

**Department for Environment, Food and Rural Affairs
and The Environment Agency**

**CONTAMINANTS IN SOIL: COLLATION OF
TOXICOLOGICAL DATA AND INTAKE VALUES
FOR HUMANS**

Publishing Organisation

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Statement of Use

This publication sets out the approach to the derivation of Tolerable Daily Soil Intakes and Index Doses for contaminants to support the derivation of Soil Guideline Values. The report has been written for technical professionals who are familiar with the risks posed by land contamination to human health but who are not necessarily experts in risk assessment. It is expected to be of use to all parties involved with or interested in contamination, but in particular to those concerned with the assessment of land contamination.

Keywords

Soil Guideline Values, land contamination, index dose, risk assessment, TDI.

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1 Introduction

- 1.1 This report describes a framework for the collation of toxicological data to support the derivation of soil contaminant intakes that are protective of human health. It has been developed by the Department for Environment, Food and Rural Affairs (DEFRA)¹ and the Environment Agency, based upon work by a number of contractors. This involves assessing the potential harm to human health from contaminants in soil and using this information for deriving *health criteria*. Tolerable daily intakes (TDIs) and minimal risk levels (termed “Index Doses”) are derived for threshold and non-threshold contaminants, respectively. The latter refers to chemicals for which a threshold for health effects cannot be assumed, such as genotoxic carcinogens and mutagens. TDIs and Index Doses are derived from expert judgement of all the relevant data on the toxicological properties of the chemical.
- 1.2 This report is one of a series published by DEFRA and the Environment Agency (the “Agency”) that is relevant to the assessment of the risks to human health arising from long-term exposure to soil contamination. These reports are set within DEFRA’s framework for risk assessment and management, and promote the use of a tiered approach to risk assessment (DETR, Environment Agency and IEH, 2000). It is important that each report in this series is read in conjunction with other relevant documentation. Table 1.1 provides more information on the content of each report. Figure 1.1 sets the reports in a much wider context, and shows how the general approach to investigating land contamination is supported by a hierarchy of guidance. This figure also provides information on where this specific guidance fits.
- 1.3 Tolerable daily intakes and Index Doses are used as the basis for deriving Soil Guideline Values. The principles behind the derivation of appropriate Soil Guideline Values and a description of the computer model used to generate these values are described in CLR10 (DEFRA, 2002d). Separate reports are also being published on the toxicological data for particular contaminants and on the derivation of Soil Guideline Values for these contaminants (DEFRA, 2002c, e).
- 1.4 This report has been written for technical professionals who are familiar with the risks posed by land contamination to human health but who are not necessarily experts in toxicology. It will enable assessors to have an understanding of the basic toxicological principles used to derive TDIs and Index Doses for the purpose of developing Soil Guideline Values as part of a risk assessment of a contaminated land site. However, those requiring more detailed information on the toxicological principles outlined in this report should refer to the original reports referenced in subsequent sections of this document or obtain specialist advice.
- 1.5 The remainder of this report has been divided into three further parts. Section 2 sets out the basic concepts and definitions of terms used together with background information on the

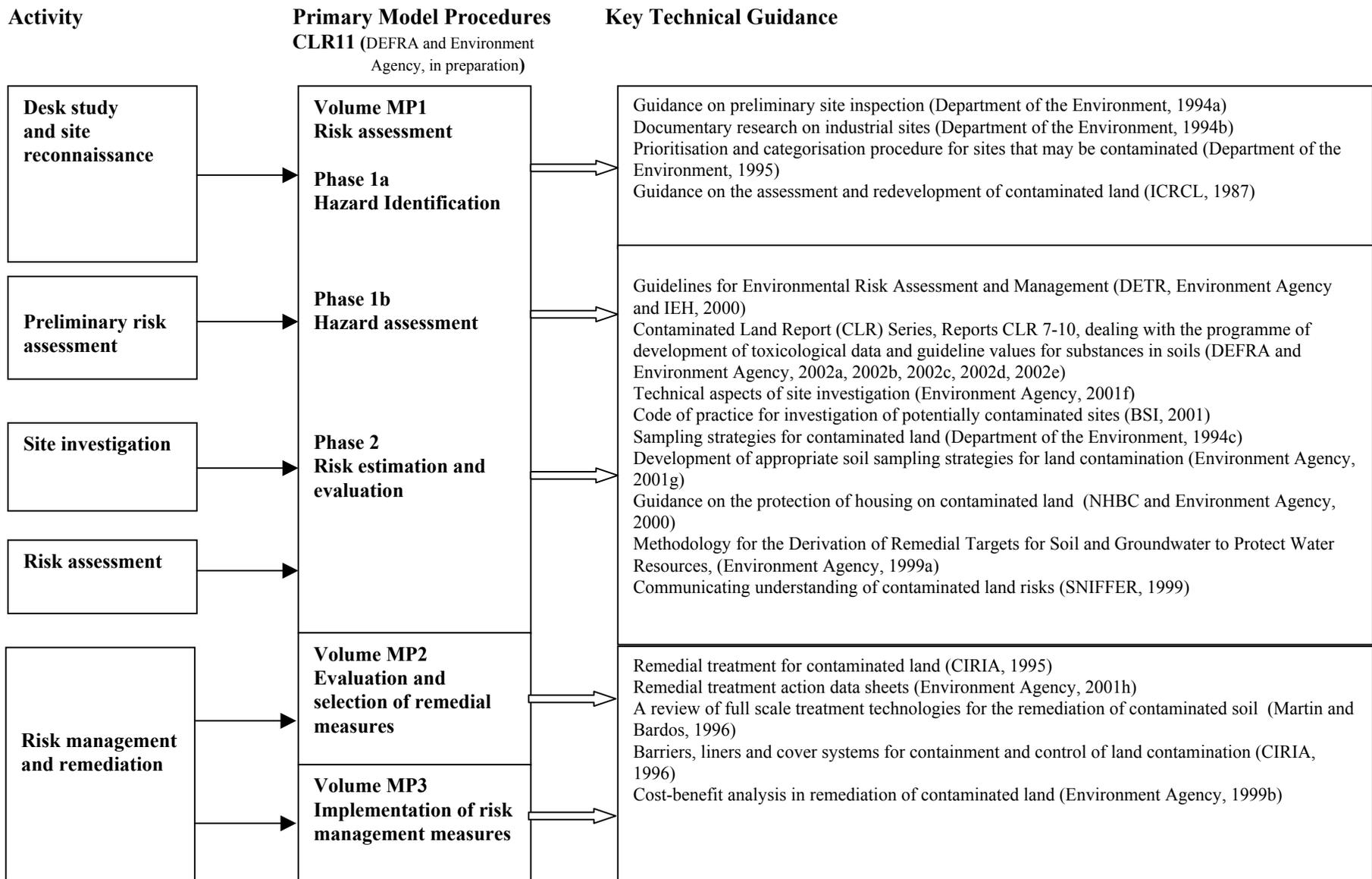
¹ Formerly the Department of the Environment, Transport and the Regions (DETR).

reasons for selecting these. Section 3 presents the framework for deriving soil contaminant intakes that are protective of human health. Section 4 gives a brief overview on how to deal with chemical mixtures in soils. Finally, Appendix A provides a summary of international approaches and definitions used for the purpose of deriving health criteria for the protection of human health.

Table 1.1 Assessment of risk to human health from land contamination. Key reports from DEFRA and the Environment Agency

<p>CLR 7 <i>Assessment of Risks to Human Health from Land Contamination: An Overview of the Development of Soil Guideline Values and Related Research</i> (DEFRA and Environment Agency, 2002a). CLR 7 serves as an introduction to the other reports in this series. It sets out the legal framework, in particular the statutory definition of contaminated land under Part IIA of the Environmental Protection Act (EPA) 1990; the development and use of Soil Guideline Values; and references to related research.</p>
<p>CLR 8 <i>Priority Contaminants for the Assessment of Land</i> (DEFRA and Environment Agency, 2002b). This identifies priority contaminants (or families of contaminants), selected on the basis that they are likely to be present on many current or former sites affected by industrial or waste management activity in the United Kingdom in sufficient concentrations to cause harm; and that they pose a risk, either to human health, buildings, water resources or ecosystems. It also indicates which contaminants are likely to be associated with particular industries.</p>
<p>This document:</p> <p>CLR 9 <i>Contaminants in Soil: Collation of Toxicological Data and Intake Values for Humans</i> (DEFRA and Environment Agency, 2002c). This report sets out the approach to the selection of tolerable daily intakes and Index Doses for contaminants to support the derivation of Soil Guideline Values.</p>
<p>CLR TOX 1–10 (DEFRA and Environment Agency, 2002d). These reports detail the derivation of tolerable daily intakes and Index Doses for the following contaminants, which are arsenic, benzo[a]pyrene, cadmium, chromium, inorganic cyanide, lead, phenol, nickel, mercury and selenium.</p>
<p>CLR 10 <i>The Contaminated Land Exposure Assessment Model (CLEA): Technical Basis and Algorithms</i> describes the conceptual exposure models for each standard land-use that are used to derive the Soil Guideline Values. It sets out the technical basis for modelling exposure and provides a comprehensive reference to all default parameters and algorithms used.</p>
<p>CLR GV 1–10 (DEFRA and Environment Agency, 2002e). These reports set out the derivation of the Soil Guideline Values for the following contaminants, which are arsenic, benzo[a]pyrene, cadmium, chromium, cyanide (free, simple, and complex inorganic compounds), lead, phenol, nickel, mercury (inorganic compounds) and selenium.</p>
<p>CLR 11 <i>Model Procedures for the Management of Contaminated Land</i> (DEFRA and the Environment Agency, in preparation). This report incorporates existing good technical practice, including the use of risk assessment and risk management techniques, into a systematic process for identifying, making decisions about and taking appropriate action to deal with contamination, in a way that is consistent with UK policy and legislation.</p>

Figure 1.1 Hierarchy of guidance on land contamination



2 Basic Concepts and Definitions

- 2.1 Many countries have undertaken work on the potential human health impact that may result from exposure to contaminants in soils. Each has developed new terminology or adopted another existing one. This section describes the principal terms used in this report, in terms of their meaning in the context of setting Soil Guideline Values for the assessment of chronic risks to human health.

Definition of exposure, intake and uptake

- 2.2 The relationship between the terms exposure, intake dose and uptake dose, as used in this report, is shown graphically in Figure 2.1.

