



Professional Practice Note:

Reviewing human health risk assessment reports invoking contaminant oral bioavailability measurements or estimates

Under Part 2A of the Environmental Protection Act 1990, local authorities are given a duty to determine land as "contaminated land" where there exists "significant harm...or...the significant possibility of such harm" arising from the intake etc. of chemicals or other substances in, on or under the land (an "unacceptable intake"). In the course of development control, potential developers are required to provide evidence to local planning authorities that, as a minimum, their land will not be determinable as "contaminated" on completion of the development.

In both contexts, reliance on total contaminant soil concentrations in the assessments of whether land is, or is not, contaminated is, however, likely to over-estimate the risks and result in unnecessary determinations and remediation with attendant blight, worry, delay and cost. While the science around it is, admittedly, incomplete, carefully invoking measurements or estimates of oral contaminant bioavailability in the process can help clarify those risks and, in any event, such data are now routinely submitted to local authorities in conjunction with third-party site reports. At the very least, they therefore need to know how to assess such data and helping them to do that is, fundamentally, the purpose of this Note.

1 Introduction

Background

1.1 A recent survey undertaken by the Environment Agency¹ indicated that many local authorities now accept the use of bioaccessibility data as part of their regulatory decision-making. The Agency nevertheless reported wide variation in the ways such data was being used and presented by risk assessors and while there are examples of good practice in the use of bioaccessibility, in some cases the data is being used inappropriately or without an understanding of its current

limitations. In addition, bioaccessibility data is sometimes being rejected when it may inform the assessment.

1.2 Despite limitations surrounding the use of such data and the need for further research aimed at filling knowledge gaps and assisting the local authorities which make the ultimate decision², CLR reports³ have for several years pointed risk assessors towards the use of bioavailability in detailed quantitative risk assessments (DQRA) and recent material in the SR

¹ Environment Agency 2006

² LAs are the lead regulator under both planning and Part 2A.

³ CLR 9 & 10 and associated "old" SGV reports were withdrawn in 2008 but reviewers are likely to come across reports prepared having regard to these for some time to come.

series⁴ maintains this advice. Oral bioaccessibility data can:

- help refine human health risk assessments of land affected by contamination and
- assist in the identification of the need for and scope of any risk management measures.

But consideration of bioaccessibility data can only make a useful contribution to the risk assessment process if:

- there is explicit recognition of its current limitations and uncertainties and
- consistent application and good practice procedures are adopted by risk assessors and regulators within the contaminated land community.

SUMMARY POINTS

Reliance on total contaminant soil concentrations is likely to over-estimate risks, resulting in unnecessary determinations and remediation.

Careful use of oral bioavailability data in DQRAs can help clarify risks and has been supported by CLRs but its limitations and uncertainties must be recognised.

Practical guidance is offered for reviewers of risk assessments and some common misuses and myths about bioaccessibility are highlighted.

1.3 Recent guidance⁵ reiterates this too: referring to DQRA, the Environment Agency advises⁶, with respect to exposure

⁴ Environment Agency, 2009a-ab comprises the most recent guidance published at the time of writing

⁵ Environment Agency, 2009a; 2009ab;

⁶ Environment Agency, 2009ab, p. 23

via soil, to: "*obtain bioaccessibility estimates for contaminants where scientific evidence supports the use of such techniques.*" Underlining the need for adequate evidence, however, in a reference specifically to arsenic, the Environment Agency's view is that "*in vitro tests should be used cautiously in assessing risks to health from arsenic in soil since the relationship between measured bioaccessibility and the relative human availability/toxicity of arsenic remains uncertain* [Environment Agency, 2005a, 2007b]. *We are not able to recommend any specific test at this time, however, provided such testing has been carried out in accordance with guidelines for good practice, we consider that the results can be useful as part of a 'lines of evidence approach' to evaluating site-specific risk, including the sensitivity of any quantitative risk assessment*"⁷.

Purposes of this Note

1.4 Bioaccessibility-based estimates of *bioavailability* are routinely applied and frequently misused in DQRA (Table 1). The aim of this Practice Note is therefore to assist report reviewers in recognising good practice while identifying and rejecting common misuses of bioaccessibility test results in DQRA.

