurements are made over averaging times of several hours or days. The sensitivity and accuracy of the instruments used for personal monitoring may be lower than those used for fixed-site monitoring, and this needs to be considered in study design. Furthermore, bias in sample selection and poor response rates mean that many studies have not used population-based samples. It can also be time-consuming and costly to obtain enough direct measurements to describe accurately the frequency distribution of exposures within a population.

In contrast, the indirect method uses computer models, in which the movement of individuals between different microenvironments is simulated by combining data on time–activity patterns, the characteristics of populations that influence exposure, and the concentrations in different microenvironments. These concentration data may be estimates from physicochemical models, estimates from empirical relationships derived from static pollution monitoring in different microenvironments, or data from direct personal monitoring (Figure 2.8; NRC, 1991). Since there is evidence, for particles in particular, that personal monitors provide different results from static

Figure 2.7 Summary of approaches to determining personal exposure to air pollutants

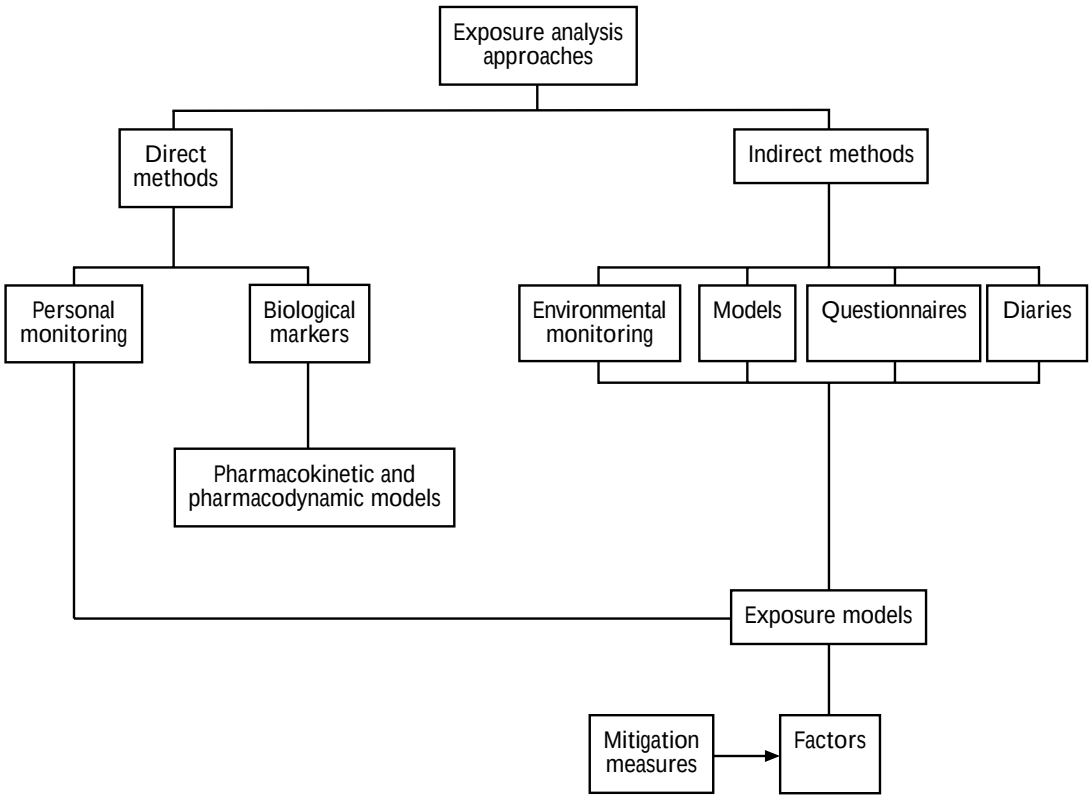
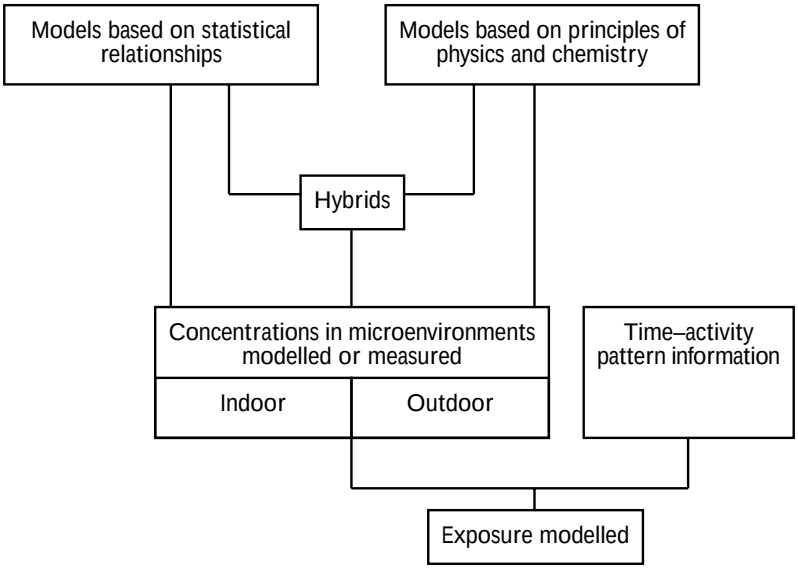


Figure 2.8 Schematic summary of model structures used in air pollution exposure assessment



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monitors in the same location (e.g. Monn *et al.*, 1997), direct personal exposure measurements are preferable. Models can allow simulation of exposures across large populations, and are well suited to assessment of the effect of policy interventions, but the validity of model assumptions needs to be carefully evaluated. Although some studies have shown good agreement between modelled and measured exposures (e.g. Leung & Harrison, 1998), the potential for bias arising from model assumptions and parameterisation is large.