- 2.3 The term **exposure** is defined as follows:

Exposure is the amount of a chemical that is available for intake by a target population at a particular site. Exposure is quantified as the concentration of the chemical in the medium (for example, air, water, food) integrated over the duration of exposure. It is expressed in terms of mass of substance per kg of soil, unit volume of air or litre of water (for example, mg kg^{-1} , mg m^{-3} or mg L^{-1}).

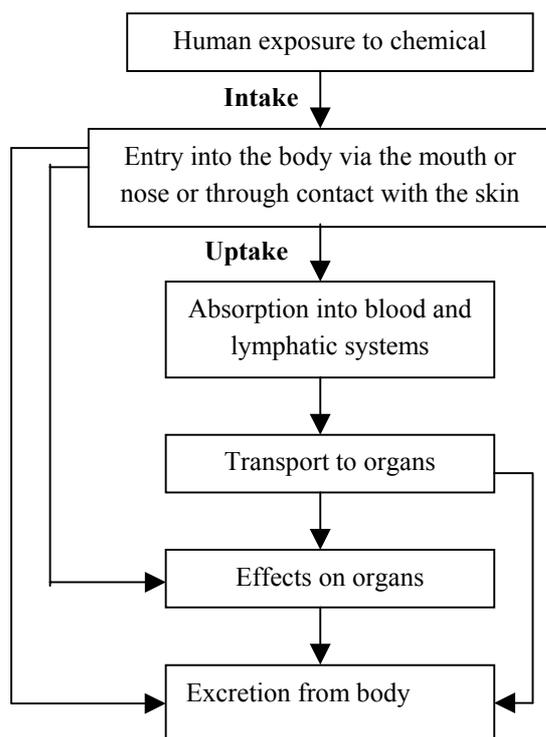
- 2.4 In the first instance, exposure to humans occurs externally. This is referred to as the **intake dose** and is defined as follows:

Intake dose is the amount of a chemical entering or contacting the human body at the point of entry (that is, mouth, nose or skin) by ingestion, inhalation, or skin contact. Actual intake will be a function of the chemical characteristics and the nature of the target population and their behaviour patterns. Intake dose is expressed in terms of mass of substance per kg body weight over a period of time (for example, $\text{mg kg}^{-1} \text{bw d}^{-1}$).

Intake dose in this document is generally abbreviated to intake.

- 2.5 In many cases there is no distinction made between the intake of contaminants that are bound to soil and those which occur as a vapour or are released during processes like digestion into solution (the so-called **bioaccessible** fraction). For example, children may ingest arsenic-contaminated soil through deliberate or inadvertent mouthing of hands or sucking soiled toys. Empirical studies have sought to demonstrate a relationship between the type of contaminated soil and the fraction of arsenic that can be dissolved by digestion (Ruby *et al*, 1999). Such studies may improve our knowledge of the intake dose of bioaccessible organic and inorganic chemicals in the future, as this parameter represents a better estimate of the intake dose than does the total concentration of soil contaminants.

Figure 2.1 Simplified diagram of the relationship between exposure, intake and uptake



2.6 Not all of the intake is absorbed by the body, and the **uptake dose** is defined as follows:

Uptake dose is the amount of a contaminant that reaches the circulating blood having been absorbed by the body through the skin, the gastrointestinal system and the pulmonary system, expressed in terms of mass of substance per unit volume of blood (for example, mg L^{-1}).

Again, uptake dose is abbreviated to uptake for the remainder of this report. In reality it is difficult to estimate uptake and its practical use is limited to exposure to a limited number of substances (for example, lead).

2.7 Uptake is commonly related to the intake by the **bioavailability** of the contaminant. This term is defined as follows:

Bioavailability is the fraction of the chemical that can be absorbed by the body through the gastrointestinal system, the pulmonary system and the skin.

2.8 For example, the body may actually absorb only a fraction of a substance ingested as it passes through the intestinal tract, with the remainder being excreted. Current knowledge of the bioavailability of many chemicals is extremely limited and it is seldom modelled, with a few notable exceptions such as lead following ingestion (USEPA, 1999) or benzene following inhalation (WHO, 1993a; ATSDR, 1997).

Local effects

- 2.9 Uptake is not relevant for contaminants that produce their principal adverse effects before transfer to the systemic circulation. An example of this kind might arise when material is deposited in the lung and is not rapidly transferred to the systemic circulation. Such material may cause local effects in the lung (for example, fibrosis, or lung cancer) and/or may reach other tissues via, for example, the lymphatic system. For contaminants such as beryllium, therefore, which are cleared from the lung very slowly and which may cause local effects in the lung, the fraction of the inhaled intake that is retained in the lung must be considered in its own right.

Systemic effects

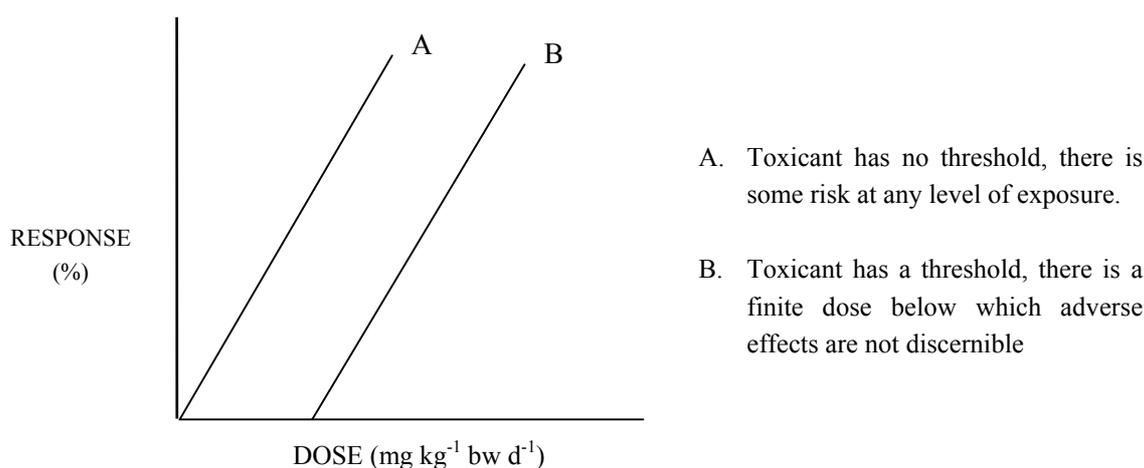
- 2.10 The amount of a chemical that actually reaches a tissue or organ in the body will determine whether damage is inflicted in that tissue/organ; for example, the kidney may be affected if the amount of cadmium that reaches it exceeds a certain level. The organs or tissues most affected are often not the site of a chemical's highest concentration, but rather the site with the greatest susceptibility to damage by the chemical or its metabolites (Covello & Merkhofer, 1993). However, as it is extremely difficult to measure or predict chemical concentrations in organs/tissues, the toxicological information is commonly derived from knowledge of the external exposure or intake, that is, the concentration of the contaminant at the point of entry, be this the mouth, nose or skin.
- 2.11 For the purpose of deriving Soil Guideline Values, contaminant intakes are generally used as a basis for health criteria for the protection of human health. There are a few exceptions to this, for example lead, where enough information is available on internal exposure (that is, uptake) and observed health effects. When conducting an exposure assessment it is important to ensure an intake is derived that is appropriate for comparison with toxicological information used to derive Tolerable daily intakes and Index Doses (see below for definition of these terms).

Threshold and non-threshold effects

- 2.12 A distinction must be made between chemicals with critical effects, for which there is considered to be a **threshold**, and those chemicals for which a threshold for health effects cannot be assumed. Figure 2.2 shows a simplified diagram that illustrates the difference between threshold and non-threshold compounds. Within toxicity, it is often assumed that there is a threshold level of toxicant that needs to be present to produce an effect (for example, inhibition of an enzyme) leading to the adverse effects. That is, there is a threshold level below which there is no effect, recognising that the precise level of this threshold may vary between individuals. However, in some areas of toxicity, specifically those for mutagenic and genotoxic carcinogens, there is no theoretical reason why a single molecular exposure should not result in a tumour or mutation, possibly expressed in subsequent generations. For these substances, no threshold can be assumed and it has to be accepted that they carry some risk at any slight level of exposure.

- 2.13 The approach used to derive toxicological criteria for the protection of human health differs for contaminants exhibiting threshold or non-threshold effects. In the context of this work, when dealing with threshold effects, a certain amount of intake of a chemical can be tolerated and the term tolerable daily intake (TDI) is used. For non-threshold contaminants, the term Index Dose is used to express minimal risk levels, with the additional requirement to keep any intake as low as reasonably practicable (ALARP). These terms are explained in more detail below.

Figure 2.2 Diagrammatic representation of the threshold and non-threshold concept



Definition and derivation of tolerable and mean daily intakes

- 2.14 The concept of an acceptable or tolerable daily intake for chemical contaminants has its origins in the setting of standards of dietary safety for food additives. The conventional toxicological approach has been to find a **no observed adverse effect level (NOAEL)** from animal studies; this is usually expressed in terms of a daily intake (μg or mg) of the chemical per kilogram body weight (kg bw) of the animal. For the purpose of this work, a NOAEL is defined as follows:

NOAEL is the greatest concentration or amount of a substance, found in experiment or observation, which causes no detectable adverse effects on the target organism under defined conditions of exposure (WHO, 1994).

- 2.15 The NOAEL is then divided by an appropriate **safety (or uncertainty) factor** (traditionally 100) to arrive at an **acceptable daily intake (ADI)** for humans (see paragraph 2.22 for further detail on safety factors). The Joint FAO/WHO (Food and Agricultural Organization/World Health Organization) Expert Committee on Food Additives (JECFA) and the WHO have defined an ADI as an estimate of the amount of a food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk (WHO, 1987).
- 2.16 During the 1970s, JECFA extended its terms of reference to include food contaminants. Whereas additives have some desirable technological purpose, contaminants have no intended

function. Therefore JECFA adopted the term “tolerable” for contaminants, with the intention of implying something rather less than “acceptable”: that is, “tolerable” should be taken to mean “permissible” rather than “satisfactory”. Therefore the term **tolerable daily intake** (TDI) was adopted (WHO, 1987) and is defined as follows:

Tolerable daily intake is an estimate of the amount of a contaminant, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk.