1.5 Its specific objectives are to:

- reinforce the formal regulatory and policy position,
- to highlight good practice,
- to highlight commonly encountered misuses (Table 1)
- to dispel myths (Table 2), and
- generally to improve the understanding of and communication between regulators and other stakeholders (e.g. developers and potential appropriate persons).

1.6 Though aimed primarily at local authority regulators, private sector risk

⁷ Environment Agency, 2009l, pp. 5-6

assessors will also benefit from this Practice Note as it highlights the essentials of good practice that they should be incorporating in their risk estimates and risk evaluations.

Context

1.7 This Practice Note is nevertheless not intended to present guidance on how to carry out DQRA or even on how to invoke bioavailability in DQRA. This is an area of rapidly developing science and policy so risk assessors and reviewers of risk assessment reports must make efforts to keep up-to-date at all times. One way is through following the contributions to the contaminated-land-strategies email discussion list. (Free) subscription is by sending an email to: jiscmail@jiscmail.ac.uk including the following text in the main message:

join contaminated-land-strategies
FirstName Surname

1.8 Reviewers should be familiar with the "regulatory science" behind bioavailability. It should be noted that this Practice Note has been written during the transition period following the withdrawal of CLR 7 – 10, CLR 9 TOX reports and CLR 10 SGV reports⁸ and the release of final versions of their replacements. References to, for example, Health Criteria Values and Soil Guideline Values are therefore to the values in the new documents. SR2 and SR3⁹ (the replacements to CLR 9 and CLR 10 respectively), were published in January 2009 and new SGV and TOX reports, as well as new LQM/CIEH GAC values, are being prepared that are compliant with this new guidance. Reviewers should confirm what if anything is written about bioavailability in revised "TOX" and "SGV" reports in due course and that the risk assessment has been carried out with such information in mind.

⁸ Defra & Environment Agency, 2002 -2004

⁹ Environment Agency, 2009 a,b

1.9 A succinct glossary is provided at the end of this document. Familiarity with the contents of the references at the end of this Practice Note is a minimum prerequisite for peer review. Several journals including the *Journal of Environmental Quality* and *Environmental Geochemistry and Health* have devoted entire special issues to bioavailability; there is a biennial international workshop on the subject and there are special sessions at many conferences including those organised by CONSOIL, CABERNET and SETAC. Finally the BARGE website¹⁰ provides helpful summaries and signposts to bioavailability related matters and some journal papers in PDF format.

Terms

1.10 Oral bioavailability has various definitions in the literature. The Environment Agency's most recent definition is used here: "*The proportion of an ingested dose (intake dose) of a chemical that is absorbed from the gut into the body and reaches the systemic circulation unchanged (i.e. without undergoing first-pass metabolism) is referred to as the 'bioavailable fraction'*"¹¹.

1.11 Bioaccessibility also has various definitions in the literature but again, the most recent Environment Agency definition: "*The proportion of a chemical released from soil following ingestion and digestion, and entering into solution, is referred to as the 'bioaccessible fraction'*"¹², is adopted here.

Comments

1.12 Comments on this Note are invited by e-mail to h.price@cieh.org

Acknowledgments

1.13 This Practice Note was drafted by

¹⁰ <http://www/bgs.ac.uk/barge/home.html>

¹¹ Environment Agency, 2009a pp 19-20

¹² Environment Agency, 2009a p. 20

Professor Paul Nathanail, Director of the University of Nottingham Masters programme in Contaminated Land Management, with input from colleagues at Land Quality Management Ltd and a review group including both local authority and private sector practitioners to whom the CIEH is grateful.

2 Legal Context

2.1 The legal context will determine when and how bioavailability estimates can, or indeed should, contribute to risk assessment. The two main contexts are, of course, the investigation of a site by a local authority and the submission of a planning application by or on behalf of a developer, however, questions of whether and how such data are used may arise in other contexts too. Any risk assessment should, however, clearly identify the legal and policy context in which it is written.