Direct measurements of personal exposure, and of the microenvironmental concentrations and time–activity patterns which determine these exposures, typically show large variation within populations. Hence, probabilistic exposure simulation models, such as the SHAPE model for carbon monoxide (Ott, 1984), which combine data on both microenvironmental concentrations and time-activity data, expressed as probability functions, are needed to simulate exposure frequency distributions. However, these models typically contain no specific spatial component, but rely on empirical relationships between outdoor concentrations at background FSMs and the mean and standard deviation of concentrations in different microenvironments; hence spatial variation is included within the input and output frequency distributions. This is not adequate in the context of air quality management, which requires a spatial component; for example, excluding certain types of traffic from a city centre may reduce exposures there, but increase them in other areas to which traffic is diverted. Although geographical methods to predict the effects of traffic management on personal exposure are being developed (Briggs *et al.*, 1998), there is a longer-term need to link three types of model to deal with these types of issue. These were first identified by Mage (1985), in the context of modelling exposure in the home, as:

- models predicting the spatial distribution of outdoor pollution concentrations, to link measurements at fixed-site stations to those immediately outside the home;
- models predicting the difference between outdoor concentrations and those in the home, as a function of building design, climate, and pollutant deposition and emission rates indoors; and
- models to predict the dispersion within the home of emissions from indoor sources.

2.7.4 UK knowledge and research priorities

Knowledge of personal exposure in the UK, obtained either by direct or indirect methods, is limited (in contrast to the situation in the USA), and more research is urgently needed to improve the basis for health risk assessment. In terms of the direct approach, a number of studies have been carried out in the UK, but few, if any, have used a population-based sample. A major multi-pollutant study, using a population-based sample of working-age adults, has recently been completed in six continental European cities (EXPOLIS: Jantunen *et al.*, 1998), and studies using this methodology are due to start in Oxford and London; these should

provide valuable comparative data. These studies need to be extended to sensitive groups, such as children and the elderly, and to specific populations with high pollution exposure. In terms of the indirect approach, similarly, relatively little UK-specific work has been carried out to date. In the context of air quality management, the need is to link current dispersion modelling of outdoor concentrations, which is being carried out in support of the National Air Quality Strategy, to exposure models which include time–activity data and models of indoor exposure. Both field studies and physicochemical model development are needed to support this approach, as is an improved national database on time–activity patterns in different groups on which to base exposure modelling.

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2.8 Occupational exposure activities in HSE

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The Health and Safety Executive (HSE) assesses exposures to chemical agents for several reasons. The mainstream activity of the Directorate of Science and Technology (DST) in this area is to provide assessments of occupational exposure which are incorporated into substance reviews for the Advisory Committee on Toxic Substances when new and revised occupational exposure limits are being considered for the Control of Substances Hazardous to Health Regulations 1994 (COSHH). In addition, the DST provides exposure assessments for the Notification of New Substances Regulations 1993 (NONS) and prepares reviews for the purposes of the Existing Substances Regulation (ESR). There are common features to these reviews, and broadly they consider the following:

- the physical and chemical properties of the substance;
- the manufacture and use of the substance in the UK;
- the occupational exposure to the substance during manufacture and use — this section covers data available from HSE's National Exposure Database (NEDB), exposure data from industry and predictive data obtained from a computer model (the EASE predictive model);
- exposure data for both inhalation and dermal exposure routes; and
- the input to a cost–benefit analysis of the effects of introducing or amending occupational exposure limits.

Reviews are also made within Health Directorate as part of the approval process for non-agricultural pesticides. Here, exposure prediction is essentially task-based and depends on a database of exposure measurements for standard processes (spraying, dusting, brush application, etc.) In addition, these reviews go beyond occupational exposure and consider both a broader exposed population (consumers, amateurs) and continuing exposure after application of the pesticide. For these pesticides reviews, 'exposure' refers both to inhalation and the dermal route, and the predicted dose is compared with toxicological end-points.

All these review processes are subject to continuing refinement and development. While they are generated in fairly standard formats, it is always the case that they are, of necessity, based on limited amounts of available information. In addition, actual exposure data are becoming very expensive to collect, and greater reliance is being placed on modelled data. Consequently, there is an emphasis on improving the accuracy and reliability of the models that are used, and this again is a continuing activity. Specifically, more work needs to be done to develop dermal prediction methods — the EASE model, particularly, is limited in this area.