- 2.17 In the UK the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) have adopted the WHO usage, and use the word “tolerable” rather than “acceptable” when referring to intakes of contaminants (Rubery *et al*, 1990).
- 2.18 In deriving a TDI, it is important to identify the **critical NOAEL** and appropriate safety factors. For an overview of the current UK approach on how to set numerical limits for intakes of chemicals, refer to Rubery *et al* (1990).
- 2.19 NOAELs may be derived from experimental animal studies and epidemiological studies. Where available, the use of sound human data should be used in preference to data derived from animal studies. Experimental animal studies have well-defined study populations and exposure regimes, but suffer from the basic limitation that the results have to be extrapolated to humans. Epidemiological studies are studies of human population groups, but the nature of the study group and their exposure pattern are largely uncontrolled. Most of the useful data come from occupationally exposed groups, where the doses are almost always higher than those resulting from environmental exposure. In making use of data from studies of occupationally exposed groups, consideration must be given to the fact that other sectors of the population (for example, the elderly or those suffering from illnesses) may be more susceptible to the effect of chemicals than a selective workforce population. In addition, occupationally exposed groups are generally exposed to substances via the inhalation route rather than the ingestion route (the one of most interest when considering contaminated soils) and do not include children, who may have higher exposure to contaminants in soils (paragraphs 3.8 and 3.9). The interpretation of toxicological data from certain studies may, therefore, require consideration of route-to-route extrapolations. Further details are given in paragraphs 3.10 to 3.14.
- 2.20 When determining the key human health effect(s) of concern from human and animal studies, it is important not to confuse the terms acute and chronic, short term and long term. Acute adverse health effects occur within seconds or days of exposure to the chemical. For example, a short-term exposure to high concentrations of organic solvents can affect nerve cells, probably from physical alteration of the cell membranes (Andrews and Snyder, 1986) and produce central nervous system effects that range from dizziness and disorientation to death from respiratory depression or cardiac arrest. Chronic adverse health effects, by comparison, last longer and develop over a longer period of time. For example, exposure to low solvent concentrations (for example, in an occupational setting) may cause neurotoxicity,

as well as cancer, reproductive, dermatological, cardiovascular, respiratory and renal effects (summarised by Roberts and Abernathy, 1996). Adverse health effects may be produced by exposures that are short-term and/or long-term. In addition, delayed or long-lasting health effects can be caused by single or multiple exposure within a short period of time.

- 2.21 The TDI is typically based on the highest dose which, given daily for a long period to laboratory animals, had no observed adverse effects. This is then divided by an appropriate uncertainty factor. The aim is to provide a wide margin of safety between the TDI and harmful intakes. This means that exceeding the TDI, particularly for brief periods, does not necessarily imply that harm will result, unless of course this short-term intake exceeds those which cause acute toxicity. For example, an individual may exceed a recommended TDI for a specific contaminant following the consumption of an unwashed vegetable that contains high levels of a metal in the soil attached to that vegetable. Provided this only occurs on rare occasions, then it would not create undue concern. However, it is difficult to make generalisations concerning the length of time during which intakes in excess of the TDI would be toxicologically detrimental. Any detrimental effect would depend on the nature of the toxicity and the biological half-life of the chemical concerned (FAO/WHO, 1989). Where acute effects are relevant, these may be taken into special account when determining the most appropriate TDI. An example of this is inorganic cyanide, where health criteria was based on short-term effects is used (see DEFRA, 2002c for further details).
- 2.22 As mentioned in paragraph 2.15, safety factors are applied to the NOAEL to estimate the TDI (Table 2.1). The use of a factor of 100 is common, and is regarded as comprising two factors of 10 each to allow for inter-species and intra-individual (intra-species) variations. More recently, additional safety factors have been incorporated to take account of, for example, deficiencies in the database, the absence of chronic data or where the key study did not identify a NOAEL. The numerical values chosen for these factors vary – usually between 3 and 10.² Various schemes have been proposed which allow for the incorporation of factors that take into account differences in chemical processes within the body; for example, absorption, distribution, metabolism and elimination and the potency at the site of toxicity (Renwick, 1993a; WHO, 1994). Although there is some general consensus as to the derivation of safety factors, many of the decisions concerned depend upon expert professional judgement, and differences in the choice of safety factors for specific chemicals often occur. The derivation of safety factors has been discussed in detail by, for example, Renwick (1993b, 1995), the WHO (1987, 1994) and RATSC (1999).

² Thus the overall safety factor can vary between 300 and 1000.

Table 2.1 Examples of safety factors used for deriving TDIs

Safety factor ^a	General comments on values
Intra-species variability	A 10-fold factor is normally used to account for variability of responses in human populations
Inter-species variability	A 10-fold factor is generally used to account for species susceptibility between humans and the animal test species
LOAEL ^b to NOAEL	A 10-fold factor may be used when a LOAEL instead of a NOAEL is used to derive a standard. For minimal LOAEL, an intermediate factor of 3 may be used
Data gaps	A factor, usually 3- to 10-fold, may be applied for “incomplete” databases (e.g. missing studies, no chronic bioassays or no reproductive toxicity data). It is meant to account for the inability of any study to consider all toxic end-points

From Renwick (1993b, 1995) and WHO (1994).

^a Professional scientific judgement is used to determine the appropriateness of each safety factor. Values ranging from 1 to 10 may be used for each, although the 10-fold value is the most commonly used.

^b The LOAEL is the lowest dose at which an adverse effect is observed.

2.23 TDIs should only be set if there are adequate data for a sufficient variety of end-points observed in the toxicological studies to allow for the establishment of a threshold level below which no adverse health effects are likely to occur (Rubery *et al*, 1990). In setting a TDI, it is important that information is provided on:

- the uncertainties in the data used to derive the TDI;
- all the studies used to derive the NOAEL(s); and
- the reasons for the size of the safety factor employed.

2.24 In the context of contaminants in soils, soil ingestion is an important route of exposure (for a review on soil ingestion studies see, for example, Paustenbach, 2000) and, where available, TDIs are normally derived from data on intakes following ingestion. TDIs have been derived from experimental animal studies involving oral intake of the substance being studied either following ingestion of food and water or by direct oral administration. However, intake by the inhalation and dermal routes can be important for some contaminants and so, when this is the case, specific consideration is given to non-ingestion routes of exposure. Separate TDIs³ may

³ The subscripts are used here to provide information on the type of study from which the TDI was derived (that is, whether the TDI was derived from oral, inhalation or dermal experimental or epidemiological studies). It does *not* imply that separate TDIs need to be derived for different exposure routes, unless there is evidence that intake via different routes may, for example, lead to different local effects or affect different target organs/systems.

then be derived for each exposure route. For example, it may be appropriate to derive TDI_{inh} , TDI_{oral} and TDI_{dermal} for nickel, as exposure to nickel above a threshold may lead to allergic contact dermatitis (or skin sensitisation) following skin contact, reproductive or fetotoxic effects following ingestion, and cancers of the lung and nasal passages if inhaled.⁴ However, this has to be decided on a case-by-case basis, based on the relevance to soils as well as the evidence and toxicological information available for the various exposure routes. For further details on route-to-route extrapolation refer to paragraphs 3.10 to 3.14.

- 2.25 Oral TDIs are usually expressed in terms of milligrams of contaminant per kilogram body weight per day ($mg\ kg^{-1}\ bw\ d^{-1}$). These are therefore applicable over the whole range of body weights, from infants and children to adults. TDI_{inh} are derived from the amount of contaminant per m^3 of air inhaled per day, making assumptions about the amount of air breathed to give the same units ($mg\ kg^{-1}\ bw\ d^{-1}$; see paragraph 3.19 for default values). Similarly, TDI_{dermal} ($mg\ kg^{-1}\ bw\ d^{-1}$) relates to the amount applied to the skin per day, making assumptions about the area of skin exposed.

Mean daily intake and tolerable daily soil intake

- 2.26 When setting Soil Guideline Values, background exposure (as defined by **the mean daily intake**, MDI) needs to be taken into account. For the UK population:

Mean daily intake is defined as the average “background intake” to which that population may be exposed (expressed in terms of mass of substance per day, for example, $mg\ d^{-1}$).

- 2.27 The MDI is estimated from published information on ambient air concentrations and average concentrations measured in water and food products. This information can be used to estimate an MDI through the inhalation route as well as an oral MDI. Where relevant, other sources should also be considered (for example, the exposure of the general population to mercury vapour from dental amalgam), though active cigarette smoking should be excluded. In estimating mean daily intakes for different exposure groups (for example children), the MDI needs to be adjusted to take into account differences in average consumption and inhalation rates by different age groups. See paragraph 3.19 and Table 3.1 for further details on default values.
- 2.28 After taking into account background exposure, a proportion of the TDI can be identified as an exposure that can be tolerated from contaminants in soil; this term is referred to as the **tolerable daily soil intake** (TDSI). Further details on how to estimate this parameter are provided in paragraphs 3.22 to 3.27.

⁴ Please note that in the example provided a TDI_{dermal} has not been derived to date for sensitisation because of the difficulties in determining this value experimentally (as this cannot be determined using the standard animal test for skin sensitisation).

Definition and derivation of Index Dose

2.29 The term **Index Dose** is adopted here for the purpose of deriving Soil Guideline Values for contaminated land for non-threshold chemicals⁵. These substances carry a putative risk at any level of exposure and, instead of a TDI, it is appropriate to allocate an Index Dose, against which the health significance of exposures to soil contaminants can be assessed. For the purpose of this work:

Index dose is defined as the dose which can be considered to present a minimal human health risk from exposure to soil contaminants. However, and in addition, efforts are still needed to reduce exposures from all routes to as low as reasonably practicable (ALARP), so that even this minimal risk is further diminished.

2.30 The Index Dose is expressed in terms of mass per kg body weight per day (same as TDI, for example $\text{mg kg}^{-1} \text{bw d}^{-1}$) and therefore is applicable over the whole range of body weights, including infants, children and adults.

2.31 As with TDIs, Index Doses are normally associated with intake by ingestion (ID_{oral}) as, in the context of contaminants in soils, ingestion is generally the dominant route of exposure (paragraph 2.24). However, intake by the inhalation and dermal routes (ID_{inh} and $\text{ID}_{\text{dermal}}$, respectively)⁶ can be important for some contaminants, and therefore specific consideration is given to non-ingestion routes of exposure, where appropriate, in this report and separate reports on individual contaminants (DEFRA and Environment Agency, 2002c). For further details refer to paragraphs 2.24 and 3.10 to 3.14. Again, as with TDIs, ID_{inh} values are derived from the amount of contaminant per m^3 of air inhaled per day, making assumptions about the amount of air breathed to give the same units ($\text{mg kg}^{-1} \text{bw d}^{-1}$; paragraph 3.19). Similarly, $\text{ID}_{\text{dermal}}$ relates to the amount absorbed through an area of skin per day, making assumptions about the area of skin exposed.

