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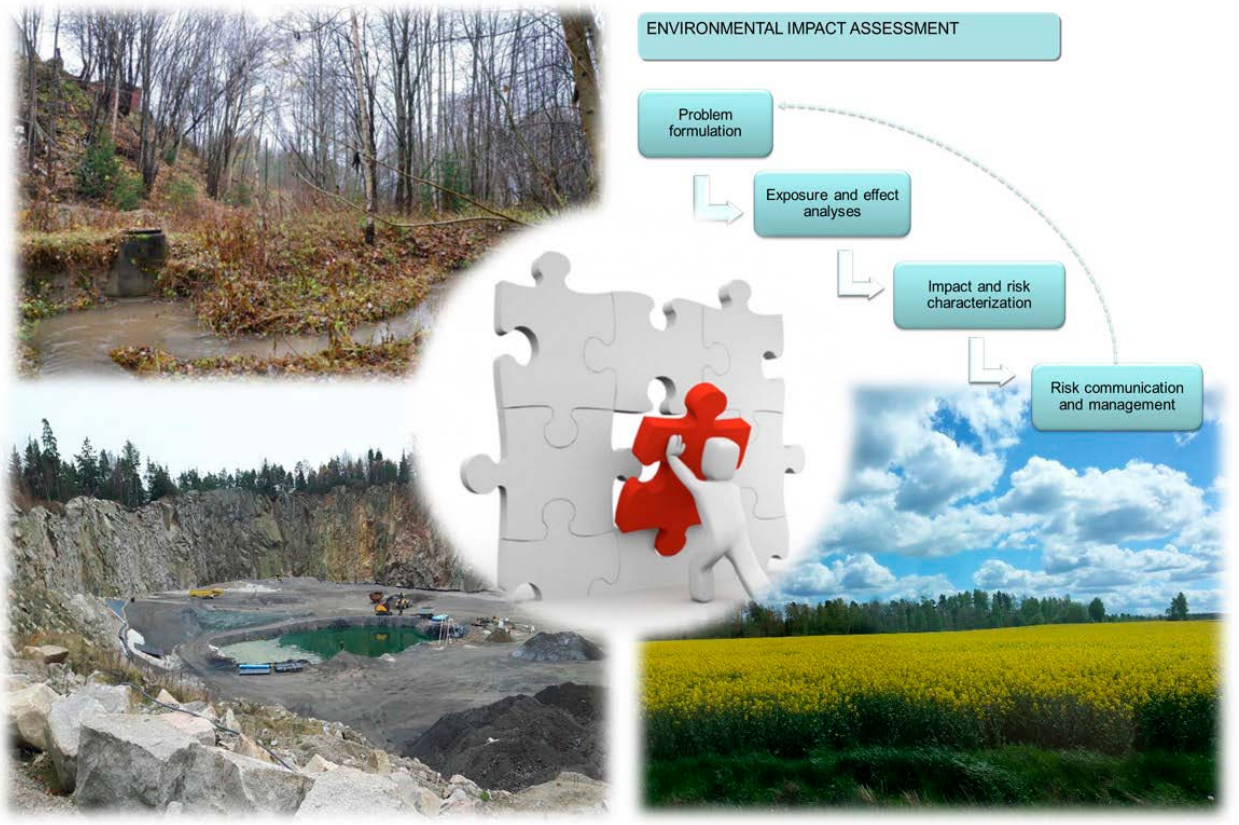
StrålevernRapport 2018:6



Study of Issues Affecting the Assessment of Impacts of Disposal of Radioactive and Hazardous Waste

Reference:
Study of Issues Affecting the Assessment of Impacts of Disposal of Radioactive and Hazardous Waste. NRPA Report 2018:6. Østerås: Statens strålevern, 2018.

Key words:
Radioactive waste, hazardous waste, waste disposal, environmental impact assessment.

Abstract:
Based on the identified need to develop coherent approaches applicable for radioactive and hazardous waste types, as well as to mixed waste such as NORM waste, a study to address the issues affecting the assessment of impacts of disposal of radioactive and hazardous waste was done internationally by members of the Bioprota forum. Details on key objectives, main findings and results of the study are given in this report.

Referanse:
Evaluering av problemstillinger knyttet til vurdering av langsiktige effekter i miljøet i forbindelse med radioaktivt og farlig avfall. Strålevern Rapport 2018:6. Østerås: Statens Strålevern, 2018.

Emneord:
Radioaktivt avfall, farlig avfall, kjemikalier, radioaktive stoffer, deponering, vudering av miljøkonsekvenser.

Resymé:
Basert på et tidligere definert behov for utvikling av en felles metode for vurdering av miljøkonsekvenser fra radioaktivt avfall og annet farlig avfall, ble det gjennomført en evalueringsstudie av problemstillinger ved metoder som i dag brukes for vurdering av miljøeffekter. Studiet ble utført av det internasjonale Bioprota forum, der Strålevernet også er medlem. Målsetninger og resultater av studiet er presentert i denne rapporten.

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Study of Issues Affecting the Assessment of Impacts of Disposal of Radioactive and Hazardous Waste

Statens strålevern

Norwegian Radiation
Protection Authority
Østerås, 2018

NRPA perspective

BIOPROTA (www.bioprota.org) is an international collaboration forum, which seeks to address key uncertainties in the assessment of environmental and human health impacts in the long-term arising from release of radionuclides and other contaminants as a result of radioactive waste management practices. The general objectives of BIOPROTA are to make available the best sources of information to justify modelling assumptions made within radiological and related assessments of radioactive waste management. Particular emphasis is on key data required for the assessment of long-lived radionuclide migration and accumulation in the biosphere, and the associated radiological impact, following discharge to the environment or release from solid waste disposal facilities. NRPA is one of the organisations within the BIOPROTA forum and actively participated in the project described in this report.

Background information

Safety and environmental impact assessments are commonly used to support decisions on the management and disposal of both radioactive and hazardous waste. Although equivalent or similar approaches might be used in these situations, different protection objectives are defined, as well as different methods of assessment and timeframes addressed.

Following that idea, two international workshops have been organised through the BIOPROTA international forum (www.bioprota.org). In the first one, held in Slovenia in 2013, the scientific basis for radiological and hazardous waste disposal assessments was evaluated and compared. In the second one, held in Norway in 2015, the focus was comparison of general safety and environmental impact assessments for radioactive waste with those for hazardous waste. This workshop was documented in NRPA report 2015:8.

The separation in approaches has been seen at international and national levels and arises for many reasons, including different historical management processes, differences in regulatory and institutional frameworks, social and cultural differences, lack of common language in addressing issues with respect to both waste types, lack of coordinated international guidance on criteria and assessments, and lack of comparable supporting scientific information. These issues lead to a need for a holistic approach for assessment of radionuclides and hazardous materials on a common risk management basis.

Needs for further international efforts and joint activities to develop coherent approaches applicable for both waste types, particularly for mixed waste such as NORM waste, were highlighted in both workshops, leading to the setting up of the project described here.

Based on the above identified needs, a further study was proposed to the BIOPROTA forum, to address the issues affecting the assessment of impacts of disposal of radioactive and hazardous waste. The proposal was accepted and supported financially by the following organisations: Low Level Waste Repository Ltd (LLWR, UK); Norwegian Radiation Protection Authority (NRPA); Nuclear Waste Management Organisation of Japan (NUMO); Nuclear Waste Management Organisation (NWMO, Canada); POSIVA (Finland); and the Swedish Nuclear Fuel and Waste Management Company (SKB). This report documents the results.

Objective

The key objective of the study was to consider all the issues of relevance to assessment of the impacts of disposal of radioactive and hazardous waste types in order to define and facilitate further steps in development of consistent approaches and methods. To meet this objective, the following activities were carried out within the project:

1. Provision of an overview of objectives and derived criteria for environmental and human health protection;

2. Review of assessment methods and data requirements for non-radiological and radiological assessments of waste disposal;

3. Review of the content and application of groundwater protection legislation as applied to waste disposal facilities;

4. Review of the design and use on toxicity indices; and,

5. Identification of factors to consider in the design of effective assessments.

Conclusions

Results have confirmed the previous position concerning the differences in assessment methods and further highlight the value of a more holistic approach, in particular the application of proportionate risk management and optimisation of the application of resources. At the same time, it has been acknowledged where and when differences in approach may be necessary or otherwise justified.

Overall, it can be seen that the non-radiological impacts associated with radioactive waste disposal have been under-investigated in the past. However, several successful examples of assessments done for a variety of radioactive wastes have been reviewed, and, in general, two overall approaches for common, holistic assessment of both radioactive and hazardous waste/waste components identified:

- Focus on radiological protection objectives and adopt the radiological assessment methods. In practice it would mean to follow the assessment practice for radioactive waste when developing the scenarios, system description and evolution, contaminant migration and accumulation, timeframes for assessment, and impacts on relevant receptors. This relies on being able to convert the different ways in which chemotoxicity expresses itself as risks to the receptors used in radiological assessment.

- Apply typical assessment methods for hazardous waste to the disposal and assessment of radioactive waste. In practice it would mean that radiation is just one more stressor alongside the multiplicity of other stressors, moderating the basic biological mechanisms that can underlie interactions between them. It also implies consideration of receptors and protection objectives commonly used for hazardous waste disposal.

However, a number of ways are identified through which assessment steps for radioactive and hazardous waste could be better aligned, so that choices between options can be made more appropriately.

The working methodology for this project, involving substantial consultation among operators, regulators and specialists in a variety of disciplines and technologies, based on waste and site specific experience, is considered the best way forward to meet the continuing challenges.

Project information

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Study of Issues Affecting the Assessment of Impacts of Disposal of Radioactive and Hazardous Waste

Version 2
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Executive Summary

Two workshops have been organised through BIOPROTA to consider the non-radiological post-disposal impacts of radioactive waste disposal. The first, held in Slovenia in 2013, addressed the scientific basis for long-term radiological and hazardous waste disposal assessments. Building on the discussion, a second workshop was held in Asker, Norway in 2015, focussing more specifically on comparisons of safety and environmental impact assessments for disposal of radioactive and hazardous wastes.

The foreword to the Asker workshop report, published by the Norwegian Radiation Protection Authority (NRPA, 2015:8), noted that "ideally, a holistic approach to assessment of radionuclides and hazardous materials should be internationally created such that consistent assumptions are employed in assessments and consistent criteria used in the evaluation of risk. Currently, the basis for separation in approaches includes traditional behaviour, regulatory and institutional differences, lack of common language in addressing things with respect to both waste types, lack of international guidance on criteria for assessments, as well as lack of supporting information from science. The development of a common set of objectives and, hence, assessment endpoints and timeframes for the different waste types would be very beneficial. In particular, this would promote the proportionate allocation of resources to the different types of hazards associated with the waste. In cases where technical differences are necessary, a clear understanding of the reasons for the different approaches should be provided to allow differences to be understood and communicated."

This report presents the results of a study organised through the BIOPROTA Forum designed with the objective of providing information to support development of a consensus on how to address the above issues, leading to the application of more coherent and consistent assessment methods. It has not been practical to account for all the latest developments in policy, management and regulatory practices, assessments approaches and tools and the under-pinning science. However, it is hoped that the report provides a substantial range of material for further developments in these areas.

The report has been developed primarily as an information resource; however, broad conclusions emerge from the study.

The work carried out in this study confirms the previous conclusions that there are inconsistencies in approaches to risk management for radioactive and hazardous waste. This creates challenges in identifying and applying optimum waste management strategies that account for all the hazards in a proportionate manner, as follows.

- Non-radiological hazards associated with radioactive wastes have been of regulatory interest for a number of years and yet the effects of non-radioactive materials within such wastes has historically been under-researched.
- Superimposition of a non-radiological performance assessment onto a radiological assessment and vice versa, taking account of different compliance points and assessment criteria, different regulatory end points and potentially the effect of additive and/or synergistic effects is difficult to fit into current regulatory frameworks that were designed separately.
- The hazard associated with non-radioactive component of radioactive waste may be greater than that of the radioactive component. Conventional landfills are generally subject to declining source terms due to leaching and biodegradation; however, the leaching potential in a radioactive waste repository will, in many cases, be much lower due to waste conditioning treatments such as cementation of radioactive wastes and there is likely to be a lack of appropriate leachate data for non-radioactive components of radioactive waste.
- Non-radiological environmental impacts arising post-disposal are not usually assessed over the long time scales required for radiological impacts, i.e. extending over thousands of years.

- Given the above, ensuring an appropriate and proportionate level of environmental protection for both radiological and non-radiological components of the waste is hard to deliver and communicate.

Despite the above, steps are being taken to address more thoroughly the chemical risks in radioactive waste management. Examples have been provided which show how relevant assessments have been carried out for near surface, intermediate depth and deep geological disposal of a variety of different radioactive wastes. These have been successful in terms of addressing current regulatory frameworks and demonstrating compliance with extant or interim protection objectives. However, regulatory development and work on compliance demonstration methods continues.

One approach is to focus on radiological protection objectives in terms of risk as opposed to dose, and adopt the radiological assessment methods, in terms of scenario development, system description and evolution, contaminant migration and accumulation, timeframes for assessment, and impacts on relevant receptors. This relies on being able to convert different ways in which chemotoxicity expresses itself as risks to the receptors used in radiological assessment. This is likely to require increased use of biokinetic models for non-radioactive contaminants, so that concentrations in key target tissues and organs can be used in the estimation of health effects, together with development of a single measure of adverse impact on health analogous to the concept of health detriment used in radiological protection.

The opposite approach would be to apply typical standards for hazardous waste to the management and assessment of radioactive waste. This would be consistent with regarding radiation as just one more stressor alongside the multiplicity of other stressors, moderating the basic biological mechanisms that can underlie interactions between them, as discussed in Appendix B. Among other things, it would imply considering much shorter timeframes for assessment and relatively limited consideration of the effects of environmental change.

In developing assessments to characterise risks associated with non-radiological substances, to ensure compliance with environmental legislation or regulatory guidelines, and/or as part of studies on optimisation or to develop waste acceptance criteria, the potential effects on human health and the environment will need to be considered. Regulatory frameworks may vary between different countries, but a range of factors has been suggested that might be considered in the design, implementation and interpretation of effective assessments of non-radiological impacts associated with radioactive waste disposal. Effective is taken to mean providing results that support the interests of decision makers, including the need for balanced and proportionate (or not grossly disproportionate) risk management, clear and consistent protection objectives and clear and consistent assessment methods. The same assessments should also support decisions on the management of radiological impacts and overall optimisation of waste management. The potential applications encompass all types of radioactive waste.

Accordingly, there are several ways in which assessment methods could be better aligned, so that choices between options can be made on a more equitable basis and more appropriately reported than at present. These ways are outlined below.

a) Radioactive and non-radioactive inventories in wastes, waste packaging and the engineered facility should be characterised quantitatively and with a proportionate degree of rigour, bearing in mind the amounts of material and intrinsic hazards. Characterisation of the non-radioactive contaminant inventory should not be viewed as a minor supplementation of the radioactive inventory, particularly in the cases of LLW and very LLW, where chemical toxicity may turn out to be of greater importance than radiotoxicity.

b) Release and transport of radionuclides and chemical contaminants from the engineered system, through the geosphere and in the biosphere, should be modelled according to the same methods, as far as makes technical sense. This is facilitated given that key non-radioactive contaminants are likely to include metals and semi-metals. The main distinction arises if an organic contaminant degrades to a more toxic form, but this is little different (in terms of performance assessment modelling) from having to handle differences in transport and impact between parent radionuclides and their progeny.

c) It is appropriate to assess exposures of humans to ionising radiations in terms of effective dose, but to assess exposures to chemical pollutants in terms of intake rates by ingestion or air concentrations. However, it is important to recognise that these are intermediate measures and that they need to be related to potential health effects. For ionising radiations in prospective assessments, effective dose can be converted to individual detriment to health using a slope factor. The slope factor generally used includes contributions from fatal cancer, non-fatal cancer and hereditary disease, and takes into account the associated years of life lost or impaired. For genotoxic, carcinogenic chemicals, slope factors are often recommended, but their use is not recommended by all authorities, due largely to uncertainties in the values of the slopes, or even whether a linear, no-threshold relationship is appropriate (noting that many of the data available on chemotoxicity are from animal studies). However, for coherence with the established approach to ionising radiations (for which similar concerns as to applicability can be raised), it is suggested that the slope factor approach should be adopted also for genotoxic, carcinogenic chemicals (assuming required data are available). However, for both ionising radiations and chemicals, it is recommended that where possible, uncertainties in the slope be propagated through the analysis together with uncertainties in the assessed levels of exposure.

d) In the context of radioactive waste disposal in purpose built repositories, tissue and organ dose rates to representative individuals are not likely to be sufficiently high to give rise to deterministic effects (except, possibly, in some human intrusion scenarios). Therefore, consideration can be directed to consideration of chemical pollutants that might give rise to deterministic effects above some threshold of exposure. The exposure-response relationship for such effects is generally strongly sigmoidal, so the range of exposures between almost no induction and induction in all sensitive individuals in a population is limited. In these circumstances, it seems prudent, and in line with the approach adopted in radiological protection, to set limits on exposure to prevent such effects. This can be achieved, as is currently done, by applying an uncertainty factor to a point of departure, to define an exposure that should not be exceeded. Because effects typically depend both on the chemical form of the pollutant and the pathway leading to exposure, more than one point of departure and uncertainty factor may be required.

e) Chemotoxic substances induce adverse health effects by a variety of mechanisms. These can have, but do not always have, commonalities with the mechanisms by which ionising radiations induce adverse health effects. Therefore, simple index quantities (weighted total exposures) cannot be recommended for application across wide ranges of chemicals or between chemicals and ionising radiations. However, there are contexts in which index quantities can be useful, notably in summing over a group of closely related chemicals, e.g. dioxins and dioxin-like compounds. This may be particularly helpful where analytical methods have difficulty in distinguishing the individual components in a mixed exposure.

f) The diversity of mechanisms involved means also that it is difficult to evaluate the effects of exposures to mixtures of toxic agents and, specifically, to determine whether synergistic interactions may enhance the effects of the agents over their individual or summed effects. For some agents, e.g. smoking and radon exposure, multiplicative or sub-multiplicative effects have been observed. In practice, where mixed exposures occur, one or, at most, a few agents will usually be found to dominate. The potential significance of the mixed exposure may then be evaluated by considering the likely response to the dominant agent or agents and then evaluating how this might be perturbed by the other agents present. This will typically require consideration of the primary toxicological literature, examining issues such as whether the target tissues and organs differ between the agents, whether one agent might act as an initiator in combination with another as a promoter, and whether the agents may affect each other's metabolism and biokinetics.

g) With genotoxic, carcinogenic agents, which are likely to be a principal cause of concern at low exposure levels, the initial adverse effect is thought to be the induction of double strand breaks in the DNA of stem cells or their immediate progenitors. It is becoming feasible to culture such cells *in vitro* and this may be a promising approach to assessing the impacts of such agents either

singly or in combination, e.g. by studying the induction of mutations, chromosomal aberrations, genomic instability or other sequelae of DNA mis-repair. However, this addresses only the initial induction of effects at the sub-cellular level. Additional modelling, supported by data, is required to interpret these results in terms of likely increases in cancer induction. Tumour initiation, proliferation and progression all need to be addressed. Multi-stage models of carcinogenesis may be useful in this context.

h) In terms of protection of the environment, although the principal interest is likely to be on environmental characteristics at the community, population or habitat level, nevertheless, for convenience, protection standards may be couched in terms of exposure of the individual organism.

i) For both exposure to ionising radiations and chemical pollutants, standards for environmental protection are generally based on precautionary approaches. These include definitions of compliance values set by reference to the sensitivity of the most sensitive species, use of precautionary uncertainty factors, and use of cautious over-estimates in exposure calculations. In some contexts, notably with ionising radiations, the compliance values are described as screening thresholds, i.e. exposures above the thresholds are an indication of a need for further investigation, but do not necessarily imply that adverse effects will be observed. This is in contrast to the approach for chemicals whereby the same approaches to deriving assessment criteria are largely applied, yet the resultant values are largely applied as limits that should not be exceeded. The adoption of precautionary approaches for individual toxic agents, with the degree of caution differing between agents, adds to the difficulty in comparing the effects of different environmental stressors or in assessing the overall impact of multiple stressors.

j) Additionally, in an environmental impact assessment, the effects of radiotoxic and chemotoxic stressors will have to be considered in conjunction with the effects of other stressors, the distributions of which will be altered by the proposed or existing development. These stressors may include thermal and noise pollution, among others. In many contexts, radiotoxicity and chemotoxicity will be minor considerations compared with these other stressors. However, even if this is the case in the short term, it may not apply in the long term, over which multiple generations will be exposed to the radiotoxic and chemotoxic materials.

k) Because of the diversity of interactions between communities and the degree to which those communities are open to changing regional influences, it is unlikely that generic, quantitative relationships can be established between levels of exposure to one or more toxic agents and responses at the community, population or habitat level. Therefore, it seems likely that ecological impact assessments will be qualitative, rather than quantitative. They may provide no more than value judgements that levels of exposure are of negligible, small, moderate or large significance.

There is a clear driver to assess the different risks in a similar and proportionate manner so as to support unbiased and reasonable decisions; however, comprehensive assessment addressing all aspects of risk in detail is likely to be impractical. Therefore, there is a continuing need for some common measure of hazard that supports identification of risk management priorities for mixed hazardous waste. This might be just as true for different types of hazardous waste as well as when radioactive waste is included.

Such a common measure needs to account not only for the basic characteristics related to toxicity of the components but also for factors concerning sources and pathways that constrain the potential for realisation of the hazard. While the overall picture, including the different regulatory contexts, remains complex, the non-radiologically hazardous components of many radioactive wastes appear to relate to relatively few elements and materials which are already reasonably well understood, such as U, Pb, Cd, and asbestos. Therefore, technical progress would appear to be most affective that focusses on a relatively limited set of hazardous components, especially for the relatively large volumes of LLW and very LLW arising in decommissioning and remediation of legacy sites. Such technical progress could benefit from parallel developments in international recommendations on management and regulation of wastes which are radioactive but also present other hazards. Such work should ideally draw a good balance between prescription and guidance, taking account of the wide range of regulatory and other contexts that arise.

Contents

Abbreviations

ADE	Average daily exposure
ADI	Acceptable daily intake
ADWG	Australian drinking water guidance
AF	Allocation factor
ALARP	As low as reasonably practicable
ALM	Adult lead model
AQG	Air quality guidelines
As	Arsenic
ATSDR	Agency for Toxic Substances and Disease Registry
B	Boron
BaP	Benzo(a)pyrene
Be	Beryllium
BHC	Below health concern
BMD	Benchmark dose
BMD_{10}	BMD producing a 10% response, or one in 10 response
BMDL	Benchmark dose lower confidence limit
$BMDL_{10}$	The lower 95% confidence limit of the BMD_{10}
C4SL	Category 4 screening level
Cd	Cadmium
CDC	Centers for disease control and prevention
CLEA	Contaminated land exposure assessment
CN	Cyanide
COC	Committee on Carcinogenicity of chemicals in food, consumer products and the environment
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
Cr	Chromium
CRI	Cumulative risk index
CSAF	Chemical-specific adjustment factor
DALY	Disability-adjusted life year
DBP	Dibutyl phthalates
DCRL	Derived consideration reference level
DGR	Deep geological repository

DiP	Decision in principle
DSB	Double strand breaks
DW	Disability weight
DWEL	Drinking water equivalent level
EAR	Excess absolute risk
EBD	Environmental burden of disease
EC	European Commission
EC_x	Effects concentration causing measured effect to x% of test population
EDTA	Ethylenediaminetetraacetic acid
EIS	Environmental impact statement
EPA	Environmental Protection Agency
EPAQS	Expert Panel on Air Quality Standards
EQS	Environmental quality standard
ERA	Ecological risk assessment
ERR	Excess relative risk
ESC	Environmental safety case
EU	European Union
EUSES	European Union System for the Evaluation of Substances
GDF	Geological disposal facility
GV	Guideline value
GW	Groundwater
GWDD	Groundwater Daughter Directive
HB	Health based
HBL	Health based limit
HCV	Health Criteria Value
Hg	Mercury
HI	Hazard index
HLW	High level waste
HQ	Hazard quotient
HR	Homologous recombination
HSC	Haematopoietic stem cell
IARC	International agency for research on cancer
ICRP	International Commission on Radiological Protection
IEUBK	Integrated Exposure Uptake BioKinetic
ILW	Intermediate level waste
INERIS	L'Institut National de l'Environnement Industriel et des Risques

IRIS	Integrated risk information system
ISO	International organization for standardization
JAGDAG	Joint Agencies Groundwater Directive Advisory Group
Kd	Sorption coefficient
L/ILW	Low and intermediate level waste
LLNA	Local lymph node assay
LLTC	Low level of toxicological concern
LLW	Low level waste
LLWR	Low level waste repository
LOAEL	Lowest observable adverse effect level
MCL	Maximum contaminant levels
MCLG	Maximum contaminant level goal
MDI	Mean daily intake
Mo	Molybdenum
MOA	Mode of action
MoE	Margin of exposure
MRV	Minimum reporting values
NEA	Norwegian Environment Agency
NEPA	National environmental policy act
NH_4	Ammonium
NHEJ	Non-homologous end joining
Ni	Nickel
NOAEL	No observable adverse effect level
NORM	Naturally Occurring Radioactive Material
NPDWR	National primary drinking water regulations
NRC	Nuclear regulatory commission
OEL	Occupational exposure limits
PAH	Polycyclic aromatic hydrocarbons
Pb	Lead
PCB	Polychlorinated biphenyls
PCE	Perchloroethene
pdf	Probability density function
PEC	Predicted environmental concentration
PHE	Public Health England
PNEC	Predicted no effect concentration
PoA	Period of authorisation

POD	Point of departure
PODI	Point of departure index
PRG	Preliminary remediation goal
PSL	Priority substances list
PTDI	Provisional tolerable daily intake
PTWI	Provisional Tolerable Weekly Intake
QALY	Quality adjusted life year
QOLS	Quality of life scale
QRA	Quantitative risk assessment
RAP	Reference animals and plants
RfC	Reference concentration
RfD	Reference dose
RG	Remediation goal
RI	Risk index
ROS	Reactive oxygen species
RSC	Relative source contribution
Sb	Antimony
Se	Selenium
SEGH	Society for Environmental Geochemistry and Health
SEIS	Supplemental environmental impact assessment
SF	Safety factor
SGV	Soil guideline value
SHS	Sodium hydrosulphite
SKB	Swedish Nuclear Fuel and Waste Management Company
SO_4	Sulphate
SPOSH	Significant possibility of significant harm
SRF	Sorption reduction factor
SSAC	Site-specific assessment criteria
SSD	Species sensitivity distribution
SSL	Soil screening level
T_{25}	Exposure producing a 25% increase in the incidence of a specific tumour above the spontaneous background rate
TCA	Tolerable Concentration in Air
TCE	Trichloroethylene
TD_{50}	Rate of exposure required to halve the probability of remaining tumourless at the end of a standard, lifespan
TDI	Tolerable Daily Intake

TDSI	Tolerable daily soil intakes
TEF	Toxic equivalency factor
TEQ	Toxic equivalent
TSPA	Total safety performance assessment
TWA	Time weighted averages
U	Uranium
UF	Uncertainty factor
UO_2	Uranium dioxide
US EPA	United States Environmental Protection Agency
V	Vanadium
VCM	Vinyl chloride monomer
WEL	Workplace exposure limits
WFD	Water Framework Directive
WHO	World Health Organisation
YLD	Years lived with disability
YLL	Years of life lost

1 INTRODUCTION, OBJECTIVES AND SCOPE

The scope of BIOPROTA activities is not limited to radionuclides. In 2008, a consultation was held among BIOPROTA member organisations on next step priorities (BIOPROTA, 2008). This identified the need to address chemical impacts of radioactive waste disposal. Chemical toxicity was of interest to several organisations and a significant range of potentially relevant chemotoxic substances was identified. Although the focus was on toxicity in humans, potential detrimental impacts on non-human species were also identified as being of potential interest. The impact of the form in which chemotoxic substances are available in the environment was identified as a significant consideration. A complicating factor is the potential for combined impacts from radiation and other stresses, creating synergistic and antagonistic effects. Concerning management and regulation, it was noted that in some situations waste is classified as hazardous[1] industrial waste, even though it contains radionuclides, and so falls within a different set of regulatory requirements for management than radioactive waste. The absence of criteria for non-radioactive contaminants that match those applied to radionuclides, e.g. in terms of addressing human health over all relevant timeframes, was noted, as was the issue of consistency between, and different degrees of conservatism in, the assessment models used in assessing the impacts of radioactive and non-radioactive contaminants.

Subsequently, two workshops have been organised through BIOPROTA to consider the non-radiological post-disposal impacts of radioactive waste disposal. The first, held in Slovenia in 2013, addressed the scientific basis for long-term radiological and hazardous waste disposal assessments (BIOPROTA, 2013). Building on the discussion at that meeting, a second workshop was held in Asker, Norway in 2015, focussing more specifically on comparisons of safety and environmental impact assessments for disposal of radioactive and hazardous wastes. The foreword to the Asker workshop report, published by the Norwegian Radiation Protection Authority (NRPA) noted that

“ideally, a holistic approach to assessment of radionuclides and hazardous materials should be internationally created such that consistent assumptions are employed in assessments and consistent criteria used in the evaluation of risk. Currently, the basis for separation in approaches includes traditional behaviour, regulatory and institutional differences, lack of common language in addressing things with respect to both waste types, lack of international guidance on criteria for assessments, as well as lack of supporting information from science. The development of a common set of objectives and, hence, assessment endpoints and timeframes for the different waste types would be very beneficial. In particular, this would promote the proportionate allocation of resources to the different types of hazards associated with the waste. In cases where technical differences are necessary, a clear understanding of the reasons for the different approaches should be provided to allow differences to be understood and communicated.”, (BIOPROTA, 2015).

The following specific points arose from the material in the Asker workshop report.

- Environmental impact assessments, and assessments of safety, human and environmental health, are used to support decisions on the management and disposal of both radioactive and hazardous wastes. Assessment of the post-disposal non-radiological impact of disposal of radioactive waste is nowadays commonly carried out for all types of radioactive waste, from high level to very low level. To carry out assessments of the non-radiological impacts, it has been natural to draw on the methods used to assess those impacts as if the waste

[1] Hazardous waste is not defined in this report due to the different definitions arising in different jurisdictions. The term is used to mean waste which presents a hazard in the general sense of the word such that it might give rise to a need for some form of regulatory control.

were not also radioactive, i.e. the assessment methods used for hazardous waste disposal in the absence of any radiological hazard. However, this gives rise to some interesting challenges.

- Although assessment methods for radioactive and hazardous waste disposal include similar modelling techniques and other procedures, different protection objectives are applied, leading to different levels of protection. This, in turn, results in inconsistencies and challenges when identifying and applying optimum waste management strategies. Even where the same protection objectives are set, the bases for demonstrating compliance with the objectives, e.g. assessment methods and issues addressed, are often different. Why, for example, is the safety of radioactive waste disposal assessed for periods up to one million years after disposal, but, generally, not even for 1000 years for non-radioactive hazardous wastes?
- Another challenge is the application of the Groundwater Daughter Directive (European Commission, 2006a) to both radioactive and other waste disposal facilities. Since many wastes are both radioactive and chemically hazardous, it can be difficult to determine which protection objectives and assessment methods to adopt. Attempts at alignment or parallel application can be hindered by institutional frameworks.

These issues complicate the design of assessments to deliver the coherent information needed by decision makers. It also complicates the provision of corresponding relevant scientific support to the assessments. The idea of creating a holistic approach for assessment of radionuclides and hazardous materials on a common risk management basis is not new (Smith et al., 1994; Little et al., 1996). Nevertheless, differences in approaches to addressing radioactive and non-radioactive materials remain in the context of radioactive waste management, both between industries and as applied by regulatory authorities at both international and national levels. Similar issues have also been recognised in the management of remediation of legacy sites, as discussed at an international workshop held in Oslo (Sneve and Strand, 2016) and in a report of strategic considerations for the sustainable remediation of nuclear installations (NEA, 2016).

The same considerations have been noted in respect of optimisation of the overall management of radioactive waste (Kessler, 2017), viz:

> "Actions to minimize, for example, health risk to the public from a disposal facility could increase the health risk to workers and members of the public in other areas of waste management, such as storage and transportation. Thus, it is entirely possible – perhaps likely – that the health risk to workers and affected members of the public from the combination of radiological and non-radiological sources is not minimized across the entire back end of the fuel cycle."

The challenges emerging from the Asker workshop were presented at the BIOPROTA Annual Meeting in May 2015 and discussed further at the Continuing Issues Workshop held in the same week. They can be summarised as including:

1. Definition of criteria for human and environmental health protection from the non radiological hazards associated with radioactive waste disposal;
2. Specification of methods and criteria for determining limits on package content of hazardous chemicals in radioactive waste packages.
3. Application of groundwater protection legislation to radioactive waste repositories, e.g. the Groundwater Daughter Directive.
4. Feasibility of developing a single toxicity index that addresses the chemical and radiation hazards associated with solid waste on a consistent and equitable basis.

5. Achievement of consistent and coherent assessments of disposal of wastes containing naturally occurring radioactive material (NORM) and other radioactive wastes in the same disposal facility;
6. Regulating the disposal of low-level and/or very low-level radioactive waste with other waste in facilities not specifically intended for radioactive waste.

This report describes a study of the issues raised above with the objective of providing information to support the development of a consensus on how to address them, leading to the application of more coherent and consistent assessment methods. It has not been practical to account for all the latest developments in policy, management and regulatory practices, assessments approaches and tools, and the under-pinning science. However, it is hoped that the report provides a substantial range of material to underpin further developments in these areas.

The scope includes the assessment of the impact of disposal of radioactive waste in land-based disposal facilities, taking account of the possible radiological impacts and non-radiological impacts due to chemotoxic substances.

The work was undertaken through a series of tasks, as follows:

- Overview of objectives and derived criteria for environmental and human health protection;
- Review of assessment methods and data requirements for non-radiological assessments of waste disposal;
- Review of the content and application of groundwater protection legislation as applied to waste disposal facilities;
- Review of the design and use on toxicity indices; and,
- Identification of factors to consider in the design of effective assessments.

Results are presented in the following sections of the report, followed by conclusions and references. In addition, three appendices are provided, as follows:

- Appendix A: Illustration of the assessment of chemical alongside radiological impacts, by reference to some relevant example contaminants being released into a realistic regional groundwater aquifer from which water is abstracted for domestic and agricultural use.
- Appendix B: Consideration of the biological mechanisms of chemical toxicity and radiotoxicity and of potential synergistic effects mediated by agents acting on the same or different stages of a toxicological response, e.g. in the initiation, promotion and expression of cancer.
- Appendix C: List of project participants and contributors.

2 Overview of objectives and derived criteria for human health and environmental protection

This section provides an overview of the objectives for human health and environmental protection from the non-radiological hazards associated with radioactive waste disposal and compares them with the radiological protection objectives. It includes accounts of international recommendations and guidance and examples of their application (or not) at the national level.

The purpose is to set out the differences between objectives and criteria for radionuclides and for chemotoxic substances, provide a perspective on why these have arisen, and comment on the implications for management and the levels of protection that are or can be achieved.

The overview then considers the quantities used in setting criteria which, if met, are taken to mean that the protection objectives have been achieved. Example criteria include individual radiation doses, individual risks, levels of exposure, levels of contamination of environmental media, protection of sites of special interest, etc. The intention is to identify both the alternatives adopted and the major differences in approaches to compliance, both in terms of the nature of the protection afforded and the level of protection.

Special consideration is given to substances, notably uranium, that can be both significantly chemically toxic and radiotoxic at the same exposure level.

2.1 Protection of people from radionuclides in waste

Dose is a commonly used term in the context of exposure to substances. In this report, dose in the context of radiation exposure is taken to mean ‘effective dose’, unless otherwise indicated. Dose is used in a very different sense with respect to toxic chemicals, where it usually refers to the amount of the chemical inhaled or ingested.

The concept of ‘effective dose’ was developed by the ICRP (ICRP, 1977a and 2007) for use in the radiological protection of workers and the public. In these applications, it is intended for use as a risk-adjusted dosimetric quantity to optimize protection from stochastic effects of exposure to radionuclides, principally cancer, comparing planned or received doses with constraints, reference levels and limits expressed in the same quantity. Its design allows all radiation exposures from external and internal sources to be considered together and summed, relying on the assumptions of a linear non-threshold dose-response relationship, equivalence of acute and chronic exposures at low doses or low dose-rates, and equivalence of external and internal exposures.

Effective dose is accepted internationally as the central radiological protection quantity (IAEA, 2014), providing a risk-adjusted measure of total body dose from external and internal sources in relation to stochastic risks of cancer and hereditary effects, expressed in terms of detriment to health. It has proved to be a valuable and robust quantity for use in the optimisation of protection, the setting of control criteria (limits, constraints and reference levels), and the demonstration of compliance with those criteria. The use of effective dose requires the assumption of a linear non-threshold dose-response relationship between dose and risk at low doses or dose-rates, and of the equivalence of effect of acute and chronic low-level exposures, and of internal and external exposures (Harrison et al., 2015). In evaluating annual exposures, effective dose is the sum of external dose received in the year and committed dose from internal exposures during that year, where committed dose is integrated over a 50-year period for workers and to age 70 years for members of the public. This procedure introduces an element of conservatism for long-lived

radionuclides with long biological half-times. While age- sex-, and population-related differences in risks per Sv are recognised, the use of constraints and reference levels that apply to all workers and all members of the public, together with optimisation, provides a pragmatic and workable system of protection that does not distinguish on an individual basis. Reference dose coefficients are provided by ICRP for various circumstances of exposure, including exposure to specific chemical and physical forms of ingested and inhaled radionuclides (ICRP, 2012). Locally relevant information on the specific chemical and physical forms of exposure should be used if available and if the level of exposure warrants more precise estimation of dose (Harrison and Leggett, 2016; Harrison et al., 2015).

Whereas radiation doses incurred at low levels of radiation exposure[2] may be measured or assessed with reasonable accuracy, the associated risks are uncertain. However, bearing in mind the uncertainties associated with risk projection to low doses, it is considered reasonable to use effective dose as an approximate indicator of possible risk, with the additional consideration of variation in risk with age, sex and population group (Harrison et al., 2015). Use of effective dose in this way is not a substitute for population- and context-specific risk analyses using best estimates of organ doses, appropriate information on the relative effectiveness of different radiation types, and age-, sex- and population-specific risk factors, with consideration of uncertainties (Harrison et al., 2015).

Given the degree of uncertainty linked generally to radiation dose assessments for post-emplacement releases of radionuclides from radioactive waste repositories and the hypothetical nature of the human populations postulated to be exposed, the use of effective dose as a safety indicator is considered justified, and, if controls are expressed in risk terms, ICRP nominal risk coefficients to convert dose to risk are also justified, albeit with appropriate recognition of the uncertainties.

In the context of geological disposal of solid radioactive wastes, radiological protection criteria have typically been considered to apply from the time of closure, or from the time at which institutional control of the site is relinquished, into the far future. These timescales can range from a few thousand years to about one million years, with the longest timescales sometimes being defined as the period of geological stability or the period over which the maximum in annual effective dose or annual risk is expressed. Where very long timescales are addressed, there can be breakpoints at which the assessment criteria change. For example, in Finland, annual effective dose is used as the appropriate measure of performance over the first few thousand years, but radionuclide release rates to the biosphere are the compliance criteria that are adopted on longer timescales. For Yucca Mountain, in the USA, although the expectation value of annual effective dose is the performance measure adopted throughout, different rules govern how it shall be calculated over the first 10 ka and beyond 10 ka, and the compliance criterion, i.e. the maximum acceptable value of the annual effective dose, differs between these two periods (see the US Code of Federal Regulations 10 CFR 63, Subpart L).

In contrast, compliance requirements for chemical hazards seldom extend or are seldom applied to more than the first millennium after disposal, notwithstanding the consideration that releases of toxic metals and heavy metals may persist over timescales similar to those applicable to releases of radionuclides (see Appendix A).

[2] The use in the literature of the term “low dose” is distinctly variable (Smith and Thorne, 2016). In this report, the term is taken to mean less than 100 mSv, based on suggestions in UNSCEAR (2015) and Harrison et al. (2015), and discussion in Smith and Thorne (2016).

2.2 Protection of people from chemotoxic substances in waste

In chemical toxicology, there is no equivalent to effective dose, thought of as a quantity that permits the adverse health impact of a wide variety of toxic agents to be expressed through a single, common measure. Instead, chemical-specific and pathway-specific relationships are developed between the degree of exposure to a chemical, typically by ingestion, inhalation or exposure of the intact skin and the adverse health impact. As noted above, this is associated with use of the term 'dose' to mean the amount of a substance to which an individual is exposed. The most usual application is for ingestion, with the 'dose' usually being expressed as the total amount of the substance ingested or the amount ingested per unit time. Furthermore, this is typically normalised by body weight, with the 'dose' being expressed as mg per kg of body mass per day. For inhalation, exposure is often measured in terms of the concentration in air (mg m^{-3}), with different limiting criteria being set depending on the duration of exposure (e.g. in an occupational context limiting criteria are often set in terms of air concentrations averaged over 15 minutes, a single eight-hour shift, or over a longer period, such as a working week, 14 days or a year).

As discussed in more detail in HPA (2007), the approaches to deriving health-based protection criteria for exposures of people can be broadly divided into two groups: one where the effect of the hazardous agent is believed to have a threshold and the other where no threshold can be assumed. Details are given in Environment Agency (2009a, b), and a summary is provided in the next section.

2.2.1 Chemicals with threshold effects

A variety of Health Criteria Values (HCVs) are derived by organisations worldwide for chemicals displaying a threshold in toxicity[3]. The most well-established of these and most universally adopted in chemical risk assessment programmes, including by the World Health Organisation (WHO) is the tolerable daily intake (TDI). The TDI is defined as an estimate of the amount of a contaminant, expressed on a bodyweight basis (e.g. mg kg^{-1} bw day^{-1}), that can be ingested daily over a lifetime without appreciable health risk.

The TDI concept has been extended from its origins in food safety to address exposure via other, non-oral, routes, such as inhalation and skin contact. In addition, for inhalation, an HCV similar to a TDI but expressed as an atmospheric concentration of the chemical (e.g. mg m^{-3}) rather than a bodyweight dose is preferred by some agencies and is commonly termed the tolerable concentration in air (TCA). For dermal studies, it would typically be the concentration of the chemical in the solvent vehicle applied to the skin.

The United States Environmental Protection Agency (US EPA) uses largely the same methodology as the WHO, but has adopted the term reference dose (RfD) instead of acceptable daily intake (ADI) or TDI, though using a very similar definition. The US EPA defines the RfD as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive groups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (US EPA, 2007). The reference concentration (RfC), also adopted by the US EPA, is equivalent to the RfD, but is based on inhalation and is defined as a concentration in air (similar to the TCA). Critically though, the RfD and RfC are based on non-cancer effects only (US EPA assesses cancer effects separately), and so may be derived by the US EPA for non-threshold genotoxic carcinogens for which a TDI would not be derived.

[3] Thresholds in toxicity can be difficult to define. For example, the threshold for subtle biochemical changes in a tissue or organ may be much less than the threshold at which clinical disease is manifest. There are also substantial inter- and intra-species variations in sensitivity and hence in threshold values. These matters are discussed in detail in later sections of this report.

Typically, the starting points will be the critical NOAEL (no observed adverse effect level) from animal data with uncertainty factors applied for both interspecies variability and individual variation in human populations. The default for each of these factors is 10 so typically the overall uncertainty factor will be 10 times 10 i.e. 100. Using this approach, an intake value can be calculated that represents a level that can be ingested daily over a lifetime by humans without appreciable health risk. This may be referred to as an ADI or TDI. It is always expressed on a body weight basis (e.g. mg per kg body weight), with the intent that it should be applicable to adults and children. The ADI or TDI is obtained by dividing the critical NOEAL by the overall uncertainty factor.

Depending on the quantity and quality of toxicity data available for an adverse effect, in addition to the NOAEL and LOAEL (lowest observable adverse effect level) – which are restricted to the 'doses' used in the toxicity studies – it may also be possible to mathematically model the dose-response curve and estimate the so-called benchmark dose (BMD) that causes a predetermined change in response (usually 5 or 10%). It is commonly the statistical 95% lower confidence limit of the BMD, termed the BMDL, that is used as a starting point for setting limits on exposure.

An alternative approach, is to estimate exposure to the compound and then to compare this with the critical NOAEL from animal data. This is often referred to as the 'margin of safety' or 'margin of exposure' approach. In general, if the margin of safety is 100 or more, a conclusion of 'no concern' is drawn. However, the value of 100 is effectively based on the same considerations as used when deriving an overall uncertainty factor to estimate an ADI or TDI, so it may be appropriate to adopt different margins of safety depending upon the chemical and route of exposure.

2.2.2 Chemicals with non-threshold effects

Mutagenic and genotoxic chemicals are often carcinogenic and are assumed not to have a threshold for their adverse effects and, therefore, it is typically recommended that exposure should be controlled to be as low as reasonably practicable (ALARP).

Two approaches exist to derive HCVs for non-threshold carcinogens: quantitative dose-response modelling and non-quantitative extrapolation.