2.9 General issues in exposure assessment: The effect and reduction of error

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2.9.1 Introduction

In studies of adverse health outcomes, exposure refers to personal contact with any agent that may have an effect on health. Such agents include those that may cause physiological effects, cause or protect from a disease, confound or modify the effects of other agents, or determine the outcome of a disease through screening or treatment.

Several practical issues confront someone assessing exposure, before any measurement is carried out. These include deciding which substances to measure, the sampling strategy and measurement method, the duration of exposure and the statistical descriptors relating exposure to effect. Exposure assessment is often ruled by practical expediency. For example, in taking a single sample of diesel exhaust, all the components could be analysed using gas or mass spectrometry. However, the findings may be of limited use because of highly reactive compounds disappearing prior to analysis, only a small number of the compounds contributing to health effects, and a single sample being of little value when assessing the overall exposure situation.

There may also be a conflict between the desire to measure contaminants and an inherent lack of information concerning toxicological factors and exposure variability. Knowledge of both the toxicokinetic processes which determine the temporal relationship between exposure and tissue concentration, and the pharmacodynamic processes which determine the temporal relationship between tissue concentration and health effects can be useful for selecting both the appropriate timescale for measurements and the combination of external and biological monitoring that will be optimal for the substance.

2.9.2 Methods of exposure measurement

General issues which should be considered before assessing exposure for the evaluation of dose–response include the following.

- Are data on individuals available or are grouped environmental data to be used as a surrogate for personal exposure?
- Are self-reported exposure data to be used or are actual physical measurements available?
- Are current exposures to be used or are past exposures, which may be more relevant if chronic diseases are of interest, to be estimated?

Exposure measurement methods can be classified as direct or indirect. Direct methods include personal monitoring and the use of biomarkers. Indirect methods include environmental monitoring, interviews, questionnaires and time–activity diaries, the use of records and archive material, and mathematical modelling.

2.9.3 The effects of error in exposure assessment

Exposure assessment error is one of the major sources of bias in studies of adverse health effects, with potentially serious consequences for the process of risk assessment and management. Two useful measures of measurement error are precision (lack of random error), that is a measure of the variation in the measurement error, and bias (average measurement error). Bias can be further classified into differential bias, in which misclassification of exposure is related to the disease of concern, and non-differential bias, in which misclassification of exposure is unrelated to the disease.

Non-differential exposure measurement error often causes an attenuation towards the null value of no association in the risk estimate between exposure and disease. This may result in false negative risk estimates. Differential error, in contrast, can cause bias in either direction, either towards or away from the null value, giving the potential for complete invalidation of a particular study. Ensuring misclassification is non-differential is a generally important consideration in any study.

It should also be noted that measurement error may affect the power of a study and the sample size needed to detect an association. Non-differential misclassification requires an increase in the sample size needed to detect an association, because the observable risk estimate is attenuated.

2.9.4 Reduction of error in exposure assessment

There are several approaches to reducing error in exposure assessment, including the use of multiple or repeated measures to enable an average to be calculated, and adjustment of the observed exposure–disease association using data from validity studies or for a covariate that is related to the exposure measurement error. Quality control procedures at all stages of a study can also help reduce exposure measurement errors.

2.10 Aggregate and cumulative exposure assessments: Experiences from the USA

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2.10.1 Background

The US Government responded to public outrage following publication of the National Academy of Sciences (NAS) report *Pesticides in the Diets of Infants and Children* (NRC, 1993) by introducing the Food Quality Protection Act.

The Act includes three specific elements that relate to exposure assessment:

- calculation of the risk presented from all sources of exposure (multi-source aggregation);
- calculation of the risk from all chemicals with similar 'mechanism of action'; and
- consideration of children as a particular 'at-risk' subgroup.

The scientific community has been challenged to develop new methods that provide realistic estimates of aggregate and cumulative exposure for adults and children.

2.10.2 Aggregate exposure

The Act requires that exposure to chemicals via all routes, that is the diet, drinking water and from residential uses, should be taken into account in determining exposure (Figure 2.9).

The initial interpretation adopted by US Environmental Protection Agency was that all possible routes of exposure could occur simultaneously and so 5–20% of the 'risk cup' was reserved for non-dietary exposure. It soon became apparent that this default approach would over-estimate total exposures in many circumstances, but on rare occasions might under-estimate exposures, for example when a home was treated to control pest infestation.

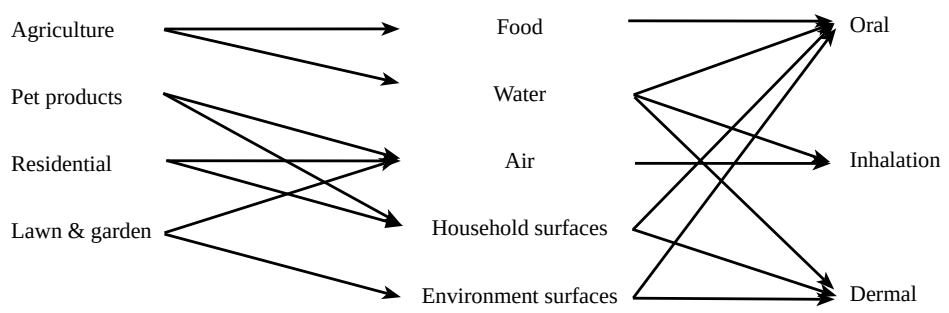
Recent developments allow the use of all available data, scientific methods and models. To avoid adding together conservative default values, probabilistic models are being developed. Using such methods it is possible to estimate the probability that exposures to chemicals via any combination of routes would occur.