2.32 The Index Dose differs from the TDI in a number of aspects as outlined in Table 2.2. Key here is that the Index Dose represents a minimal risk level and therefore these substances carry some risk at any level of exposure. Exceedance of the Index Dose, even in the short term, indicates an increase level of risk to health, which is not acceptable.

2.33 In addition, the Index Dose is set specifically for exposures from soil, and represents a *minimal* risk level from possible exposure to a particular substance from that one source, subject also to ALARP considerations. It is assumed that the risks from other sources (for example, food and air) will also be controlled by the ALARP principle. Therefore exposure

⁵ This approach has been developed in consultation with other Government departments and agencies, mainly Department of Health and Food Standards Agency, as the leading authorities in this field.

⁶ The subscripts are used here to provide information on the type of study from which the Index Dose was derived (that is, whether the Index Dose was derived from oral, inhalation or dermal studies). It does *not* imply that separate Index Doses need to be derived for different exposure routes, unless there is evidence that intake via different routes may, for example, lead to different local effects or affect different target organs/systems.

from other sources of contamination (that is, the MDI) is not considered and the Index Dose itself is the toxicological assessment parameter used for deriving Soil Guideline Values (DEFRA and Environment Agency 2002d, e).

Table 2.2 Comparisons between TDI/TDSI and Index Dose

	TDI/TDSI	Index Dose
Meaning	TDIs can be derived for substances for which a threshold for the onset of adverse health effects can be assumed. For these substances, adverse health effects are not expected to arise below this threshold dose. For example, most systemic toxicants, non-genotoxic carcinogens	Index Doses are allocated to substances for which a threshold of adverse health effects cannot be presumed. These substances therefore carry some level of risk at any given level of exposure, although this may be very low at low levels of exposure. The Index Dose is the level at which this risk is considered minimal. There is, however, the requirement to reduce exposure below this value as low as is reasonably practicable. For example, genotoxic carcinogens, mutagens
Basis for derivation	TDI is derived from NOAEL or LOAEL for critical health effect from toxicological or epidemiological studies by applying appropriate safety factors to this level.	An Index Dose can be based on a nationally or internationally agreed exposure standard from a single source. These levels may have been derived by a number of different mechanisms and they may also take into account other considerations in addition to the scientific risk assessment. However, they are considered to represent a minimal human risk level.
Applicability	The TDI relates to exposure from all sources, and pathways. A proportion of the TDI can be identified as an exposure that can be tolerated from contaminants in soil – this is referred to as the TDSI.	Relates to exposure arising <i>solely</i> from contaminants in soil. The Index Dose represents an exposure from this source that is considered to be of minimal risk, but with the requirement to reduce exposures below this as low as is reasonably practicable.
Compliance	Long-term, daily exposure to contaminants in soil that are at or below the Soil Guideline Value derived from a TDSI does not constitute an appreciable health risk.	Exposure at or below the Soil Guideline Value derived from an Index Dose carries some unquantifiable, albeit minimal, health risk. Exposure from all sources to contaminants allocated an Index Dose needs to be reduced to as low a level as reasonably practicable.
Exceedance	An exceedance of the TDSI (and therefore by definition possibly also an exceedance of the TDI) is undesirable but does not inevitably lead to increased health risk. The implications of exceedance need to be assessed on a case-by-case basis, depending on the properties and effects of the substance in question.	Exceedance of the Index Dose, even in the short term, indicates an increase in the risk to health and is not acceptable . The significance of this increased health risk may require expert judgement.
Examples	Toluene, aliphatic petroleum hydrocarbons	Arsenic, benzene, benzo[<i>a</i>]pyrene

3 Technical Framework for Deriving Soil Contaminant Intakes for the Protection of Human Health

3.1 The aim of this framework is to establish possible health effects that may arise from the exposure of humans to chemicals in the soil and to identify intakes for use as *health criteria* in the development of Soil Guideline Values that are protective of human health. This section presents the framework used to recommend threshold values and minimal risk levels, the aim being to have a structured and logical approach to deriving TDSIs and Index Doses for all the contaminants listed in CLR8 (DEFRA and Environment Agency, 2002b). The steps of this framework are summarised in Figure 3.1. Further information on specific contaminants is presented in subsequent reports (DEFRA and Environment Agency, 2002c). The same process should be followed in deriving TDSI or Index Dose for contaminants currently not in CLR8. This work should be undertaken by professionals with expertise in toxicology and risk assessment.

Step 1: Identify key characteristics for the chemical of interest

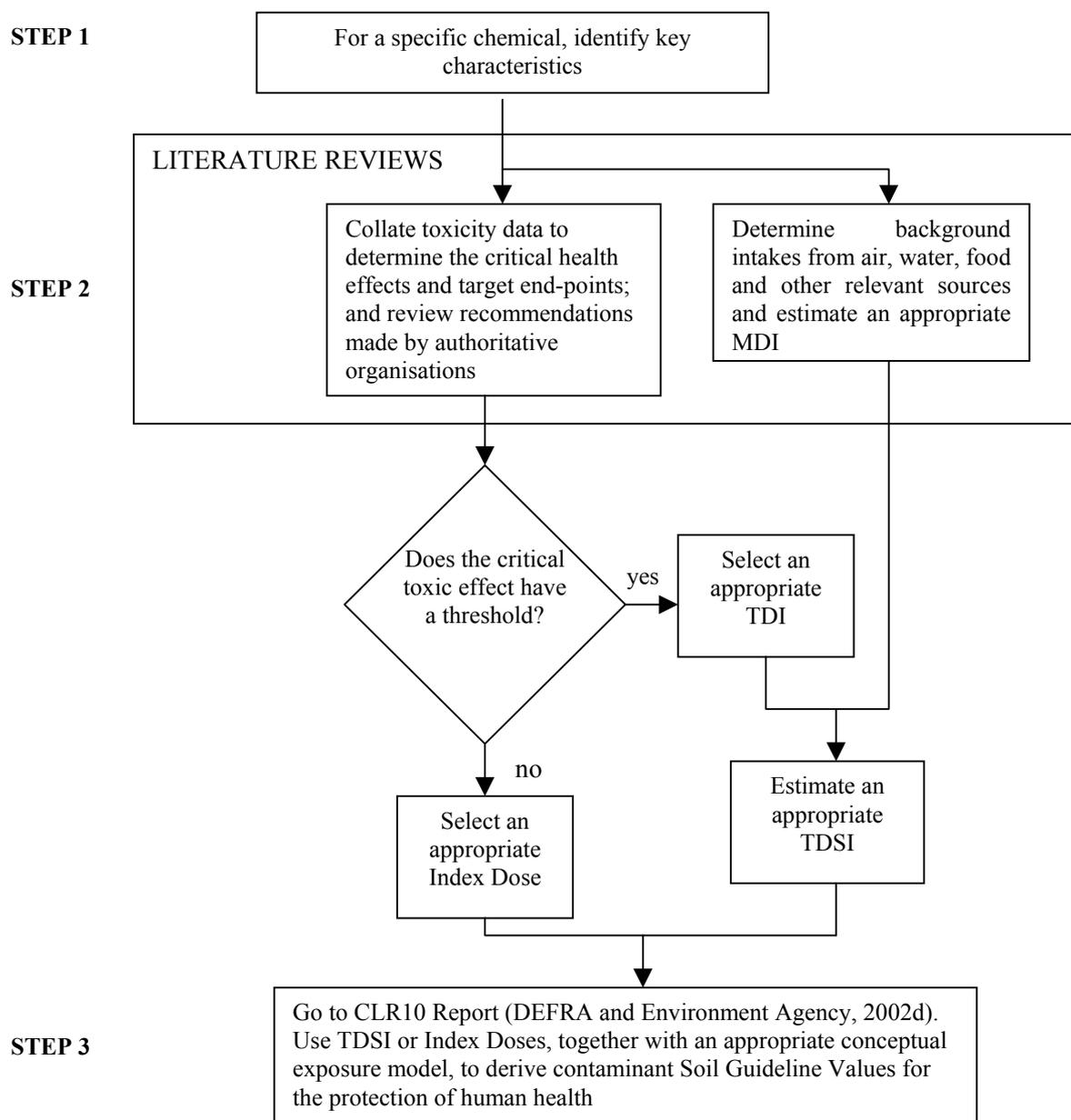
3.2 Initially, basic information needs to be collected on the chemical's identity, to include its predominant form (for example, sulphate, chloride, oxide forms), fate and behaviour in soils and factors that may influence this (for example, soil pH). It is also valuable to identify the main sources of emission (for example, incineration of wastes, combustion of coal and oil for heat and power generation or leaching from landfill sites) and how the total emissions are distributed between the different environmental media (water, soil and air).

Step 2: Literature review

Collection of toxicological data

3.3 The next step is to collate relevant toxicological data to provide basic information on the human health effects that may result following exposure to the contaminant of interest. This involves a literature search of the key publications that summarise the current "state of knowledge" on the toxicological effects for the contaminant of interest. The purpose of this exercise is to provide an overview of existing knowledge, rather than to initiate original research into the toxicology of the chemical.

Figure 3.1 Framework for deriving TDSIs and Index Doses as a basis for the derivation of Soil Guideline Values



3.4 This involves gathering and evaluating information on the adverse health effects that may be produced by the chemical in question and the exposure conditions under which damage to health may occur (van Leeuwen and Hermens, 1995). For example, a chemical does not constitute a risk to human health unless some humans are susceptible to a harmful effect and are exposed to levels that will cause the effect to occur. The aim here is to establish the highest level of exposure that appears harmless to humans. This information may be derived from environmental monitoring data and from human epidemiological and experimental animal studies.

- 3.5 In reviewing and collating toxicological data for individual chemicals, it is important that the key health effects⁷ that may arise from chronic exposure to soil contaminants are identified (paragraph 2.20). A variety of adverse health effects can be produced by exposure to soil contaminants and these can range from minor and temporary to severe and permanent. The toxicological review aims at identifying the key human health effects and chemical causes and the target organs and systems⁸ that the chemical may damage.