Part 2A of the Environmental Protection Act 1990

2.2 In the context of Part 2A, local authorities have the duty to detect any land which ought to be "determined" as "contaminated land", defined [section 78A] as:

"...any land which appears to the local authority...to be in such a condition...that significant harm is being caused or there is significant possibility of such harm being caused..."

to various receptors, most importantly human health. What "appears" to the local authority is to be determined in accordance with the statutory guidance¹³ and there is considered to be a "*significant possibility of significant harm*" when [Table B of Annex 3]:

"...the amount of pollutant...which a human receptor might take in... would represent an unacceptable intake..."

To the extent, therefore, that reliance on total contaminant concentrations is likely to overestimate the risks of a given intake, bioavailability estimates will be relevant

¹³ Defra Circular 01/2006 in England and equivalents in Scotland and Wales

considerations in risk assessments and resulting determinations will be liable to be quashed if they do not take account of them where, at least, “relevant, appropriate, authoritative and scientifically-based”¹⁴ information is available and, indeed, attention is required to be paid to the assumptions (including about bioavailability) underlying any numerical values such as the health criteria values underpinning any GACs used in the process¹⁵. The uncertainty in our ability to estimate bioavailability should, nevertheless, feature in the risk evaluation. Where a Remediation Notice is served, it will be similarly open to challenge if its requirements are based on the achievement of an unjustifiable standard.

Planning

2.3 In England, PPS 23¹⁶ requires the developer to show the land is suitable for its intended use, safe, and as a minimum will not be determinable as Part 2A contaminated land whether by reason of anthropogenic or natural contamination. Scotland and Wales have similarly worded requirements. It is the job of local planning authorities (LPAs), advised by their specialist staff, to determine applications (in the process judging whether developers have met their duty) including applying and enforcing any conditions e.g. as to the production of a risk assessment or a remediation scheme. Whereas it is open to developers to err on the safe side in their remediations if they want to (and some may wish to remediate to minimal risk levels for reasons of public confidence), LPAs are unlikely to regard their conditions as unmet where they do not include consideration of bioavailability but, as in the Part 2A situation, they may legitimately do so where over-reliance on bioavailability estimates results, in their

reasonable opinions, in falsely concluding that remediation is not necessary.

The question of longevity

2.4 The validity into the future of contemporary bioaccessibility test results must be considered by reference to the geological history of the contaminant-medium system and the extent to which stable, if not equilibrium, conditions are likely to have been achieved. For example, contaminants in made ground may be expected to have higher bioavailability than naturally occurring contaminants in soil.

2.5 In addition, land use practices can change the biochemical conditions in soil and thereby change the contaminant bioavailability. For example, liming low pH soils, the addition of phosphate fertiliser or increasing the soil organic matter content by adding manure or compost are all likely to have an effect on the mobility of lead and arsenic, do not require specific regulatory permission to be carried out and are common practices by domestic gardeners. Such changes can increase or reduce the bioavailability.

Other legislation

2.6 Consideration of other legal regimes is outside the scope of this guidance but implementation of the Environmental Liability Directive (2004/35/EC) in the UK may raise similar issues in the assessment of “environmental damage” under the Environmental Damage (Prevention and Remediation) Regulations 2009. SNIFFER has reviewed the environmental legislation related to human health protection¹⁷.

¹⁴ Para A.31 of Annex 3, *ibid*

¹⁵ Para B.48 of Annex 3, *ibid*

¹⁶ *Planning and Pollution Control*, ODPM, 2004

¹⁷ UK CC02, 200717, 200817, SNIFFER

3 General considerations

3.1 The adverse effects caused by the substance need to be understood. Bioavailability estimates are relevant to estimates of the likelihood of systemic effects, however, arguments could be made for using bioaccessibility measures in the assessment of the likelihood of localised effects.

Bioavailability of HCV

3.2 The bioavailability of the epidemiological or laboratory animal study(-ies) underpinning the derivation of the HCV must be considered before deviating from the default CLEA assumption of 100% (relative) bioavailability. Such information has usually been referred to in the main body of the relevant TOX report¹⁸. The "old" TOX report for cadmium¹⁹ is a good example. Risk assessors will need to confirm the bioavailability in the studies underpinning the revised TOX reports currently being prepared by the Environment Agency. The "new" TOX report for mercury²⁰ for example notes that the oral TDI for inorganic mercury is based on the toxicity of mercuric chloride but applied to other less bioavailable forms of inorganic mercury.