2.10.3 Cumulative exposure

Under the Act, exposures to chemical entities that share a toxicological end-point or that have structural similarities should be considered together, for example cumulative exposure to groups such as organophosphate and carbamate pesticides, which inhibit cholinesterase synthesis.

Some difficulties may arise in interpreting cumulative exposures because different compounds may have different potencies and their half-times may vary. Different potencies will be reflected in different acceptable daily intakes, and these can be taken into account by weighting intakes according to the acceptable daily intakes when calculating the cumulative risk. Differences in half-time are more difficult to resolve. For example, if an individual is exposed to two chemicals that share the same toxicological end-point sequentially (i.e. not concurrently but close together), then the extent to which the cumulative exposure should be taken into

Figure 2.9 Sources and routes of exposure to pesticides



account will depend upon the half-time of the first chemical and the time between the two exposures.

2.10.4 Intakes by children

The Act identifies children as a special subgroup by applying an up to 10-fold additional uncertainty factor. Children naturally have higher relative intakes than adults on account of their higher energy requirements to body weight ratio. In the USA, USDA food consumption survey data include small children and so their intakes can be estimated separately from those of adults. However, for cumulative toxins, relatively high exposure during childhood could be counterbalanced by lower intakes in later life. The Act does not allow this factor to be taken into account.

2.10.5 Realistic models of aggregate and cumulative exposure

It is particularly important to define as accurately as possible the period over which exposures should be averaged (Benford & Tennant, 1997). Where potential adverse health effects relate to acute end-points, then repeated low-level exposure from a variety of routes and several similar substances may be irrelevant as long as the total exposure remains below a given threshold over short periods of time. However, repeated low–level exposure to substances where the effect is related to cumulative dose may become significant after long periods of time. The actual period selected for averaging exposures should reflect any knowledge of the toxicokinetics of the specific substance concerned.

When children's intakes are estimated it is also necessary to ensure that a relevant exposure period is selected since their intakes can vary significantly from year-to-year as well as day-to-day.

Default assumptions, such as basing the intake estimate on either one day or an entire lifetime, can introduce errors and significantly over or under-estimate the true level of risk. New methods must be developed that will prevent the Food Quality Protection Act (or similar legislation elsewhere) from distorting the risk assessment process.

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2.11 Case study: Assessing exposure to BSE infectivity

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2.11.1 Introduction

The Ministry of Agriculture Fisheries and Food (MAFF) has been carrying out an experiment to find out how bovine spongiform encephalopathy (BSE) infectivity develops in an infected animal and to identify in which tissues infectivity may be detected. In mid-1997 preliminary results showed positive infectivity in a tissue connected to the spinal cord and located within the vertebral column, the dorsal root ganglia. This tissue would not be removed with the spinal cord, and was not covered by the regulations specifying the tissues banned from human consumption, thus raising the possibility that people could be exposed to BSE infectivity in food. The Spongiform Encephalopathy Advisory Committee (SEAC) requested that a risk assessment study be carried out in order to assess the potential exposure of the UK population to BSE infectivity in dorsal root ganglia (DNV, 1997). It was the discovery of infectivity in this tissue that led to the banning of beef on the bone.

This section concentrates on the approach used for the risk assessment, and how the lack of knowledge and uncertainty inherent in any assessment of BSE infectivity was dealt with.

2.11.2 Main steps

In order to assess the exposure to any BSE infectivity that may be present in dorsal root ganglia the following must be answered.

- How much infectivity will be present in dorsal root ganglia if the animal has BSE?

  MAFF has been conducting an oral challenge test on cattle to determine the minimum infective dose of BSE-infected brain tissue. Interim results indicate that this is less than 1g. The infectivity of BSE for humans is believed to be lower than in cattle because of the species barrier (Kimberlin, 1996). In the absence of experimental data on the cattle–human species barrier, a range of values from 10 to 10 000 is used. The infectivity in dorsal root ganglia is assumed to be the same as in brain tissue.

- How many animals incubating BSE are likely to be slaughtered for food?

  Preliminary results of the BSE pathogenesis experiment reported by Wells *et al*. (1998) indicate that infectivity could be detected up to 3 months before clinical onset of the disease but not at 9 months before. As all cattle for human consumption must be 30 months old or less from April 1996, the number of BSE cases with onset at 38 months or less in those animals not slaughtered would indicate the prevalence of animals with significant infectivity at the time at slaughter. Estimates of survival probability by age (Donnelly *et al.*, 1997) indicate that 46% of cattle alive at 24 months have been slaughtered by the age of 30 months. Most BSE cases have occurred in animals of about 5 years or older, but there has been a small proportion in younger animals. In 1997 there were five cases of BSE in animals less than 38 months old. Putting these factors together it was estimated that there were four animals with significant infectivity out of the total 2.25 million slaughtered for human consumption in 1997.