Review of the recommendations made by authoritative organisations

- 3.6 Once sufficient knowledge of the key health effects and toxicological end-point has been acquired, a literature review of the recommendations made by key authoritative bodies is undertaken. This information is used to come to a conclusion as to the most appropriate TDI or Index Dose in the context of soil standards that are protective of human health. In those cases where no authoritative values exist, such values will have to be derived from primary literature by expert judgement.

Principal source documents

- 3.7 Examples of the principal source documents used (in descending priority order) are as follows:

- Those produced by **authoritative bodies in the UK**, for example, the reviews of the Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COT, COM and COC), the Committee on the Medical Effects of Air Pollutants (COMEAP), the Expert Panel on Air Quality Standards (EPAQS), the Health and Safety Commission's Advisory Committee on Toxic Substances (ACTS), the Advisory Committee on Pesticides (ACP), the Working Group on Assessment of Toxic Chemicals (WATCH), and toxicological criteria documents (and summaries) produced by the Health and Safety Executive (HSE) (see paragraphs 3.8 and 3.9 below).
- Those produced by **European Commission's committees**, such as the Scientific Committee on Food (SCF) or the Scientific Committee for Toxicity, Ecotoxicity and the Environment, or by **international authoritative organisations** elsewhere, but specifically derived to estimate TDIs for ingestion of food or water (where the ingestion route is the primary source of exposure), for example, the reports of JECFA, the WHO's Environmental Health Criteria, or WHO's *Guidelines for Drinking Water Quality*.

Where inhalation (or dermal contact) is the predominant route of exposure, then it will be more appropriate to derive a TDI_{inh} (or TDI_{dermal}) derived from reports produced by authoritative organisations for the purpose of deriving air quality standards (AQSS) or guidelines for the appropriate route of exposure. Here the WHO's update and revision of

⁷ For example, cancers, anaemia, impaired development or birth defects.

⁸ For example, reproductive, nervous, lymphatic or cardiovascular systems or organs such as the kidney or lungs.

the air quality guidelines for Europe (WHO, 2000) will provide a useful source of information.

- Those prepared by **other national organisations**, such as the USEPA's reports (and their on-line database, the Integrated Risk Information System, IRIS) or the toxicological profiles of the US Public Health Service's Agency for Toxic Substances and Disease Registry (ATSDR).
- Finally, in the absence of more appropriate sources, reports produced by **authoritative organisations, but for different purposes**, for example, oral TDIs or Index Doses may be derived using information obtained from AQSs or guidelines such as those produced by WHO (2000).

Use of occupational exposure levels

3.8 Occupational exposure levels (OELs) have been derived for almost all of the chemicals of concern in contaminated land (HSE, 2001). In the absence of standards derived specifically for the general public, there has been a long tradition of using OELs as the basis for such standards. However, OELs are set in terms of a concentration in air ($\mu\text{g m}^{-3}$, mg m^{-3} or ppm) because the inhalation route is generally of prime concern in occupational exposure.

3.9 Since contaminated land assessment is concerned primarily with the ingestion route, OELs should only be considered for substances for which an inhalation intake can be validly translated into an equivalent ingestion intake, that is, for which the target organ or tissue is the same whatever the entry route (paragraphs 2.24 and below). It is important to remember here that OELs are derived for the healthy worker and are based on shorter daily exposure periods (paragraph 2.19) and may not be appropriate when estimating, for example, AQSs for the general population. In using information presented in HSE's criteria documents (for example, the NOAELs and safety factors) to derive TDIs or Index Doses, expert judgement is required and it is therefore important that simplistic approaches (such as the traditional approach of dividing by a factor of 40⁹) are not used as default.

Route-to-route extrapolation

3.10 TDIs and Index Doses (DEFRA and Environment Agency, 2002c) generally apply to ingestion routes of exposure. However, for many substances there may be little information about their human toxicity for all exposure routes. This is because many experimental animal and epidemiological studies have only examined the impacts of chemicals on the environment through one route. There are, in general, fewer studies of the effects of inhaled – compared with ingested – contaminants, and even fewer on the effects of contaminants taken up through the skin. In cases where the main exposure route is via ingestion, most studies will concentrate on determining the health impacts following ingestion and therefore less information will be available on the toxicity of the chemical of concern resulting from inhalation or dermal

⁹ To derive a standard applicable to the general population, the OEL is divided by 4 to take account of 168 hours of exposure per week for the public compared with 40 hours per week for workers, and by 10 to take account of sensitive groups within the general population (QUARG, 1993).

contact. For some contaminants, the extrapolation of toxicity information from one route of exposure to another may provide the only possible way of making an estimate of the TDI or Index Dose for a particular intake route. Indeed, for estimating the hazard via skin contact, it is usual to use data from the oral route together with information on skin absorption.

- 3.11 Occasionally it is the TDI_{inh} or ID_{inh} that is known from experimental evidence, and the TDI_{oral} or ID_{oral} that is the derived parameter. An example here is 1,1,1-trichloroethane, for which the available studies using oral administration are inadequate (for the derivation of a TDI_{oral}), but for which there is a suitable inhalation study. The WHO (1993b) have used the results of the inhalation study to derive an oral TDI and hence a drinking water standard for the concentration of 1,1,1-trichloroethane in drinking water. It must, however, be noted that the WHO stress that this value is provisional because of the use of an inhalation rather than an oral study, and recommend that an adequate oral study be conducted (WHO, 1993b).
- 3.12 Clearly, the most appropriate way of deriving a TDI or Index Dose for a particular intake route is from a study using that route of exposure. Therefore the approach of using results from a study involving a different route should always be used with caution and only in consultation with experts. For example, it would be inappropriate to use this approach for those contaminants whose end-points are different for different intake routes, as it is important to recognise that the potential harm to an organ (for example, lung) may be strongly influenced by the route of exposure (for example, inhalation). As an example, bone marrow is the target organ for benzene following exposure via inhalation or ingestion. However, inhalation of arsenic may lead to lung damage, whilst ingestion may damage the skin.
- 3.13 Some of the differences in end-points between oral and inhalation exposures are due to local action (for example, asbestos affecting the lung) rather than because of reduced or enhanced toxicity arising from chemical metabolism once the compound enters the body. However, metabolism following ingested and inhaled intake may lead to significant differences in toxicity. For example, compared to ingestion, circulating levels of chloroform in the body are higher after it is inhaled or dermally absorbed, because it is rapidly broken down in the liver after oral exposure.
- 3.14 In such circumstances a decision needs to be made as to whether it is appropriate to consider a TDI derived from one exposure route as representative of all routes of exposure or whether to consider the tolerable intake for the specific physiological pathway only. For example, can a TDI_{inh} be converted to a TDI_{oral} or is this TDI_{inh} only applicable to the inhalation route of exposure? This decision can only be made on a substance-by-substance basis after taking into account the information available on the toxicology of the substance as well as the relevant contributions made by the different exposure pathways to the overall exposure. Further information for individual chemicals is provided in separate reports (DEFRA and Environment Agency, 2002c). For information on Soil Guideline Value derivation, refer to DEFRA and Environment Agency (2002d, e).

Expert judgement

3.15 When evaluating the threshold values and minimal risk levels recommended by different agencies, authoritative bodies and organisations, it is important to take into account the quality of the data and expert judgement used in deriving the recommendations made. Expert judgement involves using a weight-of-evidence approach to draw overall conclusions in the context of TDSIs and Index Doses that are applicable to contaminated soils in the UK. This will need to consider, for example, the degree of caution incorporated into setting the recommended value. Differences may be caused by a number of reasons including:

- disagreement about the NOAEL;
- the sizes of the safety factors applied in the case of toxic effects with a threshold;
- the use of mathematical models;
- approaches to the treatment of non-threshold effects;
- treatment of data gaps and deficiencies; and
- factors that are appropriate for the protection of susceptible individuals.

Literature review to determine the most appropriate MDI

3.16 There is always some intake of contaminants from the ambient levels in food, water, air and other sources. For each contaminant this “background intake” is usefully expressed as a mean daily intake (MDI) for the UK population (paragraphs 2.26 and 2.27).

3.17 The MDI for a given chemical can be calculated from published information on the concentration of the contaminant in all media of concern, together with information on the contact rate and exposure frequency and duration.

3.18 Daily intakes from food consumption are mainly derived from the food basket surveys published by the Food Standards Agency (FSA),¹⁰ although other published sources are used for those contaminants which have not been included in any recent survey undertaken by the FSA. In addition, ambient air and water concentrations as well as average concentrations in other media (if applicable) can be obtained from the published literature. These should be based on UK data, where available; otherwise international data may be used (for example, ambient air concentrations as reviewed and summarised by the WHO). Data on the contact rate and exposure frequency and duration can be acquired from time–activity patterns that influence exposure and consumption patterns for food and water ingestion (see DEFRA and Environment Agency, 2002d for further detail).

3.19 Thus, the total dietary intakes are estimated using reported concentrations in food, air, water and other environmental media, together with appropriate default values on inhalation rate and water ingestion (ICRP, 1975) and body weight (DH, 1991a, 2000). Default values used for daily inhalation rate, daily water ingestion and average body weight for adults are 20 m³, 2

¹⁰ Formerly published by the Ministry of Agriculture, Fisheries and Food until April 2000.

litres and 70 kg respectively (DEFRA and Environment Agency, 2002c, d). Information on dietary exposures to contaminants by various population groups can be obtained from the FSA's dietary food surveys (see, for example, Ysart *et al*, 1999, or any of their Food Surveillance Information Sheets, e.g. FSA, 2000). In order to apply the adult MDI to children, it is necessary to take into account factors such as their reduced dietary intake and their different respiration rates compared to a typical adult. Table 3.1 summarises these correction factors according to age. For example, an adult oral MDI of 10 mg d⁻¹ corresponds to an oral MDI of 0.14 mg kg⁻¹ bw d⁻¹ for a 70 kg adult and to 6.2 mg d⁻¹ for a 5 to 6 year old child, or 0.31 mg kg⁻¹ bw d⁻¹ for a 20 kg child.

3.20 Full reference details of the sources of information used for deriving MDIs for specific chemicals are provided in the toxicity reviews for individual contaminants (DEFRA and Environment Agency, 2002c).