Quantitative dose-response modelling, or quantitative risk assessment (QRA) as it is more commonly known, is a procedure used by some authorities to derive limiting numerical estimates of risk (e.g. 1 in 100,000) for exposure to non-threshold carcinogens. This may be on a lifetime or on a per annum basis.

The predominant alternative (non-quantitative) approach to setting HCVs for non-threshold carcinogens involves assessment of all available carcinogenicity dose-response data to identify an appropriate dose without discernible carcinogenic effect, or the lowest dose tested if effects are apparent at all doses, and the use of expert judgement to derive a suitable margin below that dose.

Even amongst organisations that use and publish quantitative cancer risk estimates, there has been a tendency in recent years to move away from low-dose extrapolation models to simple linear extrapolation (unless there is evidence of non-linearity). In linear extrapolation, a line is effectively drawn on the dose-response curve from the point of departure to the origin. In practice, linear extrapolation is most simply achieved by calculating the BMD_{10} (the BMD producing a 10% response, or one in 10 response) or $BMDL_{10}$ (the lower 95% confidence limit of the BMD_{10}) and then dividing this by orders of magnitude to achieve the desired risk level, e.g. dividing by 10,000 to give a 1 in 100,000 risk.

In practice, the minimal risk level approach is like that for threshold chemicals, applying numerical (uncertainty) factors to a point of departure identified from the dose-response data.

2.2.3 Target risk levels

The Australian Environmental Human Health Risk Assessment guidelines (Environmental Health Australia, 2012) state that the 'target' risk level to which some Australian environmental regulatory

authorities aim is an incremental lifetime risk of developing cancer of 1 10^{-6} for chronic exposure over a lifetime. It is emphasised that this should not be misrepresented as an annual risk, although this may depend on whether the risk is associated with contamination of air, water or food, or whether the exposure is associated with a single carcinogen or is the outcome of multiple chemical exposures. In the latter case, a combined risk of 10^{-5} may be considered acceptable. The revision of the contaminated site guidelines (Australian National Environment Protection Council, 2010) proposes a carcinogenic risk 'target' of 10^{-5}, irrespective of whether a single or multiple chemical exposures contribute to the combined risk.

The Canadian regulatory agencies in general, and Health Canada in particular, tend to use risk levels ranging from 1 10^{-5} to 1 10^{-6} as the target level for lifetime cancer risk assessments (Health Canada, 1995). The Multi-Sector Air Pollutants Regulations (Environment and Climate Change Canada, 2016) require owners and operators of specific industrial facilities and equipment types to meet consistent performance standards across the country. The regulations are part of the federal government's contribution to the implementation of the 2012 Air Quality Management System. However, more detailed discussion on health-based guidance values could not be found.

In the USA, the numerical preliminary remediation goals (PRG) for contaminated sites are typically based on the upper bound excess carcinogenic risk over a lifetime of one in a million (10^{-6}) or a hazard quotient of unity. PRGs can be proportionally adjusted upward to become RGs for a higher acceptable carcinogenic risk or hazard level to account for the conservatism inherent in the PRGs (i.e. in both toxicity values and exposure assumptions). Specifically, the RG can be based on a 10^{-4} cancer risk that is still within the National Oil and Hazardous Substances Pollution Contingency Plan's acceptable range (10^{-4} to 10^{-6}) for carcinogenic risk. Similarly, the RG for a non-carcinogen can be several times higher than the corresponding PRG based on the uncertainty factor associated with the reference dose and exposure factors. In certain instances, RGs may have lower values than PRGs based on a downward adjustment because of many co-occurring principal threat chemicals and complete exposure pathways (US DoE, 1997).

The UK approach is to compare the BMDL with the modelled exposure levels to derive a Margin of Exposure (MoE). As Searle (2012) summarises 'Guidance is provided on the interpretation of the size of the MoE indicating that a MoE of 10,000 indicates that an exposure to a carcinogen at this level is unlikely to be of concern. Guidance from the UK Committee on Carcinogenicity of chemicals in food, consumer products and the environment (COC) is provided on use of the MOE approach in https://www.gov.uk/government/publications/cancer-risk-characterisation-methods.

There is a strong preference in UK regulation for controlling exposures to carcinogens to be ALARP because of the uncertainties in quantitative risk assessment. The problem with the ALARP approach, however, is that it may be difficult to prioritise actions and justify control measures in the absence of any quantitative assessment of benefit.'

As ALARP involves a weighing of risks against benefits, with the consideration that the benefits should substantially outweigh the risks (the concept of disproportion), it is difficult to see how an ALARP determination can be made without some element of quantification of risk.

A number of EU expert committees have endorsed the BMD/MoE approach to risk assessment for carcinogens (SCHER et al., 2009).

2.2.4 Routes to humans

As noted previously, human exposure to chemicals in the environment occurs via three main routes: oral (ingestion), inhalation, and dermal (via the skin). Oral limiting values may represent a regular (generally daily) ingested dose of a substance that is anticipated to be acceptable or tolerable. Examples include the ADI, TDI and RfD. Inhalation values may represent an atmospheric concentration that is expected to be without appreciable risk to humans over a lifetime. Examples include the RfC and AQG (air quality guidelines). Dermal exposure to chemicals is normally a more significant problem for occupational health than it is for environmental health, because of the

frequency of worker contact and the strength of chemicals encountered. Issues include allergic responses of the intact skin and absorption through the intact skin. Uptake through wounds is generally considered only in accident situations.

2.2.5 Consideration of different pathways in development of Health Criteria Values

Krishnan and Carrier (2013) discusses the exposure source allocation factor (AF; Health Canada, 1995; WHO, 2011) or relative source contribution (RSC; US EPA, 2000) used to apportion the acceptable dose or tolerable intake (RfD, RfC, TDI) to specific exposure sources and environmental media. In other words, a specific fraction of the total allowable exposure is allocated to each source of exposure such that the total 'dose' received does not exceed the TDI. The choice and use of appropriate AF or RSC in risk assessment is critical to ensuring that the total 'dose' from the various exposure media (e.g., air, water, soil, food, consumer products) does not exceed the TDI, as well as to ensuring that a risk assessment does not result in unreasonably small guideline values; that is, stringent regulation of a chemical due to the presence of a small amount of a contaminant in a medium that necessarily, or almost certainly, represents only a minor or insignificant source of exposure. In this regard, an AF has historically been used in Health Canada assessments to meet the need of limiting the exposure via each medium or source (i.e., air, water, soil, food, and/or consumer products), such that no single medium ends up depleting the entire TDI (Health Canada, 1995; CCME, 2006). Because people are likely to come into contact with all 5 primary exposure sources/media (i.e., air, water, soil, food, and consumer products), 20% of the TDI is apportioned to each of the 5 media (CCME, 2006), particularly when media-specific exposure data are not available or are incomplete.

The US EPA in its exposure decision tree framework (US EPA, 2000), captured the regulatory and scientific considerations as they relate to the determination of RSC. Either a subtraction or a percentage method is suggested. Both methods use a lower and an upper bound RSC value of 20 and 80%, respectively.

The exposure source apportionment is only appropriate when the risk assessment deals with systemically acting threshold toxicants. The use of AF or exposure source apportionment is conceptually not appropriate for toxicants inducing route-specific effects, nor for those toxicants (carcinogens) for which a slope factor is used in the assessment. In the case of route-specific effects, the medium/route combination may be the single most important determinant with respect to the mode of action (MOA) of the chemical, such that the concepts of total 'dose' and apportionment become non-applicable. For quantitative risk assessment of carcinogens [i.e., group I and II carcinogens for which a linear extrapolation model is used; (Health Canada, 1995)], the use of an AF is not relevant because the assessment is based on a target risk level that would be applicable independent of other sources of exposure. In other words, instead of explicitly using an AF for deriving guideline values for non-threshold carcinogens, the appropriate target risk level is specified so as to reflect the importance of a particular medium as the exposure source (e.g., drinking water) relative to the multiplicity of plausible exposure sources. This approach reflects the current strategy of regulatory agencies not to base the guideline development for carcinogens on the concept of an AF, but rather to base it on target risk levels reflective of the overall acceptable risk level for each exposure medium (e.g., drinking water).

In most countries (an exception being the UK) the approach to human health risk assessment for (potentially contaminated) soils takes account of potential contamination of the water environment and a range of possible exposure routes associated with water contamination. A review of methods to assess risks to human health from land contamination (Searle, 2012) concludes that the soil screening values between EU countries varied by an order of magnitude (Carlon, 2007) with some of the important factors being the inclusion/exclusion of "indoor air exposure" and "consumption of home-grown vegetables" and the inclusion/exclusion of exposure sources that are not related directly to soil.

The WHO Guidelines for drinking water quality (WHO, 2011) state that 'where appropriate information on exposure from food and water is not available, allocation factors are applied that reflect the likely contribution of water to total daily intake for various chemicals. In the absence of adequate exposure data, the normal allocation of the total daily intake to drinking-water is 20%, which is intended to reflect a reasonable level of exposure based on broad experience, while still being protective. In some circumstances, there is clear evidence that exposure from food is very low, such as for some of the dibutyl phthalates (DBPs); the allocation in such cases may be as high as 80%, which still allows for some exposure from other sources. In the case of some pesticides, which are likely to be found as residues in food from which there will be significant exposure, the allocation for water may be as low as 1%'.

The approaches applied to derive health criteria for drinking water, air and soil in different countries are summarised in Table 2-1.

Table 2-1. Detailing basis of HCVs for drinking water, air and soil for UK, USA, Canada and Europe.

Standards	Basis of Standards
UK	
Drinking water	Mainly taken from WHO guidelines for drinking water quality (WHO, 2011). Generally based on human toxicology data and based on TDI and $BMDL_{10}$ and a MoE of 10 000.
Air	Environmental Assessment Levels – these are derived from a Hierarchy of information - Expert Panel on Air Quality Standards (EPAQS), the World Health Organization (WHO), EU Limit Values and values derived from Occupational Exposure Limits (OELs) with the majority having been derived from extrapolation from the OELs (UK Expert Panel on Air Quality Standards, 2003). Searle (2012) states UK air quality standards for carcinogens have generally been set at levels that are about 1000 times smaller than the modelled lowest effects level in workplace studies implying a cancer risk of between about 10^{-4} and 10^{-5}. The report comments that the air quality objectives adopted in the UK are based on health-based standards but with some allowance for how readily that standard could be achieved, and are less protective than most people would imagine. Different air quality objectives apply in different parts of the UK reflecting the differences in air pollution climate and ease with which objectives can be met.
Soil	Soil Guideline Values (SGV) are based on minimal risk levels. COC (2004) defined a minimal risk level as "an estimate of daily human exposure to a chemical identified by expert judgement that is likely to be associated with a negligible risk of carcinogenic effect over a specified duration of exposure (usually a lifetime)". This is based on Tolerable Daily Intake (TDI) or if genotoxic a Margin of Exposure (MoE) of 10 000. More recently, screening levels have been developed on the basis of a low level of toxicological concern (Defra, 2012b). These values derived from same set of data as SGV but are based on BMD rather than $BMDL_{10}$ i.e. higher levels and with lower MoEs (5000 or risk of 1 in 50 000).
USA	
Drinking water	Safe Drinking Water Act - regulations include both mandatory levels (Maximum Contaminant Levels, or MCLs) and non-enforceable health goals (Maximum Contaminant Level Goals, or MCLGs) for each included contaminant. US EPA (2015) states that for chemical contaminants that are carcinogens, EPA sets the MCLG at zero if there is evidence that a chemical may cause cancer or there is no dose below which the chemical is considered safe. If a chemical is carcinogenic and a safe dose can be determined, EPA sets the MCLG at a level above zero that is safe. For chemical contaminants that are non-carcinogens but that can cause adverse non-cancer health effects (for example, reproductive effects), the MCLG is based on the reference dose. A reference dose (RfD) is an estimate of the amount of a chemical that a person can be exposed to on a daily basis that is not anticipated to cause adverse health effects over a lifetime. To determine the RfD, the concentration for the non-carcinogenic effects from an epidemiological or toxicological study is divided by uncertainty factors (for example, for sensitive subpopulations). This provides a margin of safety for consumers of drinking water. The RfD is multiplied by body weight and divided by daily water consumption to provide a Drinking Water Equivalent Level (DWEL). The DWEL is multiplied by the relative source contribution. The relative source contribution is the fraction allocated to drinking water exposure for the general population, after considering other exposure routes (for example, food, inhalation). Once the MCLG is determined, EPA sets an enforceable standard. In most cases,

Standards	Basis of Standards
	the standard is a maximum contaminant level (MCL). The MCL is the maximum level allowed of a contaminant in water which is delivered to any user of a public water system.
Air	EPA must promulgate standards for hazardous air pollutants if the source has an associated maximum individual cancer risk that exceeds 1 in one million (US EPA, 1992b). The health-based standards will be consistent with the generally acceptable risk range of 10^{-4} to 10^{-6} (40 CFR 300.430 - Remedial investigation/feasibility study and selection of remedy.)
Soil	For the ingestion, dermal, and inhalation pathways, toxicity criteria are used to define an acceptable level of contamination in soil, based on a one in-a-million (10^{-6}) individual excess cancer risk for carcinogens and a hazard quotient (HQ) of 1 for non-carcinogens. SSLs are back-calculated for migration to groundwater pathways using groundwater concentration limits (non-zero MCLGs, MCLs, or health-based limits (HBLs) (10^{-6} cancer risk or a HQ of 1) where MCLs are not available) (US EPA, 1996).
Canada	
	Decision-making for screening health assessments under CEPA (1999) is based on a "margin of exposure" approach. The "margin of exposure" is the magnitude of the ratio between the level (dose) at which the critical effect is observed in studies conducted in animals or, in some cases, humans and the upper-bound estimated (or measured) level of human exposure to a substance. Recommendations are based on the adequacy of this margin of exposure, taking into account confidence in the completeness of the identified databases on effects and exposure, within a screening context: • Generally, margins greater than 1000 are adequate as a basis for recommending no further action for substances where the databases on exposure and effects are relatively complete. • For margins of less than 1000, limitations of and confidence in the exposure and effects databases are carefully considered and documented. In some cases, consideration of some more complex information, such as that on mode of action (i.e. the way a substance induces toxic effects), and/or more refined estimates of exposure and/or assessment of critical effect levels may be required. However, in cases where an original comprehensive analysis of available data on mode of action and/or the generation of such data are warranted to more fully inform decision-making, the substance would be recommended for addition to the priority substances list (PSL) for further in-depth assessment. In some cases, where the margins of exposure are less than 1000, but the uncertainty in the available databases on exposure and/or effects is significant, a conclusion of "suspected to be toxic" is proposed as a basis to solicit additional information to permit a more definitive conclusion to be reached. For substances with high intrinsic toxicity to human health (e.g., those that cause cancer through direct interaction with genetic material), with effects where there is some probability of harm at any level of exposure, the substance would be proposed "toxic" under Paragraph 64(c) of CEPA (1999) and recommended for addition to the List of Toxic Substances under the Act, and guidance would be provided concerning priority of analysis of options to reduce exposure. For substances with potentially high intrinsic toxicity to human health, but with significant uncertainty in the available database on effects, a conclusion of "suspected to be toxic" is proposed as a basis to solicit additional information to permit a more definitive conclusion to be reached (Health Canada, 2004).
Drinking water	Health Canada considers an incremental risk of less than 10^{-5} to 10^{-6} to be “essentially negligible” for the purpose of deriving Maximum Acceptable Concentrations for carcinogenic chemicals in drinking water (Health Canada, 1995).
Soil	CCME (2006) recommends the development of a soil guideline for a non-threshold toxicant based on an incremental risk from soil exposure of 10^{-6} or 10^{-5} above background. Some provinces in Canada have adopted through policy an acceptable incremental lifetime cancer risk of 10^{-5} and other have chosen 10^{-6}. For threshold contaminants guidelines are based on Tolerable Daily Intakes using an uncertainty factor to account for uncertainty and variability in the toxicological data base of a substance. Numerical values of the uncertainty factor range from 10 to 10,000. Uncertainty factors greater than 10,000 are not applied since the limitations of such a database preclude the development of a reliable TDI. Uncertainty factors are assigned by Health Canada based on professional judgement. Health Canada has accepted the responsibility for determining the TDI.
EU	
Drinking water	The European Drinking Water Directive (European Commission, 2006a) sets essential quality standards at EU level. A total of 48 microbiological, chemical and indicator parameters must be monitored and tested regularly. In general, WHO guidelines for drinking water WHO (2011) and the opinion of the EC Scientific Committee on Health and Environmental Risks are used as the scientific

Standards	Basis of Standards
	basis for the quality standards applicable to drinking water. The Wikipedia entry states that in setting contaminant levels the Directive applies the precautionary principle. For example, the EU contaminant levels for pesticides are up to 20 times lower than those in the WHO drinking water guidelines because the EU directive not only aims at protecting human health but also the environment.
Air	Directive 2010/75/EU on industrial emissions (integrated pollution prevention and control) (European Commission, 2010), which targets certain industrial, agricultural, and waste treatment installations states that 'limit value' shall mean a level fixed on the basis of scientific knowledge, with the aim of avoiding, preventing or reducing harmful effects on human health and/or the environment as a whole, to be attained within a given period and not to be exceeded once attained; 'target value' shall mean a level fixed with the aim of avoiding more long-term harmful effects on human health and/or the environment as a whole, to be attained where possible over a given period; Air Quality Limit Values have been established to date for SO_2, NO_x, particulates (PM_{10}), lead, carbon monoxide, benzene, and ozone, polyaromatic hydrocarbons, cadmium, arsenic, nickel and mercury.
Soil	Carlon (2007) gives an overview of the derivation of soil screening levels in Europe. It states that regarding the acceptable level of incremental risk, a more or less general agreement is observed for the human health risk assessment i.e 1 in 100 000 excess lifetime cancer risk. It also comments that in some countries human health and ecological risk screening values are integrated in one value by choosing the lower of the two. When the lowest value is affected by high uncertainty, weighted averages between the lowest and the highest values can be preferred. In some other countries, the integration is avoided and both values are presented. The derivation of one reference value out of the two is made on a case by case basis (e.g., Denmark, UK, under discussion in Flanders).

2.2.6 Efforts at developing a common approach across environmental risks

The WHO has used the concept of disability-adjusted life year (DALY), a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death (WHO, 2008). DALYs are used quite extensively to evaluate public health priorities and to assess the disease burden associated with environmental exposures, particularly for microbial hazards. A key advantage of using the DALY is its aggregation of different impacts on the quality and quantity of life, and its focus on actual outcomes rather than potential risks; hence, it supports rational public health priority setting. DALYs can be used to define a tolerable burden of disease and the related reference level of risk. In the WHO Guidelines (e.g. WHO, 2011), the tolerable burden of disease is defined as an upper limit of 10^{-6} DALY per person per year. This upper-limit DALY is approximately equivalent to a 10^{-5} excess lifetime risk of cancer (i.e. 1 excess case of cancer per 100 000 people ingesting drinking-water at the water quality target daily over a 70-year period), which is the risk level used in the WHO Guidelines to determine guideline values for genotoxic carcinogens. Expressing health-based targets for chemical hazards in DALYs has the advantage of enabling comparisons with microbial risks. However, use of the DALY approach for chemicals has been limited in practice due to gaps in knowledge. For threshold chemicals, the health outcome target is based on no-observed-adverse-effect levels.

Hanninen et al. (2014) stress that it is important to prioritize environmental risk factors based on their health impact. Environmental burden of disease (EBD) measures can be used to express a diversity of health effects in one unit, such as disability-adjusted life years (DALYs). DALYs give an indication of the equivalent number of healthy life-years lost in a population due to premature mortality and morbidity. Hanninen et al. (2014) looked at nine risk factors – benzene, dioxins (including furans and dioxin-like polychlorinated biphenyls (PCBs)), sodium hydrosulphite (SHS), formaldehyde, lead, traffic noise (including road, rail, and air traffic noise), ozone, airborne particulate matter, and radon. Health end points were defined for each factor. The EBD was estimated using three methods, depending on the type of exposure-response function estimate available. Results are illustrated in Figure 2.1.

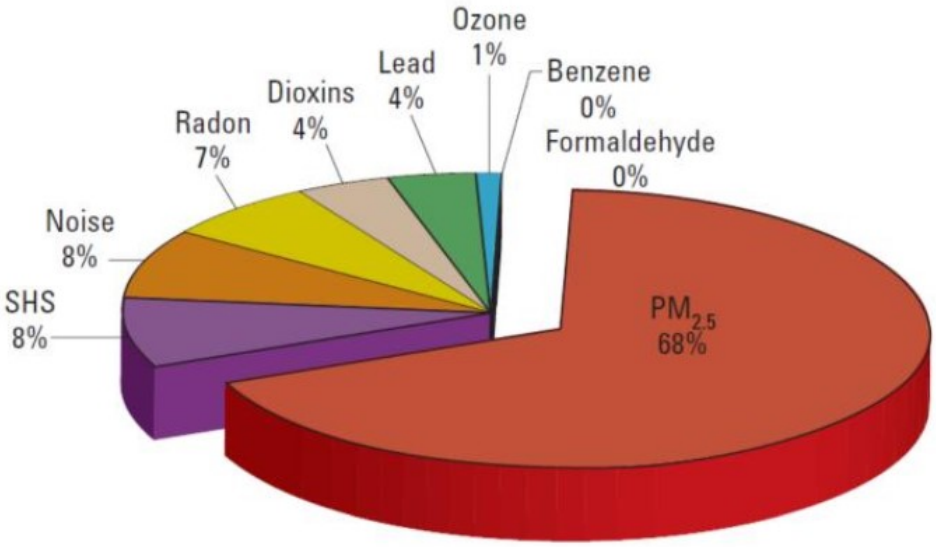

Figure 2-1. Relative Contributions of the Nine Targeted Risk Factors to the Estimated Burden of Disease attributed to these Risk Factors, averaged over the six participating countries. Adapted from Hänninen and Knol (2011).

2.3 Protection of the environment from chemotoxic substances and radionuclides in waste

In 1972, a United Nations conference on the human environment was held to address "the need for a common outlook and for common principles to inspire and guide the peoples of the world in the preservation and enhancement of the human environment" (UNEP, 1972). Several environmental protection principles were agreed as a result of the conference that have, in part, driven and supported the international development of environmental protection policies aimed at ensuring sustainable use of the environment and its resources, and to avoid irreversible impacts on non-human species and their habitats.

The objectives of protection are varied across different directives, policies and legislation, with some being very human-focussed (e.g. the protection of water from chemical pollution to maintain suitability and safety for drinking, fishing and bathing) and others being more targeted toward protection of non-human species (e.g. maintenance of the ecological quality of surface water bodies, achieving favourable conservation status of flora, fauna and habitats and maintenance of biodiversity). Protection objectives can also vary from country to country; indeed, the ICRP recognises that:

> *"no simple or single universal definition of environmental protection is applied internationally and that the concept of environmental protection differs from country to country and from one circumstance to another" (ICRP, 2008)*

Protection of the environment from ionising radiation was always a concern, as is clear from IAEA (1992) and the older references therein. The need to evaluate such protection explicitly within an international framework has been a more recent development, with specific protection objectives and assessment approaches being developed largely since the late 1990's and early 2000's. Prior to this, protection of the environment was considered by the ICRP to be implicit within the framework for the protection of people from radiation (ICRP, 1991), based on analysis of examples in IAEA (1992) and older references. Since then, a variety of more recent research and analyses has supported the development of assessment tools and criteria to allow explicit demonstration of protection of the environment from ionising radiation.

Similarities and differences in environmental protection objectives and criteria for ionising radiation and non-radioactive hazardous substances are discussed in the remainder of this section. Among other things, his draws on a previous BIOPROTA study (Smith et al., 2012) that included a review of environmental protection benchmarks for ionising radiation and their derivation.

Environmental protection from hazardous substances

As noted above, the targets for environmental protection policies are varied with some being driven by human use of the environment (e.g. maintaining water quality to support fisheries and safe bathing and drinking waters) and others being targeted toward the protection of ecosystems, communities and species and maintenance of biodiversity. For example, the European Water Framework Directive (WFD) (European Commission, 2000) calls for good ecological status to be achieved and maintained in surface water bodies and the Habitats Directive (EEC, 1992) aims to achieve favourable conservation status of important flora, fauna and habitats. More stringent water quality targets, including those for groundwater, may be applied under the auspices of the Water Framework Directive to ensure that protection targets arising from other legislation are met (WFD UK TAG, 2012). This would apply, for example, where groundwater affects surface waters or habitats, such as where groundwater feeds into a protected wetland habitat. The most stringent environmental protection requirement is applied across the different protection objectives with environmental standards being used to underpin those objectives and to guide decision making (WFD UK TAG, 2012).

Regarding waste disposal there have been a number of European Directives aiming to protect both people and the environment from associated adverse impacts. For example, the 2008 Waste Directive (European Commission, 2008a), which addresses management requirements for both conventional and hazardous waste, requires European Member States to "take the necessary measures to ensure that waste is disposed of without endangering human health and without harming the environment, and in particular:

- *without risk to water, air, soil, plants or animals;*
- *without causing a nuisance through noise or odours; and*
- *without adversely affecting the countryside or places of special interest".*

Wastes destined for landfill disposal are governed by the requirements of Directive 1999/31/EC on the landfill of waste (European Commission, 1999). The objective of the Landfill Directive is to prevent or reduce as far as possible negative effects on the environment and, particularly, on surface water, groundwater, soil and air[4]. The directive requires standard procedures to be implemented for the acceptance of waste at landfills and for limit values and other criteria to be set for waste acceptance. The directive is supported by the 2002 Council Decision establishing criteria and procedures for the acceptance of waste at landfills (European Commission, 2003a).

Predicted no effect concentrations (PNEC) and Environmental Quality Standards (EQS)[5] or threshold values (in the case of groundwater) for hazardous substances are an important means by which protection objectives for the environment can be achieved; if not exceeded, the standards are intended to ensure overall protection of the environment (European Commission, 2003a). Standards may be set nationally or internationally (e.g. through the European Environmental Quality Standards Directive for priority substances (European Commission, 2008b)) and be set in relation to environmental media (e.g. soil, sediment, air or water) or as concentration limits for biota such as fish or crustaceans. The standards may also be used as the basis for setting emission limit values for industry.

[4] http://ec.europa.eu/environment/waste/landfill_index.htm.

[5] A PNEC may be adopted as an EQS by regulators as the maximum permissible concentration of a hazardous substance in environmental media.

PNEC's are primarily derived from animal and/or plant toxicity data for individual substances through one of two approaches[6]:

- The safety factor (SF) approach; or
- The species sensitivity distribution (SSD) approach.

Which of the derivation methods is applied is largely governed by the amount and quality of toxicology data that is available for a given substance. Where data are limited, the SF approach is commonly applied whereas more extensive effects data can support the SSD approach. Both of the approaches, described further below, aim to derive an acceptable concentration for a hazardous substance that will ensure that protection objectives are met. Additional environmental factors determining toxicity, such as bioavailability and persistence can be taken into account in setting standards through the use of additional safety factors.

Safety Factor approach to deriving EQS

There is a general paucity of effects data for many chemicals, often with only short-term laboratory derived toxicity data being available. Where this is the case, an SF approach is commonly applied to derive a PNEC, which is defined as "*a concentration below which an unacceptable effect will most likely not occur*" (European Commission, 2003b). A standardised approach has been developed for application throughout European member states (European Commission, 2003b).

Effects data are often derived for a standard suite of test organisms such as fish, invertebrate and plant species representative of fresh or saline waters, or plants and soil organisms (e.g. earth-worms) for the terrestrial environment. Resultant effects data are commonly presented as either:

- Effects Concentration (EC_x) - the concentration of a substance causing a measured effect to x% (commonly 10%) of the test population; or,
- No Observable Effects Concentration (NOEC) - the highest test concentration at which no adverse effects are observable relative to controls.

Tests are commonly undertaken under controlled laboratory conditions with exposures being acute (up to 96 hours) in duration, although longer-term (chronic) effects data can be employed where available. For tests on soil organisms, it is recognised that the characteristics of the soil can vary considerably and affect the bioavailability of a substance (European Commission, 2003b). As such, it is recommended that tests of toxicity to soil organisms be conducted under conditions where the test substance is bioavailable.

The SF applied to the effects data for the most sensitive species reflects the degree of uncertainty associated with extrapolation of effects data from, for example, laboratory tests for a limited number of species to the 'real' environment and from acute to chronic exposure conditions. Guidance is provided in European Commission (2003b) as to the appropriate size of SF that should be applied based on the range of effects data available and the quality of those data. Examples are presented in Table 2-2 for freshwater/terrestrial soils and in Table 2-3 for marine water, respectively. Due to a greater species diversity in the marine environment, a greater SF may be recommended than for freshwater, to take account of the potentially increased uncertainty around the test species being representative of those that may be exposed in the environment. The SF decreases as confidence in the available data increases such that lower SF's are applied to larger and more relevant data sets, as illustrated in Tables 2-2 and 2-3.

[6] An equilibrium partitioning method is also available for deriving soil or sediment PNEC's that rely on water PNECs and soil-water or sediment-water partition coefficients. This approach, requiring PNECs as an input, is not addressed further herein. Additional information on the approach is available from European Commission (2003b).

Table 2-2. Safety factors for the derivation of a PNEC for freshwater and terrestrial soils.

Available toxicity data	Safety Factor
At least one short-term EC_{50}	1000
One long-term NOEC	100
Two long-term NOECs from species representing two trophic levels	50
Long-term NOECs from at least three species representing three trophic levels	10
Species sensitivity distribution (SSD) method	1-5

Source: European Commission (2003b)

Table 2-3. Safety Factors proposed for deriving a PNEC for saltwater.

Available toxicity data	Safety Factor
Lowest short-term LC_{50} from freshwater or saltwater representatives of three taxonomic groups (e.g. algae, crustaceans and fish) of three trophic levels	10,000
Lowest short-term LC_{50} from freshwater or saltwater representatives of three taxonomic groups (e.g. algae, crustaceans and fish) of three trophic levels plus two additional marine taxonomic groups (e.g. echinoderms, molluscs)	1000
One long-term NOEC (from freshwater or saltwater crustacean reproduction or fish growth studies)	1000
Two long-term NOECs from freshwater or saltwater species representing two trophic levels (algae and/or crustaceans and/or fish)	500
Lowest long-term NOECs from three freshwater or saltwater species (normally algae and/or crustaceans and/or fish) representing three trophic levels	100
Two long-term NOECs from freshwater or saltwater species representing two trophic levels (algae and/or crustaceans and/or fish) plus one long-term NOEC from an additional marine taxonomic group (e.g. echinoderms, molluscs)	50
Lowest long-term NOECs from three freshwater or saltwater species (normally algae and/or crustaceans and/or fish) representing three trophic levels plus two long-term NOECs from additional marine taxonomic groups (e.g. echinoderms, molluscs)	10

Source: European Commission (2003b)

SSD approach to deriving PNEC

The SSD approach can be used to derive a PNEC when a large data set is available of chronic NOEC's for a range of species representative of different taxonomic groups. It is recommended that SSD, a statistical approach to deriving a PNEC, is only applied where at least 10 NOEC's for different species covering at least 8 taxonomic groups are available (European Commission, 20003b).

The SSD approach is based around an assumption that adequate protection of an ecosystem is commensurate with protection of the majority of species and that the distribution of species sensitivities to a substance follows a theoretical distribution function (European Commission, 2003b). It further assumes that species for which data have been obtained are a random sample of all the species in the ecosystem of interest. The approach involves log-transforming effects data and fitting according to a distribution function with a percentile of that distribution, normally the 5th percentile, then being used as a protection criterion (PNEC). An SF is again applied to the PNEC to derive the protection criteria. The SF for SSD analysis ranges from 5 to 1, with the value being selected following an evaluation of the uncertainties associated with the derivation of the 5th percentile (European Commission, 2003b).

Example of the use of the application of the SSD approach as applied to mixtures of radionuclides and chemicals are provided in Garnier-Laplace et al. (2009) and Beaumelle et al. (2016), and the approach is presented and discussed in the context of releases from waste repositories in BIOPROTA (2016) and further in BIOPROTA (2017), where it was noted that that there are

limitations around the use of SSDs, with lack of species for which toxicity data are available being a primary contributor to the overall limitations.

Application of PNEC's in the demonstration of environmental protection

To demonstrate protection of the environment from hazardous substances, PNEC's (particularly when adopted as EQS's) are applied as limits against which environmental concentrations, measured or predicted, are compared. Proportions of those limits may also be used within a tiered assessment framework. For example, under the Environmental Permitting (England and Wales) Regulations 2010[7], tiered assessments must be undertaken in support of permit applications for the discharge of hazardous substances to surface waters. The Environment Agency for England and Wales and the Department for Environment, Food and Rural Affairs (Defra) have published guidance on undertaking tiered assessments (Environment Agency & Defra, 2016). The approach can be summarised as follows:

- Tier 1 – compare the concentration of a substance in the discharge effluent (measured or predicted) against the relevant EQS. If it is below 10% of the EQS, the discharge is not considered to pose a risk to the environment.
- Tier 2 – for assessments at tier 1 above 10% of the EQS, evaluate the concentration of the substance in the receiving environment, taking account of initial dilution. Where the result is less than 4% of the EQS, no further tests are required.
- Tier 3 – for assessments at tier 2 above 4% of the EQS, evaluate the predicted environmental concentration (PEC) by combining the background concentration of the substance with the process contribution. If the difference between the background concentration and the PEC is more than 10% of the EQS then modelling of the PEC will be required (tier 4) with model output being directly compared against the EQS.

If, following detailed modelling of the discharge in the receiving environment, the EQS is projected to be exceeded, it is unlikely that authorisation to discharge would be granted. The use of such a tiered assessment approach may be appropriate for discharge permit authorisations for landfill leachate collected and discharged to surface waters.

For groundwaters that may have a negative impact on surface waters or habitats, threshold values are applied. These are consistent with the PNEC approach, but are used as trigger values rather than limits. The threshold values are intended to be applied in identifying risks and to target further investigation (WFD UK TAG, 2012). The threshold values are derived from surface water standards with a dilution factor applied (WFD UK TAG, 2012). Alternatively, surface water standards may be applied to evaluate impacts of groundwater through monitoring upstream and downstream of a point source input of groundwater to a surface water body.

Environmental protection from ionising radiation

The environmental protection framework for ionising radiation is relatively new, as compared with hazardous substance environmental protection, having largely evolved since the early 2000's. This is largely due to a comprehensive protection framework being in place for people that was historically considered to provide an appropriate level of protection such that the "environmental controls needed to protect the general public would ensure that other species are not put at risk" (ICRP, 1991). Whilst this view has been maintained, the ICRP nonetheless began developing a framework for environmental protection from ionising radiation. In part, this arose from an acceptance of the difficulties associated with demonstrating that the environment is protected in situations where humans are not present, but also developments in environmental protection criteria arising from international agreements and regulations that specifically require that

[7] The Environmental Permitting (England and Wales) Regulations 2010, No. 675. http://www.legislation.gov.uk/uksi/2010/675/pdfs/uksi_20100675_en.pdf.

environmental protection is demonstrated. The resultant framework (ICRP, 2008) was developed to be consistent with that applied in the protection of people.

The objectives set by the ICRP for the protection of the environment from ionising radiation are to (ICRP, 2007):

> *"safeguard the environment by preventing or reducing the frequency of deleterious radiation effects to a level where they would have a negligible impact on the maintenance of biological diversity, the conservation of species, or the health and status of natural habitats, communities, and ecosystems"*

The focus is therefore very much more strongly on the environment itself as compared with that for hazardous substances, largely due to a framework for protection of people from ionising radiation already being in place with that for the environment being a subsequent development.

The stated objectives make clear that the focus of protection is not on individuals (with perhaps the exception of endangered species), but rather on populations or other higher organisational levels (e.g. communities, ecosystems). Natural resources such as water, soil and air are, unlike the system for protection from chemicals, not specifically included as protection targets; these being implicit in the framework for protection of people and in ensuring that environmental protection objectives are met.

Currently, there are no internationally agreed criteria for demonstrating protection of the environment from radiation, although several values (or sets of values) have been proposed by international organisations and research programmes, as illustrated in Table 2-4. National criteria have also been derived (see Appendix A of Smith et al. (2012) for further discussion).

Table 2-4. Environmental protection benchmarks and screening values and their derivation.

Source	Value (µGy/h)		Derivation	Comment
IAEA (1992)	40	Terrestrial animals	Expert judgement	Chronic exposures below which observable changes to populations unlikely
	400	Terrestrial plants & aquatic organisms		
UNSCEAR[8] (1996; 2011)	100	Terrestrial organisms	Expert judgement	Chronic exposure of most highly exposed individuals unlikely to lead to significant effects on most terrestrial communities
	400	Aquatic organisms		Chronic exposure unlikely to induce significant effects on populations
ERICA (Garnier-Laplace et al., 1996)	10		SSD*	Generic screening value across all species and ecosystems
PROTECT (Andersson et al, 2009)	10		SSD*	Generic screening value across all species and ecosystems, intended to identify situations that are below regulatory concern with a high degree of confidence
	2	Vertebrates	SSD*	Indicative, order of magnitude screening values
	70	Plants	SF*	
	200	Invertebrates	SSD*	

[8] United Nations Scientific Committee on the Effects of Atomic Radiation

ICRP Derived Consideration Reference Levels (DCRLs) for Reference Animals and Plants (ICRP, 2008)	4 – 40	Pine tree Deer Duck Rat	Expert judgement	Point of reference dose rate band within which some deleterious effects on individuals of that type of organism may occur
	40 – 400	Frog Trout Flatfish Grass		
	400 - 4000	Bee Crab Worm Seaweed		

** derived following guidance in European Commission (2003b).*

Unlike the system for environmental protection from chemicals, radiological protection of the environment does not employ limit values; rather, the values that have been derived are intended as benchmarks or screening values. Exposures above benchmark values do not imply that impacts will occur; rather, exceedance of a screening value is intended to trigger further, more detailed assessment (Smith et al, 2012). For example, the ICRP Derived Consideration Reference Levels (DCRLs) are defined as *'a band of dose rate within which there is likely to be some chance of deleterious effects of ionising radiation occurring to individuals of that type of reference animal or plant (derived from a knowledge of defined expected biological effects for that type of organism) that, when considered together with other relevant information, can be used as a point of reference to optimise the level of effort expended on environmental protection, dependent upon the overall management objectives and the relevant exposure situation'* (ICRP, 2008). Whilst limit values are not employed, the derivation of benchmarks has, in some instances, as illustrated in Table 2-4, followed the chemical hazards PNEC approach, particularly the statistical SSD approach. The use of expert judgement following review of radiation effects data or comparison of dose rate calculations against exposure to natural background have also been employed (see discussion in Smith et al, (2010)). It should be noted, however, that both the SSD and SF derivation approaches are associated with a degree of expert judgement, both in the selection of effects data upon which criteria are derived, and in the selection of appropriate safety factors. Whilst a variety of methods have been applied to derive protection criteria by several international groups and organisations, broad similarities in the derived criteria are evident.

The assessment criteria, irrespective of their derivation, are applied across all radionuclides, with differences in the biological effectiveness of different radiations being taken into account in assessments through the use of weighting factors for alpha, beta and gamma radiations.

Similarities and differences in environmental protection objectives and criteria for hazardous substances and ionising radiation

Environmental protection objectives for ionising radiation appear more focussed than those for hazardous substances. This largely results from the fact that a separate framework existed for the protection of people from ionising radiation prior to the development of the framework for environmental protection. For hazardous substances, both human protection and environmental protection objectives have largely been developed in parallel, resulting in less distinction between the protection objectives.

In terms of protection criteria, there are several differences observed, both in relation to methods of derivation and application. For example, a greater range of derivation methods have been applied for ionising radiation, with a greater emphasis on the use of expert judgement in reviewing effects data and making judgement on an appropriate level at which criteria should be set. The use of expert judgement has also allowed consideration to be given to the different radio-sensitivities

of different types of plant and animal, as evident in the ICRP DCRLs (ICRP, 2008) where different values are set for the different Reference Animals and Plants (RAPs). For chemicals, the different sensitivities of organisms are taken into account in the selection of effects data used in deriving exposure standards, but different values are not derived for different types of plant/animal.

The SF approach to deriving chemical PNEC's has also been applied to radiation, although there has been a greater focus on the use of SSD analysis over the SF approach. Throughout chemicals assessments, it is acknowledged there is a general paucity of data, yet the SF approach is routinely applied. In the field of radioecology, there has been a reluctance to apply such an approach to derive assessment criteria to evaluate and constrain the risk of impacts from ionising radiation in the environment. Indeed, where the SF approach has been used to derive criteria (i.e. the PROTECT taxa-specific criteria for plants), the output has not been recommended for use, but rather its application is cautioned as *'indicative order of magnitude values only'* (Garnier-Laplace et al, 2010). This appears inconsistent with the approach taken for chemicals and may therefore merit further consideration whilst acknowledging that the SSD approach would provide a more robust outcome should adequate data become available.

A further discrepancy is the use of criteria derived for ionising radiation using the SSD approach as screening values whereas for non-radioactive hazardous substances, criteria derived using the SF or SSD methods are applied as limits. Furthermore, protection criteria for ionising radiation tend to be more generic in their application than those for hazardous substances. For example, the ICRP DCRL's and ERICA/PROTECT screening values apply across all ecosystems and environmental media, whereas protection criteria for hazardous substances tend to be more focussed on types of environmental media such as freshwater or groundwater, soils or sediments. The different focus for hazardous substances reflects, in part, the recognition that substances may display different behaviours in different media, but primarily results from the varied legislative drivers leading to the need for the criteria to be established (e.g. legislation requiring the protection of groundwater or river basin districts). The behaviour of radionuclides in different environmental media is largely considered separately, being addressed during the assessment of environmental concentrations as opposed to being considered through the setting of different criteria for different environmental media.

In applying protection criteria, the most stringent protection standard takes precedent where multiple standards are available. For example, where a standard for drinking water quality is more protective than one for the protection of freshwater life, the drinking water standard would be applied to ensure overall protection is achieved. With generic criteria being applied in the framework for environmental protection from radiation, this is not a factor for consideration. However, the environmental protection frameworks are applied in isolation and, hence, chemical toxicity considerations associated with radioactive discharges (e.g. chemical and radiological toxicity associated with uranium) are largely overlooked. Furthermore, the use of generic screening values for radiation has been acknowledged to be potentially problematic (Copplestone et al, 2010; Howard et al, 2010; Beresford et al, 2010) since the rate-limiting organism in assessments is seldom the most radiosensitive (for example, criteria are largely governed by effects data for vertebrates, yet organisms such as phytoplankton may be the most exposed in assessments. The same is also true for chemicals, with EQS values being set on limited ecotoxicological data in many instances. However, the application of protection criteria for chemicals is different in that concentrations in environmental media are compared against the criteria, rather than concentrations in the different plants and animals being evaluated; for radionuclides, dose rates are calculated for different plants and animals and compared against the environmental benchmarks. The selection of appropriate SF's is intended to negate the risks of effects being observed in non-test species and toxicity data are generally derived for a minimum of three different taxa. A number of risk assessment approaches are outlined in Section 3, which demonstrate how toxicological criteria are used with exposure assumptions/models to either characterise risk for specific cases, or to set environmental guidelines or standards.

3 Review of assessment methods and data requirements for non-radiological assessments of waste disposal

This section provides a review of the methods used to assess whether protection objectives are met or how they would be met in the case of proposals for future disposals. Quantitative human health risk assessment methods are described in Section 3.1, and assessment methods used for non-human biota are discussed in Section 3.2.

The review of the assessment of human-health effects (Section 3.1) includes a description of source-pathway-receptor methodology, and outlines how this is applied for the derivation of both generic assessment criteria (e.g. environment guidelines for contaminants in soil, water, air) and site-specific assessment criteria.

Consideration is also given to data requirements to support the assessments and how those data can be supplied, with relevant examples. This is compared with the approaches taken for substances of radiological concern and associated data requirements.

3.1 Quantitative human health risk assessment methods

3.1.1 Generic Assessment Criteria vs. Site Specific Risk Assessment

In general, the quantitative risk assessment of chemicals is undertaken to: (1) derive public/occupational standards/guidelines; and (2) to produce site-specific, or system-specific risk assessments. However, both approaches use similar concepts, use similar toxicological data, and, therefore, have similar data requirements. 'Standards' are set to ensure compliance with a specific piece of legislation (such as drinking water standards for the public water supplies, or occupational exposure limits), whereas 'guidelines' typically characterise what is achievable by current good practice or indicate situations that would be of limited regulatory concern. Thus, quantitative guidelines are often smaller than corresponding standards, but there is not the same emphasis on a need to achieve compliance.

3.1.2 Source-Pathway-Receptor Approach

Risk assessments, either implicitly or explicitly, need to consider: sources of contaminants (their identity and properties, potential hazards they pose); pathways by which exposure can occur (e.g. ingestion, inhalation, dermal); and the identity, characteristics and behaviour of those that may be exposed, i.e. the receptor(s). For the derivation of environmental standards/guidelines (particularly for water and air) a source term must be present, along with environmental media to which humans may be exposed (such as water, soil, air and food). The key concept is that, for there to be a risk to health, there needs to be a contaminant source, exposure pathway(s) and receptor(s) that can be exposed. The lack of relevant exposure pathways and/or a receptor means that a hazard (the source) may exist, but potential risks to human health do not. When analysing situations and ensuring that all relevant pathways of exposure are considered, it is often helpful to examine the situation from source through to receptor and also from receptor to source. The latter focuses on habits and behaviour that may result in exposure to one or more of the sources present in the local environment.