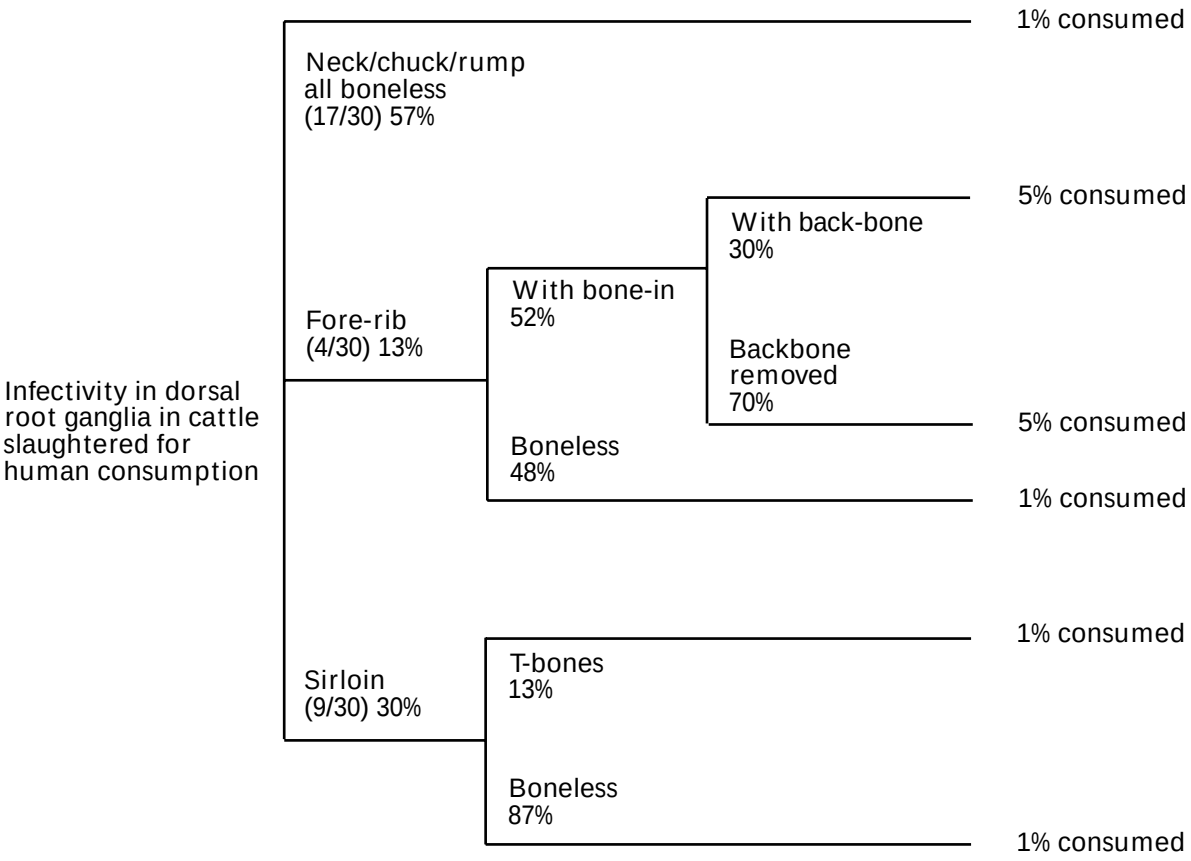
- What happens to the dorsal root ganglia when the animal is slaughtered and the carcass divided into retail cuts?

  The dorsal root ganglia are located within the vertebral column and would not be removed with the spinal cord. What happens to the dorsal root ganglia depends on how the carcass is divided into retail cuts (Meat and Livestock Commission, 1980). Most beef, even before the beef on the bone ban, was sold off the bone. Investigation by experienced butchers from the Meat and Livestock Commission showed that the dorsal root ganglia would be unlikely to be removed from the bone in a normal boning out operation. When meat was sold on the bone, for example T-bone steaks and rib of beef, it was still thought that the dorsal root ganglia would not normally be consumed. It was estimated that the dorsal root ganglia would not be removed from the bone in 1% of cases, and that the dorsal root ganglia would be consumed on 5% of occasions for meat served on the bone.

2.11.3 Risk evaluation

The data from these steps are combined in an event tree as shown in Figure 2.10. This provides a logic diagram showing what happens to the infectivity present in dorsal root ganglia and enables the infectivity consumed to be estimated. The results are obtained by evaluating the event tree using a