3.3 Of the 2002-04 vintage "old" SGVs, those for lead and cadmium assumed less than 100% bioavailability. The lead SGV incorporated bioavailability through the δ (delta) factor; the SGV assumed a value of 5 $\mu\text{g}/\text{dL}$ per 1000 $\mu\text{g}/\text{g}$ ²¹. The cadmium HCV assumed only 5% of soil cadmium reaches the kidney²².

¹⁸ The "old" TOX reports, of 2002 to 2004 vintage, were not withdrawn by the Environment Agency until 'new' replacements are published.

¹⁹ Defra & Environment Agency 2002e

²⁰ Environment Agency 2009g p. 27

²¹ Defra & Environment Agency 2002r

²² Defra & Environment Agency 2002e

Bioaccessibility testing

3.4 Bioaccessibility tests such as those reviewed by Oomen et al²³ mimic the whole or parts of the human digestive system. The Physiologically Based Extraction Test (PBET)²⁴ simulates the digestion in the stomach and small intestine and seeks to replicate the chemical but not microbiological conditions therein. The terms "PBET", "bioaccessibility" and "bioavailability" are not synonymous. Bioavailability is what is being invoked in DQRA. The bioaccessible fraction is used as an estimate or surrogate of that bioavailable fraction. The PBET is one of many available tests to measure the bioaccessible fraction. It has been the most widely used test in the UK in recent years.

3.5 The BARGE Unified Method has been derived from the Dutch RIVM physiologically based *in vitro* extraction test and may come to be commercially available in the near future²⁵. It is currently being refined and calibrated against *in vivo* data.

3.6 There is limited validation of *in vitro* tests against animal *in vivo* data, however, various bioaccessibility tests are now accepted in different countries for various substances for what we would call DQRA.

Risk assessment tools

3.7 At the time of writing, three human health "risk assessment" tools make explicit allowance for bioavailability estimates to be used in DQRA:

- CLEA 1.04²⁶

²³ 2002

²⁴ Ruby *et al.* 1996 & 1999

²⁵ Cave *et al.* 2006

²⁶ CLEA 1.03 beta also allowed site specific estimates of bioavailability to be incorporated in the derivation of site specific assessment criteria. It was released in August 2008 and withdrawn in January 2009.

- SNIFFER Updated edition
- RISC 4

3.8 Of these, only CLEA 1.04 is likely to be compatible with current technical guidance from the Environment Agency. Other public or in-house models can be used by expert risk estimators by applying bioavailability to direct soil ingestion assessment sub criteria before combining these with exposure from other pathways into an integrated site specific assessment criterion.

3.9 In addition, physiologically based tests can provide a qualitative insight into the geochemistry of the contaminant which can inform the risk evaluation stage of risk assessment.

Other considerations

3.10 While bioaccessibility tests remain the main basis for estimating bioavailability in UK risk assessment practice, it must be recognised that these empirically based tests are in effect "black boxes". Other methods of appreciating why the bioaccessibility results are what they are, are therefore useful²⁷. These can include the geological, including land use, history of the site and its vicinity. Sequential extraction tests can also be used to gain an appreciation of which mineral phase "hosts" the available and unavailable contaminant fractions²⁸.

4 Practical guidance for reviewers

4.1 Surrogates, estimates or even measures of the bioavailable fraction should be considered in conjunction with other lines of evidence (e.g. geological history, geochemical data, results of tests in the same geological material at other sites).

4.2 Risk assessors should recognise that current tests are not suitable for most contaminants. In practice, PBET results are routinely used for arsenic²⁹, occasionally used for nickel and could be used for lead if the basis for exposure assessment falls into line with the CLEA model. At the time of writing, the Environment Agency was considering using an index dose as the health criteria value for lead³⁰.

4.3 Bioavailability should be assumed to vary with soil composition and therefore separate bioaccessibility test result "samples" will be needed for each soil type across the site. Where contaminant deposition has been independent of soil type (e.g. by aerial fallout), bioavailability may vary less, if at all, with soil type and with depth. Given present understanding, this would need to be demonstrated on a site-by-site basis. Consideration should also be given on which soil fractions chemical analyses should be carried out and how the value being used as a surrogate for bioavailability has been calculated.

