ENVIRONMENTAL HEALTH SCIENCES
LIMITED

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Human Toxicology and the Work of the C4SL Project Team

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Project Background

- Defra explained its concerns regarding the historic real-world application of Part 2A and the importance of striking the right balance between the benefits and impacts of regulatory action in a consultation document issued in December 2010.
- The revised Statutory Guidance (SG - issued in April 2012) was designed to address these concerns and presented a new four category classification system, ranging from Category 4, where there is *"no risk or that the level of risk posed is low"* to Category 1, where *"there is an unacceptably high probability, supported by robust science-based evidence, that significant harm would occur if no action is taken to stop it"*.

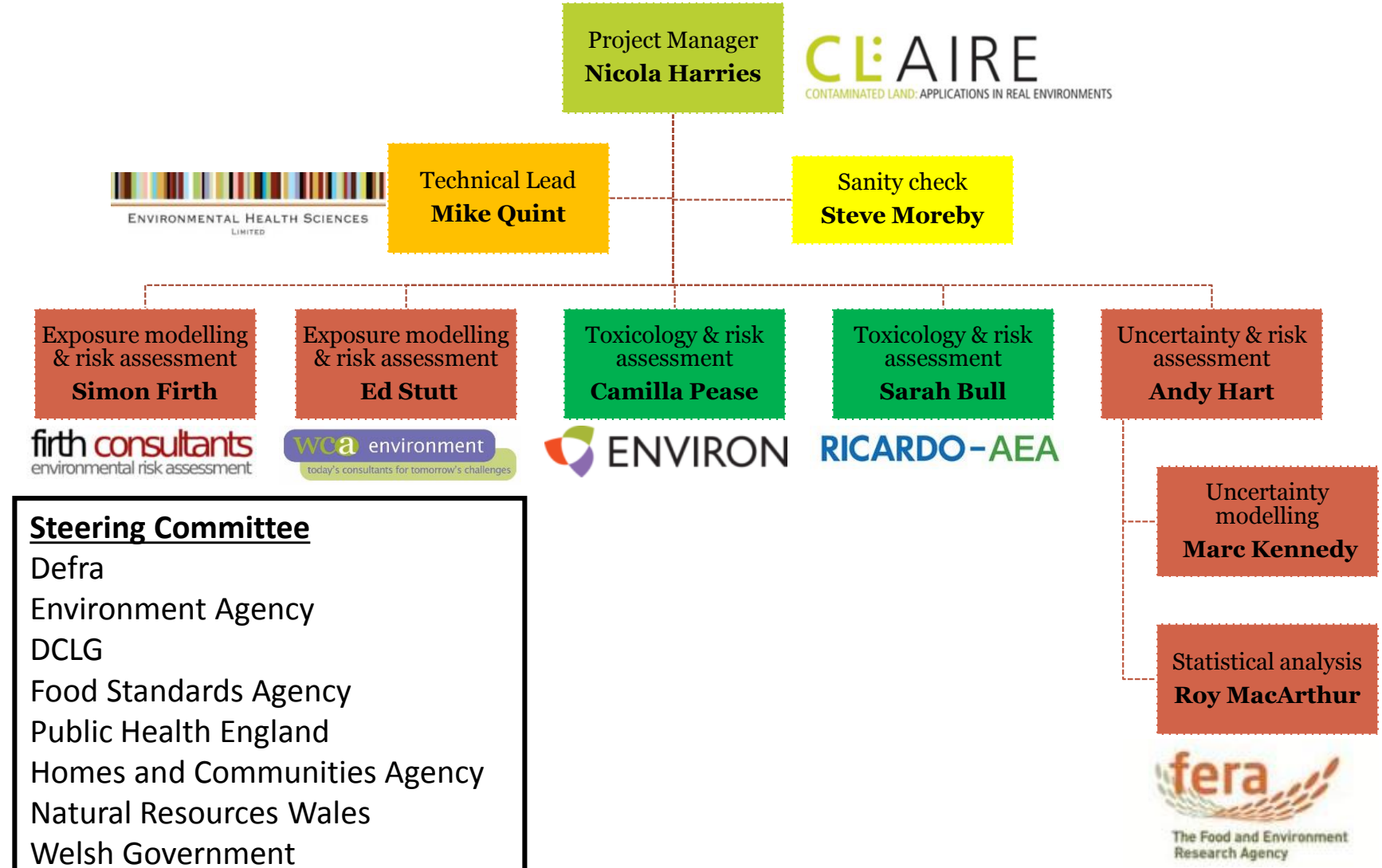
Project Background (cont)