3.1.3 Sources of Contaminants and Typical Substances of Interest

To assess the risk posed by a potentially contaminated site, or a radioactive waste repository, the identity, properties and forms of contaminants need to be ascertained, at least to some degree. There are many contaminants that can be identified as likely being of relevance to either sites where

there may be historical contamination and for either current waste disposal systems, or waste disposal systems that have only been developed at the conceptual level. The substances of interest will depend on the type of site or system being considered, e.g. historic surface or near-surface contamination, shallow or near-surface disposals, deep geological disposals. For example, asbestos is only likely to be a concern at shallow depths or at the surface, where potential receptors could be exposed to fibres that become entrained in the air which they breathe. In contrast, asbestos would be of little significance in deep geological disposal concepts, where (excluding the potential for human intrusion) there would be no exposure pathway. Other potential contaminants that are less likely to be of relevance for deep disposal systems (but are often found on former sites associated with some industries) include relatively insoluble organic compounds such as polycyclic aromatic hydrocarbons (PAH) or dioxins/furans. In general, organic compounds in themselves are of limited significance to the safety of geological repositories for radioactive wastes, because a large proportion of these compounds are degraded by microbial processes that are projected to occur either in the engineered facility or in the surrounding geosphere. Nevertheless, the effect that organic materials, or their degradation products, may have on the mobilisation of specific radionuclides and toxic metals may be of concern due to their contribution to the transport of pollutants out of the repository system. This, in the radioactive waste field, is addressed by deriving sorption reduction factors (SRFs) (e.g. Ochs et al., 2014), which quantify the level of reduction in the sorption of a given contaminant due to its complexation with organic materials in the repository. Given the high inventory of organics in some LLW stabilised in cement, most efforts in this direction are towards the estimation of SRF in cementitious environments, although organic materials may reduce sorption/retention of radionuclides under a wide range of environmental conditions.

At a recent SKB Workshop in Stockholm (Thorne and Kautsky, 2016) several organisations identified key substances as priorities for consideration for a number of different waste streams. For the Swedish SFR facility intermediate depth disposal facility for low and intermediate level waste (L/ILW), SKB noted that it will contain limited amounts of lead (Pb), asbestos and epoxy resins. However, of more interest is intermediate level waste (ILW) to be disposed to the proposed SFL facility. For this facility, Cd, Be, Pb, Cr and Hg were identified as key substances, with hazardous organic substances being only present in limited amounts. In addition, about 15 tonnes of U is provisionally to be disposed in the SFL. In France, Andra has identified the following thirteen substances as those that should be prioritised for study: Pb, B, Ni, Cr, As, Sb, Se, Cd, Hg, Be, cyanide, U, and asbestos. In the future, PAHs are likely to be added to this list. In the UK, several rounds of screening assessment and modelling studies have been undertaken. These have focused on Be, Cd, Cr, Pb and U as the key substances of concern (Wilson et al., 2011). Further consideration has been given to identification of relevant substances in RWM (2016), see page 125 *et seq*.

For the proposed HLW disposal at Yucca Mountain, the key elements were molybdenum Mo, Ni and vanadium V, arising from corrosion of the packages in which the wastes has been proposed to be emplaced (US NRC, 2016). Overall, these studies suggest that organic chemicals in various waste types are of less significance than inorganic substances (e.g. metals, metalloids) in terms of their inherent toxicological properties and can largely be addressed by limiting their disposal and by considering their degradation after disposal.

NWMO's basis for identifying potential substances of interest and the Canadian regulatory background for that approach are described in Medri (2015). NWMO has assessed the chemical hazard of a Canadian used fuel repository with copper containers, because the repository design includes significant amounts of material that can also be chemically hazardous, e.g., Cu and U. Gobien et al (2015) describe the safety criteria, screening methodology and assessment models as well as the results obtained for the two case studies based on disposal in crystalline rock and sedimentary rock. The models and scenarios were the same as those used for radiological assessment. Interim acceptance criteria for hazardous substances were based on Canadian guideline values for concentrations in environmental media relevant to human health and environmental protection. The criteria are based on federal and provincial guideline concentrations for surface water, groundwater, soil, and sediment, and in particular on Canadian Council of the Environment information. In cases

where federal guidelines do not currently exist, Ontario Ministry of the Environment guidelines and Oregon Department of Environmental Quality9 data have been adopted. Depending on the actual repository site location, the applicable provincial guidelines would be used. Hg, Pb and Cd are among the more significant substances figuring in the results, albeit at levels which are within the acceptable bounds of risk given the conservative nature of the calculation and scenarios. The results are further supported by defining and examining complementary indicators of safety on very long time frames. Natural processes carry small amounts of naturally occurring chemical elements from within the geosphere to the surface. Reference values for natural chemical element transport fluxes to the biosphere can be obtained using the elemental composition of granitic Canadian Shield crystalline rocks and Michigan Basin Sedimentary formations and the erosion rate of the formation over long time periods. The results indicate that even under the conservative assumption of the All Containers Fail Scenario, the element fluxes to the biosphere are generally much smaller than the corresponding erosion fluxes. Cu, Cr, Ni, Mn and Pb were among the more relevant elements identified in the post-closure safety assessment of L/ILW in a deep geological repository, albeit at very low levels of impact (Quintessa.et al., 2011).

In Norway, regulation of radioactive substances was placed under the Pollution Control Act in 2011, under which radioactive waste is controlled holistically, according to radioactive waste regulations, as well as the regulations concerning non-radioactive waste. Waste is regulated according to all its properties. Waste which is classified as both hazardous waste and radioactive waste, may be managed by enterprises with only a license for hazardous waste if it only contains limited amounts of radioactive waste. Even though the two waste categories are regulated by three authorities, the Norwegian Environment Agency (NEA), the Ministry of Climate and Environment and the NRPA, they are regulated under the single Pollution Control Act. This facilitates dialogue between competent authorities, makes it easier to share best practice and information of common interest and the most important makes it easier to harmonize justifiable waste management (Bratteteig, 2017). The tiered classification approach, including how it applies to NORM waste, is described by Popic in Sneve and Strand (2016). The NEA regulatory perspective, including the wider range of regulatory issues that apply to management of radioactive waste, are described in BIOPROTA (2015).

It is possible to identify several criteria by which a list of substances that may be prioritised for initial consideration can be developed. An initial attempt is as follows:

- They should be present in significant quantities in, at least some, types of solid radioactive wastes, or in encapsulation and packaging materials associated with those wastes.
- There should be significant potential for release from the wastes, grouting or packaging into the near field and for transport out of the near field into the geosphere.
- They should have the potential for relatively rapid transport through the geosphere and should not be degraded to low toxicity forms during their transport.
- They should be transported in the biosphere by a variety of pathways and should exhibit bioaccumulation (or at least not strong bioexclusion).
- There should be a reasonable degree of understanding of the mechanisms by which they induce toxic effects in humans and other biota, particularly at relatively low concentrations.

Based on the above criteria and experience in regulation and inventory, in the first instance, the following substances could be considered as being of special interest in radioactive waste from a non-radiological impact perspective: As, Be, Cd, Cr, Hg, Pb, U and asbestos. An overview of the properties of these substances is provided in Table 3-1. It is emphasised that there are extensive data on the toxicity of all these substances in humans from a variety of occupational and environmental exposure situations.

Table 3-1. Shortlist of Priority Substances.

Substance	Key Toxicological Properties (Chronic Exposures) (ref)	Notes
Arsenic (As)	Exposure may result in number different end-points, depending on form, exposure route and duration. Dermal effects, vascular effects ('Blackfoot disease) and carcinogenic properties are generally of concern for environmental exposures (1).	Common soil contaminant, especially in industrialised areas, potentially of less relevance to radioactive waste disposal compared with other inorganic substances (Pb for example).
Beryllium (Be)	Inhalation associated with chronic beryllium disease, (2, 3), lung cancer.	Significant component in some types of radioactive waste. It is difficult to argue for solubility limitation in the near field, or for substantial retardation of transport in either the near field or the far field, though slow dissolution of metal components may limit its rate of release. It exhibits multiple pathways in the biosphere and is not strongly bioexcluded, having some chemical similarities to the essential element Ca.
Cadmium (Cd)	Nephrotoxin, may cause bone disease (3).	Present in various nuclear components, as it is used as a neutron moderator. Cd is highly toxic, not strongly retarded during transport, and can exhibit a variety of chemical forms in the biosphere. It can be bioaccumulated and also converted to organic forms.
Chromium (Cr)	Hexavalent chromium (Cr{VI}) is of greater concern than trivalent Cr(III); main route of concern is inhalation exposure in relation to the element's carcinogenic properties (3).	Present in both wastes and waste packages, typically as a component of steels (as Cr(III)). Of particular interest as Cr(III) and Cr(VI) have different transport and toxicological characteristics, and there is the need to consider the potential for inter-conversion between these two forms during transport.
Mercury (Hg)	Neurotoxin, nephrotoxin, developmental effects (4).	Not always of significance in radioactive wastes, but of great significance in conventional wastes and of interest because of the existence of both inorganic and organic forms, some of which are volatile. Extensive toxicological information is available. Methyl-mercury accumulates at higher trophic levels.
Lead (Pb)	Neurotoxin (also "probably carcinogenic") (3).	Much work has been undertaken looking at blood lead levels in children and potential neurological effects.
Uranium (U)	Nephrotoxin and radioactive (5).	Of interest because of both its chemical and radiological properties. Their relative importance depends on the degree of enrichment of the uranium, its chemical form, the route of exposure, and the degree to which radioactive progeny of the element are present.
Polycyclic Aromatic Hydrocarbons (PAH)	Group of carcinogenic compounds, Benzo(a)pyrene (BaP) has been studied extensively. Carcinogen, mutagen and reproductive toxin (6, 7).	Commonly associated with industrialised areas where there has been coal burning/town gas production. Possibly of less relevance than other substances, but commonly associated with industrial sites. Could be used as an example of a non-threshold substance (risk assessments tend to focus on BaP).
Asbestos	Carcinogenic, inhalation exposure linked to increased lung cancer risk and risk of mesothelioma, as well as to the induction of fibrosis in respiratory tissues (8).	Associated with industrial sites, little authoritative guidance on environmental (public) risk assessment, reflecting difficulties associated with predicting releases from soil and exposure in ambient air outside of buildings. Workplace exposures are managed through occupational hygiene measures. Different types of asbestos vary greatly in toxicity due to physico-chemical distinctions in fibre characteristics.

Refs: (1) ATSDR (2007); (2) ATSDR (2015); (3) Wilson et al. (2009) and references therein; (4) ATSDR (1999); (5) Thorne and Wilson (2015) and references therein; (6) ATSDR (1995); (7) PHE (2015); (8) ATSDR (2001).

3.1.4 Contaminant Transport in the Environment

Contaminant transport will depend on the environment within which a contaminant is present and the form that it takes (aqueous speciation). In the context of contaminated soil, substances present (at least for any extended period) are sparingly soluble and/or have a high capacity to sorb to soil minerals, otherwise they would have largely been leached out by rainfall or the flow of water through the soil profile.

For radioactive waste disposal systems, risk assessments generally consider the potential for substances to leach from wastes due to infiltrating water or circulating or stagnant groundwater (unless the system is essentially dry, as one may expect in salt deposits for example). Transport may be primarily by advection, e.g. in fractured hard rocks, or by diffusion, e.g. in homogeneous clays and mudstones. For substances that have a very low solubility (Pb for example), one approach is to simply apply a solubility limitation without a constraint on release rate. For substances where there is a lack of solubility-limiting solid phases, or when a more realistic (possibly less conservative) release model is required, a rate can be specified. Release rates can be specified in several ways, for example the corrosion rates of metals (e.g. Kelly and Berry, 2011) and fractional release rates from waste forms such as vitrified wastes or spent nuclear fuels where the fuel pellets of uranium dioxide (UO2) are ceramic in nature. Rate laws of greater complexity that consider effects of catalysing species (e.g. H+) on rates could also be applied if considered necessary, and if data are available or can be readily acquired.

Transport parameters of contaminants are used in combination with hydrodynamics of the media to calculate contaminant transport. There are plenty of examples of conceptual models and calculation tools for this purpose. The last decades are characterised by the effort in coupling geochemistry and hydrogeology, so that the models improve their predictive potential.

Water quality preservation is of great concern, particularly in arid areas, and regulations for water protection apply to management and disposal of different type of wastes arising from different activities. For example, the Directive 2006/21/EC (European Commission, 2006b), on management of waste from extractive industry, specifically indicates that the competent authority shall satisfy itself that the operator has taken the necessary measures to meet Community environmental standards, in particular to prevent, in accordance with Directive 2000/60/EC (European Commission, 2000), the deterioration of current water status.

Section 2 (approach for metals) in Annex 7 of the Commission staff working document - Impact assessment - Proposal for a Directive of the European Parliament and of the Council on environmental quality standards in the field of water policy and amending Directive 2000/60/EC (European Commission, 2006c) states that for metals: …"dissolved concentrations (not total) are monitored which is a pragmatic approach to take account of the fact that only part of the total metal concentrations are "bioavailable". This highlights the relevance of chemical knowledge of the behaviour of contaminants, so that the correct aqueous species, presenting different transport and toxicological properties, are considered. It is recognised that such an approach may over- or underestimate the actual bioavailability. Bioavailability changes with environmental conditions, and these may vary considerably over short and long periods of time, and over various spatial scales. Overall, the use of dissolved concentrations for metals is considered as the best available proxy indicator. In this respect, the conditions that cause metals and contaminants in general to precipitate/sorb/coprecipitate and re-dissolve to the aquatic environment should be assessed, so that understanding solubility in relation to "concentration limits" is very important.

Solubility limitation is often applied in risk assessments of metals/metalloids, based on the solubility of primary, or more commonly, secondary solids that contain the contaminant of interest. The identity of solubility limiting solid phases may be ascertained through one or more of thermodynamic modelling, experimental observation and natural/industrial analogue data (e.g. Bruno et al., 2002; Duro et al., 2006; Grivé et al., 2010; Wilson et al., 2009, 2012; Wersin et al., 2014). In general, the values that are used in performance assessment models to support

environmental safety cases, are those calculated using aqueous speciation modelling tools such as PHREEQC. For the selection of "concentration limits" in performance assessment, levels measured in groundwaters of natural analogue sites and concentrations measured in laboratory experiments are used to justify the choice of solubility-limiting solid phase in calculated concentrations or provide reassurance that the values to be used in risk assessment calculations are not underestimated. Calculated and measured solubility limits can also inform the selection of values used in probabilistic risk assessment models where probability distribution functions are produced using an 'expert elicitation' approach (e.g. Garner and Jackson, 2009).

Contaminant transport through the unsaturated and saturated zones can be via diffusion and advection (depending on the environment), with retardation potentially occurring via solubility-limitation, co-precipitation reactions and ion-exchange/sorption processes. Several different models with varying levels of complexity can be used for contamination migration with compartment models often using a simple sorption coefficient ('Kd') approach (e.g. Wilson et al., 2009; Kelly and Berry, 2011) or mechanistic approaches that have a greater complexity (e.g. Savage et al., 2010; Domènech et al., 2015). In a similar way to the selection of solubility or concentration limits, performance assessment calculations require careful selection of Kd values in different media of interest (some examples are those in Bradbury and Baeyens, 2003a, 2003b; Bradbury et al., 2010; Linklater et al., 2003; Crawford, 2010; Hakanen et al., 2014, inter alia).

The pH, redox potential (Eh or pe) and concentrations of the major ions in groundwater, such as carbonates, sulphates, chlorides, calcium, etc., will affect the solubility and thus the mobility of contaminants. It is also clear that many of the "contaminant" elements may be present in rocks and soils and so background concentrations may need to be taken into account before judging groundwater quality and, as we will see This is the approach used by different countries when transposing the EC Groundwater Directive, discussed further in in section 4.

Consideration should also be taken of the site where the waste storage will be located. If the waste of interest contains elements which are redox sensitive and more soluble under oxidising than under reducing conditions, e.g. U, the site selected should ideally present reducing conditions. If carbonate affects the solubility of most of the elements of interest, the site should contain controlled concentrations of carbonate, to avoid solubilisation of the wastes with the subsequent increase in the concentrations of contaminants in groundwater.

Toxic elements of interest vary from case to case, depending on the inventory of the waste, and the conditions of the facility site, as also the background environmental levels vary from site to site. It is interesting to note that most of the toxic materials of interest are metals and that two of them (Hg and Cd) are subject to specific regulatory procedures in the European legislation ((i) The Mercury Discharges Directive (82/176/EEC) (EEC, 1982); (ii) The Cadmium Discharges Directive (83/513/EEC) (EEC, 1983) and (iii) The Mercury Directive (84/156/EEC) (EEC, 1984). It is notable that many of the elements identified as of relevance because of their chemical toxicity are not included in the safety assessment exercises on radioactive waste repositories. The different levels of complexity and comprehensiveness of radioactive and non-radioactive environmental impact assessments is translated into a general lack of structured databases for retention parameters of these compounds, in opposition to the sorption, diffusivity or solubility compilations for elements included in radioactive safety/performance assessments.

For site-specific assessments of radioactive waste disposal facilities, an initial screening approach may involve comparing calculated concentrations of contaminants in groundwater with drinking water standards/guidelines (e.g. Hunter et al., 2006; Davis et al., 2007; LLWR, 2011). A compilation of some transport-relevant characteristics of hazardous components is shown in Table 3-2. In the same table, background levels found in natural groundwaters, non-affected drinking waters and the WHO (2011) drinking limits are provided for the sake of comparison.

If more detailed biosphere models that include several additional exposure pathways are used, concentrations of contaminants in soil, irrigation water and foodstuffs (representative crops and

livestock) may also need to be calculated. In this case, a typical approach is to use compartment modelling tools (such as GoldSim[9], Ecolego[10] or AMBER[11]) to calculate transfers between different environmental media to which receptors may be exposed using transfer rates or partitioning coefficients. Such an approach has been used for calculating radiological doses to receptors (e.g. Thorne, 2007a, 2007b, 2007c) and less commonly, for considering uptakes of non-radiological contaminants via different environmental exposure pathways (e.g. Wilson et al., 2009, 2011). As in the case of mobility in the geosphere, databases of sorption coefficients in soils for contaminants have also been compiled, as well as transfer coefficients from soil to plants (Tröjbom et al, 2013; Sheppard et al., 2011).

Just as in assessments for radioactive waste disposal, tools used for calculating generic assessment criteria (such as SGVs) and site-specific assessment criteria also include the transfers of contaminants between different environmental media to which receptors may be exposed. An example of this is the approach used for the CLEA (Contaminated Land Exposure Assessment) model, that was originally developed in the UK for generating SGVs and to enable the development of site-specific assessment criteria (SSAC) (Defra/Environmental Agency, 2002a-c; Environment Agency, 2009a, 2009b). This model includes transfer of contaminants between different environmental media to which receptors may be exposed and therefore requires conceptual and numerical models along with input data for such transfers. Other models that have been developed in other countries also include re-distribution of contaminants between different media to which receptors may be exposed (e.g. Brand et al., 2007).

[9] http://www.goldsim.com/,

[10] http://ecolego.facilia.se/ecolego/show/HomePage,

[11] http://www.quintessa.org/software/AMBER/

Table 3-2. Transport-relevant characteristics of hazardous components, concentration levels in groundwater (GW) and drinking waters and drinking limits recommended by WHO (2011). BHC: Below Health Concern; HB: Health Based. References (R) are provided as footnotes.

Element	Redox states	main species in GW (pH 6 to 9)	Kd in transport (m^3/kg)	Main retention processes	Main affecting parameters	Selected concentration limits in SA µg/L	Levels in GW µg/L	Background levels in drinking Water µg/L	Drinking guidelines (WHO, 2011) µg/L
As	As(III); As(V)	H_3AsO_3; $HAsO_4^{2-}$		Sorption/co-precipitation onto HFO; Sorption to clays; Forming sulphides.	Eh S(VI) to S(-II) reduction	NSL.	<1 to 50 (R3)	<2	10
B	B(III)							< 500	2400
Be	Be(II)	BeOH+		Lack of data	F-	No qualified Thermodynamic DataBase available, so solubilities are not calculated.	<1 (R3)		12 (HB)
Cd	Cd(II)	$CdCl^+$; $CdCO_3$	7.4E-4 (2.1E-5/2.7E-2) (R4)	Sorption onto mineral surfaces Precipitation of $CdCO_3$(s), CdS(s)	(CO_3) S(VI) to S(-II) reduction (Solubility ca. 10^{-12} M)	0.45 ($CdCO_3$) (R1)		< 1	3
CN	CN-		no data					BHC	500 (HB, short exposure)
Co			7.4E-4 (2.1E-5/2.7E-2) (R4)						
Cr	Cr(III); Cr(VI)			Sorption and precipitation Cr_2O_3	Eh			<2	50 Cr total
Cu	Cu(I); Cu(II)			Precipitation of $Cu(OH)_2$ and $CuCO_3$(s) under oxic conditions; formation of native Cu and Cu sulphides under reducing conditions	Eh Microbial reduction of S(VI) to S(-II) causes Cu_2S precipitation and a decrease in solubility	0.6-0.001 (Cu0) (R2)		can be as high as 30000 µg/L	2000
Hg	Hg(I); Hg(II)					not included			6 for Hg_{inorg}
Mn						not included		BHC	400 (HB)

Element	Redox states	main species in GW (pH 6 to 9)	Kd in transport (m^3/kg)	Main retention processes	Main affecting parameters	Selected concentration limits in SA µg/L	Levels in GW µg/L	Background levels in drinking Water µg/L	Drinking guidelines (WHO, 2011) µg/L
Ni	Ni(II)	Ni^{2+} Chloride complexes dominate in brackish waters	7.4E-4 (2.1E-5/2.7E-2) (R4)	Sorption, Precipitation of NiS under reducing	Microbial reduction of S(VI) to S(-II) causes NiS ptation and decrease solubility	0.006 to 6 ($NiCO_3$) (R1)	<20	< 20	70
Pb	Pb(II); Pb(IV)	PbCl, $PbCO_3$(aq)	Pb(II): 2.5E-2 (2E-3/0.3) (R4)	Precipitation of carbonates and sulphides in reducing conditions	Eh, pH, carbonate, phosphate and chloride concentrations Microbial reduction of S(VI) to S(-II) causes PbS precipitation and a decrease in solubility	0.2 ($PbCO_3$) (R2)		< 5 (R3)	10
?Sb	Sb(0); Sb(III); Sb(V)			Sorption of Sb(V);					20
Se	Se(-II); Se(0); Se(IV); Se(VI)	HSe-; HSeO3-;SeO42-	0	Under reducing conditions:Se(0) and FeSe(s); Co-precipitation with FeS_2. oxidising conditions: sorption onto HFO	Eh Fe(II), as it will affect the formation of iron selenides. S(VI) to S(-II)	8E-4 ($FeSe_2$) to 8E-6 (Se(0)) (R1)	<80 (R3)	< 10	40
Sn	Sn(II); Sn(IV)	$Sn(OH)_4$(aq) under oxic conditions	0.16 (0.045/0.56) (R4)	Sorption Formation of SnO_2(s) and formation of sulphides in reducing conditions	Eh Microbial reduction of S(VI) to S(-II) causes SnS precipitation and a decrease	0.1 to 0.01 (SnO_2) (R1, R2)	<15 (R3)	BHC	

Element	Redox states	main species in GW (pH 6 to 9)	Kd in transport (m^3/kg)	Main retention processes	Main affecting parameters	Selected concentration limits in SA µg/L	Levels in GW µg/L	Background levels in drinking Water µg/L	Drinking guidelines (WHO, 2011) µg/L
					insolubility				
Zn							<1	BHC	3000 (HB)
U	U(VI); U(IV)	U(VI)-Ca-CO3; U(IV)-OH	U(VI): 1.1E-4 (0/2.1E-3) U(IV): 5.3E-2 (2.8E-3/0.98) (R4)	Sorption under oxidising conditions; Precipitation under reducing conditions		U(VI): 0.24; U(IV): 0.002	<20 (R3)		30
asbestos									no clear indications of toxicity by ingestion

R1. Grivé et al. (2008); R2. Duro et al. (2010); R3. data compiled in Duro et al. (2006); R4: Kd data selected in Crawford (2013).

3.1.5 Typical Exposure Pathways

When constructing human health risk assessments consideration should be given to the toxicological properties of a contaminant in terms of acute, as well as chronic exposures, and in terms of a variety of endpoints, such as carcinogenicity, genotoxicity, reproductive toxicity and teratogenicity, for several possible exposure pathways.

As noted previously, in assessing the effects of chemicals on health, these exposure pathways include: oral ingestion (of soil, dust, food), inhalation (of solid and liquid aerosols, and gases) and dermal (skin). Other pathways by which substances enter the body exist (the intravenous route for example), but these are of limited relevance in the context being considered here (though uptake from wounds or as a consequence of ritual or cosmetic damage to the skin, e.g. tattooing, cannot be entirely discounted, particularly in some cultural contexts). Exposures can also occur *in utero*, but it is the mother that would typically be considered as the receptor, even though the effect of a contaminant on the embryo or foetus would be likely to drive health protection measures.

In general, when assessing and managing risks to health, exposures can be considered within the frameworks of occupational health (or workplace exposures) and public health (or public exposures). When a worker is at their place of employment, they are subject to occupational exposure control regimes and exposures are limited to protect workers. However, when 'the worker' leaves the place of employment, they become a member of the public. This an important distinction that needs to be made when considering how exposures are assessed and managed under different legislative frameworks.

In very broad terms, occupational exposures are more likely to occur via inhalation than ingestion/skin contact and control measures can be put in place to protect worker health (e.g. room ventilation, use of fume cupboards/glove boxes, use of personal protective equipment). In contrast, members of the public may be exposed to substances by breathing ambient air, by the inhalation of aerosols and by the ingestion of soil, drinking water or food products. Individuals who consume soil compulsively in unusually large quantities, behaviour referred to as 'pica' or 'geophagy', are generally not considered specifically in risk assessments. This is a pathological condition, evaluated separately in a medical context and on a case-by-case basis. Also, the toxicity of many elements depends strongly on their chemical form. Thus, an element incorporated in food products may be much less or much more toxic than the same element in drinking water or ingested in association with soil. These distinctions may arise from differences in bioavailability, but can also be due to various chemical forms of an element having different affinities for receptor sites at the cellular level.

The exposure pathways that are included in a risk assessment will depend upon the setting of the risk assessment and the level of detail required. As previously mentioned, an initial screening for a deep radioactive waste disposal system could just include the drinking water pathway (e.g. Hunter et al., 2006). A more comprehensive approach (if considered necessary) would be like that used for radiological risk assessment, whereby other environmental media and intake of them (e.g. food in the form of crops and livestock, grown/reared on local soil) are also considered (e.g. Wilson et al., 2009).

In the assessment of land contamination, 'generic assessment criteria' may be generated for initial screening using an exposure model (e.g. SGVs in the UK (Defra/Environment Agency, 2002a, 2002b); Australian Health Impact Levels/Health Screening Levels (Government of Western Australia, 2014)) prior to the development of a site-specific risk assessment (in which more detailed consideration is given to exposure pathways, critical receptors etc.) in a 'tiered' risk assessment approach.

An example of an exposure assessment model used to generate guidelines values for soil in either a generic or site-specific context is the CLEA model (Defra/Environment Agency, 2002a-c; Environment Agency, 2009a, 2009b). In this model, consideration is given the potential for contaminants present in soil to be transferred to environmental media to which receptors may be

exposed (Figure 3-1). The primary aim of the model is to calculate the concentration of a contaminant in soil that is associated with an average daily exposure that does not exceed relevant toxicological assessment criteria, termed HCVs in the form of TDIs for threshold substances or an 'Index Dose' for non-threshold substances (Environment Agency, 2009b). Although difficult to test, consideration has been given to effectiveness of the CLEA model to predict contaminant transfers between environmental media (for example, the uptake of Cd by lettuce (Podar and Ramsey, 2005)). Other contaminated land exposure models also consider several exposure pathways, such as 'CSOIL 2000' (Figure 3-2), which has been developed in the Netherlands (Brand et al., 2007).

Models such as CLEA are generally used to determine compliance against assessment criteria based on total intake of a contaminant without the explicit consideration of the capacity of the substance to be absorbed into the body and, in the case of soil, the capacity of substances in soil to reach the systemic circulation after oral ingestion. Here it is necessary to introduce the concepts of 'bioaccessibility' (the capacity of a substance present in a soil matrix to dissolve into fluid present in the stomach and intestine) and 'bioavailability' (the capacity of a substance to reach systematic circulation). The proportion of a contaminant that is 'bioaccessible' or 'bioavailable' will depend on several factors, including the form taken by the contaminant within the soil matrix. This is considered further in Section 3.1.7.

3.1.6 Identification of Receptors and Exposure Model Assumptions

Typically, in human health risk assessment a 'critical' receptor is identified as being typical of the most susceptible individual or subgroup of a population that may be exposed. The 'identity' of the critical receptor, for example, whether they are male/female/pregnant female, adult/child, depends upon the setting in which exposure may occur (occupational/public), the environmental media being assessed and the toxicological properties of the substance(s) being considered. The identity of the receptor will determine the assumptions made in exposure assessment calculations, such the rate of consumption of drinking water or food, breathing rate and rate of ingestion of substances not directly related to food, such as the inadvertent ingestion of soil[12]. The rates of ingestion/inhalation will, therefore, influence the calculation of the amount of a substance that can be present in a given medium without toxicological criteria (such as TDI, $BMDL_{10}$ values, index doses etc.) being exceeded.

[12] Bearing in mind that some soil may be attached to, and ingested with, food items, such as salad.

Pathway	Environmental media	Chemical characteristics	Site characteristics	Receptor characteristics
Soil and dust ingestion	Soil and indoor dust	Persistence	Soil chemical concentration Fraction of soil in indoor dust	Ingestion rate Body weight
Consumption of homegrown fruit and vegetables	Produce	Persistence **Soil-to-plant concentration factors** Partitioning from soil to water Partitioning from water to lipids	Soil chemical concentration Soil type Organic matter content Plant type	Consumption rate Fraction of produce consumed that is homegrown Body weight
Skin contact (indoors)	Indoor dust	Persistence Dermal absorption fraction	Soil chemical concentration Fraction of soil in indoor dust Soil type	Contact rate Body weight Exposed skin area
Skin contact (outdoors)	Soil	Persistence Dermal absorption fraction Skin permeability rates	Soil chemical concentration Soil type	Contact rate Body weight Exposed skin area
Inhalation of dust (indoors)	Air	Enrichment potential in finer soil fractions	Soil chemical concentration Soil type Fraction of soil in indoor dust	Body weight Inhalation rate Time spent indoors
Inhalation of dust (outdoors)	Air	Enrichment potential in finer soil fractions	Soil chemical concentration Wind erosion potential Air dispersion factors Fraction of site with hard or vegetative cover	Body height and weight Inhalation rate Time spent outdoors
Inhalation of vapours (indoors)	Air	Persistence Partitioning from soil to air Diffusion through soil pores	Soil chemical concentration Soil type Building type	Body height and weight Inhalation rate Time spent indoors
Inhalation of vapours (outdoors)	Air	Persistence Partitioning from soil to air Diffusion through soil pores	Soil chemical concentration Soil type Air dispersion factors	Body height and weight Inhalation rate Time spent outdoors

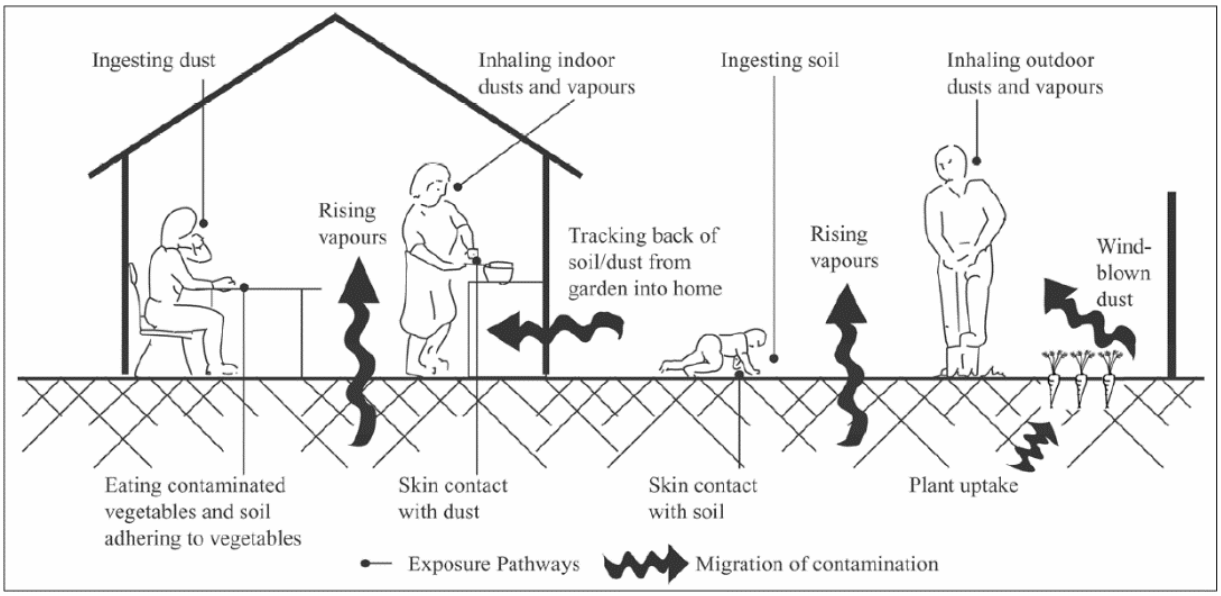

Figure 3-1. Exposure pathways and characteristics included in the UK CLEA model (Environment Agency, 2009b).

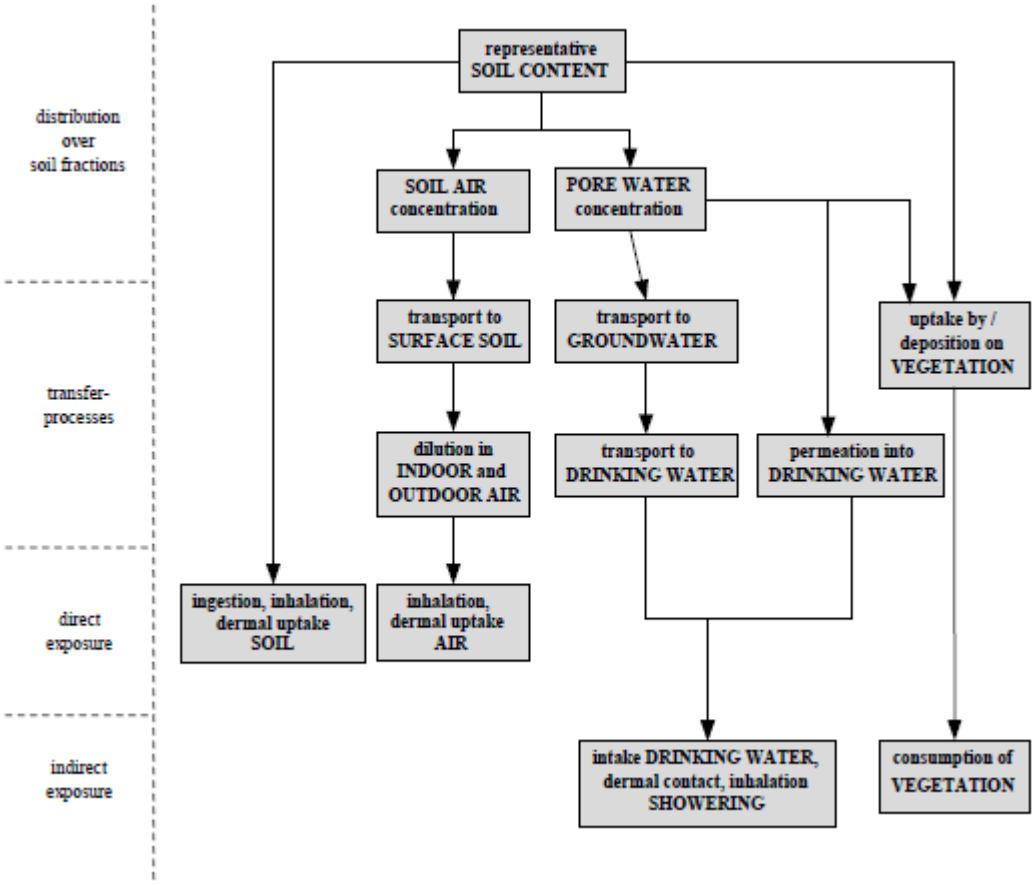

Figure 3-2. Diagram showing contaminant transfers and exposure pathways included in the contaminated soil exposure model CSOIL 2000 (Brand et al., 2007).

For recommending guidelines for drinking water quality, WHO typically considers the following receptors and drinking water ingestion rates, depending on potential susceptibility to a specific contaminant (WHO, 2011):

- 60kg adult: 2 litres of water per day.
- 10kg child: 1 litre of water per day.
- 5kg bottle-fed infant: 0.75 litre of water per day.

In recommending ambient air quality guidelines (public exposures), the susceptibility of different individuals should be considered. Increased susceptibility to air pollution has been linked to many factors, including the prevalence of chronic respiratory or cardiac diseases and diabetes, socioeconomic status and possibly nutrition (WHO, 2005).

In the assessment of potentially contaminated land, the CLEA model (Section 3.1.5) considers a critical receptor based on: susceptibility to soil contamination; the likelihood that a receptor is present based on land use category (residential, allotments, commercial); and the likely degree of contact with soil or indirect contact with other contaminated media such as home-grown produce or indoor air (Environment Agency, 2009c). In many cases, a young female child is considered the critical receptor due to a combination of higher childhood exposures for key pathways (in particular soil ingestion) and a relatively lower bodyweight (resulting in a greater intake potential per unit body weight). The duration of exposure is also considered in calculations of average daily intake.

The critical receptors for different land use assumptions and exposure pathways and durations considered in the model are:

- Residential: 0 to 6 years old female child, exposure duration of 6 years. Exposure pathways include direct soil and indoor dust ingestion, consumption of home-grown produce, consumption of soil adhering to home-grown produce, skin contact with soils and indoor dust, inhalation of indoor and outdoor dust and vapours (building is assumed to be a 2 storey, small terraced house).
- Allotment: 0 to 6 years old female child, exposure duration of 6 years. Exposure pathways include direct soil ingestion, consumption of home-grown produce, consumption of soil adhering to home-grown produce, skin contact with soils, outdoor inhalation of dust and vapours. No building.
- Commercial: working female adult (16 to 65 years old), working lifetime of 49 years. Exposure pathways include: direct soil and indoor dust ingestion, skin contact with soils and dusts, inhalation of dusts and vapours. Building is a three-storey pre-1970 office.

Given the CLEA model approach, many assumptions need to be made for the critical receptor, such as body weight, inhalation rates, along with exposed skin fraction, ingestion rates for soil and ingestion rates for different categories of home-grown produce (Environment Agency, 2009b).

In managing occupational exposures and setting exposure limits for substances that have chemotoxic properties (e.g. the UK Workplace Exposure Limits (HSE, 2011) and US Permissible Exposure Limits or Recommended Exposure Limits (OSHA, 2016)), exposure limits are for fixed time periods, and those exposure limits are sometimes defined as Time Weighted Averages (TWAs). For example, the UK 'WELs' (which were set based on Indicative Occupational Exposure Limit Values set under the Chemical Agents Directive 98/24/EC (European Commission, 1998a)) are concentrations of substances in air, expressed as TWAs, that are appropriate to 'long-term' (8 hours) or 'short term' ('15 minute') exposures.

3.1.7 Use of Toxicological Information

As outlined in Section 2, a range of different types of toxicological data can be used in human health risk assessment, when calculating generic assessment criteria (such as drinking water guidelines, air quality guidelines or soil guidelines) or for the assessment of a specific potentially contaminated site or waste disposal facility. In general, substances are considered 'threshold' or 'non-threshold' for a given exposure route and toxicological end-point. Intakes (or doses) are generally specified as mass per kg body weight per day for oral ingestion, with a similar approach being possible for inhalation, although often concentrations of substances in air are given (Section 2).

Drinking Water Guidelines

For the development of drinking water quality guidelines, WHO typically reviews toxicological data for substances of interest to determine a TDI (or a provisional TDI (PTDI) if data quality is limited) for threshold substances. The TDI is based on the most sensitive end-point, and can be based on data such as NOAEL, LOAEL or BMDL, that are then divided by an Uncertainty Factor (UF) or Chemical-Specific Adjustment Factor (CSAF). In relation to exposure of the general population, the NOAEL or BMD/BMDL for the critical effect in experimental animals is normally divided by an uncertainty factor of 100. This comprises two 10-fold factors, one for potential interspecies differences and one for inter-individual variability in humans (WHO, 2011). Extra uncertainty factors may be incorporated to allow for database deficiencies and for the severity or irreversibility of effects. Inadequate studies or databases include those where a LOAEL is used instead of a NOAEL and studies considered to be shorter in duration than desirable (WHO, 2011). Situations in which the nature or severity of effect might warrant an additional uncertainty factor include studies in which the end-point is malformation of a foetus or in which the end-point determining the NOAEL

is directly related to possible carcinogenicity. For substances for which the uncertainty factors are greater than 1000, guideline values are designated as 'provisional' to emphasise the higher level of uncertainty. CSAFs may be used instead of UFs if data on a chemical's mode of action are available, and sufficient quantitative toxicokinetic and toxicodynamic data are available.

The guideline value (GV) is then calculated as follows:

$$GV = (TDI \times bw \times P)/C$$

where bw is bodyweight of the receptor (e.g. 60 kg adult, 10 kg child, 5 kg infant), P is the fraction of the TDI allocated to drinking water and C is daily drinking water consumption (2 litres per day for adults, 1 litre per day for children and 0.75 litres per day for a bottle-fed infant).

In determining values of P, wherever possible, data on the proportion of total daily intake normally ingested in drinking-water (based on mean levels in food, drinking-water and air) or intakes estimated on the basis of physical and chemical properties of the substances of concern are taken into account (WHO, 2011). WHO (2011) noted that as the primary sources of exposure to chemicals are generally food (e.g. pesticide residues) and water, it is important to quantify the exposures from both sources. Where appropriate information on exposure from food and water is not available, allocation factors are applied that reflect the likely contribution of water to total daily intake for various chemicals. In the absence of adequate exposure data, the normal allocation of the total daily intake to drinking-water is 20%, which WHO (2011) considers reflects a reasonable level of exposure based on broad experience, while still being protective.

In setting guidelines for non-threshold substances, such as genotoxic carcinogens, values are normally determined using a mathematical model, generally the linearized multistage model. Others are considered more appropriate in certain cases (WHO, 2011). These models compute an estimate of risk at a specified level of exposure, along with upper and lower bounds of confidence on the calculation, which may include zero at the lower bound (WHO, 2011). WHO guideline values are conservatively presented as the concentrations in drinking water associated with an estimated upper-bound excess lifetime cancer risk of 10^{-5} (one additional case of cancer per 100 000 of the population ingesting drinking-water containing the substance at the guideline value for 70 years). WHO (2011) states that this value does not equate to the number of cases of cancer that will be caused by exposure to the substance at this level, rather it is the maximum potential risk, taking into account large uncertainties. WHO (2011) also notes that it is highly probable that the actual level of risk is less than this, even approaching zero, but risks at low levels of exposure cannot be experimentally verified. WHO (2011) also notes that Member States may consider that a different level of hypothetical risk is more appropriate to their circumstances, and values relating to risks of 10^{-4} or 10^{-6} additional cancer cases over a lifetime of exposure may be determined by respectively multiplying or dividing the guideline value by 10. It is also noted that the mathematical models used for deriving guideline values for non-threshold chemicals cannot be verified experimentally, and they do not usually take into account a number of biologically important considerations, such as pharmacokinetics, pre-systemic and metabolic detoxification, DNA repair or protection by the immune system. WHO (2011) also notes that such models assume the validity of a linear extrapolation of very high dose exposures in test animals to very low dose exposures in humans. As a consequence, the models used are considered conservative i.e. to err on the side of caution, although both sub-linear and supra-linear exposure-response models have been presented, each supported by some data and some theoretical arguments.

In addition to the WHO, individual countries have developed their own approaches to setting drinking water guideline values. The methodology for developing drinking water guidelines in Australia (Australian Government, 2011) is broadly like that adopted by the WHO (WHO, 2011) and the guidelines consider WHO guidance. When the guideline values derived for chemicals in the Australian Drinking Water Guidance (ADWG) differ from those recommended by the WHO, the difference usually arises in one of two ways (Australian Government, 2011):

- The ADWG use an average adult weight of 70 kg, consistent with developed countries such as Canada, whereas the WHO figure is 60 kg to cater for lighter body weights in developing countries. The use of a higher average weight can sometimes yield slightly higher guideline values, but the difference is not significant given the large safety factors used.
- For genotoxic carcinogenic compounds, WHO uses a risk assessment calculation, with the guideline value set at the concentration that would give rise to a risk of one additional cancer per 100,000 people. The Australian guideline values for these types of compounds are based on a consideration of:
    - the limit of determination based on the most common analytical method;
    - the concentration, calculated by the WHO using a risk assessment model, that could give rise to a risk of one additional cancer per million people, if water containing the compound at that concentration were consumed over a lifetime;
    - a value based on a threshold effect calculation, with an additional safety factor for potential carcinogenicity.