4.4 In keeping with long-standing guidance from the Environment Agency, risk estimates and evaluation should be anchored back into the conceptual model.

4.5 There is no simple way of estimating how many samples are needed. Land Quality Management Ltd, pioneers in the use of bioaccessibility tests results in

²⁷ see for example, Cave *et al.* 2004

²⁸ e.g. Nathanail & Smith 2007

²⁹ e.g. Nathanail & Smith 2007

³⁰ cf [CLEA FAQ page](http://www.environment-agency.gov.uk/research/planning/33718.aspx#19) [http://www.environment-agency.gov.uk/research/planning/33718.aspx#19]

DQRA, assume a minimum of ten samples per averaging zone.

4.6 Given our current lack of a predictive model of bioavailability, DQRA should be informed by site specific data. Other relevant information can constitute useful "lines of evidence" and may also be included in the risk evaluation, particularly in areas of the country and for geological conditions whose bioavailability has been widely studied.

4.7 While it is usual practice to use the maximum or a multiple of the maximum bioaccessibility test result as an estimate of bioavailability, the entire range of data should be examined and the relationship between total and bioaccessible concentrations should be considered. This will help avoid both Type I and Type II errors.

4.8 Sensitivity analysis has a long-standing role in risk evaluation. Given the move away from a probabilistic basis for CLEA, this will become important for GQRA and remain even more important for DQRA. A widely available example of a sensitivity analysis is included in SNIFFER report LQ01³¹.

4.9 Most available, and all bioaccessibility tests commercially available at the time of writing, relate to the direct soil ingestion pathway only and cannot be used to modify the relative contribution of other exposure pathways. The general principle is that the pathway being simulated by the specific test is the only one that should be modified by the test results.

4.10 Risk estimation should recognise that some contaminants have to be treated differently. These include lead, cadmium and asbestos.

Decisions for the local authority

4.11 Recent Defra guidance³² has reiterated that the onus of deciding what constitutes an unacceptable intake falls on the local authority and recognises that ultimately this will be decided by the courts³³.

How to decide when an intake is unacceptable

4.12 When bioavailability estimates are being used in a risk assessment under Part 2A, their effect is to differentiate between total intake and the systemic dose, or "the amount of a chemical that reaches the systemic circulation unchanged following absorption"³⁴ and could therefore cause systemic harm. Under Part 2A, the local authority Contaminated Land Officer's professional judgement may be exercised to decide if exceedances of a GAC in a situation where PBET results indicate a low bioaccessibility do not constitute an unacceptable intake.

³¹ Ferguson *et al.* 2003

³² Defra 2008a

³³ Defra 2008a,b

³⁴ Environment Agency 2009a p. 62

Table 1: Common misuses of bioaccessibility-based estimates

Misuses	Commentary
1. Insufficient samples	A minimum of 10 samples per averaging zone is typical in order to gain an adequate appreciation of the variation in bioaccessibility.
2. Use of peer review literature rather than site specific values	There is not necessarily a relationship between literature values and site specific bioaccessibility.
3. Application to non ingestion pathways	The PBET seeks only to simulate the direct oral ingestion pathway.
4. Application to other substances	Inappropriate appreciation of substance specific bioaccessibility.
5. Lack of line of evidence	Bioaccessibility test results may not be compatible with geological history, geochemistry.
6. Mixing samples from different soil/ ground types	Bioaccessibility varies with medium.
7. Poorly documented test procedure	Bioaccessibility tests are empirical and interpretation should be based on the specific method applied.
8. Analysis of samples not representative of concentrations of concern	Bioaccessibility varies with total concentration but the relationship is not necessarily either linear or positive.
9. Inappropriate use of statistics	Statistical summaries of bioaccessibility tests may result in discordant matching of bioavailability estimate and total concentration
10. Application of summary (average) or single values to a dataset	The relationship between total and bioaccessible concentrations is not necessarily linear.
11. Use of wrong test	Results are not relevant to the risk estimation.
12. Lack of details in reports	Reviewer cannot evaluate the robustness of the risk estimate and the compliance of the risk evaluation with the specific legal context.
13. NOT using bioavailability at all	Over conservative risk assessments and unnecessary remediation