- The revised SG states that Category 4 should include:
  - *"Land that has been excluded from the need for further inspection and assessment because contaminant levels do not exceed relevant generic assessment criteria in accordance with Section 3 of this Guidance, or relevant technical tools or advice that may be developed in accordance with paragraph 3.30 of this Guidance.*
- The C4SLs are intended to be "relevant technical tools" to help local authorities and others when deciding to stop assessing a site on the grounds that it falls within Category 4 (provided they are used correctly).

Project Background (cont)

- The role of the C4SLs was made more explicit in the October 2011 Impact Assessment (IA), which states (my underline):
  - *"The new statutory guidance will bring about a situation where the current SGV/GACs 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."*

Project Background (and Acknowledgements)



Steering Committee

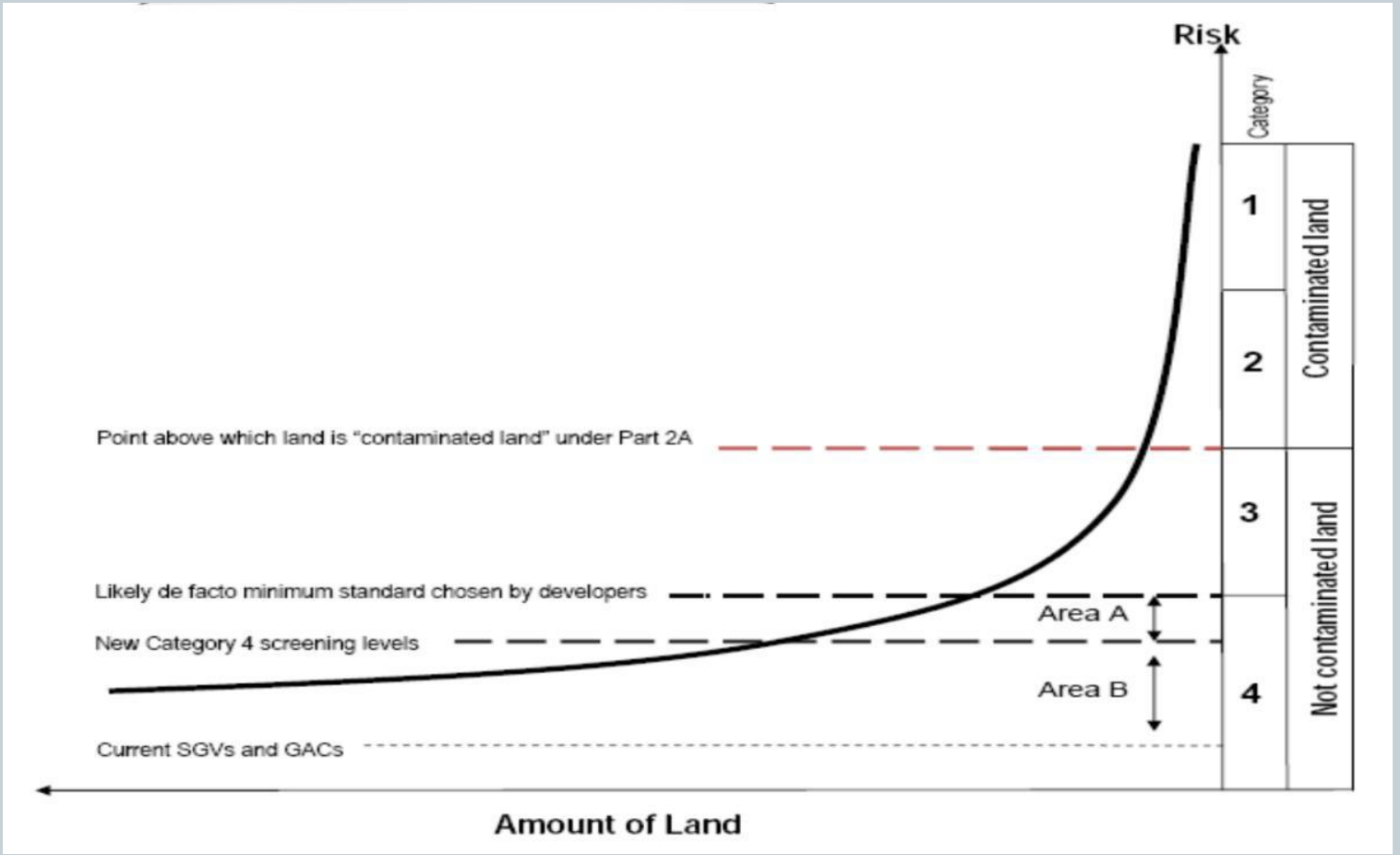
Defra
Environment Agency
DCLG
Food Standards Agency
Public Health England
Homes and Communities Agency
Natural Resources Wales
Welsh Government