In Europe, the Drinking Water Directive (Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption (European Commission, 1998b)) concerns the quality of water intended for human consumption. The Directive laid down the essential quality standards at EU level. A total of 48 microbiological, chemical and indicator parameters must be monitored and tested regularly. In general, WHO guidelines for drinking water and the opinion of the Commission's Scientific Advisory Committee are used as the scientific basis for the quality standards in drinking water (European Commission, 2016).

In the USA, the National Primary Drinking Water Regulations (NPDWR) are legally enforceable primary standards and treatment techniques that apply to public water systems. The US EPA provides a table of regulated drinking water contaminants, which include Maximum Contaminant Level Goal (MCLG) values, defined as 'the level of a contaminant in drinking water below which there is no known or expected risk to health' and Maximum Contaminant Levels (MCL), which are defined as 'the highest level of a contaminant that is allowed in drinking water'. MCLs are set as close to MCLGs as feasible using the best available treatment technology and taking cost into consideration. MCLs are enforceable standards (US EPA, 2016).

In Canada, Health Canada publish drinking water guidelines ('Maximum Acceptable Concentrations', Health Canada, 2014) with background material on how values are produced for chemical contaminants being summarised by Health Canada (Health Canada, 1995). The approach taken is broadly similar to that of other organisations/authoritative bodies, with TDI values being considered along with appropriate allocation of a fraction of the TDI to drinking water for threshold substances, and cancer risk models being considered for non-threshold substances.

It is important to note that if drinking water standards/guidelines are used outside the context of public water supply, for example, in risk assessments of radioactive waste disposal systems, that the way in which they were produced needs to be clearly understood. Although for a wide range of chemicals the guidelines are based on toxicological properties, some guidance considers whether water would be acceptable to consumers based on taste/odour or 'aesthetic' characteristics (Australian Government, 2011; WHO 2011). For example, some contaminants (e.g. petroleum hydrocarbons) can produce water that may be considered unacceptable for consumption at concentrations at, or lower than, those that would be of concern based on human health effects (WHO, 2011).

Contaminated Land Assessment

Several countries have produced guideline values and supporting exposure models for soil contamination. Examples include the UK (Defra/Environment Agency, 2002a-c; Environment

Agency, 2009a, b), the Netherlands (Baars et al., 2001; Brand et al., 2007), Australia (Government of Western Australia, 2014) and Canada (CCME, 2006).

An example of the detailed approach by which toxicological data are used is provided by the UK CLEA model, as previously described above. The CLEA model and supporting documentation were initially published by Defra/Environment Agency in 2002 (e.g. Defra/Environment Agency, 2002a, 2002b) along with a number of 'Tox Reports' in which the toxicological properties of several substances were reviewed in order to identity HCVs, generally for oral ingestion and inhalation. Rarely are sufficient dermal toxicity data available from which HCVs may be derived, therefore, the CLEA model compares both oral and dermal exposure against the oral ingestion criterion and a default assumption of 10% dermal absorption, which may be refined if dermal absorption data are available for the contaminant (Environment Agency, 2009c). In 2012, new statutory guidance was published (Defra, 2012a,b), which has resulted in a different approach being adopted subsequently. However, the methodology for generating guideline values is still relevant and it is outlined herein, along with the approaches that have been developed since 2012.

Prior to 2012, HCV values were used with generic exposure calculations to generate generic assessment criteria, SGVs (described in a series of SGV reports) and for the calculation of SSAC. For substances that exhibit threshold effects, HCVs take the form of tolerable daily soil intakes (TDSIs) (which may be better described as tolerable daily intakes from soil). The approach taken for a given substance is to identify a TDI which is expressed as the mass of a substance per unit mass body weight, per day, typically using NOAEL or LOAEL values and the application of appropriate UFs. Once a TDI has been identified, the mean daily intake (MDI) of substances from sources other than soil can be quantified (drinking water and food) to ensure that resources are not devoted to inappropriately reducing exposure to substances from soil sources. The approach taken for lead was somewhat different, in that a model relating environmental concentrations to blood lead levels was used (Defra/Environment Agency, 2002d).

For non-threshold substances, HCVs are in the form of 'Index Doses' which are daily intakes (also expressed as mass of substance per unit mass receptor body weight per day) that have a corresponding 'minimal' risk of causing adverse health outcomes, typically cancer (Wilson, 2008). Although intakes can be identified which correspond to a minimal risk, there is an additional exhortation in the UK that exposure to non-threshold substances should be kept ALARP, because no 'safe' level of exposure can be identified. Generally, it is assumed that exposures to non-threshold substances from sources other than soil will also be reduced to levels that are ALARP and, as such, intakes of non-threshold substances from sources other than soil are not considered.

The HCV values identified in the 'Tox Reports' essentially represent daily intakes that are unlikely to result in widespread manifestation of adverse health effects within a population, whereas in the UK under Part II of the Environmental Protection Act (1990)[13] 'contaminated land' is defined in terms of 'significant harm' (Wilson, 2008). Therefore, subsequent to the development of the CLEA model and its first few years of use, concern arose that exceedances of SGV values may be taken to indicate that the potential for 'significant harm' is present, when it is not certain that this is the case (Defra, 2005). This and other considerations led to a review instigated by Defra to consider a 'way forward' for contaminated land assessment (Defra, 2006). In 2009, updated guidance and documentation was published for the CLEA model, including exposure model calculations and use of toxicological data (Environment Agency, 2009a-c). The current version of the CLEA model (v 1.071) is available as an Excel workbook on the UK government website[14]. The updated CLEA model (version 1.05) has been used to generate a number of generic assessment criteria for a range of substances (3 metals and 32 organic substances) in a project involving a number of organisations

[13] http://www.legislation.gov.uk/ukpga/1990/43/part/II/enacted.

[14] https://www.gov.uk/government/publications/contaminated-land-exposure-assessment-clea-tool

(CL:AIRE et al., 2010). A limited number of updated SGV values and Tox reports were also produced and published in 2009, but uncertainties remained as to how to determine that there was the 'significant possibility of significant harm' ('SPOSH') such that land can be legally defined as being contaminated.

The updated guidance on the use of toxicological information in contaminated land assessments (Environment Agency, 2009c) aims to explain the basic toxicological principles used to derive HCVs and also directs readers to useful sources of more detailed information on the various concepts and approaches discussed. The report reviews the approaches that may be taken for threshold and non-threshold substances, including how to use 'points of departure' such as NOAELs, LOAELs and BMDLs, and UFs for the derivation of tolerable daily intakes. The approaches available for setting HCVs for non-threshold substances (quantitative dose-response modelling and non-quantitative extrapolation) are also outlined.

The report published by the Environment Agency (Environment Agency, 2009c) provides a useful summary of the issues associated with estimating cancer risks and methods of generating intake values that are protective of human health. Many of the overall approaches are the same as those typically used to derive HCV values under the 2002 guidance. The report recognises that some public health organisations and non-UK regulatory bodies (e.g. the WHO Drinking-water Guidelines Working Group and US EPA), use QRA based on animal data, but it is re-iterated that this approach has generally not been used in the UK, due to reservations expressed by the UK Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) which does not recommend its use for routine risk assessment. COC considers that the models do not simulate the carcinogenic processes adequately and is critical of the precision of cancer risk erroneously implied (COC, 1991, 2004). It is also noted that most published risk estimates are also presented as the 95% upper confidence limit on the risk rather than the maximum likelihood estimate (statistical 'best guess') and therefore, 'while such models provide quantitative cancer risk estimates, their purpose is more to be protective of than predictive of cancer risk' (Environment Agency, 2009c). The wide range of possible risks that can be calculated from observed data, depending on the model used, is illustrated in Figure 3-3.

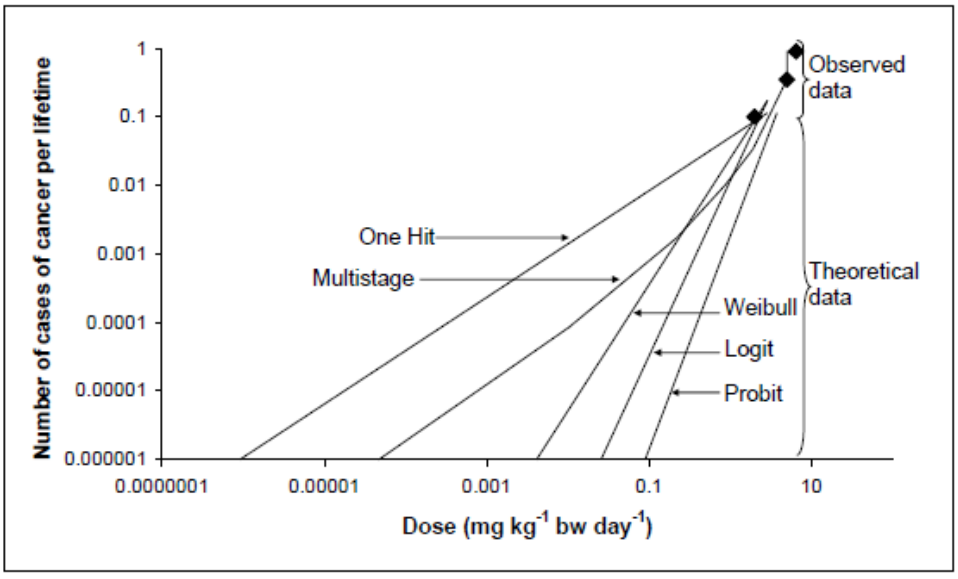

Figure 3-3. Examples of variance of quantitative cancer risk models when modelling the same dataset.

The Environment Agency (2009c) notes that there has been a tendency in recent years to move away from low-dose extrapolation models (such as those in Figure 3-3) to simple linear extrapolation (unless there is evidence of non-linearity). In linear extrapolation, a line is effectively

drawn on the dose-response curve from the point of departure to the origin. In practice, linear extrapolation is most simply achieved by calculating the BMD_{10} or $BMDL_{10}$ and then dividing this by orders of magnitude to achieve the desired risk level, e.g. dividing by 10 000 to give a 1 in 100 000 risk (Environment Agency, 2009c).

The Environment Agency (2009c) also summarised the predominant alternative (non-quantitative) approach to setting HCVs for non-threshold carcinogens. This involves the assessment of all available carcinogenicity dose-response data to identify an appropriate dose without discernible carcinogenic effect, or the lowest dose tested (if effects are apparent at all doses), and the use of expert judgement to derive a suitable margin (COC, 2004). HCVs derived using this approach have previously been called minimal risk levels by COC (noting that this is different to the Minimal Risk Levels published by the ATSDR). COC (2004) defined a minimal risk level as "an estimate of daily human exposure to a chemical identified by expert judgement that is likely to be associated with a negligible risk of carcinogenic effect over a specified duration of exposure (usually a lifetime). In practice, the minimal risk level approach is like that for threshold chemicals, applying numerical (uncertainty) factors to a point of departure identified from the exposure-response data. Where the assessment is based on animal data, it is usually not possible to identify an exposure without discernible carcinogenic effect and effect level data are therefore used. Several indices of tumour production that may be used as the point of departure are commonly reported in the experimental carcinogenicity literature. The most common are the BMDL (as for threshold toxicity), the TD_{50}, and the T_{25}. The TD_{50} can be defined as the rate of exposure required to halve the probability of remaining tumourless at the end of a standard lifespan whereas the T_{25} is defined as the exposure producing a 25% increase in the incidence of a specific tumour above the spontaneous background rate (Environment Agency, 2009c and references therein). The UF applied must account not only for the potential interspecies and inter-individual variation, but also the seriousness of the endpoint (cancer) and the assumption that there is no threshold.

The Environment Agency (2009c) notes that a MoE approach has been considered for assessing the risk posed by non-threshold substances. The MoE approach involves the evaluation of all the available toxicity data and selection of the critical point of departure. When using animal toxicity data, the point of departure is usually a NOAEL, LOAEL or BMDL for threshold chemical toxicity, or a BMDL, T25 or TD50 for non-threshold carcinogenic effects. In the MoE approach, however, the point of departure is directly compared against the estimated exposure of the human population; that is, the point of departure (in mg kg^{-1} bw day^{-1} or mg m^{-3}) is divided by the human exposure to the chemical (in the same units). The resulting ratio is the MoE. The Environment Agency (2009c) notes that the acceptability of the size of the MoE will depend on a variety of factors including the quantity and quality of toxicity data available, the species for which data are available, the critical adverse effect (including whether it is expected to have a threshold), and the expected duration of human exposure. The Environment Agency (2009c) states that: 'the MoE may be the preferred approach for an assessment when an established HCV is not available. In these instances, even when toxicity data are limited, a preliminary judgement about the potential risk posed by a chemical may be made by calculating the MoE. This can be used to inform the risk manager and decision-making process in the absence of a detailed risk assessment'.

A summary diagram is provided by the Environment Agency (2009c) on the different approaches available for considering threshold and non-threshold effects and how these fit into risk assessment (Figure 3-4).

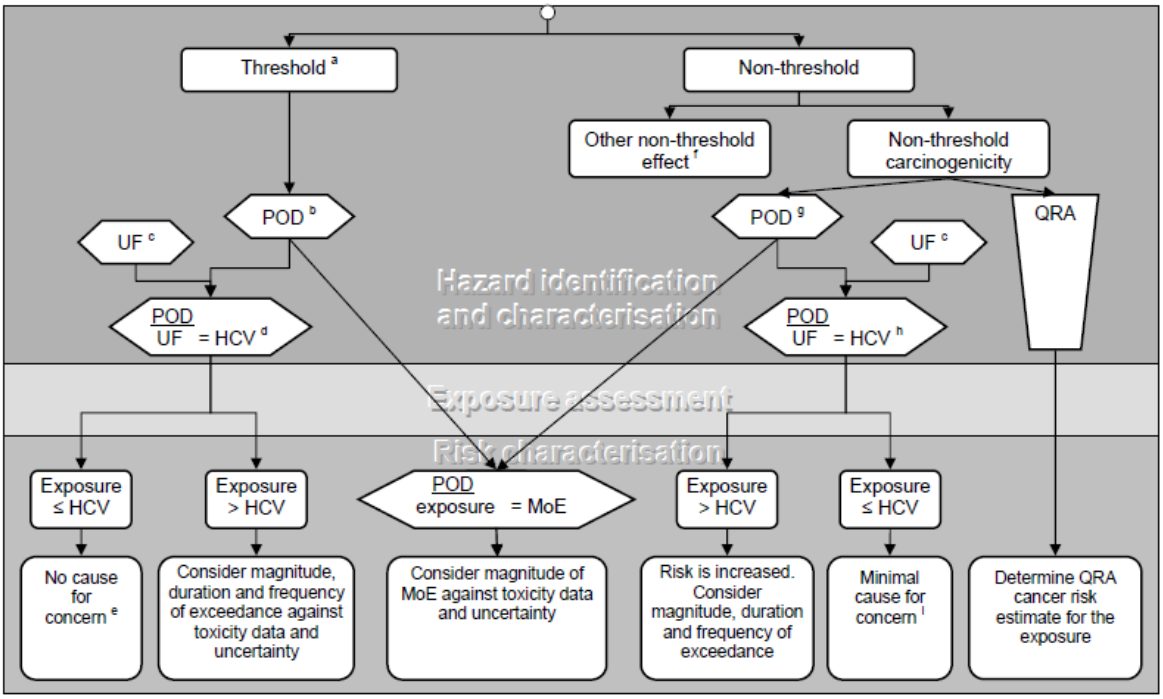

Figure 3-4. Approaches taken for assessing risks for threshold and non-threshold substances in contaminated land assessment (Environment Agency, 2002c). POD = Point of Departure, UF = uncertainty factor, HCV = Health Criteria Value, QRA = Quantitative Risk Assessment, MoE = Margin of Exposure.

In 2012, revised statutory guidance was published by Defra (2012a, 2012b), that outlines four categories of land contamination. It is stated that: 'The local authority should not assume that land poses a significant possibility of significant harm if it considers that there is no risk or that the level of risk posed is low. For the purposes of this Guidance, such land is referred to as a "Category 4: Human Health" case'.

Subsequent to the publication of the updated guidance on assessing soil contamination in the UK, a report has been published that outlines methods for developing 'Category 4 Screening Levels' (C4SLs) (CL:AIRE, 2014), which follows a similar general approach to that taken for SGVs. However, it is considered that C4SLs have a different associated level of risk than that of the former SGVs. As summarised by CL:AIRE (2014), the Defra guidance (Defra, 2012b) states that: 'The new statutory guidance will bring about a situation where the current SGVs/GACs[15] are replaced with more pragmatic (but still strongly precautionary) Category 4 screening levels (C4SLs) which will provide a higher simple test for deciding that land is suitable for use and definitely not contaminated land'.

The suggested approach for developing C4SLs includes the retention and use of the CLEA framework, modified according to considerations of the underlying science within the context of Defra's policy objectives relating to the revised statutory guidance (CL:AIRE, 2014). It is suggested that the development of C4SLs may be achieved in one of three ways, namely: (1) by modifying the toxicological parameters used within CLEA (while maintaining current exposure parameters); (2) by modifying the exposure parameters embedded within CLEA (while maintaining current toxicological "minimal risk" interpretations); and (3) by modifying both toxicological and exposure parameters. There is also a suggested check on "other considerations" (e.g. background levels, epidemiological data, sources of uncertainty) within the approach, applicable to all three options.

[15] Guideline Assessment Criteria

The issue of background levels is of relevance and recent work has attempted to describe background levels in the UK for several common soil contaminants, including: As, Cd, Cu, Hg, Ni and Pb, and benzo(a)pyrene (BaP) (Ander et al., 2013). The data given by Ander et al. (2013) suggest that background concentrations for substances such as As exceed the former SGV value in many parts of the UK (noting the former 'residential' SGV of 20 mg/kg). It has also been demonstrated by Vane et al. (2014) that background levels of some organic contaminants in parts of greater London exceed generic assessment criteria generated prior to the updated statutory guidance in 2012 (Nathaniel et al., 2009).

The C4SL guidance by CL:AIRE (2014) has been used to develop values for As, Pb, Cr(VI), BaP, benzene, Cd and Pb (provided in appendices to the main report by CL:AIRE, 2014). Many of these substances are of relevance to assessing human health risks associated with radioactive wastes. This report, along with recent updates in the UK guidance, the review of methodologies for setting HCVs, especially for non-threshold substances and the potential for the application of MoE approaches could be used in the development of future risk assessments of radioactive disposal systems, particularly those that consider exposure pathways other than just ingestion of drinking water (e.g. Wilson et al., 2009, 2012). The updated UK guidance could also be used for assessing risks posed by non-radiological substances on a particular site that is known, or suspected, to be contaminated with radioactive waste material. In addition, this material also provides a useful overview of the methods available for assessing and limiting cancer risks, which may be considered when comparing non-radiological and radiological approaches.

Contaminant Bioavailability/Bioaccessibility

Most environmental standards/guidelines, and recommended maximum intakes upon which they are based, consider animal data and, occasionally, data from human populations. In general, recommended limits on intakes (mainly oral and inhalation) are based on observations of the prevalence of disease or other indicators of adverse health effects and what intakes may lead to them. As noted previously, the points of departure used to limit intakes are typically LOAEL/NOAEL/BMDL values for threshold substances or a consideration of available dose-response data for non-threshold effects.

Although less commonly used, biokinetic modelling can also be used to set limits on intakes in order to protect human health. A recent example is the determination of intake limits for uranium compounds, to ensure that concentrations of uranium in kidney are such that adverse effects on kidney function would not be expected (Thorne and Wilson, 2015). The approach adopted allows coherent standards to be set for ingestion and inhalation of different chemical forms of the element by various age groups. It also allows coherent standards to be set for occupational and public exposures (including exposures of different age groups) and for various exposure regimes (including short term and chronic exposures). The proposed standards are more restrictive than those used previously, but are less restrictive than the MRLs proposed recently by the US Agency for Toxic Substances and Disease Registry (ATSDR). In addition, the radiological implications of exposure at those proposed limits are investigated for natural, depleted and enriched uranium.

Lead has received much attention in the development of guidelines values in soil/dust. The effects of lead on health are often considered in terms of blood lead levels. Biokinetic models have been developed to link levels of exposure with blood lead concentrations, such as the IEUBK (Integrated Exposure Uptake BioKinetic) model for children (US EPA, 1994; Hogan et al., 1998, White et al., 1998) and adults (Carlisle and Wade 1992; US EPA, 2003). The SEGH (Society for Environmental Geochemistry and Health, Wixson and Davies, 1994) model has been considered in older UK guidance, such as the original lead SGV report. Blood lead levels can be related to neurological/neurobehavioural effects in children, with a link between blood lead levels and IQ test results (Lanphear et al, 2005) and other effects in adults (renal/cardiovascular).

As noted in the C4SL report (Appendix H, CL:AIRE, 2014), to date, the 'minimal risk' situation for lead has not been defined by UK authoritative bodies. Previously, the value of 10 µg dL^{-1} blood was

selected by the Environment Agency (and was used in calculations for the now withdrawn lead SGV), but in 2011 there was published a toxicology report for lead in the light of new scientific evidence (principally the European Food Safety Authority opinion from 2010) indicating that significant health effects could be observed at levels <10 µg dL^{-1} blood. Also, in 2010, the WHO JECFA[16] committee withdrew the Provisional Tolerable Weekly Intake (PTWI) of 25 µg kg^{-1} based upon 10 µg dL^{-1} blood, as it 'could no longer be considered health protective' and they concluded that 'it was not possible to establish a new PTWI that would be health protective' (CL:AIRE, 2014). It is also noted that the ATSDR has not defined an MRL for lead. BMD models have therefore been reviewed to identify possible points of departure for neurobiological effects in children, and renal/cardiovascular effects in adults (CL:AIRE, 2014). Three possible LLTC (Low Level of Toxicological Concern) values (expressed as blood lead levels) are identified: (1) 1.6 µg dL^{-1}, derived using the BMD_{10} (adult renal toxicity); (2) 3.5 µg dL^{-1}, chosen in consideration of all 3 effects (neurobehavioural, renal, cardiovascular); and (3) 5 µg dL^{-1}, which would be a 'policy choice' based on the US CDC[17] action level. Using biokinetic models, LLTC values (as estimated dietary intake doses) were produced from the three blood lead levels for adult and child receptors (CL:AIRE, 2014). The LLTC values were then used to generate provisional C4SL values using CLEA.

Human health risk assessments for contaminated land typically include the use of generic assessment criteria or the development of site-specific criteria to which measured contaminant concentrations in soil (expressed as total mass of contaminant per unit mass of soil) are compared. Such an approach essentially means that it is assumed that all the substance present in the soil is bioaccessible after ingestion. The term 'bioaccessibility' can be defined as: 'The degree to which a chemical is released from soil into solution (and thereby becomes available for absorption) when that soil is ingested and undergoes digestion (Environment Agency, 2009c). In recent years, in-vitro methods have been developed for soil, so that the proportion of a contaminant present that is bioaccessible can be determined and taken into consideration during risk assessment. Bioaccessibility methods generally involve laboratory tests that extract metals/metalloids (such as lead and arsenic) and some organic contaminants (e.g. PAH) from soil by simulating the action of fluids present in the stomach and small intestine (e.g. Ruby et al., 1996; Environment Agency and British Geological Survey, 2002a, 2002b; Oomen et al., 2002, 2003; Lu et al., 2010; Wragg et al., 2011; Denys et al., 2012). There is a lot of debate about how realistic these methods are, whether they should be used and, if so, how. In recent years, work on validating or testing the efficacy of *in vitro* bioaccessibility tests has been undertaken by comparing *in vitro* test results with in vivo data (e.g. Drexler and Brattin, 2007; Denys et al., 2012, Juhasz et al., 2014) and, in future, it could be more widely incorporated into standard risk assessment procedures. However, some concerns have been raised in the UK by the Environment Agency as to how useful such methods are for risk assessment purposes (Environment Agency, 2005).

Assessment of Mixtures and Additive/Synergistic Effects

With regard to assessing health risks associated with exposure to a number of substances there is an issue of the potential for additive or synergistic effects. In general, four main types of additive effects can be identified comprising: 1) dose additivity; 2) response additivity; 3) supra-additivity (synergistic effects); and 4) sub-additivity (Environment Agency, 2009c and references therein). In practice, these are difficult to assess, due to a lack of toxicological data from which such effects can be readily ascertained. However, in some cases, such as that of asbestos and cigarette smoke exposure, where epidemiological data are sufficient to provide some insight (ATSDR, 2001).

For chemical congeners that share a common mode of toxic action (threshold effects), but show notable inter-congener differences in potency, a 'group TDI' can sometimes be defined in units that

[16] The Joint FAO/WHO Expert Committee on Food Additives.

[17] Unites States Centers for Disease Control and Prevention.

account for potency as well as dose (Environment Agency, 2009c). As outlined by the Environment Agency (2009c) such an approach is used for dioxin-like compounds, using Toxic Equivalency Factors (TEFs). The TEF is the potency of the compound relative to a reference compound. In this case, the most potent of the dioxin-like compounds, 2,3,7,8-tetrachlorodibenzo-p-dioxin. The index of toxicity of a dioxin-like compound is its Toxic Equivalent (TEQ), which is its concentration multiplied by its TEF. The TEQ of a mixture of dioxin-like compounds is the sum of the TEQs for the individual compounds present. The TDI for dioxin-like compounds is therefore also expressed in TEQ. The TDI set by the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT), for example, is 2 pg TEQ kg^{-1} bw day^{-1} (COT, 2001). A similar approach may also be used for non-threshold substances, if data are available (some studies, for example, have produced equivalency data for PAH, e.g. Nisbet and LaGoy, 1992; Collins et al., 1998). If TEF data are not available for a group of similar substances, a pragmatic approach is to select that with the greatest toxicity and undertake the risk assessment assuming that the toxicity of that substance applies to the mixture to which exposure occurs.

In contaminated land assessment, a simple method for addressing potential additivity of toxic action, where this is assumed to be possible, and where there is a common toxicological mode of action, is in the form of the hazard quotient / hazard index approach (Environment Agency, 2009c). The Hazard Quotient (HQ) for each chemical is calculated by dividing the estimated ADE by its TDI after consideration of MDI background exposure (i.e. TDSI), and then summing the HQs to give the Hazard Index (HI) (Environment Agency, 2009c). If the HI exceeds one, this equates to exceeding a TDSI from potential dose addition. It is therefore treated in the same way as an exceedance of a TDI by a single contaminant.

$$\mathrm{HI} = \sum_{i=1}^{n} \mathrm{HQ_i}$$

$$\mathrm{HQ}_i = \frac{\mathrm{ADE_i\,(mg\,kg^{-1}bw\,day^{-1})}}{\mathrm{TDSI}_i\,(\mathrm{mg\,kg^{-1}bw\,day^{-1}})}$$

Where HI is the Hazard Index, HQ is the Hazard Quotient, ADE is the Average Daily Exposure from soil, TDSI is the Tolerable Daily Soil Intake and n is the number of chemicals present sharing a common mode of toxicity.

Although difficult to quantify, some risk assessments have attempted to consider qualitatively the potential for additive and synergistic effects for chemical and radiological substances (e.g. Thorne and Wilson, 2009; Wilson et al., 2011).

A consideration is given to the extent to which interactions between toxic agents may need to be taken into account in regulating releases of those agents from geological facilities for the disposal of solid radioactive wastes in Appendix B. That appendix also addresses the basic biological mechanisms that can underlie such interactions and discusses *in vitro* cell-culture approaches that might be used to quantify synergistic effects.

3.1.8 Case Studies and National Approaches on the Assessment of Chemotoxic Substances Associated with Radioactive Waste Materials

In the UK, work has been undertaken to consider chemotoxic substances associated with a generic Geological Disposal Facility (GDF). Initially, work was undertaken to calculate releases from a GDF (ILW vaults) to groundwater and groundwater concentrations were compared against drinking water standards (e.g. Hunter et al., 2006). A more detailed assessment was undertaken in two parts by Wilson et al., (2009, 2011) and Thorne and Wilson (2009). The approach to assessment is illustrated in Figure 3-5. In the first part, models were constructed for an illustrative GDF present in two different types of host rock. GoldSim models were used to calculate releases of key contaminants (Be, Cd, Cr, Pb, U, identified from previous studies) from the GDF and a biosphere

model (similar to that used in the UK for assessing risks posed by radionuclides) was used to calculate contaminant transfer to different environmental media to which future humans could be exposed. A number of cases were produced using different assumptions on contaminant solubility and sorption behaviour. Three cases of decreasing conservatism in respect of release and transport were considered. Estimated exposures (oral and inhalation intakes) for the different host rocks and model cases were compared with authoritative toxicological assessment criteria (national and international guidance). In the second reported part of the work, a literature review is provided on additive and synergistic effects for radiological and chemical toxins and, using the data from the first report, an assessment is provided of the likelihood of additive and synergistic effects occurring as a result of releases from a generic GDF (Thorne and Wilson, 2009). In addressing possible combined effects between the various substances and also with exposure to ionising radiation, three topics were identified that warranted consideration:

- combined effects on the kidneys from ingestion of cadmium, uranium and lead;
- combined effects between ingested lead and exposure to ionising radiation with respect to induction of various types of cancer; and
- combined effects between all five key substances and exposure to ionising radiation with respect to lung cancer induction.

The work demonstrates a way by which synergistic/additive effects (for chemical mixtures and chemotoxic-radiotoxic interactions) can be considered proportionately. A key issue highlighted by this work relates to the availability of relevant toxicological data required as input to any quantitative assessment; as these are limited.

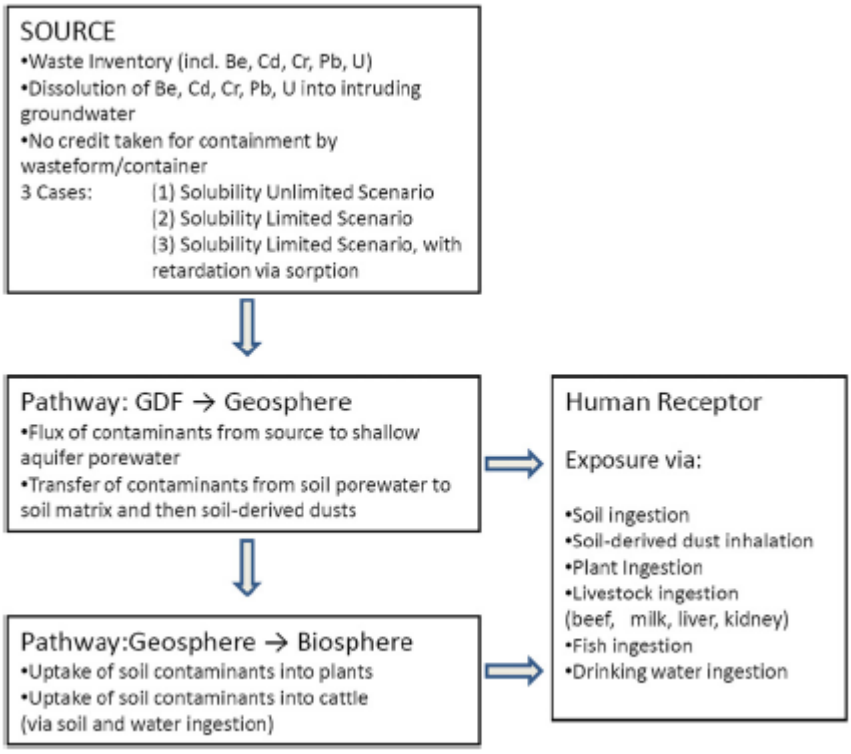

Figure 3-5. Schematic diagram of the approach taken by Wilson et al. (2009, 2011) to assess risks to human health posed by chemotoxic species in a generic UK Geological Disposal System.

Most recently, a study has been undertaken to investigate the circumstances in which either the radiotoxicity or chemical toxicity of uranium is of predominant importance (Wilson and Thorne, 2015; Thorne and Wilson, 2015). This study shows that whether chemical or radiological

considerations dominate depends on the chemical form of the uranium, the route of entry into the body, the degree of depletion or enrichment, and the presence or absence of radioactive progeny. This study is also of interest because it addresses the chemical toxicity of uranium for acute exposures of different duration, as might arise in occupational contexts.

Work has also been undertaken on non-radiological substances in the UK for the development of the 2011 Environmental Safety Case (ESC) for the Low Level Waste Repository (LLWR) in Cumbria (LLWR, 2011). The models of non-radiological contaminant behaviour included a representation of release of metals in the near field. This takes into account solubility limitation, as well as corrosion rates, including giving consideration to typical shapes of various material types, sorption of contaminants to soil in trenches and to grout in encapsulated wastes present in vaults. Two model scenarios were presented for the groundwater pathway and several cases for human intrusion and coastal erosion. These address the expected coastal erosion and delayed erosion. No credit was taken for the containment of contaminants provided by the International Organization for Standardization (ISO) containers in vaults within which grouted wastes are disposed. Chemical conditions were assumed to remain constant after few decades over the assessment period. The modelling suggested that after the end of the Period of Authorisation (PoA) there may be exceedances of the relevant assessment standards (UK drinking water standards or the relevant UK Environmental Quality Standards) in groundwater for a number of non-hazardous contaminants. In the 2011 ESC, it was demonstrated that LLWR would provide at least the same level of protection than that of a modern authorised landfill. Additionally, the 2011 ESC showed that such level of protection would be maintained for a period longer than that generally assessed for a non-radiological landfill. In terms of broad consistency with policy for the management of landfill wastes, it was suggested that limiting the disposal of common metals (some exceedances relate to contaminants that are related to such common metals) would be disproportionate. However, LLWR has stated that disposals of a few chemotoxic substances, such as asbestos and lead, should be limited.

Subsequent to the work undertaken in support of the 2011 ESC, the potential implications of organic complexation of radionuclides and chemotoxic species has been considered (Baston et al., 2013; Taylor and Baker, 2013). In particular, the potential has been assessed for complexants such as EDTA (ethylenediaminetetraacetic acid) to enhance solubilities and reduce the retardation of radioactive and chemotoxic contaminants (Kelly, 2013a, 2013b).

Work continues which seeks to better align non-radiological assessments with those used for landfill hydrogeological risk assessments.

In the US, work has recently been published on the assessment of potential releases of both radiological and non-radiological substances from the proposed Yucca Mountain repository. This is outlined in 'The Supplement to the Environmental Impact Statement (EIS) for a Geologic Repository for the Disposal of Spent Nuclear Fuel and High-Level Radioactive Waste at Yucca Mountain (Nevada)' (US NRC, 2016). A summary is as follows. Risk assessment calculations consider potential releases and contaminant transport through the volcanic-alluvial aquifer in Fortymile Wash and the Amargosa Desert, and to the Furnace Creek/Middle Basin area of Death Valley. The analysis includes the impact of potential radiological and non-radiological releases from the repository on the aquifer and at surface discharge locations of groundwater beyond the post-closure compliance location. Four non-radiological substances are addressed (Mo, Ni, V, U, noting that U is included as both a radiological substance and a chemotoxic substance). The potential for exposure to soil contamination and drinking water contamination was considered (calculated concentrations were compared with environmental standards) and intakes were also calculated and compared with US EPA limits. Molybdenum and Mo-93 in the environment have both been considered in a recent review for SKB (Lidman et al., 2017).

Calculations suggest that all four of the non-radiological chemical species in the source term from the repository (Mo, Ni, V, and U) would reach the Amargosa Farms area. The highest calculated total uranium concentration of 0.073 pCi/L in the groundwater at Amargosa Farms corresponds to

less than 0.02 µg/L (the EPA MCL for U in drinking water is 30 µg/L). While no MCLs have been established i9n the US for the metals Mo and V, the calculated groundwater concentrations for these potential contaminants are all much lower than one part per million, which is comparable to the levels occurring naturally at present. The calculated peak concentration of Ni in groundwater at Amargosa Farms, for each climate state considered, is 0.011 mg/L, and is estimated to occur at 70,000 years for a cooler/wetter climate. This concentration is much lower than the EPA National Recommended Water Quality Criteria level for Ni of 0.61 mg/L. NRC staff calculated soil contaminant concentrations using an irrigation recycling model that accounts for accumulation in the soil of both radiological and non-radiological contaminants. Non-radiological contaminants show the greatest calculated concentrations at one million years.

None of the non-radiological contaminants show any appreciable accumulation in the soil at Amargosa Farms, and all are well below soil screening levels or the natural abundance in local sediments. Potential health effects from the non-radiological contaminants were considered for a nominal intake from ingestion of contaminated water (70-kilogram person drinking 2 L of water per day). Human health impacts of the non-radiological contaminants were assessed by comparing daily intakes with EPA's Oral Reference Dose standard. In alignment with the calculations for the aquifer environment between the post-closure compliance location and Amargosa Farms, the peak daily intake for Ni was estimated to occur at 260,000 years. The estimated values of daily intake are all much lower than the EPA Oral Reference Doses.

Several features of the aquifer environment at the downstream State Line Deposits/Franklin Wells area indicate that groundwater discharge results in the accumulation of material onto sediments. The calculated soil concentrations show similar patterns to Amargosa Farms for sorbing and non-sorbing radionuclides and metals. The dose pathways for a resident of Amargosa Farms are external (body) exposure, inhalation, and ingestion of water, crops, animal products, fish, and soil. The estimated concentrations for all the non-radiological contaminants are lower than the EPA generic soil screening levels. The maximum Ni intake of 0.001 mg/kg body weight/day occurs at approximately 88 000 years after repository closure. For all the non-radiological contaminants at this location, the estimates of intake are significantly lower than the EPA Oral Reference Dose.

The Furnace Creek area and Middle Basin of Death Valley are located approximately 56 km beyond the post-closure compliance location. Under scenarios in which there is no groundwater pumping at the Amargosa Farms area, groundwater modelling indicates that most of the contaminants transported from Yucca Mountain would be discharged in Middle Basin of Death Valley. At Furnace Creek, the maximum concentration of Mo in the groundwater occurs approximately 58,000 years after repository closure for the present-day climate (under the cooler/wetter climate assumption, the peak occurs at 20 000 years after closure, at a lower concentration). The major release of this contaminant from the repository occurs fairly early after repository closure and as a non-sorbing element, transport of Mo is not significantly delayed in the aquifer. The estimate of the maximum Mo concentration in the groundwater is 0.05 mg/L. As noted previously, the EPA has not set an MCL or National Recommended Water Quality Criteria level for Mo. Mo reaches a maximum soil/evaporite concentration at about 58,000 years. The estimated maximum value is 208 ppm under the present-day climate state. The maximum value occurs slightly earlier for the cooler/wetter climate, but is lower. The maximum value decreases in the soil as the groundwater concentration decreases over time. This maximum is lower than the EPA soil screening level of 390 ppm for Mo in residential soils. The estimated maximum value of daily intake of Mo is lower than the EPA Oral Reference Dose at both Furnace Creek and Middle Basin. Compared with the dose estimates for the Furnace Creek area, peak annual dose estimates for Middle Basin are lower for both climate states, primarily due to the absence of a drinking water pathway at this location. The NRC staff concludes that the incremental impacts from non-radiological (and radiological) contaminants associated with natural groundwater discharges at Furnace Creek and Middle Basin would be small. For Alkali Flat, the NRC staff did not calculate estimates of contaminants in the groundwater (or soils). It is considered that while the exposure pathways at Alkali Flat would be the same as those for Middle Basin, Alkali Flat is further from present population centres and has even

fewer visitors or temporary occupants and therefore the impacts there would be a small fraction of those calculated for the other surface discharge locations.

In Canada, in 2015, NWMO created a document outlining their approach for defining criteria for the assessment of risks to humans and the environment from non-radiological contaminants (Medri, 2015). These criteria are being used in our current case studies. NWMO's previous safety assessments have assessed effects to chemical contaminants to the environment and people using a similar methodology, for example, inthe development of a post-closure safety assessment for the Deep Geological Repository (DGR) for L/ILW radioactive wastes. The post-closure safety assessment (Quintessa, 2011) forms part of the supporting documentation for the DGR's Environmental Impact Statement and Preliminary Safety Report which were submitted for regulatory review in April 2011. Both radiological and non-radiological contaminants were considered in risk assessment calculations (undertaken using the compartmental modelling tool AMBER) which considered both 'normal evolution' and 'disruptive' scenarios. Non-radiological substances identified in the inventory include several metals, metalloids and classes of organic compounds (PCB and PAH, Quintessa and Geofirma, 2011). Calculated concentrations were compared against environmental standards (federal and provincial guideline concentrations for groundwater, surface water, soil and sediment). For the Normal Evolution Scenario, concentrations of radionuclides and of non-radioactive contaminants in surface media are well below the relevant environmental protection criteria. For Disruptive Scenarios, impacts are also low. All non-radioactive contaminants and most radionuclides have calculated concentrations in surface media that are well below their screening concentration criteria for the base cases (some local exceedances of screening criteria for the Human Intrusion Scenario and the Severe Shaft Seal Failure Scenario did occur, but, for these scenarios, the assessment criteria are conservative and the scenarios are very unlikely).

The current situation with respect to the assessment of non-radiological substances in Belgium is outlined in notes from a recent workshop hosted by SKB (Thorne and Kautsky, 2016). LLW is to be disposed in a surface facility at Dessel. Both ILW and high level waste (HLW) are intended for disposal in a deep geological facility, but no Decision in Principle (DiP) has yet been taken. Possible disposal strata are the Boom Clay and the Ypressian Clay. ONDRAF recognises the importance of public participation in the siting process and has a strategy plan to achieve a DiP (completed 2010) aiming for a DiP at around 2020. The impact of toxic chemicals is included in the environmental impact component of the safety assessment. Currently, evaluations of the impact of toxic chemicals are based on computing concentrations in the aquifer above the Boom Clay formation and making comparisons based on drinking water standards. A major difficulty is that the composition of the waste in drums is not well known. Therefore, inverse calculations are used to calculate potentially acceptable amounts, with a view to emphasising to waste producers that this information is required. Currently, acceptance criteria are being reviewed, but none have yet been adopted.

The current situation with respect to the assessment of non-radiological substances in France (Andra) is also outlined in Thorne and Kautsky (2016). Three steps are required:

- Definition of the list of toxic substances;
- Determination of the mass inventory of each of those substances;
- Choice of reference toxicological values for each substance.

The key substances were identified as Pb, B, Ni, Cr {including Cr(VI)}, As, Sb, Se, Cd, Hg, Be, CN, U and asbestos. The selection was based on requirements in French and European legislation together with information on arisings from specific operations at nuclear facilities. In the future, PAHs are likely to be added, and specific consideration will be given to carcinogenic, mutagenic and reprotoxic agents. Risk indicators have been adopted for limiting potential exposures to these substances. For non-carcinogenic substances, the hazard index must be < 1. For carcinogens, the excess lifetime risk must be < 10^{-5}.

The impact assessment process proceeds through the following steps:

- Identification of the protection objectives;
- Identification of the potential inventory;
- Application of the same exposure scenarios (water and air transfers) as for radionuclides;
- Consideration of the specific physico-chemical behaviour of each toxic element;
- Estimation of concentrations of released material (in water and air);
- Calculation of the Risk Factor and Excess of Individual Risk with reference toxicological values (using an Andra database from national and international bibliographic data);
- Evaluation of non-cancer effects by calculation of "Hazard Factor" = level of absorption (inhalation or ingestion)/reference toxicological value and comparison with the protection objective;
- Evaluation of cancer effects by calculation of Excess Individual Risk = level of absorption (inhalation or ingestion) x reference toxicological value (also called Unit Excess Risk) and comparison with the protection objective.

Summations of Hazard Factors and Excess Individual Risks, both over substances and over ingestion and inhalation, are required in demonstrating compliance with the protection objectives. Relevant toxicological databases were identified as including those of US EPA, WHO and ATSDR. It was noted that data for sub-chronic and acute exposure situations are often limited compared with data for chronic exposure situations. Andra has asked INERIS (L'Institut National de l'Environnement Industriel et des Risques) to provide relevant toxicological values.

Regarding L/ILW in Sweden the SFR repository may contain limited amounts of Pb, asbestos and epoxy resins, but other hazardous materials are not accepted (Thorne and Kautsky, 2016). In the case of the SFL repository, for waste containing larger amounts of long-lived radionucldides, acceptance criteria have not yet been defined. Known toxic materials that might be disposed to SFL include Cd in control rods and neutron reflectors, Be in neutron reflectors and Pb, mainly as legacy shielding scrap. Lead mats may also be disposed to SFR. There are also significant amounts of Cr present in ash from incineration. Sludges, ion-exchange resins, evaporator concentrates and filter aids will contain heavy metals (mainly derived from corrosion of stainless steels), decontamination chemicals, flocking agents and bitumen (which is not considered a toxic material and is used to immobilise some of the wastes). Operational waste with trash and scrap will also contain heavy metals, again largely from stainless steels, oils, solvents, paints, adhesives and coatings, and unknown amounts of asbestos. Legacy waste with trash and scrap to be disposed in SFL is estimated to contain 68 kg of Cd and 2648 kg of Pb. X-ray analysis of legacy trash and scrap has revealed fluids suspected to be Hg. A total estimated volume of five litres has been reported. This would result in 70 kg for disposal in SFL and 31 kg disposed of in SFR. Decommissioning waste mainly consists of concrete and steel. Hazardous organic substances may be present in limited amounts, but these will likely be cleared and treated as conventional material or sent to a controlled incineration facility. Some asphalt is to be disposed, but this is not generally considered to be a hazardous waste, unless it contains coal tar.