Table 3.1 Correction factors used to derive the proportion of adult MDI applied to children of different ages

Age (years)	Oral background correction factor for adult MDI	Typical body weight (kg)	Inhalation background correction factor for adult MDI	Typical inhalation rates (m ³ d ⁻¹)
0 – 1	0.32	7	0.18	3.6
1 – 2	0.39	11	0.27	5.2
2 – 3	0.46	14	0.35	6.9
3 – 4	0.54	16	0.40	7.8
4 – 5	0.58	19	0.46	9.2
5 – 6	0.62	20	0.51	10
6 – 7	0.66	23	0.56	11
7 – 8	0.68	26	0.65	13
8 – 9	0.71	29	0.73	14
9 – 10	0.75	34	0.84	17
10 – 11	0.79	37	0.91	18
11 – 12	0.81	44	1.09	21
12 – 13	0.85	49	1.21	24
13 – 14	0.88	53	1.33	26
14 – 15	0.88	56	1.41	28
15 – 16	0.92	60	1.49	29
16 – 59	1.00	69	1.00	20
60 – 70	1.00	70	1.00	20

Step 3: Selection of appropriate TDSI or Index Dose

- 3.21 The TDSI and Index Dose (and, where appropriate, the MDI) values derived in subsequent reports (DEFRA and the Environment Agency, 2002c) have been used as the starting point in establishing Soil Guideline Values for the protection of human health. They are substance-specific and can be related to sources and routes of exposure. The following paragraphs describe the steps that should be followed in deriving these.

Selection of an appropriate TDSI for chemicals with a threshold

- 3.22 If the outcome of the toxicity review (that is, Step 2) is that the critical toxic effect of the contaminant of concern has a threshold, then a TDSI must be derived. As outlined earlier (paragraph 2.28) TDSIs for contaminants with a threshold effect are derived after taking into account the TDI and MDI. Thus, the TDSI is the difference (TDI less MDI), which is available for allocation to soil sources not included as contributors to the MDI; an example of such a source would be a contaminated site that was contributing to the contaminant intake of the local population. The MDI needs to be converted to the appropriate units before it is subtracted from the TDI (see paragraph 3.19 for further details and Table 3.1 for correction factors, typical body weights and inhalation rates for different age groups).
- 3.23 For most contaminants, the derivation of this difference is straightforward – at least insofar as the MDI is less than the TDI, and it is therefore possible to subtract the MDI from the TDI. However, there are other contaminants where this is not so, that is, where the MDI is about the same as, or greater than, the TDI (that is, $MDI \geq TDI$). It could be argued that, in such cases, there is no balance for allocation to contaminated soil. This is impracticable, and therefore an alternative approach is required.
- 3.24 There is the perspective provided by the actual daily intakes of a particular contaminant, via food and other pathways. Bearing in mind the very wide range of intakes that the MDI of any particular contaminant represents, it is difficult to argue that an intake from contaminated soil, which is only a small increment of the MDI, is not tolerable. The FSA has published estimates of intakes of a number of contaminants from the typical UK diet, based on the analysis of samples from the UK Total Diet Study. These reports show that for most contaminants the estimated exposure from the total diet for a high-level (97.5 percentile) consumer is two or more times greater than the exposure of the mean consumer. In the report of the Office of Population Censuses and Surveys (OPCS) on their dietary survey of adults (Gregory *et al*, 1990), the intakes for the upper and lower 2.5 percentiles are given for a number of minerals and trace elements. There is typically a factor of about 5 between the upper and lower figures. When the intakes from non-food sources are taken into account, this factor can be expected to be larger.
- 3.25 Thus, a contaminant may have a MDI of, say, $30 \text{ mg kg}^{-1} \text{ bw d}^{-1}$. The daily intakes for the upper and lower 2.5 percentiles might be expected to be about 80 and $17 \text{ mg kg}^{-1} \text{ bw d}^{-1}$ respectively, assuming the factor of 5 variation between upper and lower percentiles described above. With a UK population of about 60 million, these upper and lower groups would each consist of about 1.5 million people, which are large sub-populations.

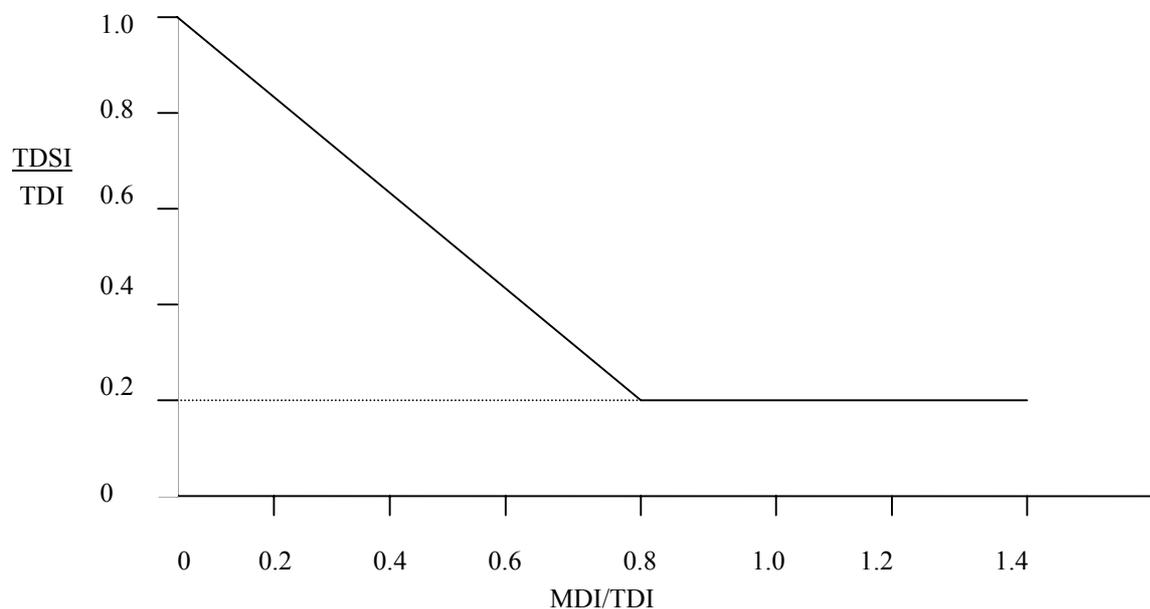
Considering the upper daily intake of $80 \text{ mg kg}^{-1} \text{ bw d}^{-1}$, an incremental intake of, say, 20% of the MDI ($6 \text{ mg kg}^{-1} \text{ bw d}^{-1}$) represents a relatively small (7.5%) addition to the existing intake for the upper group, and is still only a 30% increase for the lower group. Such increases would be likely to be undetectable in the general background variations in the actual intakes.

3.26 On this basis, in cases where the MDI is close to or exceeds the TDI, it is proposed to allocate a standard increment of intake as a basis for deriving a Soil Guideline Value. The value of 20% of the MDI, when the MDI is close in value to the TDI, has been considered. However, if the MDI greatly exceeds the TDI, then using a standard proportion of MDI would result in progressively larger allocation of intake to soil as the intakes from other sources increase – clearly an unsatisfactory outcome. It is therefore proposed to use an allocation of 20% of the TDI when $\text{MDI} \geq 80\% \text{ TDI}$. This gives a minimum allocation for the purposes of deriving a Soil Guideline Value. In summary:

- where the $\text{MDI} < 80\% \text{ TDI}$, then the $\text{TDSI} = \text{TDI} - \text{MDI}$
- where the $\text{MDI} \geq 80\% \text{ TDI}$, then the $\text{TDSI} = 0.2 \times \text{TDI}$

This is illustrated graphically in Figure 3.2.

Figure 3.2 Graphical representation of the approach for selecting an appropriate TDSI



3.27 In some cases, an approach based on the use of other health-based criteria might be more appropriate, where the data are adequate. Such is the case for lead, where there are extensive

data relating blood lead concentrations to health effects in children which can be used as a basis for deriving a Soil Guideline Value (DEFRA and Environment Agency, 2002c).

Selection of an appropriate Index Dose for non-threshold contaminants

- 3.28 The Index Dose represents an exposure level from a single source (that is, from a soil contaminant) which can be considered to present a minimal human health risk. Therefore, the Index Dose is applicable to this source alone without the need to make any further allowance for intakes from other sources, such as food ingestion (paragraphs 2.33 and Table 2.2).
- 3.29 A number of approaches have been used by UK and other regulatory bodies to identify exposure levels for non-threshold substances that can be considered to represent minimal health risk. These approaches (outlined in subsequent paragraphs) may be utilised to set Index Doses, but the examples should not be considered as generically applicable, since the actual method used will depend on the quality and completeness of the available toxicological data. Expert judgement will always be required in determining an appropriate Index Dose.
- 3.30 **Statutory and non-statutory recommended exposure levels.** For many non-threshold substances, both of these levels have been adopted by UK regulatory bodies; these usually relate to exposure from a particular source – for example, drinking water or air. It is assumed, for non-threshold substances, that human exposure below the levels specified in the standards carries minimal human health risk from that particular source. This is in accord with the definition of an Index Dose. So, a drinking water standard value specified in the UK Water Supply (Water Quality) Regulations 2000 (WQ Regs, 2000) or an air quality standard set by the Expert Panel on Air Quality Standards (EPAQS) may be a candidate value for deriving an Index Dose.
- 3.31 **Drinking water standards.** For example, the drinking water standard for arsenic ($10 \mu\text{g L}^{-1}$) set in the WQ Regs (2000) can be regarded as an exposure from one source (water) which is considered to carry a minimal health risk. Consequently the same level of exposure from another source (that is, contaminated land) can itself also be regarded as constituting minimal risk and this can be a basis for setting an Index Dose. For arsenic, therefore, the drinking water standard can be used as the basis for setting an oral Index Dose for this soil contaminant.
- 3.32 **Air quality guidelines.** EPAQS have set ambient air standards for three genotoxic carcinogens, substances which may carry some risk at any given exposure. For benzene and 1,3-butadiene (EPAQS 1994a, b), the starting point for the EPAQS approach was to identify, from occupational epidemiological studies, an exposure level at which there is no *detectable* human carcinogenic effect for each substance. For benzo[*a*]pyrene (BaP) (EPAQS 1999), in the absence of being able to identify an exposure without carcinogenic effect, the lowest occupational exposure at which cancer was observed was taken as the starting point. To these exposure levels a number of safety factors were applied to derive an exposure level for the general population. The safety factors used for BaP were as follows:
- a factor of 10 for the use of a LOAEL rather than a NOAEL;

- a factor of 10 to account for the difference between a working lifetime (77,000 hours) and a chronological life (660,000 hours); and
 - a factor of 10 to account for particularly sensitive groups in the population.
- 3.33 The resultant standards are considered to be exposure levels to substances in air below which the health risks were judged to be “minimal”. The meaning of these AQSs is consistent with the definition of the Index Dose, and therefore can provide, in some circumstances, a suitable basis for setting an Index Dose for exposure to soil contaminants by the inhalation pathway.
- 3.34 In setting an Index Dose, it is important to note that UK experts generally do not consider mathematical models based upon results of animal carcinogenicity studies, as used by the USEPA, to be appropriate for use in risk assessment.