Project Background (cont)

Stakeholder Meetings

Association of Geotechnical and Geoenvironmental Specialists (AGS)	Local Authorities - South Coast Region
British Geological Survey (BGS)	Local Authorities - South East Region
British Land Reclamation Society (BLRS)	Local Authorities - West Midlands Region
British Property Federation	Local Authorities - West of England Region
British Standards Institution (BSI) - EH/4 Soil Quality Committee	Local Authorities– Yorkshire Region
British Toxicology Society (BTS)	National House Building Council (NHBC)
Chartered Institute of Environmental and Water Management (CIWEM)	North-West Brownfield Remediation Forum (NWBRF)
Chartered Institute of Environmental Health (CIEH)	Planning Officers Society
Chemical Industries Association (CIA)	Professor Chris Collins, University of Reading
City of London Law Society	Professor Len Levy, Cranfield University
Civil Engineering Contractors Association (CECA)	Professor Paul Nathanail, University of Nottingham
Committee on Toxicity (COT)	Professor Simon Pollard, Cranfield University
Energy Institute	Register of Ground Engineering Professionals (RoGEP)
Environmental Industries Commission (EIC) – Contaminated Land Working Party	Royal Institution of Chartered Surveyors (RICS)
Environmental Protection UK (EPUK) – Land Quality Group	Royal Society of Chemistry (RSC) – Toxicology Group
Geological Society of London (GeolSoc)	Royal Town Planning Institute (RTPI)
Greater Manchester Contaminated Land Officers Group	Society for Environmental Geochemistry and Health (SEGH)
Health and Safety Laboratory (HSL)	Society of Brownfield Risk Assessment (SoBRA)
Home Builders Federation (HBF)	Society of Chemical Industry (SCI)
Institution of Civil Engineers (ICE)	Soil and Groundwater Technology Association (SAGTA)
Institution of Environmental Sciences (IES)	Specialist in Land Condition (SiLC)
Local Authorities - East Midlands Region	UK Contractors Group (UKCG)
Local Authorities - East of England Region	UK Environmental Law Association (UKELA)
Local Authorities– London Region	Waste and Resources Action Programme (WRAP)
Local Authorities - North East Region	Welsh Contaminated Land Working Group