In the SKB workshop (Thorne and Kautsky, 2016), the purpose and scope of the Merlin-Expo Tool that has been developed since 2007 in a series of EU-funded projects was outlined. The initial project developed a prototype that has subsequently been developed for marketing. This Tool integrates within an overall software framework models for contaminant transport, accumulation in environmental media, and behaviour affecting exposure, as well as physiologically-based pharmacokinetic, plus biological response models. A library of such models is available and these can be used in various combinations. The system also incorporates advanced functionality for uncertainty and sensitivity analyses. In terms of a tiered approach to assessing the impacts of releases of toxic chemicals to the environment, the Merlin-Expo Tool is envisaged as being applied at the highest tier of detailed, site-specific assessments. Simpler tools will generally be more

appropriate in more generic assessments. Merlin-Expo has been benchmarked against EUSES (the European Union System for the Evaluation of Substances). Model scenarios that have been simulated include internal exposures to PAHs following atmospheric dispersion, distribution of BaP in a freshwater system and resulting internal exposures via drinking water, and assessments of impacts on biota of persistent organic pollutants (PCBs). Reverse modelling has also been undertaken for the reconstruction of past exposures, e.g. reconstruction of exposures of Italian women to PCBs through measurements of concentrations in breast milk. The extension of the modelling framework to estimating impacts on non-human biota is a recent development. In the study of the impact of PCBs in the Venice lagoon, a classic food-web approach was used and good agreement between measured and predicted concentrations was obtained. Other recent work has used the modelling system to investigate specific processes.

3.1.9 Summary of Data Requirements for Quantitative Human Health Risk Assessments of Chemotoxic Substances

The data required for human health risk assessment reflect contents of Sections 3.1.1 to 3.1.8 and can be considered within the source-pathway-receptor framework.

In assessing potential land contamination, source(s), identities and quantities of hazardous substances present in environment media are required. It may be the case that a complex mixture of a group of substances is present (examples could include PAH, dioxins/furans) and only a selection of individual compounds within the group may be included in chemical analyses of environmental media. Generally, regarding land that might be contaminated, the focus of chemical analysis is soil, with releases of substances from soil to other environmental media being calculated in exposure assessment tools (such as CLEA, Environment Agency, 2009a-c). However, if there is concern over the effect of contamination on water or air quality, environmental sampling and analysis could include these media.

For assessing existing radioactive waste disposal sites and uranium mining liabilities, site monitoring data may be used along with inventory data in risk assessments. For planned disposals, existing or predicted inventory data (based on rate of waste generation and time to which disposals will begin) will be required. Inventory data tend to include masses of metals/metalloids, other inorganic substances and organic compounds for different waste streams. For some contaminants, the compounds in which they are likely to occur will be required in consideration of their potential for release (generally to groundwater). For example, U may exist in different redox states. The distribution of materials amongst underground vaults will also need to be considered in risk assessment (to determine the potential for interactions and to characterise release pathways).

Regarding contaminant transport in contaminated land assessment, the following will need to be considered:

- the identity and nature of transport pathways between different environmental media (e.g. soil, soil adhered to home-grown produce, soil-derived dusts, vapours, home-grown produce)
- the identification of most appropriate models for modelling contaminant transport, which could consider simple rates of transfer between different media, coefficients to describe partitioning of substances between different media, or more complex ‘mechanistic’ models.
- Input data for the transport models: physical and chemical properties of the contaminants (such as water solubility, vapour pressure), transfer rates/partitioning coefficients for contaminant distribution between different environmental media, other input that may influence such properties, such as soil type, pH, organic matter content.

For radioactive waste disposal systems, the release rates of contaminants from wastes or waste forms will be of interest, either as simple fractional release rates (or corrosion rates), or from more

complex kinetic models requiring a consideration of reaction rates and surface areas. Credit may be taken for waste containers (if present) to delay releases. In general, container lifetimes are estimated based on general rates of corrosion and container wall thicknesses. Models for performance assessment developed using compartment modelling tools (such as GoldSim and Amber, inter alia) are likely to be informed by other more complex models (e.g. of regional groundwater flow). Generally, rates of water flow are required for releases from the near to the far field (though releases can be diffusion dominated in some contexts), with, where relevant, the application of solubility limits and a consideration of contaminant retardation, which is generally modelled using a K_d approach, with values being needed for each substance (noting redox dependence for some substances). Solubility limits for some substances could also be applied in the geosphere instead of K_d values, if solubility limitation is the dominant control. These data allow fluxes of contaminants to be calculated and input into biosphere models/sub-models which consider all the different relevant exposure pathways (e.g. Figure 3-5). As in contaminated land assessment, the equations used in the models to describe transfer of different contaminants between different media will require input data often in the form of partitioning coefficients of concentration factors (potentially for both outdoor and indoor environments).

The nature of the biosphere model or sub-model will determine the data required for it. For contaminated land assessment in the UK, a female child has been taken to be a critical receptor in residential land use settings, whereas an adult female has been adopted as the critical receptor for commercial/industrial land use. To calculate exposures to environmental media (in particular, intakes via oral, inhalation and dermal pathways) assumptions have to be made on the duration of exposures to different environmental media (often reflecting behaviour), and oral ingestion/inhalation rates and skin fraction exposed.

In general, risk assessments for radioactive waste disposal facilities consider similar receptors (e.g. individuals representative of the more exposed in the population) and similar data are needed for calculating intakes, if such an approach is used rather than the comparison of calculated concentrations of contaminants to relevant standards/guidelines.

3.1.10 Comparison with Radiological Risk Assessment Approaches

To a large extent, the approach to be adopted in modelling the impact of non-radiological contaminants is like that adopted for radionuclides. In the near-field of a repository, the radiological risk assessment needs to address releases of radionuclides from the wastes, and the effects of solubility limitation and sorption. The main difference is that most radionuclides will be present at trace levels, so, for example, solubility will be controlled by co-precipitation with other chemical species present at larger mass concentrations. In the geosphere, solubility limitation is seldom invoked for radionuclides, but sorption remains an important consideration. In the biosphere, similar modelling approaches can be used for both radionuclides and non-radioactive contaminants, particularly the metals and metalloids.

The main difference in approach between non-radioactive contaminants and radionuclides comes in the assessment of impacts. For non-radioactive contaminants, concentrations in air or rates of intake per unit body mass are generally related directly to the likelihood of occurrence and/or severity of health effects. Only in a few special cases is an additional step introduced in which tissue concentrations are calculated as an intermediate to health effect estimation. These special cases include the estimation of blood Pb levels in children and the estimation of peak kidney concentrations of U in occupationally or environmentally exposed individuals. In contrast, for radionuclides, all exposures both external and internal are expressed in terms of radiation dose. Furthermore, because the doses and dose rates are generally assessed as low, deterministic effects (tissue reactions) are not of relevance and effective dose (or committed effective dose for internal exposure) provides a single measure that can be summed over all radionuclides and exposure pathways and used to estimate the risk of induction of cancer in the exposed individual or serious hereditary disease in their descendants. Thus, within the framework of radiological protection,

effective doses from different radionuclides are treated as additive, irrespective of the key target tissues and organs, different degrees of protraction of exposure, and different types of radiation involved. Thus, radiological protection sidesteps the issue of synergies between different components of exposure, although investigation of this topic remains an active area of radiobiological research (see Appendix B).

Furthermore, radiological protection has introduced the concept of health detriment. Thus, a tissue weighting scheme has been introduced that includes fatal cancer, non-fatal cancer and hereditary disease in a single measure of the adverse impact on human health. For non-radiological contaminants, no such measure exists, so each health effect must be treated separately in the standards setting process. As these health effects range from subtle biochemical changes or decreases in functionality in a particular tissue to the induction of gross malformations in utero and fatal cancer, the development of a single measure of adverse impact is likely to be difficult. One possibility is to base such a measure on years of life lost or impaired, with a weighting for the subjectively assessed degree of impairment, as discussed in ICRP (1977b).

Thus, in summary, release and transport calculations for non-radiological contaminants and radionuclides can be very similar. However, considerable new work is required to develop a commonality of approach to evaluating impacts on human health. This is likely to require increased use of biokinetic models for non-radioactive contaminants, so that concentrations in key target tissues and organs can be used in the estimation of health effects, together with development of a single measure of adverse impact on health analogous to the concept of health detriment used in radiological protection.

3.2 Ecological risk assessment

Ecological risk assessment[18] (ERA) is the process of evaluating the nature and likelihood of effects of human-induced stressors on animals, plants and the environment. The approach has been developed from the established risk assessment framework for human health (Section 3.1) and there are, therefore, close similarities between human risk assessment and ERA (Suter et al, 2000). ERA is a useful risk management tool that helps identify and prioritise the greatest risks to the environment, which in turn supports the allocation of resources, and allows the consequences of management actions such as clean-up options to be evaluated through exposure and effects analysis (SETAC, 1997). A harmonised approach to risk assessment for human health and the environment also helps to avoid unnecessary duplication of effort, particularly regarding data requirements for source characteristics and environmental transport (Björk and Gilek, 2005).

3.2.1 Overview of ERA approach

The principal stages of an ERA (US EPA, 1992a; SETAC, 1997; Gormley et al, 2011) are as follows, and illustrated in Figure 3-6:

1. **Problem formulation:** clearly defining the problem and scope of the assessment. This should involve the development of a conceptual model that identifies the hazards and their source and the ecological receptors of interest and particularly any protected habitats or species. The components of the problem formulation stage are: framing the problem (risk of what to which environmental receptor, when and where); conceptual model development; risk assessment planning; screening and prioritising risks to be assessed. In the context of hazardous waste disposal, questions such as ‘what is the risk of an environmental release from an engineered, contained system?’, ‘what area and how many people will such a release affect?’ and ‘for how long will they be affected?’ may be appropriate.

[18] Alternatively referred to as ‘environmental risk assessment’

2. **Analysis**: identification of hazards and characterising the potential or existing exposure of biota within ecosystems to those hazards and the associated effects. Hazard identification involves considering various stressors that could lead to harm, including consideration of secondary effects such as biomagnification of a substance through the food chain. Exposure assessment involves quantifying the concentration in environmental compartments and media (e.g. air, soil, and water), taking into account transport pathways, degradation and retention in different media. The spatial and temporal patterns of exposure and their magnitude are therefore estimated. *Effects assessment* then considers the incidence and severity of effects that may arise at the levels of exposure that may occur. Describing and estimating the level of uncertainty associated with exposure and effects assessment may also be appropriate. Source-pathway-receptor analysis can be useful in conceptual model development, allowing processes and features to be screened from further analysis.
3. **Risk characterisation:** integrating exposure and effects profiles and estimating risk. The incidence, severity and probability of effects likely to occur due to actual or predicted exposure to a substance or substances is estimated through, for example, the calculation of the ratio between contaminant concentrations in environmental media and guideline values or quality standards (i.e. the PEC/PNEC ratio or risk quotient).
4. **Planning the assessment and engaging with stakeholders** are important additional aspects that may help to ensure the output will provide the required information and address the appropriate ecological concerns (US EPA, 1992a). The overall decision-making process may also require cost/benefit analysis, technical feasibility studies and consideration of legal mandates and political requirements (SETAC, 1997). In undertaking an ERA, a tiered approach to assessment is often employed, whereby the complexity of the assessment and the associated data requirements increase with each tier, whilst the level of conservatism decreases. Such an approach allows resources to be focussed where they are most required (Björk & Gilek, 2005). The procedure is illustrated in Figure 3-7.

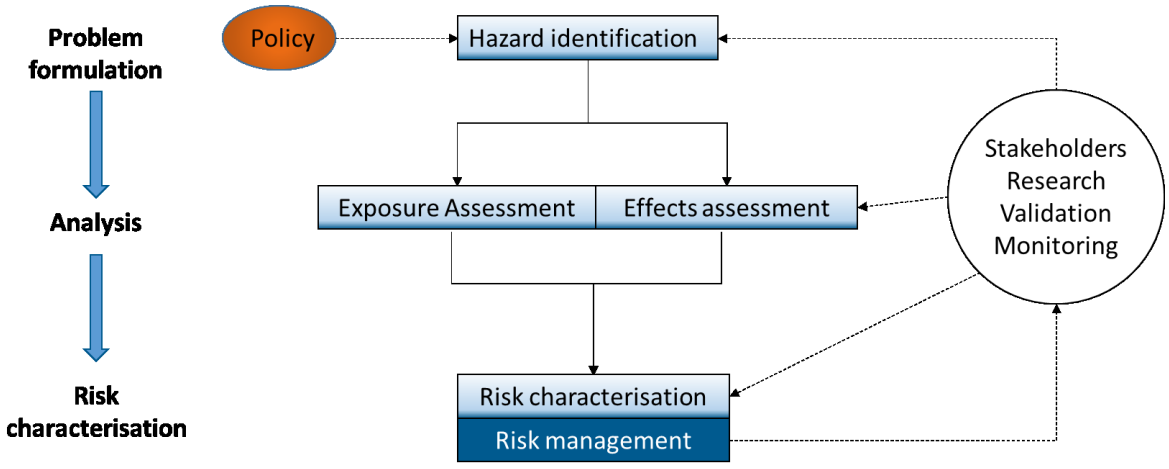

Figure 3-6. Stages in an ERA (adapted from Björk and Gilek (2005)).

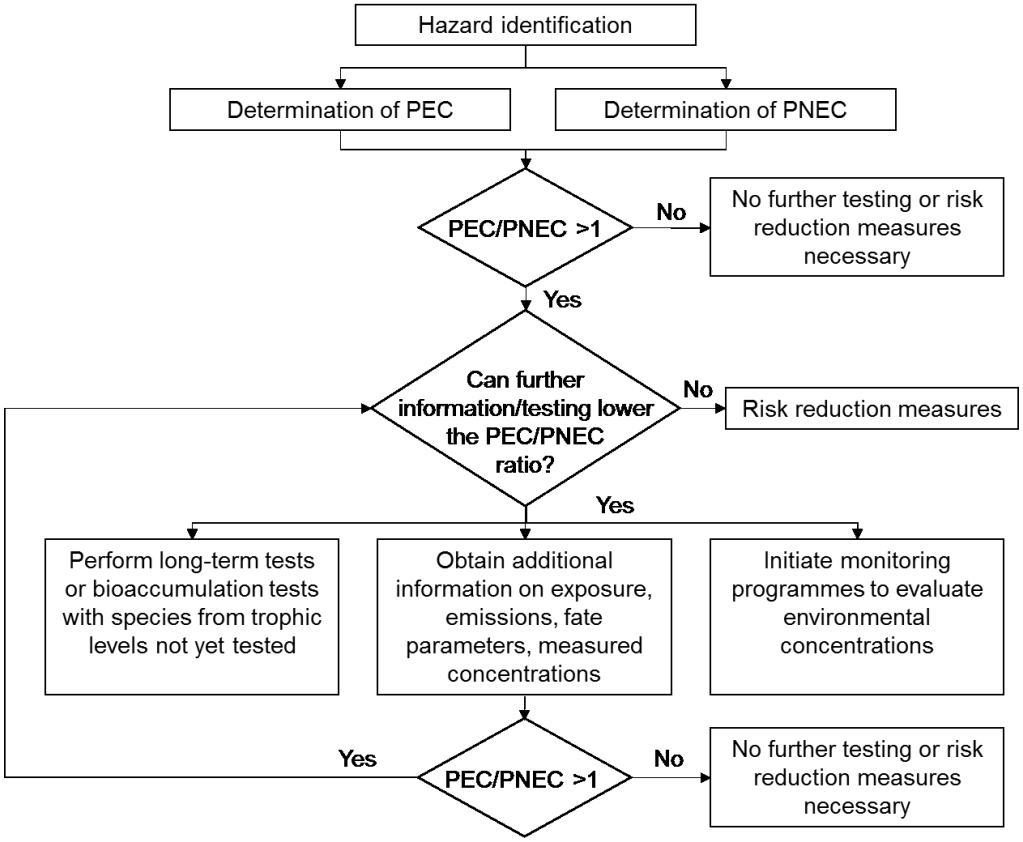

Figure 3-7. General procedure for ecological risk assessment (adapted from European Commission (2003b)).

Bioavailability is increasingly considered when evaluating the risk to the environment from hazardous substances, with EQS values being increasingly derived that relate to the bioavailable concentration of a substance (Bass et al, 2008). The persistence of a substance in the environment is also normally considered, although degradation products are seldom evaluated for their effects on the environment (Björk and Gilek, 2005). The risk to the environment, as illustrated in Figure 3-7, is evaluated by assessing the concentration in the environment arising from a source (the PEC) and comparing this against a relevant benchmark or standard (the PNEC). Where concentrations remain below the standard, risk to the environment can be considered low. Whilst a ratio of 1 is illustrated in Figure 3-7 for triggering decisions, different fractions of a PNEC may be applied at different tiers of assessment to ensure screening assessments are associated with a high degree of confidence.

3.2.2 ERA in a radiological assessment context

A tiered ecological risk characterisation methodology has been developed for ionising radiation within the EC ERICA project (Beresford et al, 2007), which drew largely on the ERA approach for hazardous substances, in recognition of the similar requirements in terms of evaluating exposure and effects irrespective of the type of ecological stressor (Björk and Gilek, 2005). The steps associated with a radiological ERA are therefore consistent with those illustrated in Figure 3-6. There are, however, some differences that arise as a result of the nature of the hazard. The primary differences between the radiological and non-radiological approaches stem from the fact that the former is assessed based on absorbed dose rate-response relationships whereas the latter is based on exposure concentration-response relationships. Dose rate takes into account both internal and external exposure whereas for hazardous chemicals, the focus is on internal exposure, since external exposure to a chemical is seldom deleterious unless there are toxic or allergenic reactions

with epidermal tissues. However, dermal absorption can contribute to internal exposure and may need to be taken into account.

In assessing the risk of adverse effects of ionising radiation on the environment, common practice is to evaluate the absorbed dose rate from exposure to all radionuclides of interest for a range of organisms that are representative of the environment. In some contexts, the contributions to absorbed dose rate from high- and low-LET radiations may be evaluated separately. With external exposure being part of the evaluation, the occupancy of organisms in different environmental media is also considered (e.g. occupancy of the soil surface or within the soil column). This contrasts with the approach for hazardous substances for which an environmental concentration is evaluated for the media of interest (e.g. soil, sediment, water) and compared directly with assessment benchmarks or standards derived from exposure-effect data; uptake into biota is not specifically evaluated. Assessment benchmarks for ionising radiation are derived using broadly consistent approaches to those for hazardous substances, but the exposure assessment is more complex, requiring absorbed dose rates for different types of animal and plant to be evaluated in terms of both internal and external exposure, and for high- and low-LET radiations.

Because it is not feasible to obtain toxicity data for all organisms in an ecosystem and for all chemicals to which they may be exposed, representatives of major taxonomic groups are usually used as test organisms to act as surrogates for the whole ecosystem (European Commission, 2003b). With the lack of effects data for individual substances, risk assessments involving multiple stressors can be a particular challenge (see Appendix B)[19], as can consideration of population and ecosystem effects from information on individual organisms and species[20] (SETAC, 1997). This is less of an issue for ionising radiation where absorbed dose rates are summed across all radionuclides, taking account of the relative biological effectiveness of different radiations. Furthermore, for radionuclides, radioactive decay and the ingrowth of progeny needs to be considered, with progeny potentially leading to an increased hazard, whereas for hazardous materials, the environmental effects of degradation products are not commonly evaluated (Björk and Gilek, 2005), though biochemically mediated processes can sometimes produce degradation products that are more toxic than the originating substance. This is the case, for example, for vinyl chloride monomer, which is degraded in the liver of mammals by the mixed-function oxidase system (Thorne et al., 1986).

3.2.3 Future directions

In assessing the environmental impacts of exposure to either ionising radiation or toxic chemicals, it is typically the case that effects are studied at one level of biological organisation, whereas the primary interest is often in the expression of effects at a different level or levels. For example, effects may be studied at the level of the individual cell (e.g. in *in vitro* cell cultures), in individual tissues or organs (either in vivo or as ex vivo preparations), in intact organisms, or in populations (e.g. multi-generation colonies maintained in laboratory conditions) or communities. The observed effects will then need to be related to impacts at the individual, population, community, habitat or ecosystem level. Furthermore, effects observed under laboratory conditions will need to be translated into implications for impacts in field conditions, where both genotypes and phenotypes may be more diverse, and where key impacts may relate not to the viability of individual organisms, but to broader-based concepts such as biodiversity, sustainability, ecosystem stability, habitat diversity, and the continued provision of ecosystem services. Development of an ecosystem

[19] One approach for addressing multiple hazardous substances within effluents is to undertake a Direct Toxicity Assessment whereby the toxicity of the mixture of substances is evaluated in rapid screening toxicity tests.

[20] Ecosystems and communities are highly complex and factors such as resilience and recovery, among others, are important in determining the long-term effects of contaminants on ecosystem structure and function.

approach to environmental protection, including radiological hazards, is discussed in Bréchignac et al (2012).

The complexities outlined above strongly suggest that experimental and field observations need to be embedded and utilised within an appropriate theoretical framework. It seems likely that the most appropriate such framework is that of systems ecology. Systems ecology is an interdisciplinary field of ecology that takes a holistic approach to the study of ecological systems, especially ecosystems (Shugart and O'Neil, 1979; Odum, 1983). Systems ecology is an application of general systems theory to ecology. Central to the systems ecology approach is the idea that an ecosystem is a complex system exhibiting emergent properties. Systems ecology focuses on interactions and transactions within and between biological and ecological systems, and is especially concerned with the way the functioning of ecosystems can be influenced by human interventions. It uses and extends concepts from thermodynamics and develops other macroscopic descriptions of complex systems.

A key consideration in adopting a holistic approach to biological systems is the primary role played by interactions between the components of the system, whether they be individual cells within a multicellular organism or individual organisms within a community. At the community level, those interactions may be described as the rules of engagement. Those rules of engagement vary considerably from one community to another. Broadly speaking, there are three models of how species richness relates to ecosystem performance (defined in terms of fluxes of energy and matter). The redundant species hypothesis suggests that there is a minimum of species diversity necessary for ecosystem functioning, but, beyond this minimum, most species are redundant in their roles. In contrast, the cumulative hypothesis postulates that all species are important, so that ecosystem processes are progressively more impaired as species are lost from the system (Lawton, 2000; Thorne, 2012).

The idiosyncratic hypothesis postulates that the identities of particular species matter more than species richness per se. In consequence, ecosystem processes might change erratically and unpredictably if species are lost in an arbitrary sequence from the system (Lawton, 2000). Under both the redundant species and idiosyncratic hypotheses, species could be lost from an ecosystem without affecting its performance. Although local biodiversity would be impaired, global biodiversity might be unaffected. Furthermore, if exposure to a stressor or stressors caused the local mix of species to change, biodiversity might be increased, because the area of high stress would constitute a new and distinctive habitat patch.

It should also be recognised that communities do not exist in a vacuum. Rather, they are strongly determined by the regional 'pool' of species that exists within a biogeographic region extending over a spatial scale several orders of magnitude larger than that of the local community. Local communities establish themselves from this 'pool' through a series of filters. First, species must arrive before they can establish populations. The probability of this occurring depends on the structure of their geographic ranges. If a species can reach a site, it may still find the environment unsuitable. More subtle filters operate at the landscape scale. Here the effects of number, area, shape and spatial arrangement of habitat patches can strongly mould the characteristics of local assemblages. Overall, from a consideration of regional influences, Lawton (2000) draws the following three conclusions:

- The richness of local species is not only determined by their interactions. For a majority of systems, richness in assemblages of species and in local guilds appears to be primarily determined by changes in the size of the regional species pool.
- Local population dynamics are also not solely the product of local interactions. They too are modified and influenced, sometimes strongly, by regional processes.
- The role that any one species plays within the community varies spatially within its geographic range.

Together, these conclusions suggest that ecologists will neither be able to understand or predict the consequences of change for ecological communities by considering only local processes. Events well beyond the immediate area of the community can drive significant local changes in species richness, as well as in species composition, population abundances and the dynamics of local assemblages. Discerning the local effects of exposure to stressors such as ionising radiation or toxic chemicals in communities that are so strongly influenced by external factors is likely to be difficult, unless the effects of exposure are both gross and distinctive (Thorne, 2012).

Given the importance of regional factors, it is not surprising that important processes and community dynamics differ, often markedly, from system to system. Although there is now a good understanding of how several local sets of interacting species work in nature, there is currently no way to predict which processes will be important in particular systems. As Lawton (2000) has said, 'by painstakingly detailed studies of particular local systems, it is possible to understand the local rules of engagement for interacting species at one place and time. However, almost every place, time and species assemblage is sufficiently different to make more general rules and patterns impossible to find.'

In the context of the above remarks, it is clear that progress in evaluating the environmental significance of stressors such as ionising radiation and toxic chemicals has to proceed at several different levels, but that there should also be cross-cutting research, including mathematical modelling, to establish relationships between observations made at these different levels.

At the most detailed level, it is important to develop an understanding of the biochemical mechanisms that determine the impact of stressors. This is necessary because it will never be possible to investigate directly the significance of exposures to different levels of stressors, singly or in combination, for the wide diversity of organisms present in the environment. However, by developing an understanding of the underpinning biochemical mechanisms, it may be possible to generalise observations with particular stressors and types of test organism to a wide variety of situations of interest. For example, the degree to which reactive oxygen species are induced in the intra-cellular milieu may provide a common basis for assessing the likely effect of both ionising radiation and various cytotoxic and genotoxic chemicals.

On a related point, development of an understanding of biochemical mechanisms and their significance may be facilitated by the identification and exploitation of suitable biomarkers, i.e. biological changes indicative of exposure to a particular stressor or class of stressors. These may be either biomarkers of exposure, with the level of expression related to the degree of exposure to the stressor, or biomarkers of impact, with the level of expression related to the degree of adverse effect. In this context, studies of epigenetic effects may be of particular interest (see COMET, 2013, for background). In the context of ionising radiation, this was the topic of a recent workshop (COMET, 2015), where it was concluded that the revolution in understanding of epigenetic mechanisms that has occurred over the last decade has provided environmental toxicologists with access to a wealth of new methods and tools. Although the main focus to date has been DNA methylation, the widespread availability of methods for analysis of miRNAs and histones suggests that these should also be a focus of study. Key areas of future work that emerged from discussion are as listed below.

- Fundamental studies of genome-wide methylation patterns across species from different taxa to assess the different roles of DNA methylation in gene regulation, including expression levels and alternative splicing.
- Further work on the role of DNA methylation as a first case study of the role of epigenetic mechanisms in species responses to radionuclide (and chemical) exposure.
- Studies to assess the specific role of DNA methylation as a potential biomarker of exposure, including the potential for cytosine modifications to act as a 'memory' of exposure for individuals that have been subject to time varying exposures.

- Studies using non-coding RNAs in radiological and ecotoxicological reference species, including assessment of the link between the changing non-coding RNA complement and gene expression.
- Assessing comparative radio-sensitivities and chemical sensitivities for different organisms of different phylogeny to allow assessment of the role of physiological traits, including the epigenome, in sensitivity.
- To determine what protection goals are most important in various contexts, and to understand how information gained from epigenetic studies can support decision making in these contexts.

However, the focus should not solely be on epigenetics. Studies of other endpoints are also important including those related to macrophenotypes (growth, development, reproduction etc.) and effects on genome architecture. These have been identified as being of vital relevance when considering the nature of transgenerational effects (COMET, 2015). COMET (2015) particularly emphasises the need to link detailed studies of mechanisms to a programme of observations at the level of the phenotype. Thus, a key cross-cutting element of the research agenda needs to be experimental and modelling studies that relate changes at the sub-cellular level to changes at the levels of tissues, organs and the whole organism. Furthermore, as in the COMET programme, sub-cellular changes and their sequelae at the organism level need to be explored in a variety of types of organism representative of different taxa. For convenience of comparisons between the effects of different stressors, it is appropriate to adopt a standard set of model organisms. Typical model organisms used in ecotoxicology are zebrafish, *Lemna* (duckweed), earthworm, *Caenorhabditis elegans* (roundworm) and *Daphnia* (COMET, 2015).

In order to relate effects at the individual organism level to effects at the community or ecosystem level, it might be thought necessary to develop systems models. However, as stressed above, responses in different ecosystems or communities with similar characteristics may be significantly different. Therefore, a more realistic aim may be to determine levels of exposure to stressors that cause changes in the behaviour or physiology of organisms that are substantially less than the variability in behaviour or physiology observed in natural communities or ecosystems. Specifically, it may be appropriate to examine variability in communities or ecosystems subject to gradients in the particular stressors of interest and other factors, so that changes in laboratory and field conditions, and in the presence of confounding factors, may be compared. The observatory sites being developed in collaboration with the COMET programme, e.g. in the Chernobyl exclusion zone and at Fukushima, should facilitate such laboratory-field comparisons, and samples are being acquired from the observatory sites for epigenetic analysis with this intent.

4 Review of content and application of groundwater protection legislation as applied to waste disposal facilities

This section provides examples of regulatory requirements and guidance specifically related to protection of groundwater, e.g. the European Commission's Groundwater Directive (European Commission, 2006a; 2014), a daughter directive to the EU Water Framework Directive (2000/60/EC, European Commission, 2000). This legislation has implications for the assessment of disposal of radioactive and hazardous wastes. Similar legislation exists in other parts of the world.

4.1 Groundwater and protection of humans and as a resource

In the EU, groundwater protection is achieved through the EU Groundwater Daughter Directive (GWDD), as amended (European Commission, 2006a; 2014). This requires that inputs (or discharges, though the two terms are not precisely equivalent) of pollutants to groundwater are either prevented or limited, to avoid or control groundwater pollution. In so doing, such measures should also prevent the deterioration of the chemical status of groundwater bodies and avoid (environmentally) significant and sustained upward trends in the concentration of pollutants in groundwater. An important consideration is that the quality of groundwater should be preserved in the potential presence of multiple sources of contamination. Thus, releases of radionuclides and non-radiological contaminants from a repository for radioactive wastes are only one potential source of degradation of groundwater quality.

According to the underpinning WFD (European Commission (2000)) the member states must elaborate specific measures to prevent or to limit the input of contaminants with the aim to ensure that the status of groundwater is not deteriorated and the contaminants do not show an upward trend. The contaminants to be controlled and limited are listed in WFD Annex VIII: organo-halogen compounds, organo-phosphorous compounds, organo-tin compounds, substances which have been proved to possess carcinogenic or mutagenic properties, persistent hydrocarbons, and persistent and bioaccumulating organic toxic substances, cyanides, metals and their compounds, arsenic and its compounds, biocides, materials in suspension, nitrates, phosphates and substances which have an unfavourable influence on the oxygen balance, and other contaminants of concern for each Member State. The limits must include the attenuation capacity of the unsaturated zone.

Subsequently, the GWDD ((2006/118/EC) was issued. This covers preventing and controlling groundwater pollution, setting measures for assessing the chemical status of groundwater, and measures to reduce the presence of pollutants.

The GWDD responds to the requirements of Article 17 of the WFD and introduces, for the first time, quality objectives obliging Member States to monitor and assess groundwater quality, based on common criteria, and to identify and reverse trends in groundwater pollution. This Directive aims to ensure good status of all waters in the EU by means of pressure and impact analysis results (Article 5 and Annex 2) and setting quality threshold values.

The objective of the GWDD is to protect groundwater against pollution and deterioration through the establishment of specific measures to protect and control groundwater pollution. The Directive requires identifying the chemical status of groundwater. Specifically:

- It fixes the limits for nitrate and pesticide concentrations; and

- It requires Member States to establish threshold values for As, Cd, Pb, Hg, ammonium (NH4), chlorine (Cl), sulphate (SO4), perchloroethene (PCE), trichloroethylene (TCE) and electrical conductivity. These threshold values must take into account the intrinsic or natural concentrations.

The so-called intrinsic or natural concentrations may significantly vary among different groundwater bodies. Therefore, in 2014, a relevant amendment to the GWDD appeared (European Commission, 2014) where the approach to fixing background levels in areas with elevated levels of substances or ions due to hydrogeological causes is specified as follows.

'Wherever elevated background levels of substances or ions or their indicators occur due to natural hydrogeological reasons, those background levels in the relevant body of groundwater shall be taken into account when establishing threshold values. When determining background levels, the following principles should be considered:

a. The determination of background levels should be based on the characterisation of groundwater bodies in accordance with Annex II to Directive 2000/60/EC and on the results of groundwater monitoring in accordance with Annex V to that Directive. The monitoring strategy and interpretation of the data should take account of the fact that flow conditions and groundwater chemistry vary laterally and vertically;

b. Where only limited groundwater monitoring data are available, more data should be gathered and in the meantime background levels should be determined based on those limited monitoring data, where appropriate by a simplified approach using a subset of samples for which indicators show no influence of human activity. Information on geochemical transfers and processes should also be taken account of, where available;

c. Where insufficient groundwater monitoring data are available and the information on geochemical transfers and processes is poor, more data and information should be gathered and in the meantime background levels should be estimated, where appropriate based on statistical reference results for the same type of aquifers in other areas having sufficient monitoring data.'

Also, in 2013, Directive 2013/39/EC appeared (European Commission, 2013), amending Directives 2000/60/EC and 2008/105/EC as to priority substances in the field of water policy.

As can be inferred from the previous paragraphs, there is no unique way to implement the GWDD, and threshold values for contaminants may strongly depend on background levels.

4.1.1 Groundwater Protection in the UK

The primary sources of guidance for assessment of a radioactive waste repository are the Environment Agency and Northern Ireland Environment Agency (2009) and Environment Agency et al., (2009), for geological and near surface disposal respectively. The potential implications of the EU GWDD are most readily illustrated by considering how they have been translated into legislation and regulations.

In the UK, the regulatory context is most readily defined by reference to the environmental permitting guidance relating to groundwater activities (Defra, 2010). In this context, groundwater activities refer to the discharge of a pollutant that results in or might lead to a direct or indirect input to groundwater, together with any other discharge that might lead to direct or indirect input of a pollutant to groundwater. Groundwater is very broadly defined as all water that is below the surface of the ground in the saturation zone and in direct contact with the ground or subsoil. However, this does not distinguish water in aquifers from water in other strata, nor does it distinguish waters that are more readily accessible, e.g. aquifers at shallow depths, from waters that are less accessible, e.g. waters at great depths in lower permeability formations. This point is addressed, to some degree, at paragraph 3.5 of Defra (2010), where it is stated that 'It will continue to be a technical decision of the Environment Agency to determine what is groundwater in certain

circumstances for the purposes of the Regulations. For example, in very low permeability strata, such as clays, evaporites and dense crystalline rocks it may not be possible to define a zone of saturation because the water is bound to the rock or is relatively immobile.'

However, although the Environment Agency is prepared to consider arguments that water present in geological strata is not groundwater, these arguments would probably need to be made in relation to specific sites and multiple lines of argument would likely be needed to support them.

Pollution is also defined broadly in the UK. It comprises the direct or indirect introduction, because of human activity, of substances or heat into the air, water or land, which may be harmful to human health or the quality of aquatic ecosystems or terrestrial ecosystems directly depending on aquatic ecosystems, which result in damage to material property, or which impair or interfere with amenities or other legitimate uses of the environment. Pollutants are defined in the EU GWDD to comprise both hazardous substances and non-hazardous substances, where hazardous substances are those substances or groups of substances that are toxic, persistent and liable to bio-accumulate, and other substances or groups of substances which give rise to an equivalent level of concern. In the UK, radionuclides are defined as hazardous substances.

There are no longer specified lists of substances over which control may be exercised under the GWDD and the UK Regulations. All substances that are not determined to be hazardous are potentially non-hazardous pollutants. This enables control to be exercised over polluting substances which have hitherto been beyond control purely because, regardless of their impact, they were not listed in the GWDD. In practice, the Environment Agency will need to deal with substances which are current priorities of concern and not expand the field to include all other substances in all circumstances unless they are liable to cause pollution (Defra, 2010).

In this context, it is noted that, for clarity, the Environment Agency is required to maintain and publish a list of hazardous substances (Defra, 2010). For non-hazardous pollutants, the focus is on input to groundwater bodies, where a groundwater body is a distinct volume of groundwater within an aquifer or aquifers that is either exploited by man or supports surface ecosystems. This indicates that the Environment Agency is likely to take a broader view of what constitutes groundwater in respect of a hazardous substance than what constitutes a groundwater body in respect of a non-hazardous pollutant. This needs to be kept in mind when selecting compliance points. Specifically, an aquifer at depth might be considered to contain groundwater, but not to constitute a groundwater body, whereas immobile water in a clay formation might not even be considered as groundwater.

The identification of hazardous substances is the responsibility of the Environment Agency on the recommendation of the Joint Agencies Groundwater Directive Advisory Group (JAGDAG). JAGDAG comprises a committee of experts drawn from the UK environment agencies, research and consultancy interests, the water industry and various other sector interests. In the absence of formal JAGDAG determinations, the Environment Agency may make preliminary determinations to enable it to fulfil its statutory duties. All such interim determinations are to be referred to JAGDAG for prompt review (Defra, 2010).

For hazardous substances, the requirement is to prevent their entry into groundwater. However, the term 'prevent' is used in a restricted sense. As stated in Defra (2010), during negotiations on the GWDD the nature of the duty to prevent was discussed at length and the European Commission subsequently issued Common Implementation Strategy guidance on the implementation of the Water Framework Directive and the GWDD, by way of clarification (CIS Guidance Note No. 17 – Guidance on preventing or limiting direct and indirect inputs in the context of the Groundwater Directive 2006/118/EC, section 3.4.)

This guidance (European Commission, 2007) states that (emphasis added):

> "The broadening of controls on pollutants by the WFD noted above is now balanced by a series of exemptions introduced by the GWDD (Article 6.3). It is indeed not technically

> feasible to stop all inputs of hazardous substances, and some small inputs are environmentally insignificant and therefore do not present a risk to groundwater. Without these exemptions, the "prevent" requirement would imply an onerous and sometimes unfeasible task. Each exemption applies to both the 'prevent' and the 'limit' objective (both hazardous and non-hazardous substances) but must not override other more stringent requirements in other EC legislation.
>
> To "prevent" an input into groundwater means: taking all measures deemed necessary and reasonable to avoid the entry of hazardous substances into groundwater and to avoid any significant increase in concentration in the groundwater, even at a local scale. "Reasonable" means technically feasible without involving disproportionate costs. How to define "disproportionate costs" depends on the local circumstances".

Thus, 'prevention' appears not to be an absolute requirement. Schedule 22 of the Environmental Permitting (England and Wales) Regulations 2010 states that, for the purposes of implementing the GWDD, the Environment Agency must take all necessary measures to:

> a) Prevent the input of a hazardous substance to groundwater
>
> b) Limit the input of non-hazardous pollutants to groundwater so as to ensure that such inputs do not cause pollution to groundwater

Both assessment criteria and compliance points differ for hazardous substances and non-hazardous pollutants.

Nevertheless, the term 'prevent' has been interpreted in England and Wales to mean that 'there are no discernible concentrations of hazardous substances attributable to the discharge in groundwater immediately down-gradient of the discharge zone, subject to adequate monitoring (or in the case of new discharges a detailed predictive hydrogeological impact assessment)'. (Defra, 2010, paragraph 4.18). However, it is noted that paragraph 4.18 offers the further option that prevention could be achieved if there are (or are predicted to be) discernible concentrations of hazardous substances in the groundwater down-gradient of the discharge zone attributable to the discharge, subject to all the following conditions applying:

> a) Concentrations will not result in any actual pollution or a significant risk of pollution in the future;
>
> b) There is no progressive increase in the concentration of hazardous substances outside the immediate discharge zone, i.e. there will be no statistically and environmentally significant and sustained upward trend or significant increasing frequency in pollutant "spikes"; and,
>
> c) All necessary and reasonable measures to avoid the entry of hazardous substances into groundwater have been taken.

It is important to recognise that the UK regulations now include radionuclides and other hazardous substances within the same framework. As stated at paragraph 4.11 of Defra (2010), due to their nature, it is considered that all radioactive substances are hazardous substances. This is not the case in Norway (Bratteteig, 2017).

Hazardous substances may be introduced directly or indirectly to groundwater. This distinction is generally made in terms of percolation through unsaturated soils and sub-soils, which may act to attenuate the flux. However, Defra (2010) has some comments on direct and indirect entry at paragraphs 4.24 and 4.25. These paragraphs are reproduced in full below.

4.24 The definition of 'direct' in relation to inputs to groundwater mirrors the definition used in the 1998 Regulations in respect of 'direct' discharges. As described above, this definition is interpreted to mean that, for a discharge to be construed as direct, there will have been an input to groundwater with no percolation through the soil or ground or other natural or artificial barrier.

This includes, for example, an engineered barrier or geological barrier in the case of solid waste disposal facilities.

4.25 An indirect input to groundwater is one where the input to groundwater occurs via percolation (seepage) through the soil or subsoil, including through the unsaturated zone of the aquifer in which the groundwater occurs or through a natural or artificial barrier, as noted above.

For radionuclides, 'prevention' is clearly not required to achieve 'no discernible concentrations'. Rather, Defra (2010) emphasises that inputs may be environmentally insignificant and subject to exemption. For radionuclides, Defra (2010) states at paragraph 4.28 that 'consideration should be given to the significance of any input in respect of the radiation doses which might be received by people and non-human species due, for example, to plausible future abstractions of drinking water and to natural processes involving the return of groundwater to the other environmental media.' Also, Defra (2010), at paragraph 4.29, states that 'when considering which measures are "reasonable", the radiation protection principle of optimisation should be observed.' Consideration of optimisation necessarily involves a balancing of the adverse impacts of a release against the resource requirements involved in reducing or preventing that release.

These remarks are consistent with paragraph 4.31, which states that:

> 'For disposals of any solid wastes, absolute and indefinite containment of pollutants within a disposal facility will not be achievable. At some point after a disposal facility has closed, there will eventually be some inputs into groundwater. These facilities should be designed such that the long-term inputs of hazardous substances to groundwater will be insignificant from an environmental and human health perspective.'

Note that this paragraph relates to both radioactive and non-radioactive hazardous materials.

The use of MRVs for compliance purposes was discussed in Environment Agency (2010) and Environment Agency (undated). The practical interpretation of no discernible discharge given there was that hazardous substances must not exceed the MRVs at the point of compliance. Environment Agency (2010) was almost entirely directed to the issue of downward percolation to the water table or a confined aquifer. In this context, it notes that 'typically processes of dispersion and dilution can reduce concentrations by 1-10 times, perhaps up to 100 times, depending on the size and frequency of your discharge'. Thus, dilution and dispersion in an aquifer beneath the unsaturated zone were envisaged. However, updated guidance has since been issued at https://www.gov.uk/government/collections/risk-assessments-for-specific-activities-environmental-permits

The potential for taking dilution and dispersion into account is related to the topic of compliance points. Environment Agency (2010) states that:

> 'Compliance points can be located at a number of different points between your activity's discharge and the identified receptor(s). Their purpose is to define a (modelled or real monitoring) point where, if a compliance value is achieved, the receptor(s) will be protected. Where the compliance point is set between the receptor and the activity's discharge, compliance values are based on the justified and predicted effects of dilution and attenuation/degradation downstream at the receptor. The compliance point could even be the discharge itself and in this case the compliance value is referred to as the limit value. Where the compliance point is the receptor, the compliance values will be the water quality targets.'

The above discussion emphasises the point made earlier that a simplistic evaluation against MRVs at a location immediately downstream of a release may not be appropriate. If compliance is to be established immediately downstream, an alternative measure may be appropriate. Alternatively, given the difficulty of defining an appropriate point of compliance close to a source, the point of compliance may be better defined in an exploitable aquifer where MRVs may be more appropriate.

It is also noted in Environment Agency (2010) that some sources may be screened out from further consideration if the presence of unproductive drift or unproductive bedrock strata and remoteness from surface waters mean that risk to any identified groundwater-fed receptor is very low.

Although MRVs are sometimes used for hazardous substances as the principal criteria for compliance, it should be noted that MRVs are not directly related to toxicity. Specifically, MRVs represent the smallest quantity of a substance that can be accurately determined at a given laboratory. Therefore, it may be appropriate to complement comparisons with MRVs with comparisons against EQSs or concentrations corresponding to MRLs as recommended by the US ATSDR for typical rates of water ingestion. This may also help in setting compliance values for substances for which MRVs are not available.

4.1.2 Groundwater Protection in Other European States

Several publications exist on how the WFD has been implemented in various countries. In Vilanova et al. (2012) an example is given where the implementation in five countries has been compared, with the aim of identifying the degree to which the GWDD implementation would depend on the previous procedures followed. Each river basin district has adopted the best methodologies to study the intrinsic characteristics of their respective territory based on EC guidance documents. The presentation and publication of results depends on the legal framework of each country in terms of groundwater competencies. It was shown that, despite the use of these common documents, the results were not homogeneous. Local characteristics such as land use, available data or groundwater management structure were determinant factors in the achievement of results, besides the procedures adopted for carrying out the impact analysis. It was observed that one of the most important factors for obtaining an accurate risk evaluation was the delimitation of the affected groundwater bodies.

As each water body has its own background level, the environmental risk assessment of any facility of hazardous wastes should account for the specific background level of the site where the waste will be stored and/or the environment where long-term discharges from the facility are expected to occur. Examples of approaches followed to assess the impact of storage and disposal of hazardous wastes and how groundwater quality is accounted for, are given in the following sections.