Table 2: Myths about bioaccessibility

Myth	Consequence	Truth
1. The EA completely rejects the use of bioavailability	Over conservative risk assessments and unnecessary remediation	The EA cautions that bioavailability may only be useful in limited circumstances
2. Bioavailability is positively correlated with total concentration	Use of low bioaccessibility results underestimates risks posed by high total concentrations	The relationship between total and bioavailable fractions is much more complex.
3. No other country uses bioaccessibility test results	Reluctance to inform risk evaluation with estimates of bioavailability	Several countries accept various in vivo and in vitro based approaches to incorporating bioavailability in risk assessments.
4. PBET is the only show in town	Less than optimal test conditions for specific circumstances.	The PBET is only one of several physiologically based tests available worldwide.
5. All laboratories carry out the 'PBET' in the same way	Lack of comparability between results	Different laboratories may well have made minor modifications to improve efficiency or reduce costs.
6. All laboratories carry out 'total' analysis in the same way	Lack of comparability between results	Laboratories may differ in the way extraction and analysis is carried out.
7. The EA does not allow the use of bioaccessibility in human health risk assessment	Over conservative risk assessments and unnecessary remediation	The EA cautions that its use may only be justified in limited cases.
8. We understand why a given soil has the bioavailability it has	Over reliance on lines of evidence and literature values rather than site specific measurements	We are only just beginning to understand the biogeochemical controls on bioavailability.

Glossary of key terms

BARGE	BARGE (the Bioaccessibility Research Group of Europe) is a European network bringing together international institutes and research groups to study human oral bioaccessibility of priority soil contaminants such as arsenic, lead and cadmium. (http://www.bgs.ac.uk/barge/home.html)
Bioaccessibility	"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 2009a). In the context of this Practice Note the term refers to humans.
Bioavailability	"The degree to which a substance is absorbed and becomes available to the target tissue (without first being metabolised)" (Environment Agency 2009a). In the context of this Practice Note the term refers to humans.
CLR	Defra & Environment Agency Contaminated Land Report (CLR reports 9 & 10 formed the basis for the 'old' SGVs).
DQRA	Detailed quantitative risk assessment involving the derivation of site specific assessment criteria. DQRA is usually carried out either in the absence of relevant generic assessment criteria (GAC) or to consider site specific parameters where site contaminant concentrations exceed a GAC.
GAC	Generic Assessment Criterion
Health Criteria Value	"A generic term used ... to describe a benchmark level of exposure to a chemical derived from available toxicity data for the purposes of safeguarding human health (e.g. a tolerable daily intake)" (Environment Agency 2009a).
Intake dose	"The amount of a chemical entering the human body at the point of entry (that is, mouth, nose or skin) by ingestion, inhalation, or skin contact" (Environment Agency 2009a).
JISCMail	The National Academic eMailing List Service (www.jiscmail.ac.uk). The contaminated-land-strategies list provides a forum for exchange of information on all aspects of risk based contaminated land management.
Lines of evidence approach	"The lines of evidence approach means that no single piece of evidence such as the outcome of an in vitro test should be solely relied on to make a decision about health risks. But alongside other investigations, such as a greater understanding of soil chemistry, in vitro tests may inform a site specific risk evaluation" (Environment Agency 2009 p. 6).
Oral Bioaccessibility	Bioaccessibility through ingestion.

Oral Bioavailability	Bioavailability through ingestion.
Part 2A	Part 2A of the Environmental Protection Act 1990; referred to as Part IIA in Scotland; not in force in Northern Ireland.
PBET	The Physiologically based extraction test (PBET) is a sequential extraction test that mimics the effect on soil contaminants of the stomach and upper intestine.
Safe and suitable for use	The condition developer has to demonstrate the land is in under PPS 23.
Soil Guideline Values	"Non statutory, scientifically based generic assessment criteria [GAC] for assessing the risk to human health from chronic exposures to chemicals in soil" (Environment Agency 2009a).
SR	Environment Agency Science Report (the replacements to the CLR reports have an SR designation).
Unacceptable intake	Contaminant intake that would result in a significant possibility of significant harm.

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Items in bold are recommended as core reading.

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