Figure 2.10 Event tree for dorsal root ganglia



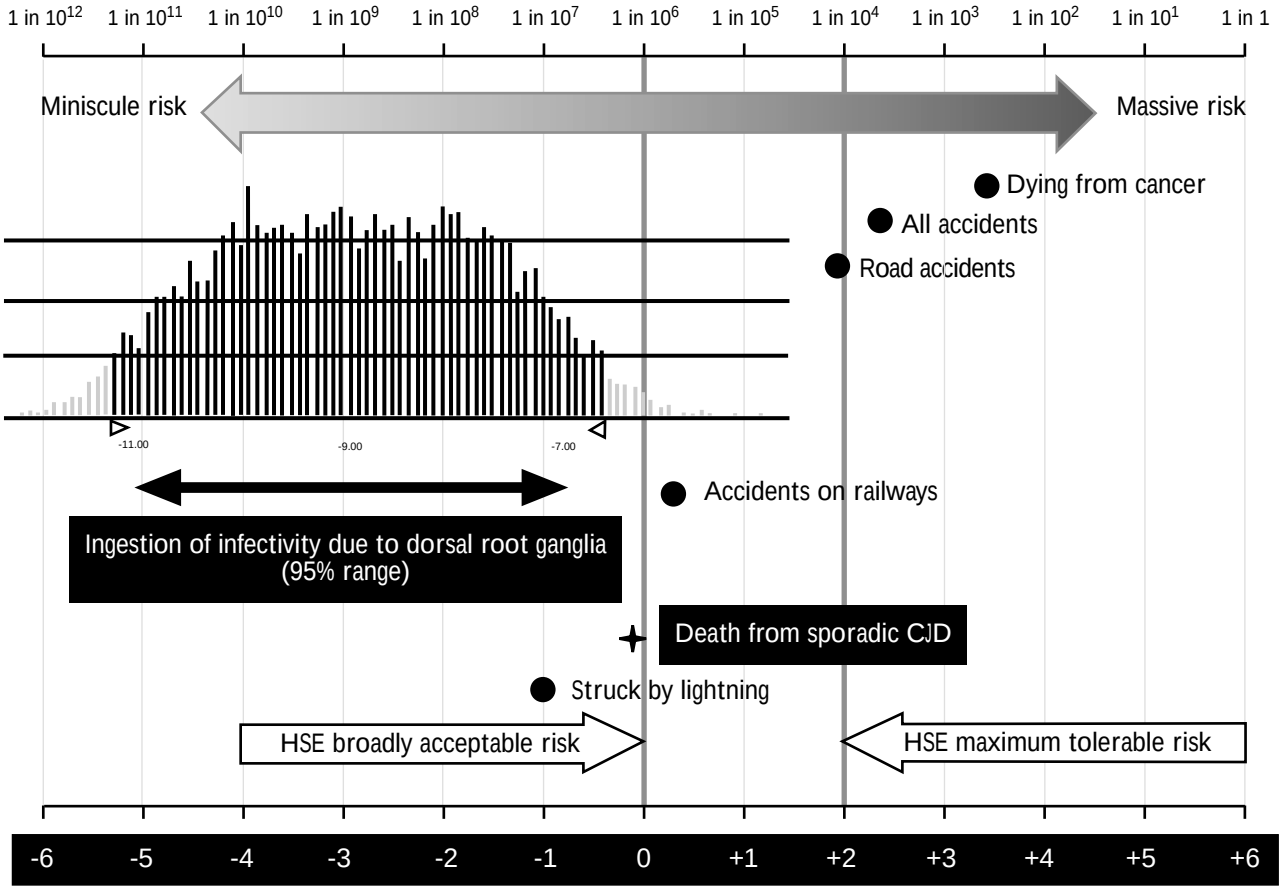
Monte Carlo simulation tool (Crystal Ball, 1996) to take account of the uncertainty in the input parameters. Each variable is defined as a distribution of values rather than as a single point value, and the result is calculated many times using the simulation program. This gives a distribution and range of values for the risk results.

Two measures of risk have been determined, both of which are based on the consumption of human oral ID_{50} units (the dose which will cause infection in 50% of the exposed population). The first measure is the total consumption per year of human oral ID_{50} units for all people in the UK. This is a measure of societal or group risk. The second measure is the individual risk, which is represented by the expected consumption per year by any one individual of human oral ID_{50} units.

The median value of the total ingestion of infectivity from infectivity in dorsal root ganglia of cattle with infectivity in the central nervous system at less than 30 months of age, has been estimated to be 0.05 ID_{50} units over the whole UK population in 1997. The 95% range is from 10^{-4} to 11 ID_{50} units. Of this total ingestion, 24% of infectivity is from meat sold on the bone (range 10%–45%).

The median value of the individual risk of ingestion has been estimated to be about one in a billion per person per year. The 95% range is from 5×10^{-12} to 2×10^{-7} ID_{50} units per person per year, which is some four orders of magnitude. These results are illustrated on a risk perspective scale in Figure 2.11. This shows the frequency distribution of the log of the individual risk on a scale that allows the results to be compared with other risk values.

Figure 2.11 Risk comparisons for individual risk of infection



Derived from John Paling © The Environmental Institute, 1992

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3 Conclusions and recommendations

The conclusions and recommendations in this section are based on considerations of the questions set out in Section 1 of this report, taking into account the reviews presented in Section 2.