In Spain, the water authority is organised in water basins. Each river basin is managed by the River Basin Authority. Those organisations are called Agencia del Agua (Water Agencies) and belong to the Autonomous Government if the river basin is fully enclosed into the Autonomous Community (administrative organisation of Spain). If the river basin extends beyond an Autonomous Community, then the organisation is called a Confederación Hidrográfica and belongs to the Ministry of the Environment (Central Government).

The most commonly used criteria for comparison of the groundwater quality are the Maximum Concentration Levels for drinking water (Spanish Law RD 140/2003) and other international rules for drinking water. In Spain, the remediation targets for a polluted soil or the maximum contamination levels are also set by means of a site-specific risk assessment as regulated in the Spanish law RD 9/2005. This law affects all industrial activities having a potential risk of contaminating the soil. Waste management and disposal facilities are included in the list.

Often, the Dutch standards for soil and groundwater remediation are used in Spanish technical reports.

In addition, the Catalan Water Agency has developed the Quasar project to set reference levels (generic values) for chemical pollutants depending on the different uses of the groundwater, based on risk assessment (ACA, 2007). As a result, a list of values was generated for five metals and eighteen organics with two indicative thresholds. The lower threshold is the generic accepted risk under present-day uses of the soil at the site.

Above this threshold, a monitoring programme should be set in place and, if the value is over the maximum threshold, corrective actions should be designed and executed to decrease the concentration and reduce the risk to an acceptable level.

In a similar way, the Ebro river basin Water Agency (Confederación Hidrográfica del Ebro) obtained a list of generic values (CHE, 2013). The list is a little longer than that of the Catalan Water Agency, but also has two thresholds, defined in the same way.

4.2 Groundwater and the protection of the environment

Groundwater has a very important role in the environment, supporting rivers, lakes and wetlands with upwelling groundwater being important in supporting the baseflow of rivers and for the health of aquatic wildlife; all rivers are partly fed by groundwater and some rivers and wetlands are completely dependent on groundwater (Environment Agency, 2013). As such, groundwater protection legislation has been developed, including the WFD (European Commission, 2000) and the GWDD (European Commission, 2006a), as amended (European Commission, 2014). Together, these Directives aim to ensure that groundwater inputs to associated surface waters do not result in failure to meet the environmental objectives of those waters under the WFD or result in deterioration in the ecological or chemical quality of those waters (European Commission, 2015).

The WFD (European Commission, 2000) requires that registers of protected areas be established that take account of habitats and species that are directly dependent on water, including habitats and species falling under Natura 2000 protection status[21]. The Directive furthermore requires that all groundwater bodies achieve 'good' water quality status, with water quality status being evaluated against thresholds for the chemical constituents of groundwater and their impact on ecosystems (Environment Agency, 2013). The GWDD (European Commission, 2006a), which complements the WFD, requires quality standards to be established for groundwaters, taking into account local or regional conditions, and requires hazardous substances to be prevented from entering groundwater and the input of non-hazardous substances to be limited, as discussed above. It is not only hazardous substances that are of interest regarding groundwater protection; nutrients are also an important consideration with nitrogen and phosphorous in groundwater posing a risk of eutrophication to surface waters (European Commission, 2014).

In considering protection objectives, the GWDD requires that "the relationship between bodies of groundwater and the associated surface waters and directly dependent terrestrial ecosystems" be established (European Commission, 2014). Furthermore, Member States are required to establish standards and threshold values for substances in groundwater that take account of the likelihood of adverse effects on associated aquatic ecosystems and dependent terrestrial ecosystems and the environmental quality objectives and other standards for water protection that exist at national or international levels. The threshold values relate to good chemical status and are required to be set at the level of Member States, taking account of the potential for impact on surface waters, wetlands and dependent terrestrial ecosystems and knowledge on ecotoxicology, in addition to human toxicology (European Commission, 2006a). Annex II of the GWDD provides guidelines for establishing threshold values. With regard to environmental protection, these guidelines stipulate that the determination of threshold values should be based on the extent of interactions between groundwater and associated aquatic and dependent terrestrial ecosystems, along with the hydro-geological characteristics of the substances, background levels, dispersion tendency and their persistence and bioaccumulation potential (European Commission, 2006a).

Groundwaters that may have a negative impact on surface waters or habitats often have threshold values established. These are intended to ensure that adverse impacts do not occur and to help

[21] Natura 2000 is a network of sites selected to ensure the long-term survival of Europe's most valuable and threatened species and habitats.

identify risks for further investigation (WFD UK TAG, 2012). These threshold values may be derived from surface water standards with a precautionary dilution factor applied (WFD UK TAG, 2012; European Commission, 2015). Alternatively, surface water protection standards may be applied directly to evaluate impacts of groundwater through monitoring upstream and downstream of a point source input of groundwater to a surface water body (WFD UK TAG, 2012).

In protecting groundwater from hazardous substances associated with waste disposal, siting is an important consideration. Locations selected for waste disposal should ensure that environmentally sensitive locations are avoided and optimum locations in terms of geology and hydrogeology are selected (Environment Agency, 2013). Regulatory guidance in England suggests that relevant factors for consideration in terms of environmental impacts from waste disposal sites include (Environment Agency, 2013):

- The proximity of the surface water;
- Directness of the hydraulic connection;
- Quality and quantity of both the groundwater and the receiving surface water;
- The consequences of the potential impact on the surface water quality; and
- The consequences of the potential impact on the ecology of the surface water due to changes in quality or level.

5 Review of the design and use of toxicity indices

Toxicity indices have been widely used as indicators of the hazard linked to radioactive and other hazardous wastes. Toxicity of a material has been used as a basis for categorising waste as requiring specific measures to be used in its management and/or to show that particular legislation applies to its management.

A question that may be posed is whether it would be possible to develop a single toxicity index that would work for both radionuclides and non-radioactive chemicals. Were this possible, the hazards from radioactive and chemical wastes could be compared on the same scale. This would allow the determination of which characteristics of a waste stream should be the focus of more detailed risk assessments, in terms of mitigating the risks and to help in balanced and proportionate decision making. Such an index would also support communication with stakeholders e.g. in explaining the reasoning for why particular emphasis is given to specific waste management strategies or aspects of such strategies, and could assist in the development of waste acceptance criteria.

The intention here is to review the nature and application of toxicity indices for radioactive and hazardous wastes, with a view to providing evidence to support the design of a single common index and/or to identify the difficulties, e.g. relating to different shapes of exposure-response relationships and the different types of impacts applicable to different chemical substances, or to different physical forms of those substances. It is noted that consideration of the difficulties of taking into account multiple radiotoxic and chemotoxic effects is needed in any case; otherwise decisions will be taken without due consideration of relevant issues.

Approaches that have been considered for developing an index of harm for radiological substances are discussed in 5.1, whereas approaches for non-radiological substances are outlined in 5.2.

5.1 Radioactive substances

It has long been recognised that the deleterious effects of exposure to ionising radiations may be of many kinds. In consequence, as long ago as 1977 the ICRP introduced the concept of detriment to identify, and where possible to quantify, all those deleterious effects. They defined the detriment in a population as the mathematical expectation of the harm incurred from an exposure to radiation, considering not only the probability of each type of deleterious effect, but also the severity of the effect. Interestingly, at that time they included both the effects on health and other effects (ICRP, 1977a; paragraphs 15 and 16). It was also in 1977 that the ICRP introduced the concept of effective dose, determined using radiation and tissue weighting factors, though these names were not then in use, with the term effective dose equivalent subsequently used (ICRP, 1984), but with this, in turn, being replaced by effective dose in the 1990 recommendations of the ICRP (1991).

In practice, in 1977, the ICRP defined tissue weighting factors and set occupational exposure limits by reference to occupational fatality rates (ICRP, 1977a; paragraph 96). They commented that other criteria than fatality rates could have been used and that, ideally, account should be taken of all components of harm or detriment, including the sum of all accidents, illnesses, genetic defects and fatalities involved, as well as the anxieties of workers or their families about the hazards or conditions of work in various industries. However, they considered that an assessment based on mortality criteria was conservative, since experience had shown that the non-fatal effects of radiation are much less frequent than the non-fatal effects encountered in other safe occupations (defined as those in which the average annual mortality did not exceed 1×10^{-4}) (ICRP, 1977a, paragraph 97). No specific remarks were made in ICRP (1977a) on the role of harm or detriment in

setting criteria for limiting exposure of members of the public, but the basis of the approach adopted is clearly similar.

A detailed commentary on the limitations of using fatality as a criterion was included in ICRP (1997b). These included the neglect of non-fatal injuries, diseases and permanent disabilities; the lack of distinction between a certain frequency of immediate deaths from accidents and of delayed deaths from various forms of malignant disease (with the greater apprehension that is likely to attach to the latter); and the consideration that the length of life lost is more important than the fact of death alone. A further distinction that was noted was that accidents may be attributed, rightly or wrongly, to a lack of skill by the victim, whereas occupational diseases are less likely to be so attributed. Thus, in many respects, ICRP (1977b) anticipates the extensive literature on risk perception that has developed subsequently (e.g. Breakwell, 2007).

ICRP (1977b) includes a detailed analysis and comparison of risks in various industries and those arising from exposure to ionising radiations. It emphasises that no single index can be scientifically defensible, but that there is nevertheless a requirement for a single quantitative index that is consistent with reasonably informed opinion. An index is proposed, but it is emphasised that this index addresses only the harm from events and does not deal adequately with that from anxieties about their occurrence, although these anxieties may be very different in different occupations and may vary according to any recent publicity, secretiveness or chance occurrences related to malignant diseases. Although these anxieties may not involve harm comparable with that of the actual diseases or deaths that occur, they may affect large numbers of workers who will never develop such diseases.

A more detailed comparison between occupational risks and those due to exposures to ionising radiations was included in ICRP (1985). This re-emphasised that no simple numerical index of total occupational or other harm can be regarded as complete or compelling. However, it was also pointed out that the discussion of such indices, and of the bases on which they are formulated, should help in defining the components of harm to which importance should be attached, and the weight that is held to apply to each component, when comparisons need to be made between the amounts of harm due to different occupations or activities. Overall, the use of total periods of health or life lost was considered to allow a rather fuller assessment of total harm than can be obtained from mortality rates alone. However, it was considered that additional consideration needs to be given to:

- The relative weights that would attach to illnesses of various kinds, to periods off work because of injury, and to periods of lost life expectancy;
- The relative weight applicable to years of lost life or activity at different ages, at least insofar as the ages at which life or activity is lost may differ in the contexts being considered;
- The difference in weight between an immediate sudden death and a later death from cancer;
- The relative weight that should be given to disabilities in exposed individuals or in any of their descendants;
- The component of anxiety in respect of risks that may be expressed in the future, rather than at the time of exposure.

The index of harm defined in ICRP (1985) is closely related to the Quality Adjusted Life Year (QALY) used in assessing the value of medical interventions (Mortimer and Segal, 2008). The QALY takes account of both the quality and quantity of life lived, with 1 QALY representing one year in perfect health. The utility of a year of less than perfect health is assessed using standard methods employed in multi-attribute utility analyses, e.g. time trade-offs, standard gambles and visual analogue scales. In terms of quality of life, a useful concept is the Quality of Life Scale (QOLS) applied in evaluating the significance of chronic illness. The QOLS was originally a 15-item

instrument that measured five conceptual domains of quality of life: material and physical well-being, relationships with other people, social, community and civic activities, personal development and fulfilment, and recreation. After descriptive research that queried persons with chronic illness on their perceptions of quality of life, the instrument was expanded to include one more item: independence, the ability to do for yourself. The QOLS has been found to provide a widely applicable, meaningful way of determining the impact of health care when a cure is not possible (Burckhardt and Anderson, 2003).

Because of the difficulties of defining a single index of harm (or detriment), in its 1990 recommendations, the ICRP modified its definition of detriment (ICRP, 1991; paragraphs 47 to 51). Although the general aim was still to find a quantitative way of expressing a combination of the probability of occurrence of a health effect and a judgement on the severity of that effect, a single index quantity was not considered adequate. Because of a need to use detriment for several different purposes and because detriment intrinsically has many different aspects, the ICRP replaced its previous concept of detriment by a multi-dimensional concept, with only a limited attempt to aggregate those facets into a single index of harm. Aggregation was primarily used for defining tissue weighting factors, because the choice of tissue weighting factors is not very sensitive to the procedure for aggregating different aspects of detriment.

Detriment is similarly defined in the most recent recommendations of the ICRP (2007). There it is defined as the total harm to health experienced by an exposed group and its descendants as a result of the group's exposure to a radiation source. It is further stated that detriment is a multi-dimensional concept and that its principal components are the stochastic quantities probability of attributable fatal cancer, weighted probability of attributable non-fatal cancer, weighted probability of severe heritable effects, and length of life lost if the harm occurs.

In summary, use of a single index of health has been considered and advocated in the field of radiological protection. However, its limitations have been recognised and the most recent recommendations from the ICRP define health detriment as a multi-dimensional concept considering the probabilities of occurrence of a variety of health-related endpoints. Although the potential importance of anxiety concerning radiation exposures and associated health risks has long been recognised, to date this aspect has not been considered in defining overall detriment. In the future, there may be merit in establishing closer links with the medical community, as they have considerable experience in evaluating the quality of life experienced in different states of illness, and in expressing this in quantitative terms such as are expressed through the QALY and QOLS. Specifically, the QOLS provides a very broad valuation of an individual's perception of their own degree of personal and relational well-being. Anxiety could readily be represented within a similar broad framework for evaluating overall well-being.

5.2 Non-radiological substances

Non-radiological substances, or those that present a hazard due to their chemical properties (or in the case of some substances, such as uranium compounds, a combination of radiological and chemical) can act on several different biological tissues in different ways. Chemotoxicity tends to be assessed in terms of threshold and non-threshold effects, or toxicological end-points, over acute and chronic durations of exposure (Section 2). The relatively large number of possible end-points and 'points of departure' (NOAEL, LOAEL, BMD_{10}, excess cancer risk estimates) that are used in setting exposure standards or guidelines for acute or chronic exposures result in a lack of a single applicable metric for comparing the potency of chemicals with each another.

For acute toxicity, measurements aim to investigate effects after a single exposure for period of up to 24 hours using dermal, oral or inhalation routes are appropriate (Fielder, 2008). One metric by which chemicals may be compared is the LD_{50}, the dose of a toxic compound that causes death in 50% of a group of experimental animals. LD_{50} values can be categorised to provide an indication of relative potency. However, this approach is generally only applicable to acute exposures and has

been heavily criticised due to animal welfare considerations and as being scientifically unnecessary (Fielder, 2008) and in fact it could be said to be inappropriate given the potential for different mechanisms to occur at very high exposures compared with the much lower exposures that are typically of interest in environmental protection and exposure management. Instead, methods have been recommended in more recent years that emphasise determining the onset and duration of signs of toxicity (Fielder, 2008), such as that suggested by the British Toxicology Society which does not use death as an end-point, but instead the maximum dose level used is designed to produce 'evident' toxicity, i.e. clear signs of toxicity such that the next higher dose level is expected to result in mortality or severe pain and distress (Fielder, 2008). In addition to acute toxicity, methods exist for assessing skin and eye irritation and skin sensitisation. Methods for investigating irritancy have included use of the rabbit model, although considerations of the physico-chemical properties of chemicals and the use of a wide variety of *'in vitro*' (literally 'in glass', or so called 'test tube') methods often allows the potential for severe effects to be predicted without using live animals (Fielder, 2008). Hybrid methods can also be used in which cells are exposed to toxic chemicals *in vitro*, but their carcinogenic potential is evaluated by injecting them into intact animals (Combes et al., 1999). The ability of a chemical to cause skin sensitisation has been assessed using the Guinea Pig Maximisation Test and more recently a mouse model referred to as the Local Lymph Node Assay (LLNA) (Fielder, 2008). Several techniques, both *in vivo* (in living organisms) and *in vitro*, have been developed to measure a variety of other toxic effects including reproductive/developmental effects, mutagenicity and carcinogenicity *inter alia* (Timbrell, 2002; Fielder, 2008).

Regarding carcinogenicity, the International Agency for Research on Cancer (IARC) assesses the carcinogenicity of different substances and classifies chemicals into several groups (IARC, 2006):

- Group 1: The agent is carcinogenic to humans
- Group 2A: The agent is probably carcinogenic to humans
- Group 2B: The agency is possibly carcinogenic to humans
- Group 3: The agent is not classifiable as to its carcinogenicity to humans
- Group 4: The agent is probably not carcinogenic to humans.

However, it should be noted that the IARC categories are hazard based, not risk based, and so there is a wide range of the degree of toxicity of chemicals in Group 1 and it is possible that there are chemicals in group 2A (or even 2B or 3) that could be just as concerning as those in Group 1.

Considering threshold substances (or more correctly, substances where there is a threshold in dose-response data for a specific exposure route) in risk assessments, toxicological assessment criteria in the form of tolerable intakes (e.g. TDI) are often based on different points of departure (such as LOAEL, NOAEL and BMD_{10} values) for different toxicological end-points. Therefore, beyond a comparison of TDI values for different substances, it is difficult to assess the degree of harm that may result in a population that is exposed to chemical mixtures (leaving aside issues of additive or synergistic effects, which are discussed elsewhere in this report), especially if different end points are associated with the different substances in the mixture. The difficulties associated with considering the cumulative risks associated with exposures to mixtures of chemicals are reviewed by Sarigiannis and Hansen (2012) who provide a summary of typical approaches, including the use of a hazard index (HI):

$$HI = \sum_{i=1}^{n} \frac{exp_i}{ref_i}$$

where *exp* is an exposure, ref is reference intake (e.g. TDI) for a mixture of several substances Si, (i = 1,2,….n).

This approach does not allow the prediction of the overall health effect of the mixture, but does attempt to combine the degree of risk. If HI > 1, the concern warranted would be the same as that if an individual chemical exposure exceeded its reference intake by the same proportion. Another approach is the Point of Departure Index (PODI) which is the sum of exposure of each compound divided by its respective point of departure (POD) (Sarigiannis and Hansen (2012):

$$PODI = \sum_{i=1}^{n} \frac{exp_i}{POD_i}$$

where the POD can be a NOAEL or a BMD. For the evaluation of potential risk, the PODI of a mixture is then used in combination with a group safety factor (often 100), where the product of PODI and the uncertainty factor should be less than 1.

The MoE approach can also be used for mixtures, whereby the combined margin of exposure of a mixture (MOE_{mix}) can be calculated as:

$$MOE_{mix} = \left(\frac{1}{MOE_1} + \frac{1}{MOE_2} + \cdots \frac{1}{MOE_n}\right)^{-1}$$

The margin of exposure index of a mixture is compared with an agreed 'acceptable' threshold (noting that criteria for determining what this may be are not widely agreed upon). Note that the MoE approach is essentially the inverse of an index quantity and therefore, these approaches are not distinct.

A further approach is the use of a cumulative risk index (CRI) that combines MoEs for chemicals with different uncertainty factors. The Risk Index (RI) of a single chemical is the reciprocal of the hazard quotient and is given by (Sarigiannis and Hansen (2012):

$$RI_i = \frac{NOAEL_i}{exp_i \cdot UF_i} = \frac{ref_i}{exp_i}$$

where UF is an uncertainty factor. The CRI of a mixture of chemicals is defined as (Sarigiannis and Hansen (2012):

$$CRI = 1/\sum_{i=1}^{n} \frac{exp_i}{ref_i}$$

i.e., CRI is the reciprocal of the hazard index.

The HI approach may be used as a screening tool, but the outputs will not necessarily represent a concern for health, rather a need for further refined assessment which is likely to be on a chemical by chemical basis. In the majority of instances, HI is more likely and appropriate to be used when there is concern over a common mode of action or target organ, but is often not used due to the wide range of substances with differing modes of action that are found in waste disposal systems.

For compounds that are structurally similar and can be considered to have a similar mechanism of action, TEFs can be used, whereby the TEQ is simply the summation of the concentrations or doses of mixture components multiplied by their respective TEF.

Even though such simple approaches exist, it should be noted that the exceedance of a TDI value does not necessarily guarantee that an adverse health effect will be identifiable in the exposed population and it is likely to be a non-trivial task to determine what degree of an exceedance of a TDI would be of greater concern if more than one TDI is exceeded.

If a scenario occurred whereby a population was exposed to a number of different chemicals but they tended to affect the same target organ, it may be possible to consider (to some degree) the relative impact of each along with the potential for additive or synergistic effects and a number of

methods have been suggested for considering interactions (see reviews by Thorne and Wilson, 2009; Sarigiannis and Hansen, 2012; Kienzler et al., 2016 *inter alia*), even though it is generally difficult to assess potential interactions between different contaminants in a truly quantitative way, given a lack of toxicological data to constrain models of interactions.

Work has been undertaken in recent years on considering how population-level exposure to chemicals may be assessed in terms of burden of disease using a DALY approach. DALY is expressed as the number of years lost due to ill-health, disability or early death (thereby combining mortality and morbidity into a single metric, an approach slightly different to the QALY, which has a greater emphasis on the perceived quality of life). For example, Fewtrell et al. (2004) estimated that lead causes nearly 1% of total global burden of disease and Prüss-Üstün et al. (2011) calculated that exposure to a variety of chemicals, including lead, second-hand smoke and asbestos accounts for 5.7% of total global DALYs and 8.3% of total global deaths. In their systematic review, Prüss-Üstün et al. (2011) state that chemicals with known health effects, such as dioxins, cadmium, mercury or chronic exposure to pesticides could not be included due to incomplete data and information. QALY has also been used as an evaluation tool in a health surveillance programme, where it has been applied to health-related effects of PCB exposure (Esser et al., 2014). Regarding assessing the burden that exposures may impose on a population, a distinction can be made on whether the aggregate quantity used is for assessing the possible detriment in quality of life that members of the population may experience (including their perceived health status) or whether the metric is to be used to provide an indication of the burden that may be placed on medical resources, where components such as anxiety would feature less importantly.

An example on the use of DALYs is that by Chatham-Stephens et al. (2013), who undertook a study on burden of disease from toxic waste sites in India, Indonesia and the Philippines (chosen as low to middle income countries). The study involved combining estimates of disease incidence from environmental exposures with population data to calculate DALYs attributable to exposures at each site. In brief, the approach taken was as follows:

- Identification and screening of contaminated sites (including environmental sampling and analysis)
- Estimating the population at risk for each site identified (number of people regularly coming into contact with a contaminant, considering distribution by age)
- Calculating risk per person for cancer and non-cancer effects. The US EPA regional screening level calculator for chemical contaminants was used for this, calculated as cancer probably per unit mass of environmental medium. For non-cancer effects reference doses (RfD) and concentrations (RfC) were taken from the US EPA Integrated Risk Information System (IRIS) and were applied to exposure pathways and contamination levels at each site (noting the assumption of linear dose-response relationship and associated health outcome). Lead was given a separate treatment.
- Calculating incidence of disease. For each chemical, up to three environmental media (soil, water, air) and two routes of exposure (ingestion/dermal and/or inhalation) risk per person was calculated from the level of contaminant in the relevant environmental medium. The use of linear slope factors resulted in very high concentrations of contaminants having very high estimates of disease incidence, and as such, disease incidence was arbitrarily capped at 5% (it is not clear why this value was chosen and the need for such a cap arguably highlights a deficiency in the approach). For lead, the incidence of mild mental retardation and anaemia in children was calculated, along with cardiovascular disease in adults resulting from lead-induced increases in blood pressure, taking into account blood lead levels resulting from exposures that were calculated using the US EPA IEUBK (Integrated Exposure, Uptake and Biokinetic Model for Lead) and Adult Lead Methodology (ALM).

- Calculating YLD (Years Lived with Disability) and Years of Life Lost (YLL), as DALY is a sum of these two components. YLD and YLL were calculated for each exposure pathway. YLD is the product of estimated years of life with a given disability multiplied by a specific Disability Weight (DW). For each chemical, the relevant type of cancer or non-cancer health effect and corresponding DW were assigned, reportedly considering data from the US EPA IRIS database and WHO (2008). A number of assumptions were made in the calculations concerning life expectancy, application of DW to different stages of cancer, cancer incidence and survival data.
- Sensitivity Analysis. In addition to calculating DALYs with varying rates and weights, assumptions on population risk and the use of different disease incidence caps were explored.

The study by Chatham-Stephens et al. (2013) estimated that, in 2010, 8.62 million individuals were at risk of exposure to industrial pollutants at 373 toxic waste sites in the three countries, with exposures resulting in 828,722 DALYs (ranging from 814, 934 to 1,557,121 depending on the weighting factors used). The authors compared this with estimated burdens for outdoor air pollution (1,448,612 DALYs) and malaria (725,000 DALYs) in these countries. Lead and hexavalent chromium were found to account for 99.2% of the total DALYs for the chemicals investigated. The authors recognised the study's limitations and suggested that further research should consider improved exposure measurements by linking environmental sampling levels, biomarkers of disease and health outcomes, with focusing on vulnerable populations (e.g. pregnant females, children and the elderly). Of note in these studies is the difficulty of characterising actual exposures (hence the recommendation for linking environmental sampling to biomarkers).

A recent study by Caravonos et al. (2016) used an exposure assessment method and DALY approach similar to that described by Chatham-Stephens et al. (2013) to estimate the burden of disease resulting from exposure to lead at toxic waste sites in three Latin American countries (Argentina, Mexico and Uruguay) in 2012. The study found that ~316,703 individuals were at risk of exposure to pollutants at 129 sites, and that exposure to lead was estimated to result in between 51,432 and 115,042 DALYs depending on the weighting factors used. The estimated burden of disease is estimated to be comparable with estimates for Parkinson's disease and bladder cancer in these countries. As in the study by Chatham-Stephens et al. (2013), the US EPA's IEUBK model and associated tools were used to estimate mean blood lead levels.

It is emphasised that the above discussion is entirely in terms of impacts on human health and wellbeing. However, radionuclides and toxic chemicals can also have adverse impacts on the environment, as is discussed elsewhere in this report. It is emphasised that these two aspects of impact cannot be kept entirely separate, since degradation of the environment will also adversely impact human health and wellbeing. Therefore, both components will require evaluation in a wider environmental impact assessment context, where their interactions with each other and with other relevant factors can be addressed.

5.3 Towards a measure of 'harm' for radiological and non-radiological substances

There seems to be general agreement that harm is best described in terms of several components (e.g. years of life lost, years of life impaired in different ways, overall well-being, financial burden, ability to participate in social activities, anxiety concerning the possibility of future disease). Thus, harm is a multi-dimensional quantity, and we can express our degree of aversion to each of these in terms of a disutility, where a disutility of zero corresponds to no adverse impact and a disutility of one corresponds to the maximum possible disutility. Thus, for years of life lost, zero would correspond to no life shortening and one would correspond to the death of a young person. It is emphasised that with radiotoxic or chemically toxic materials, two steps of assessment are involved. The first step relates exposure to adverse effect on health and is susceptible to objective

evaluation. The second step relates adverse effect on health to the disutility of that degree of adverse impact. This is a subjective judgement dependent on the views of the individual or stakeholder group.

Disutility is a function (not necessarily linear) of the appropriate measure of each component (e.g. years of life lost is a measure of life shortening). Generally, disutility can be regarded as a precise function for any one person, but for a stakeholder group it is likely to be variable, reflecting different views in the group. Thus, disutility could be defined in terms of a probability density function (pdf) $p_i(e_i|r_i)$, where r_i is the measure of harm component i, e_i is the disutility and $p_i(e_i|r_i)$ is the probability density function for e_i given specified r_i. Relationships between r_i and e_i can be established for individuals using standard elicitation techniques (e.g. odds ratio equivalent gambles). These individual relationships can then (in theory) be combined to give pdfs.

A stakeholder group will also have views as to the relative weight to be assigned to the different types of disutility. Again, there will be variations between individuals, so these weights are best expressed as pdfs denoted $q_i(w_i)$. It may be useful to subject these pdfs to a constraint that the weights sum to unity. However, this is not essential and it may be more convenient to treat them as independent and not require that they sum to unity. If this latter approach is adopted, we can give a precise estimate of the overall disutility, D, as:

$$D = \sum_{i=1}^{i=n} \int_0^{\infty} w_i q_i(w_i) \mathrm{d}w_i \int_0^1 e_i p_i(e_i | r_i) \, \mathrm{d}e_i$$

Note that the two integrals are separable, i.e. the expectation value of the disutility can be first estimated and then multiplied by the expectation value of the weight. More generally, percentiles and higher moments of the distributions can be computed, if these are useful. However, the above equation may generally suffice, as it allows uncertainties to be elicited and represented, but still provides a precise index quantity for comparative purposes. Note that the above discussion is restricted to one stakeholder group, where divergences of opinion may be assumed to be limited. For multiple stakeholder groups, different estimates of *D* would generally be derived. These different values and their bases of derivation would provide a basis for discussion between stakeholder groups as to actions to be taken, i.e. the computation of disutility values for individuals, or collective disutility values for populations, is envisioned as providing a decision-aiding tool. Disutilities evaluated on this basis might be used in comparative contexts, e.g. in national comparisons of industrially induced and naturally occurring diseases, or as an input to a multi-attribute utility analysis, together with financial and other considerations, targeted at identifying the preferred option for managing a specific situation, such as the clean-up of a contaminated site.

With harm described as a multi-dimensional concept, there is no problem, in principle, in representing different health outcomes along the various dimensions, and in aggregating those health outcomes to provide one or more overall measures of disutility. However, it does require that the health outcomes are estimated realistically, rather than adopting index quantities that intrinsically contain conservatisms. Such conservatisms may be explicit, e.g. uncertainty factors, but they may be implicit, such as the use of a NOAEL that is some undetermined factor lower than the LOAEL for the same substance and exposure route.

There are also problems in realistically interpreting how intact animal or *in vitro* toxicity data should be interpreted in terms of human health impacts. For ionising radiation, this is less of a problem than with many chemicals, because the LNT approach is founded on various epidemiological studies on a variety of populations that are broadly consistent with each other. In view of these considerations, it may be better to carry forward different aspects of harm separately into comparisons or optioneering studies, so that stakeholder groups can see explicitly the different aspects of the comparisons and/or trade-offs involved between options rather than them being hidden in a single measure of disutility. For example, in a comparison between two options

for clean-up in which one gave a high cancer risk to remediation workers, but a low risk to members of the public, and a second that gave a low cancer risk to workers, but left residual contamination assessed as giving a high risk of neurological effects in children exposed to that contamination, it would be irresponsible to present a single collective disutility for each option as a basis for decision making. The two impacts are sufficiently different in kind that an explicit choice would need to be made between the options in full appreciation of the different health impacts involved.

In summary, aggregated indices of health detriment or quality of life may be useful in providing summary measures of impact, e.g. in national comparisons of industrially induced and naturally occurring diseases, but excessive aggregation should be avoided, as this could be seen as an attempt to obscure salient considerations, or may result in choices being made on the basis of summary information that oversimplifies the implications of those choices.

Although the approach outlined above has considerable power in comparing alternatives and encouraging stakeholder dialogue, it does not address directly the issue of setting quantitative standards limiting exposure to one or more toxic agents. This requires the further step of defining a limiting level of disutility. This can be back-converted to the magnitude of health impact associated with a toxic agent that would give rise to that level of disutility (dependent upon stakeholder views on the relation between the health impact due to a toxic agent and the associated disutility). In turn, the health impact can be back-converted to a corresponding level of exposure, which can then be used to establish an associated compliance requirement (introducing a suitable precautionary factor, e.g. an uncertainty factor, as required by regulatory policy).

An advantage of this is that exposures to multiple toxic agents can be addressed by partitioning the limiting disutility between the toxic agents, and then back-calculating separately for each agent, as described above. Threshold and non-threshold agents are both handled correctly by this approach, because threshold agents typically have disutility that rapidly increases from zero to one above the threshold. Thus, the regulatory standard effectively becomes the threshold divided by the associated precautionary factor, or the product of precautionary factor and partitioning factor for exposure to multiple agents. In contrast, if a non-threshold factor is associated with a slope factor, then that factor is employed in the step in which health impact is back-converted to the corresponding exposure. Where a quantitative model does not exist relating exposure to health effect, then a policy decision will need to be taken on the model to apply for regulatory purposes. This might range from a slope factor model to a step function, which would be the limiting case of a threshold model in which there was no variability in the exposure at which the health impact increases from zero to its maximum value.

6 Factors to consider in design of effective assessments

In this section, a range of factors are outlined that might be considered in the design, implementation and interpretation of effective assessments of non-radiological impacts associated with radioactive waste disposal. Effective is taken to mean providing results that support the interests of decision makers, including the need for balanced and proportionate (or not grossly disproportionate) risk management, clear and consistent protection objectives and clear and consistent assessment methods. The same assessments should also support decisions on the management of radiological impacts and overall optimisation of waste management. The potential applications encompass all types of radioactive waste, including, for example:

- assessment of disposal at facilities receiving waste containing naturally occurring radioactive material (NORM) and other waste in the same disposal facility; and
- disposal of low-level and/or very low-level radioactive waste with other waste in facilities not specifically intended for radioactive waste.

6.1 Human health risk assessment

In developing assessments to characterise risks associated with non-radiological substances, either to ensure compliance with environmental legislation or regulatory guidelines, or as part of studies on optimisation, the potential effects on human health will need to be considered. Regulatory frameworks may vary between different countries, but several general “good practice” principles can be identified for undertaking risk assessments.

In general, the level of detail of a risk assessment will depend on its intended purpose, and as with other environmental risk assessments (such as those related to general land contamination, Section 3), a ‘phased’ or ‘tiered’ approach may be taken (and this may also be the case for an ecological assessment, Sections 3.2.1 and 3.3.1). An initial assessment may identify substances of concern based on their toxicological properties and occurrence in waste, and calculated concentrations of those substances in environmental media can be compared with ‘generic’ environmental standards or guidelines (such as those for drinking water) assuming that they are available for the substances of interest. This approach has been used for example, in ‘generic’ studies underpinning an illustrative risk assessment of a GDF in the UK (Hunter et al., 2006) (Section 3.2.8). Such as approach has also been used for the LLW repository in the UK (Kelly and Berry, 2011; LLWR, 2011) (Section 3.2.8) and the DGR in Canada (Section 3.2.8). A more detailed approach to risk assessment may include calculation of specific intakes of substances and comparison against toxicological assessment criteria that have been identified from authoritative sources (national or international regulatory or advisory bodies), such as the approach taken by Wilson et al. (2011) (see Section 3.2.8).

Regardless of the level of detail, a useful conceptual framework typically used in risk assessments is the ‘source-pathway-receptor’ methodology (Section 3.2.2) as described in Sections 3.2.1-3.2.7 and this approach should be used for assessing non-radiological substances associated with radioactive materials, with consideration being given to data typically required (see Section 3.2.9). To date, most of the environmental risk assessments developed for non-radiological substances associated with radioactive materials have used either published guidelines or standards for environmental media or have considered intakes in those media. In either case, the toxicological data used in the assessments are typically those recommended by “authoritative bodies” either at a national or

international level. Of course, data from the primary scientific literature could be used, but it would need to be carefully evaluated, and any evaluation would require a consideration of guidelines on data use which may be specific to a given nation. For example, the UK COC does not recommend the use of quantitative cancer risk models based on animal data for routine risk assessment (COC, 1991, 2004). See also https://www.gov.uk/government/publications/cancer-risk-characterisation-methods.

In general, toxicological assessment criteria for non-radiological substances are based on limiting intakes to those that either fall well below a threshold above which deleterious effects can occur, or that correspond to a very small risk of non-threshold effects (such as cancer, Sections 2, 3). Typically, it is difficult to consider synergistic effects (either due to mixtures of substances with different toxicokinetic properties and/or the presence of radionuclides), but attempts have been made (e.g. Thorne and Wilson, 2009). At least a degree of recognition of the potential for such effects should be included in risk assessments, even if effects cannot be readily quantified at present, due to lack of fundamental toxicological data (see discussion in Appendix B). Where a quantitative analysis cannot be undertaken, it may still be possible to infer something as to the possibility of synergistic effects by reference to the relative levels of exposure to the different agents and their modes of action, e.g. one agent may dominate the mixture toxicologically and the other agents may have modes of action that are unlikely to influence the mode of action of the primary agent. Where more information is available, numerical approaches have been suggested that would allow quantitative evaluation. Some approaches exist for considering additive effects for substances with similar toxicological properties (e.g. the use of TEFs, Section 3.2.7) or for considering relative contributions that different substances may make to an overall measure of risk (Section 5.3). In the case of uranium, exposures may result in harm due to both its chemical and radiological properties and recent work has been undertaken to compare possible effects given different modes of intake, degrees of enrichment, and characteristics of the exposed individual (Thorne and Wilson, 2015).

There are similarities in aspects of risk assessments for non-radiological and radiological substances, but there are clear differences associated with evaluating health detriment (Section 3.2.10). Some approaches have been suggested that look at the overall detriment of exposures on populations, such as the QALY or DALY metrics, but the application of the latter with regard to non-radiological substances is challenging (Section 5.3) and it has not yet been applied to chemotoxic substances present in radioactive waste disposal facilities. However, a potential framework for considering harm due to exposure to both radiological and non-radiological substances is suggested in Section 5.4. The application of such an approach could be the subject of further research.

6.2 Ecological risk assessment

Many of the considerations that arise in human health risk assessments apply also in ecological risk assessments. However, whereas the focus in human health risk assessments is generally on the individual (though impacts on populations may be addressed in optimisation studies), in ecological risk assessments the focus is typically on communities, populations and habitats. This introduces additional considerations of the spatial and temporal scales over which impacts should be assessed. Furthermore, the main consideration may be on wider measures of system characteristics, such as the maintenance of biodiversity or the provision of ecosystem services. Thus, relevant measures of performance may be measures of fertility and fecundity averaged over populations.

Although the principal interest is likely to be on environmental characteristics at the community, population or habitat level, nevertheless, for convenience, protection standards may be couched in terms of exposure of the individual organism. This applies both to ionising radiation, for which RAPs are defined (ICRP, 2008) and to chemical pollutants, though, for the latter, environmental quality

standards are more likely to be specified. Thus, the regulatory standards often lack guidance on the spatial scale over which they should be applied.

For both exposure to ionising radiations and chemical pollutants, standards for environmental protection are generally based on precautionary approaches. These include definitions of compliance values set by reference to the sensitivity of the most sensitive species, use of precautionary uncertainty factors, and use of cautious over-estimates in exposure calculations. In some contexts, notably with ionising radiations, the compliance values are described as screening thresholds, i.e. exposures above the thresholds are an indication of a need for further investigation, but do not necessarily imply that adverse effects will be observed. The adoption of precautionary approaches for individual toxic agents, with the degree of caution differing between agents, adds to the difficulty in comparing the effects of different environmental stressors or in assessing the overall impact of multiple stressors.

Additionally, in an environmental impact assessment, the effects of radiotoxic and chemotoxic stressors will have to be considered in conjunction with the effects of other stressors, the distributions of which will be altered by the proposed or existing development. These stressors may include thermal and noise pollution, and mechanical disturbance of the environment. In many contexts, radiotoxicity and chemotoxicity will be minor considerations compared with these other stressors. However, even if this is the case in the short term, it may not apply in the long term, over which multiple generations will be exposed to the radiotoxic and chemotoxic materials.

Because of the diversity of local rules of engagement between communities and the degree to which those communities are open to changing regional influences (Lawton, 2000), it is unlikely that generic. quantitative relationships can be established between levels of exposure to one or more toxic agents and responses at the community, population or habitat level. Therefore, it seems likely that environmental impact assessments will be qualitative, rather than quantitative. They may provide no more than value judgements that levels of exposure are of negligible, small, moderate or large significance. It may be possible to quantify whether compliance has been demonstrated with numerical environmental quality standards, but this simply transfers the issue, since the question then becomes the relationship of the compliance standards (and fractions and multiples of those standards) to impacts at the community, population or habitat level.

7 Overall conclusions

The work carried out in this study confirms the previous conclusions that there are inconsistencies in approaches to risk management for radioactive and hazardous waste. This creates challenges in identifying and applying optimum waste management strategies that account for all the hazards in a proportionate manner. Lean (2017) recently summarised the challenges as follows, consistent with the above study findings.

- Non-radiological hazards associated with radioactive wastes have been of regulatory interest for a number of years and yet the effects of non-radioactive materials within such wastes has historically been under researched.
- Superimposition of a non-radiological performance assessment onto a radiological assessment and vice versa, taking account of different compliance points and assessment criteria, different regulatory end points and potentially the effect of additive and/or synergistic effects is difficult to fit into current regulatory frameworks that were designed separately.
- The hazard associated with non-radioactive component of radioactive waste may be greater than that of the radioactive component. Conventional landfills are generally subject to declining source terms due to leaching and biodegradation; however, the leaching potential in a radioactive waste repository will in many cases be much lower due to waste conditioning treatments such as cementation of radioactive wastes and there is likely to be a lack of appropriate leachate data for non-radioactive components of radioactive waste.
- Non-radiological environmental impacts arising post-disposal are not usually assessed over the long time scales required for radiological impacts, I.e. extending over thousands of years.
- Given the above, ensuring an appropriate and proportionate level of environmental protection for both radiological and non-radiological components of the waste is hard to deliver and communicate.

Despite the above, steps are being taken to address more thoroughly the chemical risks in radioactive waste management. Examples have been provided which show how relevant assessments have been carried out for near surface, intermediate depth and deep geological disposal of a variety of different radioactive wastes. These have been successful in terms of addressing current regulatory frameworks and demonstrating compliance with extant or interim protection objectives. However, regulatory development and work on compliance demonstration methods continues.

One approach is to focus on radiological protection objectives in terms of risk as opposed to dose, and adopt the radiological assessment methods, in terms of scenario development, system description and evolution, contaminant migration and accumulation, timeframes for assessment, and impacts on relevant receptors. This relies on being able to convert different ways in which chemotoxicity expresses itself as risks to the receptors used in radiological assessment. This is likely to require increased use of biokinetic models for non-radioactive contaminants, so that concentrations in key target tissues and organs can be used in the estimation of health effects, together with development of a single measure of adverse impact on health analogous to the concept of health detriment used in radiological protection.

The opposite approach would be to apply typical standards for hazardous waste to the management and assessment of radioactive waste. This would be consistent with regarding radiation as just one more stressor alongside the multiplicity of other stressors, moderating the basic biological mechanisms that can underlie interactions between them, as discussed in Appendix B. Among other things, it would imply considering much shorter timeframes for assessment and relatively limited consideration of the effects of environmental change.

In developing assessments to characterise risks associated with non-radiological substances, to ensure compliance with environmental legislation or regulatory guidelines, and/or as part of studies on optimisation or to develop waste acceptance criteria, the potential effects on human health and the environment will need to be considered. Regulatory frameworks may vary between different countries, but a range of factors has been suggested that might be considered in the design, implementation and interpretation of effective assessments of non-radiological impacts associated with radioactive waste disposal. Effective is taken to mean providing results that support the interests of decision makers, including the need for balanced and proportionate (or not grossly disproportionate) risk management, clear and consistent protection objectives and clear and consistent assessment methods. The same assessments should also support decisions on the management of radiological impacts and overall optimisation of waste management. The potential applications encompass all types of radioactive waste.