Step 4: Derivation of a Soil Guideline Value that is protective of human health

- 3.35 Once the TDSI or Index Dose has been derived, this should be used, together with appropriate conceptual models such as those embedded in the Contaminated Land Exposure Assessment (CLEA) model, to calculate Soil Guideline Values that are protective of human health. For further details refer to CLR10 (DEFRA and Environment Agency, 2002d).
- 3.36 Where a TDSI and/or Index Dose has been derived for more than one route of entry (for example, oral and inhalation) then these values should be considered when deriving Soil Guideline Values. As an example, for cadmium, it is appropriate to derive both an oral TDSI and an Index Dose for the inhalation route as cadmium may cause renal damage via the oral route and lung cancer (and kidney toxicity) if inhaled (see DEFRA and Environment Agency, 2002c for further details). In such cases the Soil Guideline Value that is most protective of human health should be selected as being the most appropriate (for further details in DEFRA and Environment Agency, 2002d).

4 Dealing with Mixtures of Contaminants

- 4.1 Tolerable daily intakes and Index Doses are mainly based upon studies in which large doses of single chemicals are administered to experimental animals, and almost all of the comparatively few human studies that provide adequate exposure/effect data are also concerned with a single contaminant. Although the reality is that most of the pollution sources to which the general population is exposed produce a wide range of individual contaminants, knowledge about the toxicity of any particular group of contaminants in combination is rarely available. For a review of the different approaches available for dealing with mixtures of contaminants, refer to Environment Agency (2002). It is also important to recognise the practical difficulties of testing mixtures in view of the huge numbers of contaminants encountered compared to individual chemicals.
- 4.2 As a consequence, TDSIs and Index Doses are generally derived for individual substances, although in some instances – for instance, dioxins – these may be set for a class of substances with similar effects, and likely to be present in combination. There may be concern about the possible effects of exposure to other chemicals in combination, even when the Soil Guideline Value derived for each chemical is not exceeded. In practice, this is likely to be an issue only when there is enough evidence that two or more chemicals found in soil share the same toxicological pathway leading to identical effects on the same target organ. If the chemicals are considered to have a threshold, the question is whether the combined exposure would exceed the threshold. If, on the other hand, the chemicals are thought to be harmful at any exposure (for example, genotoxic carcinogens), the question is whether the combined risk is excessive.
- 4.3 Many approaches to these questions have been proposed, but the data to choose between them rarely exist. For chemicals thought to share a common toxicological pathway, but also believed to have a threshold of effect, it is reasonable to assume that the exposures, weighted by relative toxicity, are additive. A common approach, which assumes that the reciprocal of the TDI is a rough index of relative toxicity, is to divide, for each chemical to be combined, the estimated exposure by the TDI. These fractions are then added. If the sum is lower than 1, there is no cause for concern. If the sum exceeds 1, further expert consideration of the toxicology of the individual chemicals is needed (Environment Agency, 2002).
- 4.4 Such an exercise requires the calculation of total intake to include background intakes (not just intake from soil) from the soil guideline value (following the principles highlighted in paragraphs 3.22 to 3.27 for estimating the TDSI). It is not valid simply to calculate the sum of the fractions “soil concentration divided by soil guideline value”, and compare this with 1. The exercise is therefore time-consuming. Furthermore, chemical analyses of soil could reveal many combinations of possible concern.
- 4.5 For chemicals with no threshold, a parallel approach (using Index Doses instead of TDIs) would in essence assume that Index Doses represent risks that are quantitatively fairly similar. Unfortunately, for most such chemicals, sufficiently reliable estimates of risk are not possible. Consideration of the consequences of exposure to a relevant combination of non-

threshold chemicals must be a matter for expert judgement, in the light of the need to keep levels as low as reasonably practicable.

- 4.6 Based on the above, for the purpose of deriving TDSIs and Index Doses for the protection of human health, chemical mixtures should only be considered where there is sufficient evidence that effects are mediated through the same receptor or where substances may act on the same target organ or system. For example, effects caused by dioxins and polychlorinated biphenyls (PCBs) are mediated through the same receptor and therefore an additive approach (for example, the Toxic Equivalent or TEQ approach) may be used in deriving TDIs for this group of contaminants. This must be done on a case-by-case basis using expert judgement. Further details on whether this approach is appropriate for individual chemicals/groups of chemicals are provided in individual toxicity reviews (DEFRA and Environment Agency, 2002c).

Appendix A

Overview of International Approaches used for the Purpose of Deriving Health Criteria for the Protection of Human Health

A.1 An array of different definitions and approaches are used elsewhere for the purpose of deriving health criteria for the protection of human health. These have been briefly summarised below to:

- ensure that the reader understands the differences and similarities of approach between the UK and other countries;
- aid risk assessors and toxicologists who work across international boundaries; and
- provide clarity of terminology used in the UK and overseas.

Approaches used for assessing threshold effects

A.2 Many organisations express the acceptable long-term exposures to background levels of chemical contaminants to the general public in terms of provisional tolerable weekly intakes (PTWIs). This term is similar to the TDI insofar as it is an estimate of the intake of a substance over a lifetime that is considered to be without any appreciable health risk (WHO, 1994). PTWIs are provisional because they are often based on weak toxicological supporting data; they are also based on weekly intakes as a recognition of the long-term cumulative nature of many environmental contaminants.

A.3 The United States Environmental Protection Agency (USEPA) use the same methodology as JECFA/WHO but have adopted the term “**reference dose**” (RfD) instead of ADI or TDI and use a very similar definition. They have defined this RfD as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive groups) which is likely to be without an appreciable risk of deleterious effects during a lifetime (Barnes and Dourson, 1988). The USEPA have adopted the term “**uncertainty factor**” to replace the traditional “safety factor” and this newer term is now also being used by other organisations.

A.4 A comparatively recent approach to the derivation of TDIs is the use of the **benchmark dose** (BMD) method (Haag-Grönlund *et al*, 1995; Barton and Das, 1996; Gaylor *et al*, 1999). BMD is defined as the dose corresponding to a specified increase in effect (usually 1 or 10%) found from this dose–response curve and is derived on the basis of data from the entire dose–response curve for the critical effect rather than from the single-dose group at the NOAEL. This facilitates comparison of results between different studies on the same chemical and allows for the comparison of the potencies of different chemicals (WHO, 1994). It also takes into account the statistical power and quality of the data as the confidence interval around the dose–response will be wider for smaller and/or poorly designed studies, leading in turn to a lower benchmark dose, reflecting the greater uncertainty of the database (WHO, 1994). A

disadvantage of this method is currently that the determination of a benchmark dose is limited to specific toxic effects and it requires studies in which there are a number of experimental data points. It has not as yet been widely used as an alternative to the NOAEL approach, although the USEPA have made use of it in their derivation of RfDs for a few substances.

- A.5 Traditionally doses at or below the TDI (or RfD) are considered to be without a health risk and doses above the TDI are assumed to have some (unknown) probability of causing adverse health effect. Price and co-workers (Price *et al*, 1997) have developed an approach that provides **quantitative estimates** of a non-carcinogenic response at any specific dose above the RfD. This approach extends the traditional methodology to estimate the probability of adverse effects occurring in a population exposed to dose rates in excess of the RfD by using probabilistic techniques (Monte Carlo analysis) to characterise the uncertainty in the response estimates. The risk above the RfD is estimated using a linear model of response. This is based on the traditional system of applying uncertainty factors in setting the RfDs, together with other information such as benchmark doses, NOAELS, LOAELs and doses in which adverse effects are observed in 50% of test animals (Price *et al*, 1997).

Approaches used for assessing non-threshold effects

- A.6 A number of approaches, largely based on the characterisation of dose–response, have been adopted by different organisations for the assessment of non-threshold effects (WHO, 1994). Whilst these approaches have not been adopted in the UK, they are summarised in subsequent paragraphs for information.
- A.7 Health risks from non-threshold substances may be estimated by extrapolating dose–effect relationships derived from animal or epidemiological studies. This procedure is usually called **quantitative risk assessment (QRA)** and entails the use of numerical estimates of cancer risk based on extrapolation from animal and/or human data. Whilst QRA is generally acceptable when based on good epidemiological data, low-dose extrapolations from the very high doses used in animal studies have raised doubts as to the validity of the risk estimates derived from them. The models used for extrapolating the animal data are not generally based on biological mechanisms (Maynard *et al*, 1995), data are often inadequate and models cannot be validated. Therefore results from the various models can lead to a wide variation in risk estimates depending on the model adopted. These may give an impression of precision that cannot be justified in light of the approximations and assumptions upon which they are based (DH, 1991b).
- A.8 Some organisations use QRA, or consider it a standard method for assessing health risks from environmental pollutants, but recognise and stress the uncertainties inherent in the estimates. For example, QRA based on epidemiological studies and the assumption of a linear relationship over the extrapolated range is an approach used by the WHO in deriving some of its drinking water and air quality guidelines (WHO, 1993; 1996a, b). It is also used by the USEPA in deriving cancer risk factors for some carcinogens. However, because the estimates are likely to be subject to substantial error, the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) do not support the routine use of QRA based on animal data for non-threshold chemicals (DH, 1991b; Maynard *et al*, 1995).

However, the situation is different if there are large amounts of human data from which a dose– response can be estimated, for example, asbestos (Doll and Peto, 1985; HSE, 1996) and ionising radiation.