Current exposure estimates, possible improvements and the role of probabilistic modelling

Exposure assessments are carried out for a variety of reasons, for example, as part of the risk characterisation, for qualitative screening and for prioritisation. It is generally the case that current exposure estimates could be improved There is a need to distinguish between crude exposure estimates (e.g. calculations of exposure based on sales of a product, or production volume of a chemical divided by population size) and detailed measurements (e.g. of personal exposure). The amount of detail necessary in an exposure estimate should be tailored to its purpose, and the sophistication of the exposure assessment methodology should be matched to the quality of the supporting data and underlying science. Sometimes a tiered or iterative approach with increasing degrees of complexity may be appropriate. However, such an approach might be seen as manipulating the estimate and so should be used with care. Any approaches used should be transparent. There is also a need for those carrying out exposure assessments within different media to share expertise and experience and to develop new approaches.

Generic exposure models should be developed for screening purposes, directed both at chemicals and at pathways of exposure. The value of personal exposure measurement rather than generic measurement should be considered.

Further consideration is needed about how best to address multiple pathways of exposure. A number of tools are available, such as event-tree analysis, which can combine different pathways of exposure and be used in probabilistic models, so that the outcomes of various exposure scenarios can be examined. Another technique available is the 'risk cup' approach, where a 'total human dose', for example an acceptable daily intake (ADI), can be apportioned to different routes of exposure. However in some cases each portion is so small that it becomes unmanageable, and a mechanism for integrating the different routes and associated uncertainties is needed. Comparing the need for or stringency of standards or guidelines for different routes of exposure, for example ADIs, occupational exposure standards (OES) or environmental quality standards, which are derived in different ways, can be difficult. A probabilistic approach could potentially be the most useful.

Probabilistic approaches could be used as part of a tiered approach to risk assessment. Such approaches will allow the identification of key determinants of exposure, and the evaluation of the likelihood of exposure by particular routes. By building a model, the key uncertainties in the estimates of frequency distribution of exposure can be identified and the sensitivity of the output to different input conditions can be examined. Such sensitivity analysis is very important. True variation in exposure within the population (e.g. variation in levels of contaminants or variation in space and time because of different activity and consumption patterns) should be separated from uncertainty in the input parameters, although it may not be possible to disaggregate them completely.

Probabilistic models do, however, need to be validated. Current models use frequency distributions rather than discrete data, and actual or fitted distributions can be accommodated. Uncertainties might be greater at the top end of the frequency distribution, which is the portion most likely to be of interest.

Probabilistic methods, such as Bayesian, fuzzy arithmetic and simulation of the entire population, should be evaluated and developed to investigate whether these might have advantages over Monte Carlo approaches to risk assessment, either generally or in particular circumstances.

As probabilistic approaches allow analysis of different scenarios, they could aid policy development. Probabilistic modelling is already in use in some Government departments; however it is recognised that there is a need for further discussion, in order to share experience, pool expertise and clarify some of the current assumptions being made. The lack of data and skills and the time and computing resources required to analyse and present outputs are seen as key limitations, at present, for the use of probabilistic approaches.

There are often problems with availability of, access to and quality of data. The data available have often been collected for a variety of purposes (e.g. general surveys of exposure in the population, monitoring to ensure that levels are not increasing, research purposes) and therefore they are not always in the most appropriate form to feed into a risk characterisation. Collection and use of exposure data could be shared much more profitably than at present among Government departments, agencies, academic institutions and industry.

'Average' or 'worst case' assumptions

Current approaches to exposure estimation use both 'average' and 'reasonable extreme case' assumptions, as there is rarely information available on the 'worst case'. There are difficulties in defining a sensible 'reasonable extreme', as there may be differences in opinion as to what constitutes 'extreme' and what constitutes 'normal'. There are always difficulties in deciding which levels of exposure to include in a population distribution, owing to varying patterns of behaviour or even abuse. It is generally not possible to protect very extreme consumers. Clarity and transparency are important in defining both the particular situation being examined and the rationale behind the choice of 'reasonable extreme case'.

Efforts should be made to understand the uncertainties present at each stage of the exposure assessment and the implications of the combined uncertainties for the final exposure estimate; again, probabilistic approaches may have a useful role.

Different exposure estimates and the effectiveness of current default values for some population subgroups

In estimating exposure it is necessary to decide who (e.g., the general population or special groups such as children or sensitive subpopulations) is to be protected and to what level, and whether some risk is acceptable. Uncertainty factors are often used to deal with some of these concerns. However there remains a need for greater clarity and transparency when making such decisions.

Three types of special groups can be identified based on biological, social/cultural or ethnic characteristics (see Table 3.1). Potentially these groups are sufficiently different to justify separate exposure estimates, although the need for this should be considered on a case by case basis. This has already been done for exposure from food, where dietary data have been collected by age, sex, social class and ethnicity and exist for groups such as vegetarians, diabetics and pregnant women. For other routes of exposure such detail generally does not exist. Estimates of current exposure are often made only in healthy adults, and often only in males; special groups are only occasionally addressed and generally in an inconsistent and superficial manner. If special groups have characteristics that lead to exposures at the extreme ends of those of the general population then focusing on these groups will improve exposure estimates at the tails of the general distribution, generally the weakest areas in data sets.

The current default values used for anatomical and physiological parameters are considered to be of limited use. Databases often become out of date quickly, and there are considerable cost and resource implications in updating them. In general, the quality of data for special groups is considered to be poor.