Accordingly, there are several ways in which assessment methods could be better aligned, so that choices between options can be made on a more equitable basis and more appropriately reported than at present. These ways are outlined below.

a) Radioactive and non-radioactive inventories in wastes, waste packaging and the engineered facility should be characterised quantitatively and with a proportionate degree of rigour, bearing in mind the amounts of material and intrinsic hazards. Characterisation of the non-radioactive contaminant inventory should not be viewed as a minor supplementation of the radioactive inventory, particularly in the cases of LLW and very LLW, where chemical toxicity may turn out to be of greater importance than radiotoxicity.

b) Release and transport of radionuclides and chemical contaminants from the engineered system, through the geosphere and in the biosphere, should be modelled according to the same methods, as far as makes technical sense. This is facilitated given that key non-radioactive contaminants are likely to include metals and semi-metals. The main distinction arises if an organic contaminant degrades to a more toxic form, but this is little different (in terms of performance assessment modelling) from having to handle differences in transport and impact between parent radionuclides and their progeny.

c) It is appropriate to assess exposures of humans to ionising radiations in terms of effective dose, but to assess exposures to chemical pollutants in terms of intake rates by ingestion or air concentrations. However, it is important to recognise that these are intermediate measures and that they need to be related to potential health effects. For ionising radiations in prospective assessments, effective dose can be converted to individual detriment to health using a slope factor. The slope factor generally used includes contributions from fatal cancer, non-fatal cancer and hereditary disease, and takes into account the associated years of life lost or impaired. For genotoxic, carcinogenic chemicals, slope factors are often recommended, but their use is not recommended by all authorities, due largely to uncertainties in the values of the slopes, or even whether a linear, no-threshold relationship is appropriate (noting that many of the data available on chemotoxicity are from animal studies). However, for coherence with the established approach to ionising radiations (for which similar concerns as to applicability can be raised), it is suggested that the slope factor approach should be adopted also for genotoxic, carcinogenic chemicals (assuming required data are available). However, for both ionising radiations and chemicals, it is recommended that where possible,

uncertainties in the slope be propagated through the analysis together with uncertainties in the assessed levels of exposure.

d) In the context of radioactive waste disposal in purpose built repositories, tissue and organ dose rates to representative individuals are not likely to be sufficiently high to give rise to deterministic effects (except, possibly, in some human intrusion scenarios). Therefore, consideration can be directed to consideration of chemical pollutants that might give rise to deterministic effects above some threshold of exposure. The exposure-response relationship for such effects is generally strongly sigmoidal, so the range of exposures between almost no induction and induction in all sensitive individuals in a population is limited. In these circumstances, it seems prudent, and in line with the approach adopted in radiological protection, to set limits on exposure to prevent such effects. This can be achieved, as is currently done, by applying an uncertainty factor to a point of departure, to define an exposure that should not be exceeded. Because effects typically depend both on the chemical form of the pollutant and the pathway leading to exposure, more than one point of departure and uncertainty factor may be required.

e) Chemotoxic substances induce adverse health effects by a variety of mechanisms. These can have, but do not always have, commonalities with the mechanisms by which ionising radiations induce adverse health effects. Therefore, simple index quantities (weighted total exposures) cannot be recommended for application across wide ranges of chemicals or between chemicals and ionising radiations. However, there are contexts in which index quantities can be useful, notably in summing over a group of closely related chemicals, e.g. dioxins and dioxin-like compounds. This may be particularly helpful where analytical methods have difficulty in distinguishing the individual components in a mixed exposure.

f) The diversity of mechanisms involved means also that it is difficult to evaluate the effects of exposures to mixtures of toxic agents and, specifically, to determine whether synergistic interactions may enhance the effects of the agents over their individual or summed effects. For some agents, e.g. smoking and radon exposure, multiplicative or sub-multiplicative effects have been observed. In practice, where mixed exposures occur, one or, at most, a few agents will usually be found to dominate. The potential significance of the mixed exposure may then be evaluated by considering the likely response to the dominant agent or agents and then evaluating how this might be perturbed by the other agents present. This will typically require consideration of the primary toxicological literature, examining issues such as whether the target tissues and organs differ between the agents, whether one agent might act as an initiator in combination with another as a promoter, and whether the agents may affect each other's metabolism and biokinetics.

g) With genotoxic, carcinogenic agents, which are likely to be a principal cause of concern at low exposure levels, the initial adverse effect is thought to be the induction of double strand breaks in the DNA of stem cells or their immediate progenitors. It is becoming feasible to culture such cells *in vitro* and this may be a promising approach to assessing the impacts of such agents either singly or in combination, e.g. by studying the induction of mutations, chromosomal aberrations, genomic instability or other sequelae of DNA mis-repair. However, this addresses only the initial induction of effects at the sub-cellular level. Additional modelling, supported by data, is required to interpret these results in terms of likely increases in cancer induction. Tumour initiation, proliferation and progression all need to be addressed. Multi-stage models of carcinogenesis may be useful in this context.

h) In terms of protection of the environment, the principal interest is likely to be on environmental characteristics at the community, population or habitat level. However, for convenience, protection standards may be couched in terms of exposure of the individual organism.

i) For both exposure to ionising radiations and chemical pollutants, standards for environmental protection are generally based on precautionary approaches. These include definitions of compliance values set by reference to the sensitivity of the most sensitive species, use of precautionary uncertainty factors, and use of cautious over-estimates in exposure calculations. In some contexts, notably with ionising radiations, the compliance values are described as screening thresholds, i.e. exposures above the thresholds are an indication of a need for further investigation, but do not necessarily imply that adverse effects will be observed. This is in contrast to the approach for chemicals whereby the same approaches to deriving assessment criteria are largely applied, yet the resultant values are largely applied as limits that should not be exceeded. The adoption of precautionary approaches for individual toxic agents, with the degree of caution differing between agents, adds to the difficulty in comparing the effects of different environmental stressors or in assessing the overall impact of multiple stressors.

j) Additionally, in an environmental impact assessment, the effects of radiotoxic and chemotoxic stressors will have to be considered in conjunction with the effects of other stressors, the distributions of which will be altered by the proposed or existing development. These stressors may include thermal and noise pollution, among others. In many contexts, radiotoxicity and chemotoxicity will be minor considerations compared with these other stressors. However, even if this is the case in the short term, it may not apply in the long term, over which multiple generations will be exposed to the radiotoxic and chemotoxic materials.

k) Because of the diversity of local rules of engagement between communities and the degree to which those communities are open to changing regional influences, it is unlikely that generic, quantitative relationships can be established between levels of exposure to one or more toxic agents and responses at the community, population or habitat level. Therefore, it seems likely that ecological impact assessments will be qualitative, rather than quantitative. They may provide no more than value judgements that levels of exposure are of negligible, small, moderate or large significance.

There is a clear driver to assess the different risks in a similar and proportionate manner so as to support unbiased and reasonable decisions; however, comprehensive assessment addressing all aspects of risk in detail is likely to be impractical. Therefore, there is a continuing need for some common measure of hazard that supports identification of risk management priorities for mixed hazardous waste. This might be just as true for different types of hazardous waste as well as when radioactive waste is included.

Such a common measure needs to account not only for the basic characteristics related to toxicity of the components but also for factors concerning sources and pathways that constrain the potential for realisation of the hazard. While the overall picture, including the different regulatory contexts, remains complex, the non-radiologically hazardous components of many radioactive wastes appear to relate to relatively few elements and materials which are already reasonably well understood, such as U, Pb, Cd, Cr and asbestos. Therefore, technical progress would appear to be most affective that focusses on a relatively limited set hazardous components, especially for the relatively large volumes of LLW and very LLW arising in decommissioning and remediation of legacy sites. Such technical progress could benefit from parallel developments in international recommendations on management and regulation of wastes which are radioactive but also present other hazards. Such work should ideally draw a good balance between prescription and guidance, taking account of the wide range of regulatory and other contexts that arise.

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Appendix A. Illustration of the assessment of chemical alongside radiological impacts

A.1. Background and objectives

The purpose of this illustration is to show how chemical impacts can be assessed alongside radiological impacts on the environment in a complementary fashion that allows the two sets of impacts to be assessed against each other in a coherent manner. The illustration is taken from the US Department of Energy (DOE) radiological impact assessment for Yucca Mountain, as described in its License Application and License Application Update (US DOE, 2008a and b) complemented by information from the US Nuclear Regulatory Commission (NRC) Supplemental Environmental Impact Assessment (SEIS) (NRC, 2016).

A.2 Assessment context for the illustration

The Total Safety Performance Assessment (TSPA) modelling reported in the License Application Update for Yucca Mountain relates only to the radiological impact assessment of Yucca Mountain. This impact arises because infiltration percolating through the unsaturated zone of the mountain can corrode and penetrate the waste containers leading to release of radionuclides. These radionuclides are then transported downward through the lower part of the unsaturated zone, enter the regional aquifer where they are transported sub-horizontally to Amargosa valley. The radionuclide plume is then taken to be captured by groundwater wells, with the contaminated water that is abstracted used for both domestic purposes and irrigation. Although evaluation of the radiological impact of the repository is sufficient for addressing compliance with the Code of Federal Regulations at 10 CFR 63, it is not sufficient to address the requirements of the US National Environmental Policy Act (NEPA) (https://www.epa.gov/nepa), which requires consideration of the degradation of water quality in the regional aquifer due to both radioactive and non-radioactive contaminants.

In this context, the US NRC reviewed the US DOE's 2002 "Final Environmental Impact Statement for a Geologic Repository for the Disposal of Spent Nuclear Fuel and High-Level Radioactive Waste at Yucca Mountain, Nye County, Nevada" and 2008 "Final Supplemental Environmental Impact Statement for a Geologic Repository for the Disposal of Spent Nuclear Fuel and High-Level Radioactive Waste at Yucca Mountain, Nye County, Nevada," in accordance with the findings and scope outlined in the NRC staff's 2008 "Adoption Determination Report for the U.S. Department of Energy's Environmental Impact Statements for the Proposed Geologic Repository at Yucca Mountain." Based on that review, the NRC found that DOE's environmental impact statements (EISs) did not adequately characterise impacts from potential contaminant releases to groundwater and from surface discharges of groundwater.

Specifically, the NRC found that the DOE analysis did not provide adequate discussion of the cumulative amounts of radiological and non-radiological contaminants that may enter the groundwater over time and how these contaminants would behave in the aquifer and surrounding environments. Because the DOE would not commit to providing the additional analyses required, the NRC developed a supplement to the SEIS to provide the information the NRC Staff identified as necessary. Two distinct but related aspects of potential impacts on the groundwater system were addressed in that supplement. These are (i) the nature and extent of the repository's impacts on groundwater in the aquifer (beyond the post-closure compliance location) and (ii) the potential impacts of the discharge of potentially contaminated groundwater to the ground surface.

This appendix does not address all aspects of the NRC analyses. Instead, it focuses on the single issue of the way in which the NRC aligned its assessment of cumulative releases of metals to the regional aquifer with the approach that the DOE adopted in its License Application.

A.3. Illustrative calculations

The release rate model that the NRC adopted was based on that used by the DOE, which used the following assumptions and values.

- The materials that corrode to produce the metals of interest (Mo, Ni and V) include construction material, all waste package material, and internal fuel assemblies and spent fuel. The number of failed waste packages was taken from the TSPA output for the combined scenario case (including the nominal, early failure, igneous intrusion and seismic ground motion - fault displacement scenario classes).
- The mobilisation rate for each element was calculated based on the corrosion rate used in the DOE Safety Assessment (US DOE, 2008a and b) and the exposed area of all external material (from construction and waste packages) and internal material (exposed in failed waste packages). The release ends when the thickest component has been completely corroded.
- The mobilisation rate was applied at the unsaturated-saturated zone boundary, i.e. any delays due to transport in the unsaturated zone were neglected, and a transport model based on breakthrough curves from the TSPA was used to determine the mass flux reaching the post-closure compliance location at 18 km from the repository.

The mass fluxes released from the repository and arising at the regulatory compliance location are shown in Figure A-1 of the SEIS. That figure is reproduced as Figure A-1 below.

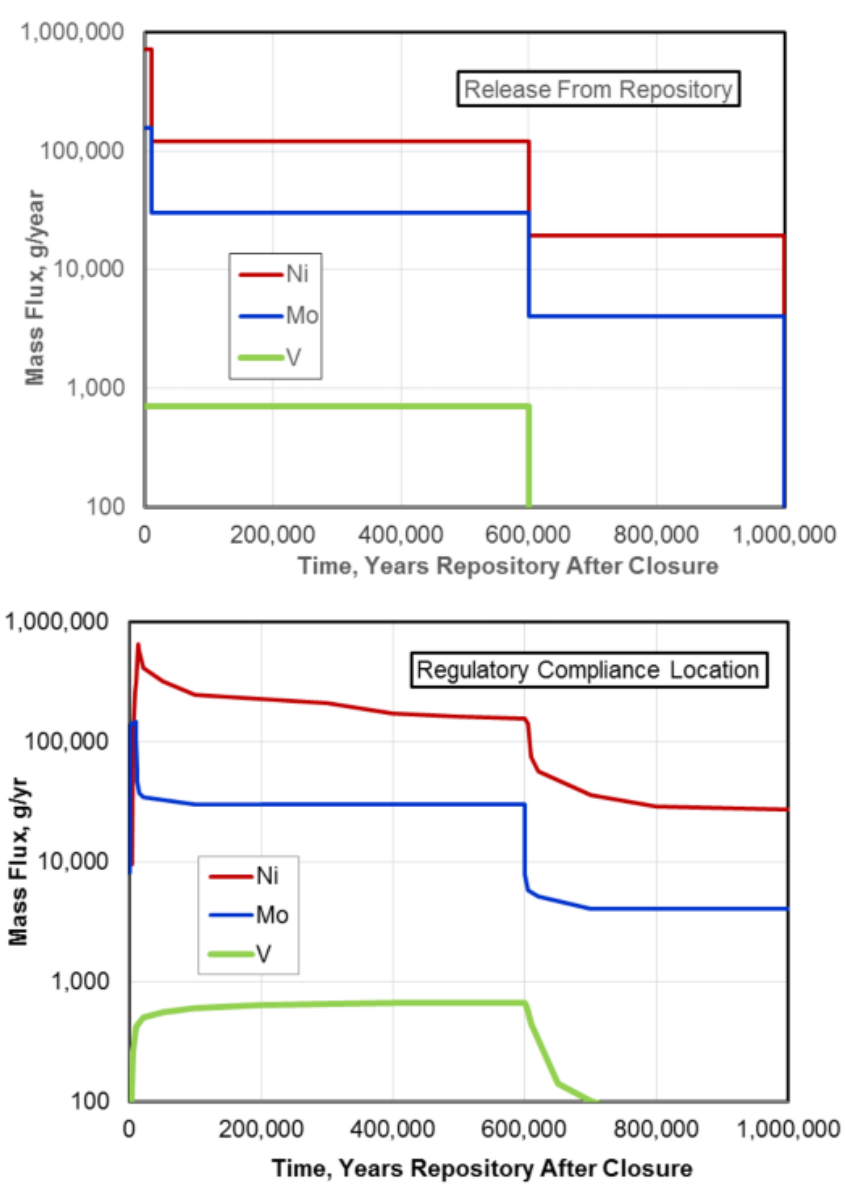

Figure A.1. Reproduction of Figure A-1 of the SEIS showing Mass Fluxes of Molybdenum, Nickel and Vanadium.

A key point to note is that the transit times through the saturated zone to the compliance location are generally short compared with the timescales of release, such that the mass fluxes are not substantially modified in transit through the aquifer. Secondly, the corrosion rates assumed mean that much of the mass flux of each element is uniformly distributed over 600,000 years. By reading the mass fluxes and periods over which those mass fluxes apply from the upper part of Figure A-1, the totals shown in Table A-1 are obtained.

Table A-1. Estimated Releases of Molybdenum, Nickel and Vanadium over Different Periods from Figure A-1 of the SEIS.

Metal	Mass Flux (kg/y) 0	$1\ 10^4 – 6\ 10^5$ y	$6\ 10^5 – 1\ 10^6$ y	Total Mass Released (kg) $0 – 1\ 10^4$ y	$1\ 10^4 – 6\ 10^5$ y	$6\ 10^5 – 1\ 10^6$ y
Mo	154	29.4	3.92	$1.54\ 10^6$	$1.73\ 10^7$	$1.57\ 10^6$
Ni	698	115	19.1	$6.98\ 10^6$	$6.79\ 10^7$	$7.64\ 10^6$
V	0.698	0.698	0	$6.98\ 10^3$	$4.12\ 10^5$	0.0

Thus, the total releases estimated are $2.05\ 10^7$ for Mo, $8.25\ 10^7$ kg for Ni and $4.19\ 10^5$ kg for V. For comparison, information on releases given in Tables 3.1a and 3.1b of the NRC supplement to the DOE EIS (NRC, 2016) are shown in Table A.2. The two sets of results are very similar, showing that almost all the released material eventually accumulates in the Amargosa Farms area having been transported through the aquifer.

Table A-2. Information on releases of metals reproduced from Tables 3-1a and 3-1b of the NRC Supplemental Environmental Impact Assessment (SEIS, NRC, 2016).

Amount of Selected Metals from the Repository in the Aquifer Environment between the Post-closureCompliance Location and Amargosa Farms (kg)				
Metal	**Present-day Climate**		**Cooler/Wetter Climate**	
	10,000 years	**1 million years**	**10,000 years**	**1 million years**
Molybdenum (Mo)	$1.3\ 10^5$	$8.9\ 10^4$	$1.1\ 10^5$	$9.5\ 10^4$
Nickel (Ni)	$4.2\ 10^6$	$7.3\ 10^6$	$1.7\ 10^7$	$3.3\ 10^6$
Vanadium (V)	$2.2\ 10^3$	$2.6\ 10^3$	$2.2\ 10^3$	$1.3\ 10^3$
Amount of Selected Metals from the Repository accumulated at the Amargosa Farms Area (kg)				
Metal	**Present-day Climate**		**Cooler/Wetter Climate**	
	10,000 years	**1 million years**	**10,000 years**	**1 million years**
Molybdenum (Mo)	$1.3\ 10^6$	$2.1\ 10^7$	$1.3\ 10^6$	$2.1\ 10^7$
Nickel (Ni)	0	$7.3\ 10^7$	0	$7.7\ 10^7$
Vanadium (V)	0	$4.0\ 10^5$	0	$4.0\ 10^5$

Figure A-1 and Table A-1 emphasise that the major part of the release occurs between 1 10^4 y and 6 10^5 y, i.e. slow corrosion of the waste packages is assumed to persist throughout that period (the rock bolts, tunnel and drift liners, and other installed rock supports are stated in the Appendix A of the SEIS to be assumed to be completely corroded in 1 10^4 years, internal waste package components are assumed to completely corrode in 5 10^5 years, and Alloy 22 is assumed to completely corrode over 6 10^5 years).

Also, from Table A-1, the SEIS estimates that releases to the aquifer in the first 1 10^4 years would be 1.54 10^6 kg for Mo, 6.98 10^6 kg for Ni and 6.98 10^3 kg for V. From Table A-2, the amounts of these elements in the aquifer between the post-closure compliance location and Amargosa Farms at 1 10^4 years under present-day climate are 1.3 10^5 kg for Mo, 4.2 10^6 kg for Ni and 2.2 10^3 kg for V. These amounts correspond to 0.084, 0.602 and 0.315 of the released, Mo, Ni and V, respectively. These fractions differ because these three elements are subject to different degrees of retardation in the aquifer.

Given these metal burdens in the aquifer, it is important to address the concentrations in groundwater that could result. The volume used by the NRC is described at page A-12 of the SEIS. They cautiously neglect lateral and vertical dispersion and treat the plume as a rectangular volume 3 km wide, 100 m thick and 17 km long between the post-closure compliance location and Amargosa Farms. The SEIS references the transport properties of the flow paths to DOE, Analysis of Postclosure Groundwater Impacts for a Geologic Repository for the Disposal of Spent Nuclear Fuel and High-Level Radioactive Waste at Yucca Mountain (US DOE, 2014).

At page B-5 of that report, the porosities of the carbonate aquifer and the alluvial deposits are given as 0.01 and 0.18, respectively. These are used to provide average porosities over the whole flow path. For the pumped flow path to Amargosa Farms, the weighted porosity is 0.16. Table B-1 of that report (at page B-6) also gives the distribution coefficients, K_d values, adopted for Mo, Ni and V as 0.0, 0.015 and 0.008 $m^3\ kg^{-1}$, respectively.

The aquifer has a volume of 3 10^3 × 1 10^2 × 1.7 10^4 = 5.1 10^9 m^3. With a porosity of 0.16, the volume of water contained within it is 8.16 10^8 m^3. However, when sorption to solids is considered, the effective volume is 5.1 10^9 ($\varphi + \rho K_d$), where φ is the porosity and ρ (kg m^{-3}) is the dry bulk density (taken as 2 10^3 kg m^{-3} from Table B-1 of DOE (2014)). Thus, using the K_d values adopted by the NRC from the DOE, the effective volume of the aquifer is 8.16 10^8 m^3 for Mo, 1.54 10^{11} m^3 for Ni and 8.24 10^{10} m^3 for V.

Based on these effective volumes and the amounts of these three elements present in the aquifer at 1 10^6 years, as estimated above, the concentrations of these elements in groundwater are estimated as follows:

- Mo: 8.9 10^4 / 8.16 10^8 = 1.1 10^{-4} kg m^{-3} or 0.11 mg L^{-1}
- Ni: 7.3 10^6 / 1.54 10^{11} = 4.7 10^{-5} kg m^{-3} or 0.047 mg L^{-1}
- V: 2.6 10^3 / 8.24 10^{10} = 3.2 10^{-8} kg m^{-3} or 3.2 10^{-5} mg L^{-1}

For comparison, the NRC at Table 3-2 of the SEIS gives peak concentrations in the aquifer at Amargosa Farms over one million years of 0.0073 mg L^{-1} for Mo, 0.0056 mg L^{-1} for Ni and 3.2 10^{-5} mg L^{-1} for V. These are 0.07, 0.12 and 1.0 of the values given above, respectively, with the difference largely reflecting distinctions in the location at which the concentration is estimated (i.e. at Amargosa Farms compared with the average in the aquifer between the compliance location and Amargosa Farms) and differences in retardation within the aquifer.

As the NRC comments at page 3-10 of the SEIS, no EPA MCLs have been established for Mo, Ni or V in drinking water. However, the WHO has provided water quality guidelines for Mo and Ni (but not for V). These guidelines are given in WHO (2011).

For Mo, the WHO comments that concentrations in drinking water are usually less than 0.01 mg L^{-1} and that in a 2-year study of humans exposed via drinking water the NOAEL was found to be 0.2 mg L^{-1}. As Mo is an essential trace element, the WHO considered that a safety factor of three applied to this concentration would be adequate to reflect intra-species variation and, therefore, recommended a health-based guidance value of 0.07 mg L^{-1}. This is below the average aquifer value of 0.11 mg L^{-1} estimated above. However, an individual consuming two litres of water per day would have an intake of 0.22 mg d^{-1} of Mo, which is similar to the total estimated daily requirement of 0.1 to 0.3 mg given by the WHO.

For Ni, the WHO also provides a guideline value of 0.07 mg L^{-1}. This is based on a TDI of 12 µg per kg body weight, assignment of 20% of this to drinking water, and a 60 kg adult drinking 2 litres per day. The WHO comments that this guideline value is close to the acute LOAEL, but that the LOAEL is based on total exposure from drinking water, and absorption from drinking water on an empty stomach is 10- to 40-fold higher than absorption from food. Thus, the WHO concludes that basing total acceptable intake for oral challenge from studies using drinking water on an empty stomach can be considered a worst-case scenario. However, set against this the data relate to a LOAEL rather than a NOAEL, which would be expected to be lower.

The guideline value of 0.07 mg L^{-1} is a little larger the assessed average concentration in the aquifer of 0.047 mg L^{-1} derived above.

A.4 Comment

This study illustrates that a similar model can be used to represent both radionuclide and chemical contaminant transport from a repository, but that the source terms for the two calculations may be very different, i.e., in this case spent nuclear fuel for radionuclide releases, but near-field engineered components and waste packages for other contaminants. In turn, this means that the timescales for release can be different. It also illustrates a regulatory regime in which the cumulative load of contaminants in the aquifer is important and not just the peak concentrations that arise at specific locations. Finally, it shows that, even in a large aquifer and with corrosion-resistant waste packages, the concentrations of non-radiological contaminants may be significant in comparison with WHO drinking water standards.

Appendix B. Consideration of synergistic effects

B.1 Introduction

Toxic chemicals and ionising radiations (hereafter collectively described as toxic agents) can induce adverse effects in organisms through a wide variety of mechanisms that are often only poorly understood. Furthermore, even a single toxic agent can operate through a variety of mechanisms, e.g. both initiating and promoting carcinogenesis. The nature of the mechanism or mechanisms involved will determine the overall shape of the exposure-response relationship and whether there is a threshold for clinically or environmentally significant adverse effects or whether there is a possibility of such effects occurring in some individuals even at very low exposures, with the magnitude of the exposure primarily determining the likelihood that the effect occurs rather than its severity. Where an organism is exposed to several toxic agents, the relationship between the pattern of exposure, the frequency of induction of deleterious effects and the severity of those deleterious effects may be extremely complex. The situation is further complicated by the consideration that the effects of exposure to a toxic agent or agents may be affected by aspects such as the period of exposure, the age or stage in its life cycle of an individual, and the impact on that individual of environmental stressors other than the toxic agent or agents under consideration.

In this appendix, consideration is given to the extent to which interactions between toxic agents may need to be considered in regulating releases of those agents from geological facilities for the disposal of solid radioactive wastes. Consideration is given to the issue as to whether such agents might act synergistically, i.e. exposure situations in which their combined effect might be greater than the sum of their effects considered separately. In addressing this issue, consideration is given both to potential adverse effects on humans and potential adverse effects on non-human biota. In these two contexts, the key issues are rather different. For humans, the focus is on the health status of the individual, so attention is given to the induction of clinically significant conditions, notably cancer, but also a wide variety of other pathological conditions, such as impaired tissue and organ function. For non-human biota, less emphasis is placed on the health of the individual and more on the maintenance of viability of populations and communities, e.g. by considering the need not to adversely impact biodiversity. Thus, endpoints such as fertility, fecundity and age-specific mortality become of greater interest, though other considerations, such as the genetic load carried by a population, may be of relevance as indicators of its long-term sustainability.

Clearly, a comprehensive account of issues relating to the induction of adverse effects by a wide range of toxic agents acting individually or in combination would be an enormous undertaking. Therefore, this appendix focuses only on some general issues, illustrated, as appropriate, by model calculations and information from the literature. Following this introduction, Section B.2 addresses mechanisms of induction of adverse effects in humans and Section B.3 provides a corresponding account for non-human biota. Section B.4 then gives examples of where synergistic effects have been observed in practice, Section B.5 presents a simple example showing how synergistic effects can arise in a multi-stage model of carcinogenesis that includes cellular proliferation and Section B.6 illustrates how synergistic effects may be described in terms of non-linear exposure-response surfaces in two or more dimensions. Conclusions from this review and analysis are given in Section B.7.

B.2 Mechanisms of induction of adverse effects in humans

In humans exposed to ionising radiations, the main adverse effect of concern at low doses and dose rates is the induction of cancer. This is also the case for many chemicals, particularly those that act

as genotoxic agents. Thus, here attention is focused on mechanisms of carcinogenesis, with some final remarks on adverse tissue reactions that are considered to have a threshold (either in radiation dose or in chemical exposure) for their induction.

Mechanisms of carcinogenesis have recently been discussed in detail by the ICRP (2015) in the context of the role of stem cells and the effects of radiation on those stem cells and their descendants. Although oriented towards the effects of ionising radiation, the discussion of the role of stem cells in carcinogenesis is of wider relevance and is adopted here as a basis for description of the key biological processes and issues.

Carcinogenesis from radiation is considered to be a stochastic event, originating in a single transformed target cell. Generally, the target cells are considered to be the stem cells, and possibly some of their progenitor cells, in each tissue. These target cells have tissue-specific characteristics and reside in micro-environmental 'niches' that regulate their proliferation and differentiation (ICRP, 2015).

B.2.1 Characteristics of Stem Cells

Stem cells differ between early embryogenesis, foetal development and after the establishment of adult tissues. Embryonic stem cells are totipotent and have the capacity to differentiate into all tissue types. In the foetal stage, stem cells are lineage-committed, to some extent, and contribute to specific tissues in the adult. In these two stages, stem cells mainly undergo symmetric division to produce two daughter stem cells associated with an increase in size of the embryo or foetus (although asymmetric division, see below, also occurs during foetal development) (ICRP, 2015).

In contrast to the embryonic and foetal stages, adult tissue stem cells are mainly fully committed with restricted differentiation capabilities, and they usually divide in asymmetric fashion, resulting in a daughter stem cell and a second daughter, progenitor cell that is subject to differentiation as it proliferates (ICRP, 2015).

Progenitor cells then divide further to increase in number and differentiate into functional cells that are eventually lost by senescence after having served their required functions. Whereas stem cells often (but not always) exhibit long cell-cycle times and are referred to as quiescent, progenitor cells generally divide more rapidly, but with limited proliferative capacity. Although stem cells were once considered to have an unlimited proliferative capacity, it now seems that their proliferative capacity may be large, but finite, since they have been found to demonstrate telomere shortening because of successive cell divisions. Loss of telomeres can result either in cell senescence or in genomic instability potentially leading to cancer induction (ICRP, 2015; Bristow and Harrington, 2005). Cells that continue to proliferate, such as cancer cells, must maintain their telomeres. In cancer cells this is often achieved by activation of the enzyme telomerase that adds new telomere DNA to chromosome ends (Bristow and Harrington, 2005).

The differential roles of stem cells and progenitor cells is part of a strategy for maintenance of the long-term integrity of the genomic characteristics of stem cells, by minimising replication-mediated mutations while supplying many cells to the functional component of a tissue. The progression from stem cell to differentiated functional cell is generally unidirectional, but de-differentiation and transformation can occur, such as when stem cells are lost for some reason and vacant stem-cell niches become occupied by a neighbouring stem cell or de-differentiated progenitor cell (ICRP, 2015).

The number of lineages supplied by a type of stem cell varies greatly. In the epidermis, stem cells supply a limited number of lineages, whereas haematopoietic stem cells (HSCs) supply a wide variety of lineages. The number of divisions between the stem cell and its fully differentiated functional descendant also varies greatly, depending on the number of lineages supported, the numbers of functional cells required for each lineage, and the rate of turnover of those functional cells (ICRP, 2015).

As mentioned above, the body requires a strategy for maintaining the genomic integrity of tissue stem cells throughout the lifetime. This is achieved by minimising DNA damage and cell division, and DNA replication, while maximising repair of DNA damage and eliminating damaged or mutated cells. Abundance of antioxidants in stem cells and the provision of a hypoxic micro-environment by the stem-cell niche can contribute to minimising DNA damage, while quiescence facilities DNA repair (by providing an extended period over which it can occur) and minimises replication-mediated mutation. Damaged stem cells can be eliminated by apoptosis or by differentiation. Also, competition of stem cells for the occupancy of a limited number of niches is likely to help in eliminating damaged stem cells (ICRP, 2015).

Quiescence may itself be maintained by existence in a hypoxic micro-environment, e.g. high concentrations of Reactive Oxygen Species (ROS) can force HSCs into cell cycling. However, quiescence poses its own problems in respect of DNA repair. A key mechanism by which ionising radiation induces the DNA damage that may underlie radiation carcinogenesis is the induction of double-strand breaks (DSBs). These are repaired either by homologous recombination (HR) or non-homologous end joining (NHEJ) (ICRP, 2015; Bristow and Harrington, 2005). HR is potentially error free, as it takes place in S- and G2-phase cells, by copying the intact part of the sister DNA strand. NHEJ takes place in non-cycling cells and in all phases of the cell cycle, but is intrinsically error prone. However, there are two NHEJ error repair systems one that is more accurate and an 'alternative' that is highly error prone, and that catalyses many genomic rearrangements, some leading to oncogenic transformations. Only the NHEJ error repair systems are available to quiescent cells. Operation of these repair systems has the potential to enhance the survival of quiescent stem cells, but may also result in the induction of chromosome mutations (ICRP, 2015). Cell-cycle checkpoints exist that help ensure successful and accurate DNA replication and repair prior to mitosis (Bristow and Harrington, 2005).

To avoid naturally occurring mutations accumulating in stem cells, these cells may adopt an alternative strategy, as proposed by Cairns (1975), in which asymmetric segregation of the DNA strands occurs. The stem cell retains the template DNA strand after each round of DNA synthesis, whereas the progenitor cell inherits the daughter strand. In this way, replication errors are routed to the progenitor cell. Currently, this 'immortal strand' hypothesis remains controversial and further evidence is required to determine to what extent, and in what contexts, it occurs (ICRP, 2015).

Stem cell niches differ between tissues and within a single tissue. Thus, in bone marrow, there are three types of niches for HSCs. These are an osteoblastic niche, a vascular niche and a medullary niche. HSCs residing in the osteoblastic niche are of primitive and less committed types, and this type of niche seems to be particularly hypoxic to afford specific protection to these more primitive cells (ICRP, 2015).

Although tissue stem cells normally divide asymmetrically, this is not always the case. Stem cells can divide symmetrically. This can give rise to an excess of stem cells competing for a limited number of niches, with elimination of less competitive cells. Stem cells can also divide into two progenitor cells, leading to the existence of a vacant niche that can be occupied by a surplus stem cell or de-differentiated progenitor cell. Together, these mechanisms result in turnover of the stem cell 'pool'. For example, a single clone of mutant stem cells has been observed to take over an entire intestinal crypt in 5-7 weeks in the colon and 12 weeks in the small intestine after mutagen treatment in mice. In perinatal and post-natal life, overall growth of the body can lead to an increase in the number of stem cell niches available, providing accommodation for a growing number of stem cells derived from symmetric division (ICRP, 2015).

B2.2 Role of Stem Cells in Carcinogenesis

The target cells for carcinogenesis are considered to be tissue stem cells and their proximal progenitor cells. This judgement is based on the many resemblances between tissue stem cells and cancer cells, and the observation of cancer stem cells in human leukaemia and in various solid

tumour types arising in the breast. Also, stem cells are the only cell type that has a sufficiently long residence time in the body to accumulate multiple mutations and gain a malignant phenotype. There is also some evidence that the risk of carcinogenesis in different tissues correlates with the estimated size of the stem cell 'pool' or with the product of stem cell number and the lifetime number of cell divisions per stem cell. However, there are examples suggesting that progenitor cells can also be a target for carcinogenesis, particularly where they have a high proliferative capacity (ICRP, 2015).

The current model of radiation carcinogenesis assumes that radiation acts as a mutagen, and gives possibly one or two carcinogenic mutations to a target cell (ICRP, 2007; 2015). Radiation is known to induce DSBs that are prone to result in large mutations, such as deletions and translocations. Deletion mutations can inactivate tumour-suppressor genes, whereas translocation can activate proto-oncogenes by juxtaposing them to strong transcription promoter elements or making fusion genes with oncogenic functions (see Oster et al., 2005 for a detailed account of oncogenes and tumour-suppressor genes). Thus, one or two damage events (giving a linear-quadratic dose response relationship) can result in multiple changes to the genome and the potential for progression to overt cancer. In addition, radiation has been found to readily induce micronuclei and it has recently been discovered that micronuclei have a role in the process of chromothripsis, in which multiple genomic rearrangements occur within sharply circumscribed regions of one or a few chromosomes. Thus, again, one or two damage events can result in multiple changes to the genome (ICRP, 2015).

It is emphasised that radiation also acts in a non-targeted fashion, inducing transient changes in gene expression and genomic instability, where the effect is not expressed until after many cycles of cell division. These effects may be induced either in irradiated cells or in unirradiated, bystander cells at distances of as much as a few millimetres from the irradiated cells. These effects may be mediated by cell-to-cell communication via tight junctions or by the movement of transmitter molecules through the intercellular medium. The role of such non-targeted effects in human carcinogenesis is yet to be established, but is a currently active area of research (ICRP, 2015). Genomic instabilities may arise from gene mutation, but may also occur due to gene amplification and the epigenetic modification of gene expression through gene methylation and gene acetylation (Bristow and Harrington, 2005). A popular account of epigenetic processes and effects is given by Carey (2012).

Based on the epidemiological evidence, the ICRP (2007) uses both relative risk and absolute risk models in transferring radiation risks from one population to another. The absolute risk model assumes that the risk of incurring a cancer per unit radiation exposure is the same in the two populations irrespective of the background risk of the cancer in those two populations. The relative risk model assumes that the ratio of the induced risk to the background risk per unit of radiation exposure is the same in the two populations. The absolute risk model can be interpreted as implying that radiation-induction and background processes both operate at the same stage of carcinogenesis, presumably induction of the initiating lesion, whereas the relative risk model can be interpreted as implying that they operate at successive (though not necessarily immediately successive) steps. This might arise if radiation and stem-cell replication both induced DSBs and that these DSBs then gave rise to cancer through processes affected by factors such as age, gender, ethnicity, diet and state of health. In the absolute and relative risk models, the background risk is generally subtracted, so risk is expressed either as Excess Relative Risk (ERR) or Excess Absolute Risk (EAR). The models themselves are, therefore, often described as ERR or EAR models.

Genotoxic chemical carcinogens have a wide diversity of chemical structures, but all of them are electrophilic, either directly or after enzymatic conversion. Reactive electrophiles interact readily with negatively charged, electron-rich groups on biological molecules, such as proteins and nucleic acids, forming covalent adducts. These, if not repaired prior to the next cycle of DNA replication, may lead to errors in DNA replication and hence to fixation of the damage. Most genotoxic carcinogens require enzymatic bioactivation in order to damage DNA. The enzymes involved are

typically active with a wide range of substances, since their primary role is to convert toxic lipophilic compounds to water-soluble compounds that are readily excreted (Okey et al., 2005).

With a few exceptions, both direct-acting carcinogens and those requiring prior metabolic activation interact with DNA by three general types of reaction chemistry. These reactions involve transfer of an alkyl group, an arylamine group or an aralkyl group. These different types of DNA-reactive chemical agents tend to produce distinctive adducts on the individual DNA bases (Okey et al., 2005).

Although most of the chemicals that have been identified as probable human carcinogens are genotoxic, a large fraction of the chemicals that are carcinogenic in rodent bioassays are not genotoxic. Whereas genotoxic carcinogens usually induce tumours in many animal species and varied anatomic sites, non-genotoxic carcinogens tend to be much more restricted in their action. This suggests that non-genotoxic carcinogens exert their effects by altering functions in specific regulatory pathways. Non-genotoxic carcinogens, in general, share with tumour promoters an ability to stimulate cell proliferation (Okey et al., 2005).

B.2.3 The Progression from Initial Lesion to Malignancy

The discussion so far has related to the target cells for cancer induction due to ionising radiation or other agents and their transformation from a normal to a malignant phenotype. However, the induction of a malignant phenotype in one, or a limited number, of target cells does not necessarily imply that the individual will experience a clinically diagnosed cancer within their lifetime. The progression from initial lesion to malignancy in radiation- and chemically induced carcinogenesis has been succinctly summarised by Okey et al. (2005).

Early experiments led to a multistep model that divided the carcinogenic process into the three stages of initiation, tumour promotion and tumour progression. In practice, the process does not always neatly compartmentalise into these three stages, and more stages may occur. Nevertheless, this remains a useful framework for description.

An initiated cell is one in which an alteration has occurred in the genome predisposing a cell and its progeny to carcinogenesis, i.e. a malignant phenotype has been established. At least three cellular functions are important in initiation. These are DNA damage, DNA repair and cell proliferation. DNA damage may be direct or indirect by ionising radiation, and may involve metabolism of a chemical to activate the carcinogenic form of that chemical and/or inactivate it. DNA repair may occur by the HR and NHEJ mechanisms described in Section B.2.1. Cell proliferation is required to permanently embed the change in the genome, as non-reproducing, quiescent cells have the potential to implement DNA repair on long timescales.

Although initiation is irreversible, not all initiated cells will go on to establish tumours because many will die by apoptosis. An initiated cell is not a tumour cell, because it has not yet acquired autonomy of growth. The DNA alteration may remain undetected throughout the lifetime of the organism, unless further events stimulate development of a tumour.

In general, tumour promotion is the clonal expansion of an initiated cell with altered gene expression that gives the cell a selective growth advantage. Chemicals that act as tumour promoters cause cells to proliferate, but not to terminally differentiate, resulting in the proliferation of preneoplastic cells and the formation of benign lesions, e.g. papillomas, nodules or polyps. Where initiating and promoting agents are applied to an animal, no excess of tumours arises if the promoting agent is applied alone or before the initiating agent.

Tumour progression describes the process whereby the tumour acquires the ability to grow, invade local tissue and establish distant metastases. Increased genomic instability and karyotypic alterations are hallmarks of progression. Inherited or acquired mutations can increase rates of mutation in other genes thereby accelerating accumulation of further mutations. At the later stages of tumour progression, cell proliferation and cell death, and hence the growth of the

tumour, depend strongly on the rate and effectiveness with which angiogenesis results in the development of functional blood vessels within the tumour and the supply of oxygen to the proliferating cells. Although hypoxia may slow tumour growth, it may also promote rapid progression of tumour cells to a more malignant phenotype (Donovan et al., 2005).

Together, the processes of initiation, promotion and progression explain why a latent period of a considerable fraction of a lifetime may occur between exposure to ionising radiation or a toxic chemical and the clinical manifestation of a resulting malignancy.

B.2.4 Threshold and Non-Threshold Effects

In previous sections, it has been emphasised that both radiation-induced and chemically induced carcinogenesis can arise from one or two DNA changes in a single somatic cell resulting in transformation from a normal to a malignant phenotype. Clonal expansion, differentiation, genomic instability and escape from normal processes controlling cell division can lead to development of a clinically diagnosable cancer (either a leukaemia or a solid tumour). In principle, transformation of a single cell could result in the development of a clinically diagnosable tumour, so a response without threshold might be expected. However, this does not necessarily imply that the exposure-response relationship will be linear. With radiation, both one-hit and two-hit events may be implicated in the initial DNA damage, resulting in a linear-quadratic relationship. However, this linear-quadratic shape may be modified by processes of cell killing, induced or saturable repair processes, effects of cell proliferation, variations in individual sensitivity and the influence of competing causes of death. This last effect occurs because of the long latency periods involved. At low exposures, only a few cells may be transformed with none of them progressing to clinical malignancy within the lifespan of the individual. At higher exposures, more cells will be transformed and the chance of at least one of them progressing rapidly to clinical malignancy will be increased. Thus, even with genotoxic, carcinogenic agents, the exposure-response relationship may be highly non-linear and may exhibit a quasi-threshold below which clinically diagnosable effects are not observed. This is well illustrated by the threshold exposure-response relationships for 3-methylcholanthrene and BaP in mice shown at Figure 3.12 in Okey et al. (2005). In the case of non-genotoxic agents, there is no reason to suppose that a non-threshold relationship would apply even in relation to the initial stage of damage induction.

With toxic chemicals, a further consideration is that the active agent may be a metabolic product of the chemical to which the individual is exposed. Thus, the exposure-response relationship will be conditioned by the extent and rate of metabolic conversion of the original chemical to its active metabolite, and the rate of loss of that active metabolite from the body by excretion or further metabolism. This is well exemplified by the case of vinyl chloride monomer (VCM), which is metabolised to chloroethylene oxide by the mixed-function oxidase system present in the liver. The chloroethylene oxide is then further metabolised by a variety of pathways eventually leading to thiodiglycollate, a significant urinary metabolite. At low exposure levels, the rate of metabolism of VCM is at its maximum. However, at higher exposures the initial stage of metabolism saturates and the fraction of VCM metabolised decreases as the level of exposure increases (Thorne et al., 1986).

Where a threshold exists in the exposure-response relationship, the characteristic form of the relationship observed is an S-shaped curve. Below the threshold, incidence of the effect is zero. Above the threshold, the incidence rises, at first slowly and then more rapidly. However, as the exposure increases further, the rate of increase in incidence declines and the incidence eventually saturates at a maximum value. This maximum value may be unity if all the population is susceptible (as is the case for the haemopoietic syndrome arising from short-term, whole body irradiation by ionising radiation) or it may be less than unity if only a susceptible sub-population is affected. Empirically, a good representation of such exposure-response relationships is often the logistic relationship:

$$I(x) = F/(1 + \exp\{-k(x - x_0)\})$$

where I(x) is the incidence at exposure level x, F is the sensitive fraction of the population, k is the maximum slope of the incidence-exposure relationship and x_0 is the exposure at which the incidence is half its maximum value. Illustrative logistic relationships are shown in Figure B-1, taking F = 1 and x_0 = 3.

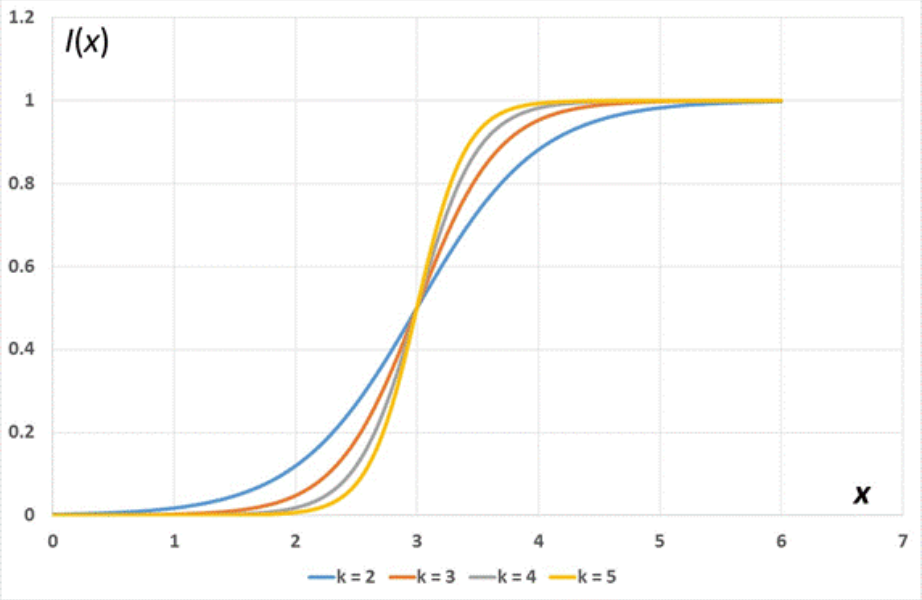

Figure B-1. Logistic relationships for F = 1, x_0 = 3 and various values of k.

If the logistic relationship is not sufficiently general, alternative relationships can be obtained by making x a monotonic function of exposure, e.g. x = ln(y), where y is the actual exposure and x is the derived value used in the logistic relationship.

B.2.5 Synergistic Interactions

For ionising radiation and genotoxic chemicals, the principal insult resulting in carcinogenesis is likely to be damage to nuclear DNA resulting in DSBs. Deletions or translocations may occur resulting in the activation of oncogenes or the deactivation of tumour-suppressor genes. Thus, a common measure of insult that could be estimated across a wide range of genotoxic agents would be the induction of DSBs (or their sequelae in terms of deletions and translocations) in stem cells of different types (both totipotent and pluripotent). The ability to achieve relatively pure cultures of stem cells is developing rapidly (ICRP, 2015), so such assays should be feasible soon. The advantage of such assays is that exposure-response relationships could be established both for individual toxic agents and for combinations of such agents. Thus, synergistic or antagonistic effects between agents could be investigated experimentally.