- A.9 To apply the concept of QRA to derive an acceptable numerical level of risk for non-threshold chemicals, it is necessary to take a view about the “acceptability” of levels of additional risk. Organisations such as the WHO and the USEPA use the simple “attributable lifetime probability of death” as the prime measure of risk,¹¹ often referred to as “**lifetime excess risk**”. The acceptable lifetime excess risk, for an individual member of the public, can range over orders of magnitude (for example 10^{-2} to 10^{-6}) between different organisations.¹² This is largely attributable to differences in the meanings of the various terms used (for example, maximum tolerable risk, acceptable risk or negligible risk) and to differences in application. For example, does the value refer to the sum of all the risks from a particular situation or activity, or to the risk from a single contaminant in a single environmental medium? In the UK, the figures quoted for an acceptable risk have usually been in the context of the risk from a particular industrial installation, or from a particular consumer product. On the other hand, the WHO, in its guidelines for drinking water quality (WHO, 1993b), allows a risk of 10^{-5} in respect of each carcinogenic contaminant considered. It follows that the total risk from drinking water as a whole (possibly containing several carcinogenic contaminants) could be greater than that estimated for an individual contaminant.
- A.10 Despite the wide-ranging values reported by different authoritative organisations, there is some consensus for selecting a figure of 10^{-4} as the upper bound of “acceptable” additional lifetime risk from exposure to environmental contamination from any one source (such as, for example, a contaminated site). This corresponds to an annual excess risk of cancer of about 10^{-6} (one in a million per year). However, making a decision as to what is an acceptable level of risk to individual members of the public from exposure to ambient levels of an environmental pollutant is a value judgement. Although knowledge of some background scientific and technical information is necessary, the essential decision is one that involves socio-political judgements. The estimate of risk from a source such as a contaminated site, and an understanding of the uncertainties inherent in the estimate, can only help to guide decisions on action, which inevitably depend also on factors such as practicality, cost and competing priorities.
- A.11 Comparison of human exposure to the chemical’s carcinogenic potency¹³ in the experimental range is another approach that can be used to indicate the magnitude of risk as a basis for deriving guideline values (WHO, 1994). Various approaches have been used for deriving

¹¹ It should be noted here that “risk of cancer” and “risk of death” are sometimes used as though they are synonymous, which is not always so. For example, the fatality rates in the UK for non-melanoma skin cancer are quite low (at most, a few per cent), whilst for lung cancer they are in the region of 95%. In quoting an excess cancer risk, it is important to always state whether this refers to a risk of developing cancer

¹² See for example recommendations/reviews made by Royal Society (1983, 1992), HSE (1988, 1992), NRPB (1987, 1991, 1993), WHO (1993), or Travis *et al* (1987).

¹³ Potency is the intrinsic strength or the ability of a substance to cause a particular type of harm to health.

carcinogenic potencies. An example of such a measure is the Tumorigenic Dose₅ (TD₅), which is defined as an estimate of the daily human intake or exposure divided by the intake or exposure associated with a 5% incidence of tumours in animal or epidemiological studies (as summarised by WHO, 1994). The carcinogenic potency of a chemical can also be estimated using a range of other measures, such as the T₂₅ or TD₅₀. The T₂₅ can be defined as the daily dose (as mg kg⁻¹ bw d⁻¹) resulting in a tumour incidence of 25% at a specific site, after correction for spontaneous incidence, within the standard study period for that species (DH, 1996). The TD₅₀ can be defined as the daily dose rate required to halve the probability of remaining tumourless at the end of a standard lifespan.

- A.12 Finally, another approach is to divide the highest dose at which there is no observed or detectable increase in tumour incidence (in comparison with controls) by a large composite uncertainty factor, the magnitude of which should be a function of the weight of evidence available (WHO, 1994). This approach has been used, for example, by the Expert Panel on Air Quality Standards (EPAQS) to derive an appropriate standard for air for benzene, which is a known genotoxic carcinogen (see for example EPAQS, 1994a, b, 1999).
- A.13 Approaches used to deal with non-threshold compounds differ between different organisations. For example, the Dutch use the term “maximum permissible risk” to refer to both threshold and non-threshold toxicants, TDI and Tolerable Concentration in Air (TCA) for threshold substances and CR_{oral} and CR_{in} to refer to health criteria for non-threshold substances for oral and inhalation routes respectively (CR being Cancer risk; Lijzen *et al*, 2001). In deriving the values for non-threshold substances an estimated additional lifetime risk of 10⁻⁴ is used (van den Berg *et al*, 1993). The WHO (1993b) base their guidelines for drinking water quality (1993) on an upper 95% confidence limit estimate of additional lifetime risk of 10⁻⁵. For some substances for which there is limited evidence of carcinogenicity, the WHO derive a TDI incorporating an additional uncertainty factor of 10; hexachlorobutadiene is an example of a substance treated in this way.

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Abbreviations

ACP	Advisory Committee on Pesticides
ACTS	Advisory Committee on Toxic Substances
ADI	Acceptable Daily Intake
ALARP	as low as reasonably practicable
AQS	air quality standard
ATSDR	Agency for Toxic Substances and Disease Registry of the US Department of Health and Human Services
BaP	benzo[<i>a</i>]pyrene
COC	Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
COM	Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
COMEAP	Committee on the Medical Effects of Air Pollutants
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
CR _{in}	Cancer risk for the inhalation route
CR _{oral}	Cancer risk for the oral route
DH	Department of Health
EPAQS	Expert Panel on Air Quality Standards
FAO	Food and Agricultural Organization of the United Nations
FSA	Food Standards Agency
HSE	Health and Safety Executive
ID _{oral}	Index Dose derived from oral studies
ID _{inh}	Index Dose derived from inhalation studies
ID _{dermal}	Index Dose derived from dermal studies
IRIS	Integrated Risk Information System
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOAEL	Lowest observed adverse effect level
MAFF	Ministry of Agriculture, Fisheries and Food
MDI	mean daily intake
NOAEL	No observed adverse effect level
NRPB	National Radiological Protection Board
OEL	occupational exposure limit/level
OPCS	Office of Population Censuses and Surveys
PCBs	polychlorinated biphenyls

PTWI	provisional tolerable weekly intake
QUARG	Quality of Urban Air Review Group
QRA	quantitative risk assessment
RCEP	Royal Commission on Environmental Pollution
RfD	reference dose
SCF	Scientific Committee on Food
TCA	Tolerable concentration in air
TDI	tolerable daily intake
TDI _{oral}	tolerable daily intake derived from oral studies
TDI _{inh}	tolerable daily intake derived from inhalation studies
TDI _{dermal}	tolerable daily intake derived from dermal studies
TDSI	tolerable daily soil intake
TEQ	Toxic Equivalent
USEPA	United States Environmental Protection Agency
WATCH	Working Group on Assessment of Toxic Chemicals
WHO	World Health Organization

Glossary

Adverse effect	A change in morphology, physiology, growth, development or lifespan of an organism which results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increase in susceptibility to the harmful effects of other environmental influences (WHO, 1994). Decisions on whether or not any effect is adverse require expert judgement.
Carcinogen, genotoxic	A chemical that induces tumours via a mechanism involving direct damage to the deoxyribonucleic acid (DNA).
Critical effect	The adverse effect judged to be the most important for setting a tolerable daily intake. This is usually the most sensitive adverse effect (that is, the lowest effect level) or sometimes a more severe effect, not necessarily having the lowest effect level.
DNA	deoxyribonucleic acid is the chemical substance containing the genetic code.
Dose	The amount of a substance available for interaction with metabolic processes or biologically significant receptors after crossing the outer boundary of a person. For example, the amount of a chemical ingested, inhaled or applied to the skin (see intake), or the amount of chemical taken up by the body (see uptake) or the product of the ambient exposure concentration and the duration of exposure (see Exposure).
End-point	An undesirable health event such as the occurrence of disease or death. In general, an end-point is the undesirable health consequence of some exposure.
Epidemiology	The study of the incidence, prevalence and distribution of diseases (or injuries) in human populations in order to ascertain the determinants or causes of those diseases.
Exposure	The amount of a chemical that is available for intake by a target population at a particular site. Exposure is quantified as the concentration of the chemical in the medium (for example, air, water, food) integrated over the duration of exposure. It is expressed in terms of mass of substance per kg of soil, unit volume of air or litre of water (for example, mg kg ⁻¹ , mg m ⁻³ or mg L ⁻¹).
Gastrointestinal	Pertaining to or communicating with the stomach and intestines.
Index Dose	The daily dose of a chemical that can be considered to present a minimal health risk from exposure to soil contaminants.
Intake	The amount of a chemical entering the human body at the point of entry (that is, mouth, nose or skin) by ingestion, inhalation, or skin contact.
Inter-species variability	Relates to the variability in sensitivity among members of different species, for example, humans and other animals.
Intra-species variability	Relates to the variability in sensitivity among the same species. For example, variability within the human population to account for genetic diversity, age, health status, personal habits, diet and smoking habits.
LC ₅₀	The concentration required to kill half the population of a particular organism.
LOAEL	The lowest concentration or amount of a substance, found by experiment or observation, which causes an adverse alteration of morphology, functional capacity, growth, development or lifespan of the target organism

	distinguishable from normal (control) organisms of the same species and strain under the same defined conditions of exposure (WHO, 1994).
Mutagen	A chemical that can produce permanent heritable change in the amount or structure of the genetic material of cells or organisms.
NOAEL	The greatest concentration or amount of a substance, found in experiment or observation, which causes no detectable adverse alterations of morphology, functional capacity, growth, development or lifespan of the target organism under defined conditions of exposure (WHO, 1994).
Non-genotoxic carcinogen	A chemical that induces tumours via a mechanism that does not involve direct damage to DNA.
Potency	The intrinsic strength or the ability of a substance to cause a particular type of harm to health.
Route of Exposure	The way the chemical enters a person after contact (for example, ingestion, inhalation or dermal absorption).
Systemic circulation	Internal system for distributing blood to systems and organs in the body.
T ₂₅	The daily dose resulting in a tumour incidence of 25% at a specific site, after correction for spontaneous incidence, within the standard study period for that species.
Target	Actual cells, organ or system where chemical actually causes an adverse health effect. For example, target organs such as kidneys or lungs or target system such as the lymphatic or reproductive systems.
TD ₅₀	The daily dose estimated to halve the population of tumour-free animals.
Toxicity	The ability to cause injury or an adverse effect in a living organism.
Tumorigenic Dose ₅ or TD ₅	This is an estimate of the daily human intake or exposure divided by the intake or exposure associated with a 5% incidence of tumours in animal or epidemiological studies.
Uptake	The amount of a contaminant that reaches the circulating blood having been absorbed by the body through the skin, the gastrointestinal system and the pulmonary system.