Exposure data should be collected on susceptible groups in the population and a survey of data sources should be conducted.

For some subpopulations, currently used methodologies for obtaining exposure estimates could be improved. For example, questionnaires are a commonly used approach but are often produced only in English. Measuring devices may be inappropriate; for example, measurement of personal exposure to air pollutants may require heavy monitoring equipment to be carried, making it unsuitable for very young, sick or elderly people. Furthermore, there may be difficulties with access

Table 3.1 Identification of special groups

Biological	Social/cultural	Ethnic
Age group (e.g. infant, elderly)	Diet	Genetic
Sex	Smoker/non smoker	Social - diet
Disease state/medication	Alcohol/drugs	
Genetic susceptibility	Social circumstances (e.g. low income/homeless)	
Pregnancy	Religion	
Physiological variation (e.g. weight)	Quality of housing	
	Location of housing	
	Work circumstances	

to some special groups; for example, a food survey of homeless people might present particular challenges. Ideally exposure estimates should be of consistent quality for all groups being examined so that comparisons can be made, and the planning stages of any survey should consider the need to obtain data about special groups.

Consistency in collection and analysis of exposure data in different media

Although consistency in data collection and analysis is desirable, harmonisation, where feasible and appropriate, is more important than standardisation of sampling and measurement methods and analysis. Clear and transparent guidelines should be developed to promote such harmonisation.

Setting standards for a single medium and the use of data from other media

Although a case by case approach is needed, in principle, data from all exposure routes should be taken into account in standard-setting. When exposure is from multiple pathways, the various routes of exposure may have different impacts on the total exposure and this should be taken into account. In some cases ADIs have been apportioned between media, although sometimes arbitrarily. When exposure is to mixtures, it may be appropriate to aggregate exposure to chemicals that have similar mechanisms of effect. Again there is room for a more co-ordinated approach between those bodies responsible for setting standards, and the Interdepartmental Liaison Group on Risk Assessment (ILGRA) and the Risk Assessment and Toxicology Steering Committee, in combination with the Society for Risk Analysis, might provide an appropriate forum.

Models are needed for dealing with total exposures to particular chemicals and mechanisms should be developed for addressing mixtures, both in terms of evaluating their toxic effects and in terms of exposure estimation; models are also needed for dealing with bioaccumulation in estimating exposure and in risk assessment.

Dealing with uncertainty in exposure estimates and with sparse data

There is a need for an increased awareness about uncertainty and how to incorporate it into exposure assessments. The process used for any exposure estimate should be transparent so that uncertainties can be traced and the process can be audited. Uncertainties could be categorised as due to either inherent variability or inadequate information. As noted above, probabilistic approaches may have a role in investigating the implications of uncertainties, for example by sensitivity analyses. Again, the development of a harmonised approach and clarity and transparency are important, as is successful communication about how uncertainty and sparse data are dealt with.

Models for dealing with uncertainty in exposure estimates and guidance on their interpretation should be developed.

Improvements in the incorporation of exposure assessments into risk characterisation, and in risk communication

At all stages of the risk assessment process, from hazard identification and characterisation and exposure assessment to the overall risk assessment, better communication is needed between the experts involved. This will facilitate the optimal integration of all stages to produce the final overall assessment. Furthermore, the earlier stakeholders

are included in the process the sooner limitations pertaining to clarity and transparency in the selection and use of methodologies and procedures can be identified and resolved.

Harmonisation of approaches and use of terminology (rather than standardisation) would benefit communication. There are a number of areas which could be harmonised, for example the definition of frequency distributions, the definition of cut-off points and approaches for dealing with lack of data.

Successful communication with the general public is vital. This is a two-way process and should include taking account of the concerns of the general public as well as providing information. Methods for communicating with the general public about the process of risk assessment and the issue of uncertainty should be improved. More openness about uncertainty issues and greater attempts to explain these to the public would be valuable. However, identifying uncertainties may be interpreted by some as 'fudging' and could lead to difficulties in acceptance of the subsequent risk assessment. The presentation of uncertainty must be transparent. Stakeholders should be involved, ideally throughout the process of communication to the public. Intermediaries such as health care workers and teachers might play a useful role.

Communication with the general public, including susceptible groups within the population, should be improved. Presentational aspects, for example visual displays, should be considered.

An interdepartmental approach

Throughout the exposure assessment process there is a need for a more harmonised approach and better pooling of expertise, and for improved clarity and transparency regarding both the choice of procedures, models and other factors to be used in the assessment and the communication of the outcome. To this end it is recommended that Government departments establish a specific forum to address issues common to all departments. Suggested issues for such a forum include:

- harmonisation of approaches where feasible;
- development of guidelines;
- ensuring that total exposure to a chemical being examined is considered;
- the establishment of multidisciplinary groups, both in terms of media being addressed (e.g., food, occupational, environmental — water, air, soil), and the expertise involved (e.g., toxicology, epidemiology, chemistry, regulatory);
- common approaches to the use of expert judgement; and
- shared methods for communicating with the general public.

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