It is emphasised that such studies would primarily shed light on the interactions between toxic agents at the sub-cellular level. The exposure-response relationships observed would not necessarily translate into similar exposure-response relationships for clinically significant effects, due to the influence of a wide variety of processes that affect cell proliferation and tumour progression. Nevertheless, one could hope to develop conversion factors that would allow exposures to various toxic agents singly or in combination to be converted to a single aggregated measure of exposure that could be used to assess the overall impact on health from any specified exposure situation.

Whereas ionising radiation directly damages DNA and induces DSBs, with toxic chemicals it may be a metabolic product rather than the original chemical that is the genotoxic factor. This means that any *in vitro* assay must include a substrate that converts the toxic chemical to its active product. This would be analogous to the variant of the Ames Test in which a liver homogenate is added to the bacterial test system to metabolise the potentially toxic agent under test (Ames et al., 1973).

However, for non-genotoxic agents in combination with each other or with genotoxic agents, the situation is more complex, since one agent may influence the initiation process whereas the other may affect proliferation or tumour progression. In these circumstances, additive, sub-multiplicative, multiplicative and supra-multiplicative interactions are all possible. These types of interactions are explored further in the modelling studies described in Sections B.5 and B.6.

B.3 Mechanisms of induction of adverse effects in non-human biota

In the case of non-human biota, exposure-response relationships at the individual organism level will exhibit the variability of shapes described for humans in Section B.2. However, it seems likely that the exposure-response relationships for overall mortality, fertility and fecundity, which relate to the killing or sterilisation of substantial fractions of specific cell populations rather than the induction of mutagenic DNA damage in a few cells, are likely to exhibit sigmoidal shapes with thresholds or quasi-thresholds, as illustrated in Figure B-1. However, effects at the individual level will not often be of primary interest. Rather, attention should focus on considerations such as the sustainability of populations, communities and habitats and on the maintenance of biodiversity. Thus, effects on the individual organism need to be evaluated and interpreted in a wider ecological context.

It is emphasised that protection of individuals is not assured by the protection of a population, so long as that population remains sustainable. Protection of a community does not guarantee the protection of either individuals or populations. The converse of this is also true, i.e. it is not always necessary to protect specific populations to preserve ecosystem function. This is emphasised by lessons learned from community ecology (Lawton, 2000).

Broadly speaking, there are three models of how species richness relates to ecosystem performance (defined in terms of fluxes of energy and matter). The redundant species hypothesis suggests that there is a minimum of species diversity necessary for ecosystem functioning, but, beyond this minimum, most species are redundant in their roles. In contrast, the cumulative hypothesis postulates that all species are important, so that ecosystem processes are progressively more impaired as species are lost from the system (Lawton, 2000).

The idiosyncratic hypothesis postulates that the identities of species matter more than species richness per se. In consequence, ecosystem processes might change erratically and unpredictably if species are lost in arbitrary sequence from the system (Lawton, 2000). Under both the redundant species and idiosyncratic hypotheses, species could be lost from an ecosystem without affecting its performance. Although local biodiversity would be impaired, global biodiversity might be unaffected. Furthermore, if exposure to toxic agents caused the local mix of species to change, biodiversity might be increased, because the area or areas of high exposure would constitute new and distinctive habitat patches.

It must also be recognised that communities do not exist in a vacuum. Rather, they are strongly determined by the regional 'pool' of species that exists within a biogeographic region extending over a spatial scale several orders of magnitude larger than that of the local community. Local communities establish themselves from this 'pool' through a series of filters. First, species must arrive before they can establish populations. The probability of this occurring depends on the structure of their geographic ranges. If a species can reach a site, it may still find the environment unsuitable. There are also subtle filters that operate at the landscape scale. Here the effects of number, area, shape and spatial arrangement of habitat patches can strongly mould the

characteristics of local assemblages. Overall, from a consideration of regional influences, Lawton (2000) draws the following three conclusions.

- The richness of local species is not only determined by their interactions. For most systems, richness in assemblages of species and in local guilds appears to be primarily determined by changes in the size of the regional species pool.
- Local population dynamics are also not solely the product of local interactions. They too are modified and influenced, sometimes strongly, by regional processes.
- The role that any one species plays within the community varies spatially within its geographic range.

Together, these conclusions suggest that ecologists will neither be able to understand or predict the consequences of change for ecological communities by considering only local processes. Events well beyond the immediate area of the community can drive significant local changes in species richness, as well as in species composition, population abundances and the dynamics of local assemblages. Discerning the local effects of exposure to toxic agents in communities that are so strongly influenced by external factors is likely to be difficult, unless the effects of exposure are both gross and distinctive.

Perhaps it is not surprising in the light of the significance of regional factors that important processes and community dynamics differ, often markedly, from system to system. Although there is now a good understanding of how several local sets of interacting species work in nature, there is currently no way of predicting which processes will be important in which types of system. As Lawton (2000) has remarked, by painstakingly detailed studies of local systems, it is possible to understand the local rules of engagement for interacting species at one place and time. However, almost every place, time and species assemblage is sufficiently different to make more general rules and patterns impossible to find.

In practice, ecological concerns are likely to arise in the context of spatially extensive sites at which several toxic agents are present, but with different spatial distributions of the individual toxic agents. Furthermore, these sites are likely to have been perturbed by human actions and there are likely to be stressors additional to the toxic agents and gradients in those stressors across the sites. Furthermore, the sites will be embedded in larger ecological regions to and from which migration of populations can occur on a variety of timescales. Both the spatial patterns of contamination with toxic agents and the magnitude and spatial patterns of other stressors are likely to change with time.

In these circumstances, predicting the impact of exposure to multiple toxic agents and other stressors is likely to be impossible, so any regulatory regime is likely to require that the overall environmental stress is kept sufficiently low that adverse effects are unlikely to occur. Thus, a realistic approach may be to set EQSs for individual toxic agents using substantial uncertainty factors, to ensure that exposure to several agents at EQS levels would be unlikely to adversely affect ecosystem functioning or biodiversity.

B.4 Examples of synergistic effects

In the context of radiation exposure, the most compelling evidence of the significance of interactions between radiation and other toxic agents arises in the case of exposures to radon and its progeny in relation to the effects of smoking (which results in exposure to a variety of carcinogenic agents by inhalation). This has been investigated in relation to both underground miners and domestic exposures. In the case of underground miners, the various case-control studies that have been undertaken demonstrate a sub-multiplicative interaction between radon exposure and smoking status. Thus, in contexts where the smoking status is known, the ERR is generally larger, even if not significantly, among non-smokers than smokers (ICRP, 2010).

In the case of domestic exposure, large cohort sizes are required for evaluation. Thus, over the last 20 years, several joint analyses have been undertaken. These have integrated basic individual data from cases and controls over several studies. Three such joint analyses have been conducted based on data from Europe (Darby et al., 2005), North America (Krewski et al., 2005; 2006) and China (Lubin et al., 2004). Each analysis showed evidence of the risk of lung cancer increasing approximately linearly with cumulative domestic exposure to radon, and the ERR was 0.08, 0.10 and 0.13 at 100 Bq m^{-3} for Europe, North America and China, respectively. In the European joint analysis, the ERR per 100 Bq m^{-3} was 1.11 (95% confidence interval of 1.00 to 1.28) for lifelong non-smokers. In the North American study, the ERR for non-smokers was similar, but not significant (0.10, 95% confidence interval -0.09 to 0.42) (ICRP, 2010). These results are consistent with the ERR due to radon exposure being the same for smokers and non-smokers. However, because the baseline lifetime lung cancer risk is about a factor of 25 larger for smokers than non-smokers, the absolute excess risk to smokers is much larger than the absolute excess risk to non-smokers from the same level of radon exposure. For example, based on the European pooled analysis, the cumulative risk of lung cancer up to 75 years of age is estimated for lifelong non-smokers as 0.4%, 0.5% and 0.7% for radon activity concentrations of 0, 100 and 400 Bq m^{-3}, respectively. For lifelong smokers, the corresponding values are close to 10%, 12% and 16%, respectively (ICRP, 2010).

Thus, in summary, the effects of smoking and radon appear to combine multiplicatively or sub-multiplicatively. Additivity of effect is strongly ruled out by the available data. In the domestic studies, excess risks were detectable at air concentrations of below 200 Bq m-3 (ICRP, 2010). The dosimetry of 222Rn and its progeny has been extensively discussed in the peer-reviewed literature. Estimates of effective dose per unit exposure have been obtained both by a dosimetric approach and through an analysis of the epidemiological data on lung cancer induction due to exposure to 222Rn and its progeny. Based on the epidemiological approach, the ICRP has recommended, in its Statement on Radon, a detriment-adjusted nominal risk coefficient for a population of all ages (mixed adult population of non-smokers and smokers) of 8 10-10 per Bq h m-3 for exposure to 222Rn gas in equilibrium with its progeny (ICRP, 2010). Taking the risk coefficient for such a population to be 0.057 Sv-1 (ICRP, 2007), the implied effective dose per unit exposure is 8 10-10/0.057 = 14 nSv per Bq h m^{-3}. In practice, in domestic premises, the concentration of ^{222}Rn progeny is typically about 0.4 of the equilibrium value (ICRP, 2014). Thus, a ^{222}Rn concentration of 200 Bq m-3, would correspond to an equilibrium equivalent concentration of about 80 Bq m^{-3}. For an occupancy of 7,000 hours per year, this would give an annual effective dose of 8 mSv. Thus, multiplicative effects between smoking and exposures to high-LET radiation occur down to effective dose rates of a few mSv per year.

It is perhaps worth noting that there is a need to investigate whether synergistic effects can occur between different types of ionising radiations. As Baverstock and Thorne (1998) pointed out, at a subcellular level there is little overlap in the spectra of energy deposition between photon irradiation and alpha-particle irradiation, so there is no a priori reason that the effects of these different types of irradiation should arise through the same mechanisms. This is a matter that can be investigated experimentally in *in vitro* studies. For example, Sollazzo et al. (2016) have analysed clonogenic cell survival and mutation induction in TK6 wild type (wt) cells and in TK6 cells with a knocked down hMYH glycosylase. The results showed a synergistic effect of mixed beams of x-rays and alpha particles on clonogenic cell survival in TK6wt but not TK6hMYH- cells. There was no evidence of synergistic effects on mutation, but the mutation results exhibited a high-degree of variability that may have obscured such an effect.

An interesting possibility for the occurrence of synergistic effects arises in the case of asbestos. Although the precise mechanisms by which asbestos fibres causes toxic injury have not been determined, data are available that indicate that both direct interaction between fibres and cellular components and cell-mediated pathways may be involved. In addition, the physico-chemical nature of the fibre appears to be an important determinant of toxicity (ATSDR, 2001). Specifically, the nature of fibre surfaces appears to play a role in the induction of adverse health effects by asbestos, with surface charge density having an important role. This is indicated by the observation

that modification of the surfaces of asbestos fibres can both increase and decrease their biological activity (ATSDR, 2001). Thus, other toxic agents present on asbestos fibre surfaces could enter cells upon complete or partial phagocytosis of the fibres and contribute to its toxic action. As one mode of action of asbestos is through the intra-cellular formation of ROS (ATSDR, 2001) interactions with other agents, such as ionising radiation, that induce ROS are possible. The induction of lung cancer as affected by both asbestos and smoking has been investigated. Three models were investigated. These comprised an additive model, a multiplicative model and an amplifier model in which asbestos can only increase lung cancer incidence in the presence of smoking. Of these, the additive model was found to be the least plausible, the amplifier model was contradicted by one sub-set of data, whereas the multiplicative model was not refuted, at a probability level, p, of 0.05, by any one of the sets of data examined (Smith et al., 1986). Additionally, asbestos and BaP interact synergistically in lung cancer induction in rats. This may be either because asbestos delays clearance of BaP from the lower respiratory tract or because it augments carcinogenesis at that site (Smith et al., 1986).

B.5 SYNERGISTIC EFFECTS IN A MULTI-STAGE MODEL OF CARCINOGENESIS

Herein an illustrative multi-stage carcinogenesis model is presented to show how two agents may interact to increase cancer incidence. The general form of the model is illustrated in Figure B-2.

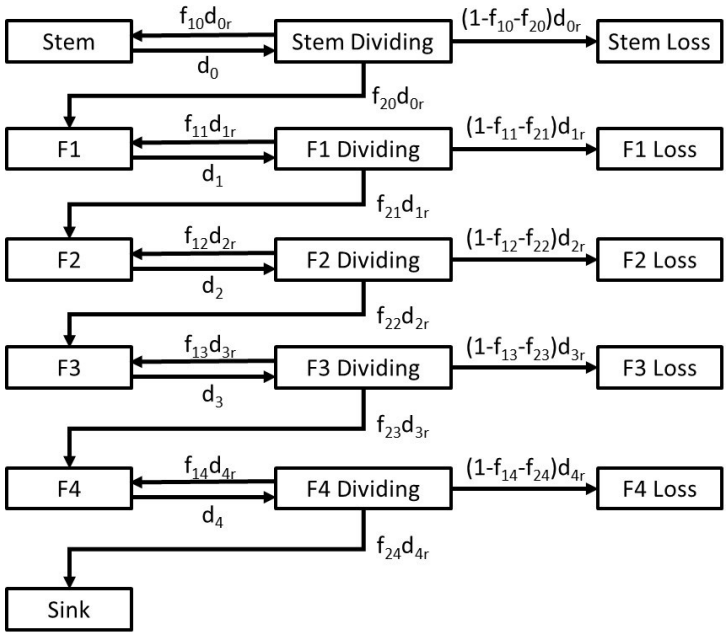

Figure B-2. General Structure of the Multi-Stage Carcinogenesis Model.

Stem cells are taken to divide at a rate d_0 (day^{-1}). The division results in 2 cells, one of which remains a stem cell. This is achieved in the simulation package used (AMBER 6.0) by treating the compartment Stem as non-depleting. The second cell enters the Stem dividing compartment, where its fate is determined. Turnover in this notional compartment is rapid and is determined by the value of d_{0r} (day^{-1}), which may be thought of as the time during cell division over which the cell's fate is decided). Three alternative fates are possible. The cell may become an additional stem cell (probability f_{10}), in which case the stem cell pool will grow with time (as occurs in the foetus and in childhood as the body mass increases). Alternatively, the cell may be transformed into an abnormal F1 type (probability f_{20}), which is the next stage in the carcinogenesis process. If neither of these things happens, the cell may either proceed by normal differentiation or may die. As these eventualities need not be distinguished in the carcinogenesis model, they are assigned the residual probability of $1 – f_{10} – f_{20}$ and routed to a stem loss compartment that is essentially a sink and plays no further part in the model.

The approach to offspring generations F1 to F4 is similar. When cells divide, one is assumed to retain the same phenotype (again achieved by treating the compartment as non-depleting). The second is assigned either to the same phenotype (probability f_{1x}, where x = 1 to 4), or is transformed to the next stage (probability = f_{2x}) or is lost from the carcinogenesis process (probability = $1 - f_{1x} - f_{2x}$). It is considered that a cell that reaches F4 will give rise to a tumour. Note that the model computes the expectation numbers of cells in each compartment as a function of time.

For the reference case, the following parameter values are used:

$$d_0 = 0.001 \qquad d_1 = d_4 = 0.01 \qquad d_2 = d_3 = 1.0$$

i.e. stem cells have slow turnover, but abnormal phenotypes divide more rapidly, though at two different rates;

$$d_{0r} = d_{1r} = d_{2r} = d_{3r} = d_{4r} = 1.0$$

i.e. arbitrary but rapid determination of fate on division;

$$f_{10} = f_{11} = f_{12} = f_{13} = f_{14} = 0$$

i.e. none of the cell pools expands by reproducing additional cells of the same phenotype;

$$f_{20} = f_{21} = f_{22} = f_{23} = f_{24} = 0.00005$$

i.e. there is a low probability per cell division of moving to the next stage of malignancy.

For initial conditions, 10,000 cells are placed in the stem cell compartment and all other compartmental contents are set to zero. Results from the reference case are shown in Figure B-3.

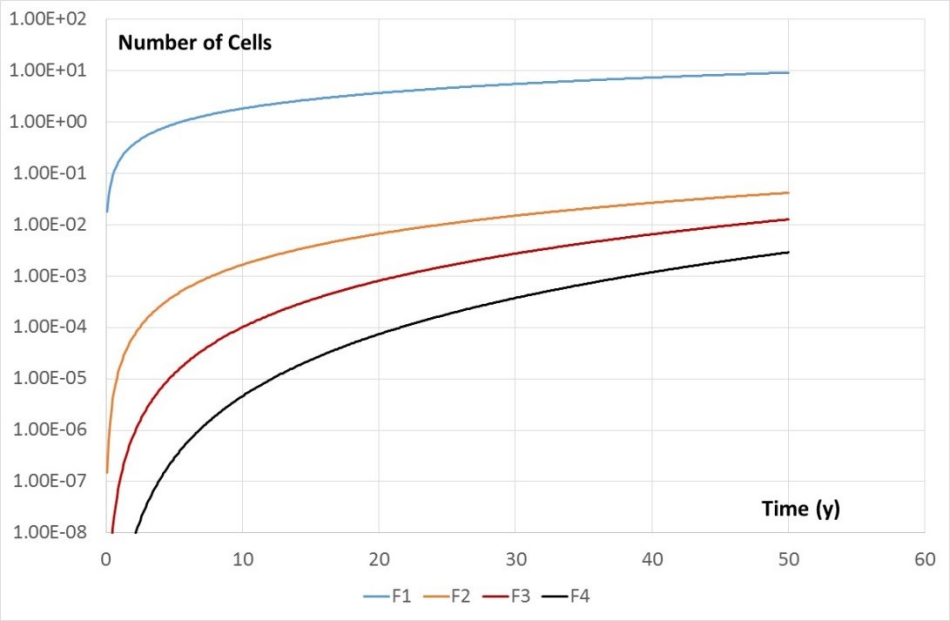

Figure B.3. Results from the Reference Case.

This shows that there is a successive delay in the build-up of cells in moving from F1 through to F4. The curves are like those expected for a multi-compartment chain with constant input, because no proliferation of phenotypes at any stage is included.

Six variant cases were then studied, changing only f_{21} and f_{23}. This simulates two agents acting at different stages of the carcinogenic process, i.e. stimulating abnormal phenotype production from F1 and F3 cells, respectively. The six cases are listed in Table B-1, together with the expectation numbers of

F4 cells present at the end of the 50-year simulation period and the ratios of these numbers of cells to the number present in the reference case.

Table B-1. Comparison of the Reference Case and Six Variants.

Case	f_{21}	f_{23}	Number of F4 cells	Ratio to Reference Case
Reference	5E-5	5E-5	2.89E-3	1.0
1	1E-4	5E-5	5.79E-3	2.0
2	5E-5	1E-4	5.79E-3	2.0
3	1E-4	1E-4	1.16E-2	4.0
4	1E-3	5E-5	5.79E-2	20
5	5E-5	1E-3	5.79E-2	20
6	1E-3	1E-3	1.16E+0	400

Results are as expected. The fractions of cells progressing from one abnormal stage to the next are small and there is no cellular proliferation at any stage, so the two effects act sequentially as perturbations and are thus multiplicative. However, this is a multiplicative effect in respect of the expectation numbers of F4 cells present. If the presence of such a cell ensures that it will proliferate to lead to a tumour and the numbers of such cells present obey a Poisson distribution, then the probability of occurrence of a such a tumour is 1 – exp(-F4), where F4 denotes the number of F4 cells present. Results at 50 years are presented in Table B-2.

Table B-2. Probabilities of Cancer for the Reference Case and Six Variants.

Case	Number of F4 cells	Probability of Cancer	Ratio of Probability of Cancer to the Reference Case
Reference	2.89E-3	2.89E-03	1.00E+00
1	5.79E-3	5.77E-03	2.00E+00
2	5.79E-3	5.77E-03	2.00E+00
3	1.16E-2	1.15E-02	4.00E+00
4	5.79E-2	5.63E-02	1.95E+01
5	5.79E-2	5.63E-02	1.95E+01
6	1.16E+0	6.87E-01	2.38E+02

Because there cannot be more than unit probability of cancer (though multiple primaries or foci could arise), a multiplicative effect for number of cells corresponds to a multiplicative model for cancer induction at low exposures, but a sub-multiplicative model at high exposures.

A second interesting case is where the two effects occur for the same cell, but have different influences. In this case, the same reference case is adopted, but with the three variants and results shown in Table B-3.

Table B-3. Comparison of the Reference Case and Three Additional Variants.

Case	f_{11}	f_{21}	Number of F4 cells	Ratio to Reference Case
Reference	0.0	5E-5	2.89E-3	1.00
7	0.01	5E-5	4.38E-3	1.51
8	0.0	1E-3	5.79E-2	20.0
9	0.01	1E-3	8.76E-2	30.3

Again, the results are multiplicative. The increased ‘pool’ of F1 cells gives rise to proportionately more F2 cells, and the increased probability of transformation acts proportionately on this increased pool.

Interestingly, this multiplicative effect occurs even where the result from the model is strongly non-linearly related to the value of f_{11}. This non-linearity is illustrated in Figure B-4, where only f_{11} is varied from the reference case value of 0.0 and an upward curvature is observed even when the logarithm of F4 is plotted.

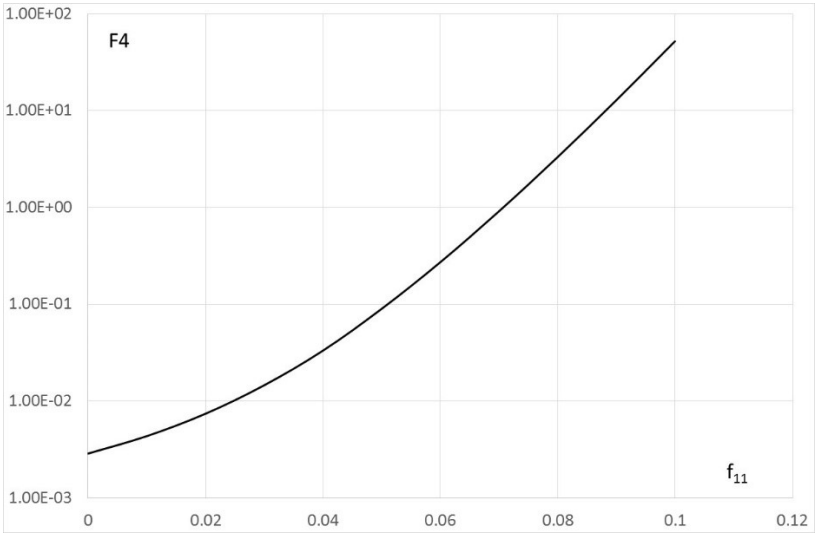

Figure B-4. Number of F4 Cells as a Function of f11 relative to the Reference Case.

Increasing f_{11} grows the pool of F1 cells exponentially as f_{11} increases, hence the highly non-linear effect. It is, therefore, interesting to examine the case in which two agents affect the proliferation of different cell pools. This is illustrated in Cases 10 to 12, summarised in Table B-4.

Table B-4. Comparison of the Reference Case and Three Further Variants.

Case	f_{11}	f_{12}	Number of F4 cells	Ratio to Reference Case
Reference	0.0	0.0	2.89E-3	1.00E+00
10	0.05	0.0	9.02E-2	3.12E+1
11	0.0	0.0005	9.02E-2	3.12E+1
12	0.05	0.0005	5.64E-1	1.95E+2

In this case, a sub-multiplicative effect occurs, since $31.2^2 = 973 > 195$. The difference between the effects of changes in f_{11} and f_{12} arises because f_{11} acts on a cell population that divides 100 times more slowly than does the cell population acted on by f_{12}. The cell growth curves for the four cases are shown in Figure B-5. In Case 10, where $f_{11} = 0.05$ and $f_{12} = 0.0$, all four cell generations show a continuing increase compared with the Reference Case, due to the proliferation of F1 cells, which drives the descendent populations. In Case 11, in contrast, the F1 cells behave as in the Reference Case, but F2 to F4 show continuing increases due to F2 proliferation ($f_{12} = 0.0005$; $f_{11} = 0.0$). Finally, in Case 12 ($f_{12} = 0.0005$, $f_{11} = 0.05$) all four cell generations show a continuing increase, mainly driven by F1 proliferation, but with some contribution from F2 proliferation (Compare, for example, F4-11 and F4-12.)

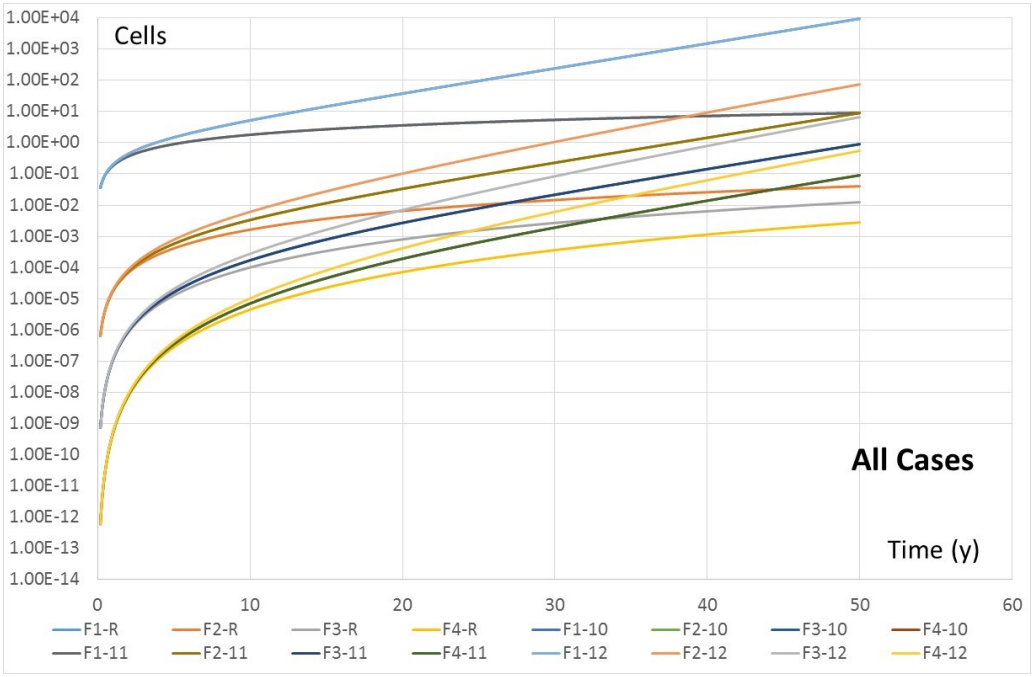

Figure B-5. Cell Populations for the Reference Case (R) and Variant Cases 10, 11 and 12.

These few cases illustrate the power of this simple model to explore different relationships between one or more toxic agents and the induction of cancer. In further studies, it could be used to illustrate a wide variety of potential synergistic and anti-synergistic relationships.

B.6 Development of non-linear exposure-response surfaces

A simple model calculation is set out below to illustrate some of the issues that arise from adopting a simple index formulation for limiting exposure to multiple toxic agents and how these may be overcome. For this simple calculation, only two interacting agents are addressed.

The effect of exposure to two agents, 1 and 2, is characterised as $E(x_1, x_2)$, where x_1 and x_2 are dimensionless measures of exposure {$x = I/I_0$, where I is the exposure measured in convenient units and I_0 is a unit exposure, e.g. the TDI. Now, in general:

$$E(x_1, x_2) = f(x_1, x_2)$$

where f is a general non-negative function that is only defined for non-negative values of x_1 and x_2. Typically, this function will not be separable, since the two agents can act together on the organism. However, for this illustration the view is taken that the exposures to the two agents are sufficiently low that their actions can be separated, i.e. one perturbs the system and then the other acts on the perturbed system. Thus:

$$E(x_1, x_2) = f_1(x_1)\, f_2(x_2) \qquad \text{(multiplicative model)}$$

$$E(x_1, x_2) = f_1(x_1) + f_2(x_2) \qquad \text{(additive model)}$$

Note that the multiplicative model is an amplifier-type model in which each agent is ineffective in the absence of the other. This differs from an ERR model, in which each agent modifies either the baseline incidence or the perturbed baseline incidence. This point is discussed further at the end of this section.

It is also assumed that the response of the system to either agent is monotonic (reasonable at low levels of exposure) and is no higher than a second-order polynomial. Ignoring effects that occur in the absence of exposure:

$$f_1(x_1) = a_1x_1 + b_1x_1^2$$

$$f_2(x_2) = a_2x_2 + b_2x_2^2$$

$$E(x_1, x_2) = (a_1x_1 + b_1x_1^2)(a_2x_2 + b_2x_2^2) \text{ (multiplicative model)}$$

$$E(x_1, x_2) = (a_1x_1 + b_1x_1^2) + (a_2x_2 + b_2x_2^2) \text{ (additive model)}$$

It is assumed that the aim is to limit the effect to below some value, E_{Limit}. This is expressed on an $x_1 – x_2$ diagram as being below the contour of height E_{Limit}. Figure B-6 shows the additive model with $a_1 = a_2 = 1$, $b_1 = b_2 = 0$.

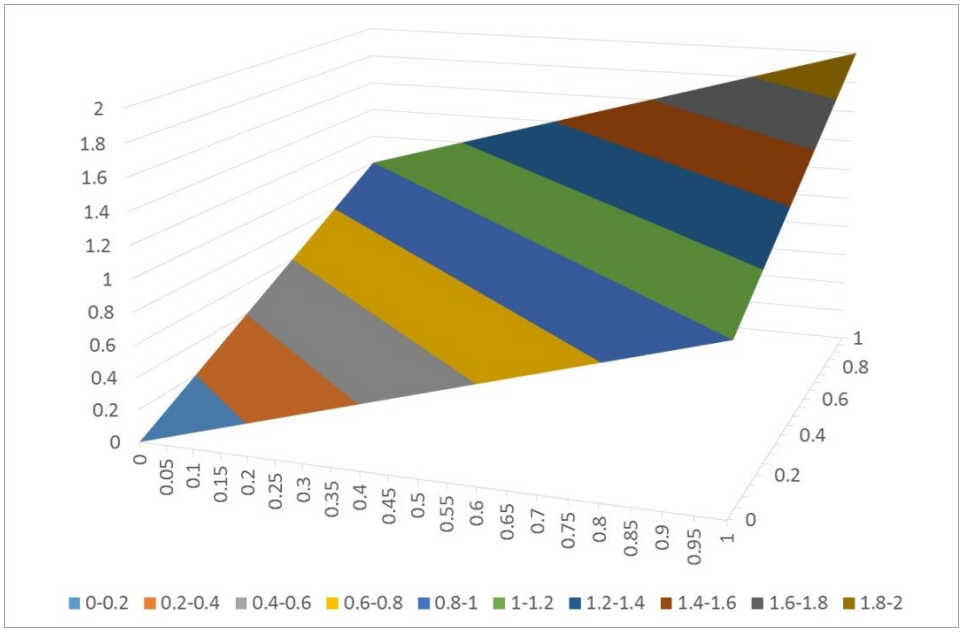

Figure B-6. Additive Model with a1 = a2 = 1, b1 = b2 = 0.

Contours of equal effect are linear and run diagonally across the model space. This arises because an increment in the amount of one agent can be exactly compensated by an equal decrement (in normalised terms) of the other agent. However, for a purely quadratic form of the additive model, $a_1 = a_2 = 0$, $b_1 = b_2 = 1$, the result is as shown in Figure B-7.

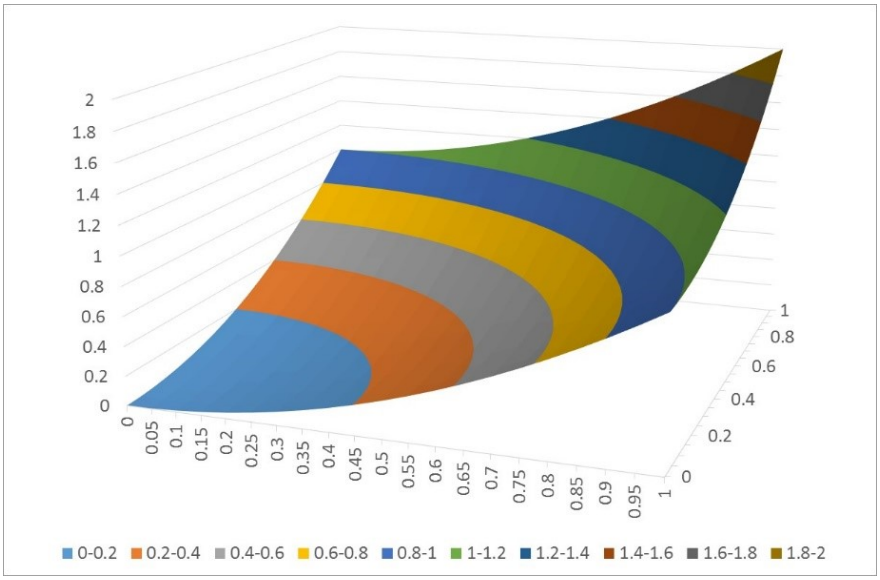

Figure B-7. Additive Model with a1 = a2 = 0, b1 = b2 = 1.

Contours now correspond to the circumferences of circles centred on the origin.

Finally, for the additive model, Figure B-8 shows the case of linear and quadratic components of comparable importance, $a_1 = a_2 = 1$, $b_1 = b_2 = 1$.

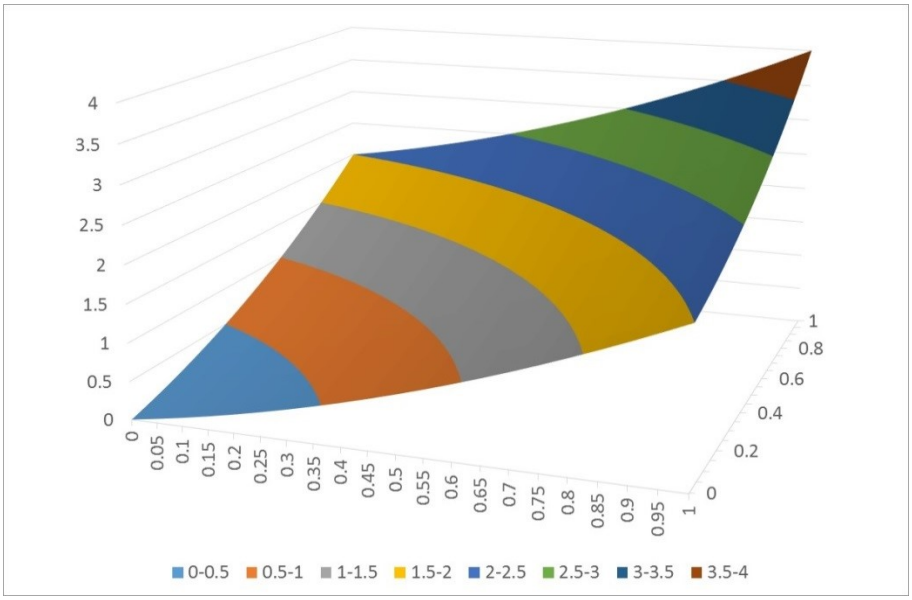

Figure B-8. Additive Model with a1 = a2 = 1, b1 = b2 = 1.

In this case, the curvature of the contours is intermediate between that of Figures B-6 and B-7.

For the multiplicative model, Figure B-9 shows the case of $a_1 = a_2 = 1$, $b_1 = b_2 = 0$.

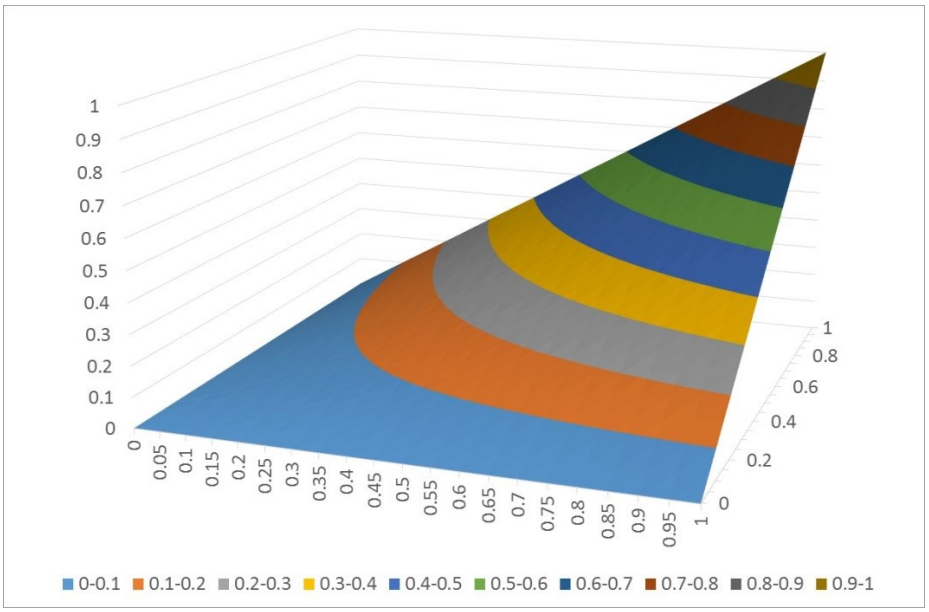

Figure B-9. Multiplicative Model with a1 = a2 = 1, b1 = b2 = 0.

In this case, the contours exhibit the opposite curvature to the additive model. This is because two parameters that sum to a constant value give their maximum when they are equal (e.g. 0.5×0.5 = 0.25, but 0.1×0.9 = 0.09). Thus, the linear contours of the additive model become pulled downhill along the axis of equal values in the multiplicative model.

For the purely quadratic multiplicative model, $a_1 = a_2 = 0$, $b_1 = b_2 = 1$, results are shown in Figure B-10. The contours are rather more linear than with the linear model, but with a greater overall steepening towards $x_1 = x_2 = 1$.

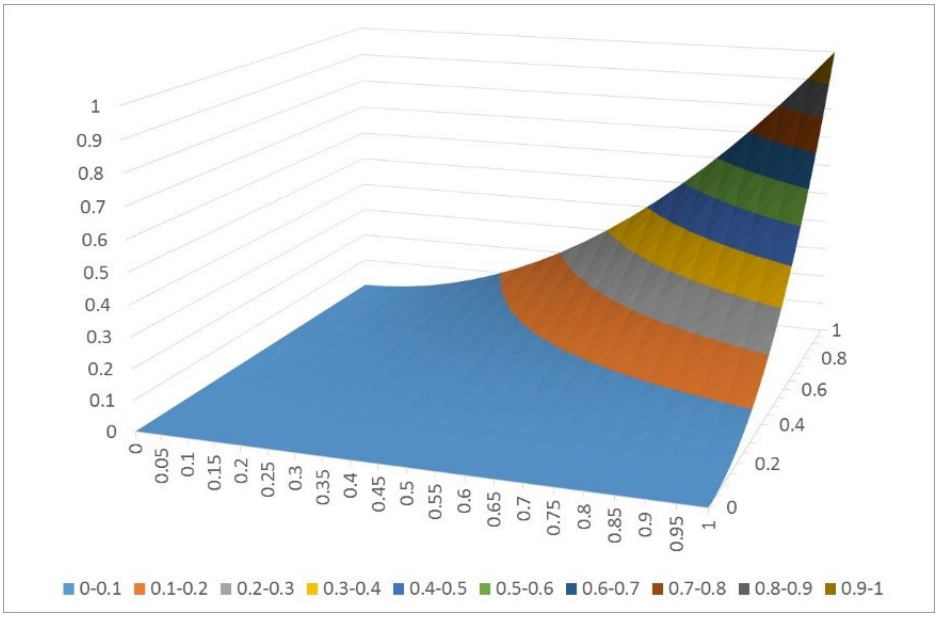

Figure B-10. Multiplicative Model with a1 = a2 = 0, b1 = b2 = 1.

The composite case, with $a_1 = a_2 = 1$, $b_1 = b_2 = 1$ is shown in Figure B-11.

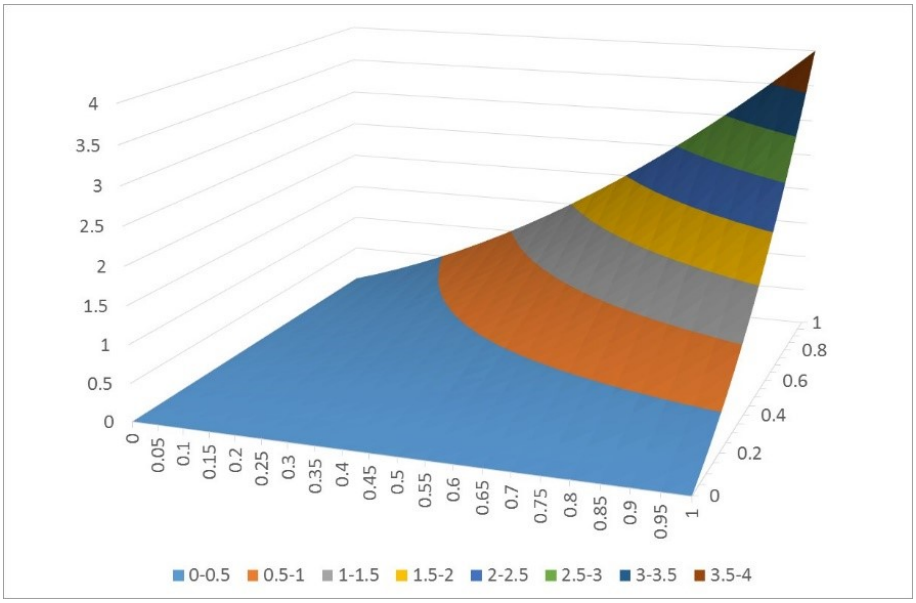

Figure B-11. Multiplicative Model with a1 = a2 = 1, b1 = b2 = 1.

In these examples, the multiplicative model assumes that the two agents are separately ineffective. A more realistic approach to a multiplicative model is to assume that each agent multiplies a baseline incidence, *B*, in the population. Thus, for the two agents operating separately:

$$E(x_1) = B\{1 + f_1(x_1)\} - B = Bf_1(x_1) \qquad E(x_2) = B\{1 + f_2(x_2)\} - B = Bf_2(x_2)$$

For the two agents operating together:

$$E(x_1, x_2) = B\{1 + f_1(x_1)\}\{1 + f_2(x_2)\} - B = B\{f_1(x_1) + f_2(x_2) + f_1(x_1) f_2(x_2)\}$$

Thus, an ERR model for two agents, in which one perturbs the baseline incidence and the second perturbs the baseline incidence as perturbed by the first agent corresponds to an overall model that is an equally weighted sum of the purely additive and multiplicative models described previously. An EAR model corresponds to the purely additive model described previously.

These simple calculations show how an index-based methodology can readily be extended into an iso-effect based methodology using simple formulae for representing the interactions between two or more toxic agents.

B.7 Conclusions

The handling of synergistic effects between toxic agents has not been adequately explored in the literature. In terms of hazards to human health arising from environmental exposures to toxic agents at low levels (i.e. low concentrations or doses and dose rates), cancer induction is likely to be the primary interest. A considerable amount is known about the likely target cells for cancer induction, these being either tissue stem cells or their proximal progenitor cells, and about subsequent cell proliferation and tumour progression. Genotoxic agents may act individually or in combination to generate DSBs and hence DNA deletions and translocations that can activate oncogenes or deactivate tumour-suppressor genes. There is the potential to investigate the response to individual agents or mixtures of agents in *in vitro* stem-cell preparations, possibly with added substrates to facilitate metabolic conversion of toxic agents to their active form. Non-genotoxic agents may act at later stages of tumorigenesis. The joint effects of agents that act at different stages may be explored in multi-step models of carcinogenesis, as illustrated herein in terms of a four-step model. Although the primary damage arising from genotoxic agents is likely to exhibit a non-threshold, linear-quadratic response, a variety of factors operating during the

subsequent expression of that damage may result in a threshold or quasi-threshold exposure-response relationship for clinically determinable disease. The overall response to multiple genotoxic agents is likely to be best evaluated in terms of iso-effect levels of DNA damage or changes in gene expression. At any such iso-effect level, implications for cancer induction could then be estimated by using an agent-independent mapping from iso-effect level to the expression of clinical disease. Such an approach cannot be applied to situations involving agents that operate at later stages of cell proliferation or tumorigenesis. In such cases, it is likely to be necessary to develop specific multi-stage models of the processes involved.

If appropriate models can be developed for toxic agents operating separately or in combination, these models can be used for limit setting. The limits imposed are likely to be expressed through iso-response surfaces for multiple agents rather than by use of the simple index quantities that have been employed to date and that imply linear, additive exposure-response models. EAR and ERR models for individual toxic agents have different implications for mechanisms of action and hence for how those agents should be considered in combination.

In terms of impacts on non-human biota, the complexities of individual organism responses to multiple toxic agents are compounded by the way in which those responses are translated into responses at the population, community or habitat levels. The rules of engagement of such systems are strongly context dependent. Also, these are open systems that are strongly influenced by regional characteristics at much larger spatial scales. In realistic environmental situations, with multiple stressors and gradients in those stressors, and with changes in those stressors with time, it is likely to be impossible to make predictions of the impacts of multiple toxic agents. Therefore, protection of the environment is likely to require the setting of precautionary EQS values derived using large uncertainty factors relative to exposures at which adverse effects have been observed.

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