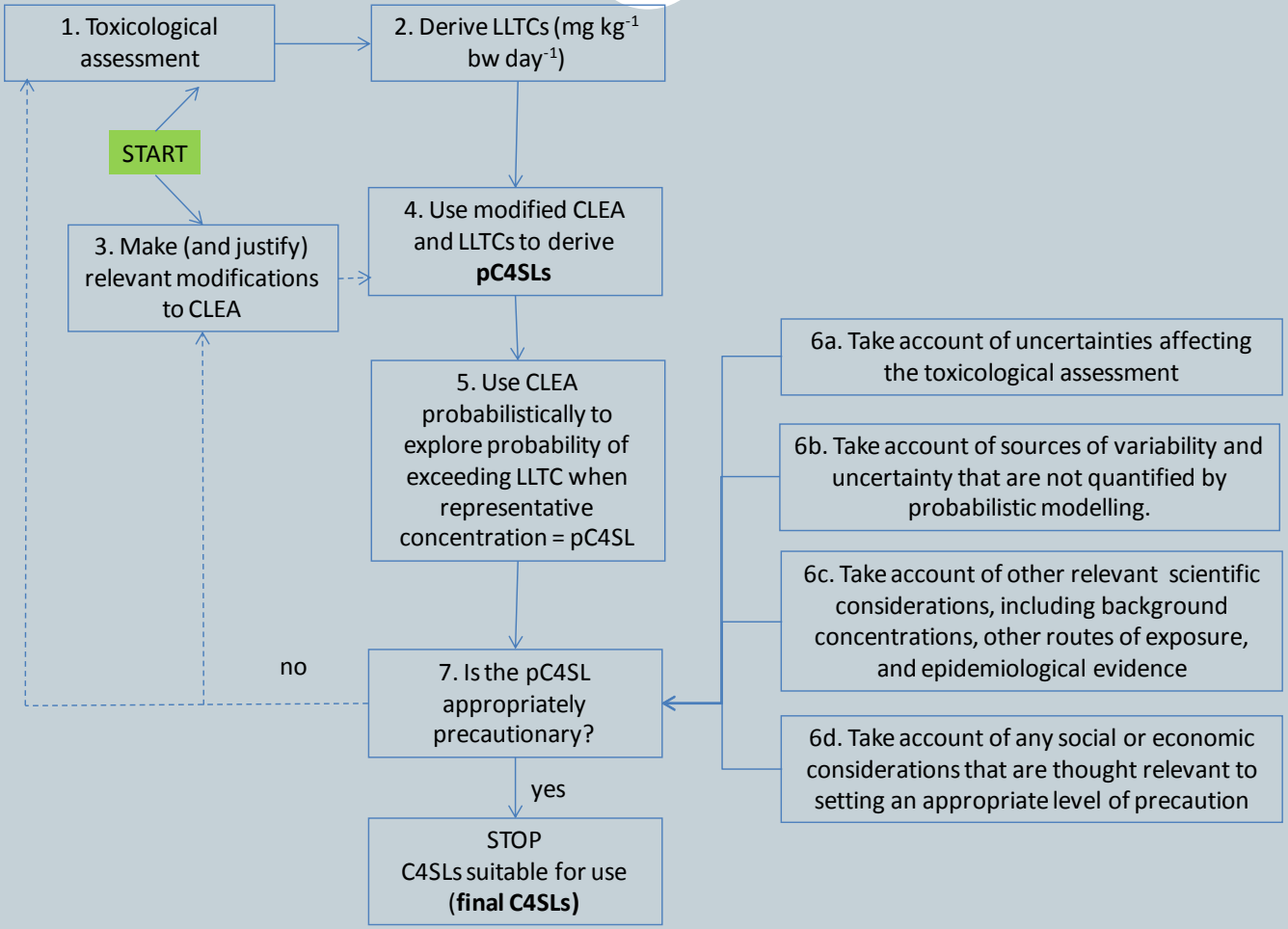
Overview of Methodology



Overview of Methodology (cont)

- Retained and used the CLEA framework
- Modifications relating to:
  - toxicological parameters;
  - exposure modelling (inc new exposure scenarios);
  - consideration of uncertainty; and
  - considerations in the setting and use of C4SLs.

Overview of Methodology (cont)



Toxicological Assessment

- Retained much of the existing framework described in SR2, except:
  - Take account of all critical health effects, not just most sensitive
  - Use benchmark dose (BMD) modelling to set a point of departure (POD)
  - Use central measure of BMD rather than the lower confidence limit (BMDL)
  - Use scientifically based chemical specific adjustment factors (CSAFs) or chemical specific margins (CSMs), rather than default uncertainty factors or generic margins, where possible
  - Use a generic margin of 5,000 to derive a “low level of toxicological concern” (LLTC), where appropriate
  - Use an excess lifetime cancer risk of 1 in 50,000 to derive a LLTC for carcinogens with human epidemiological data, where appropriate

Toxicological Assessment (cont)

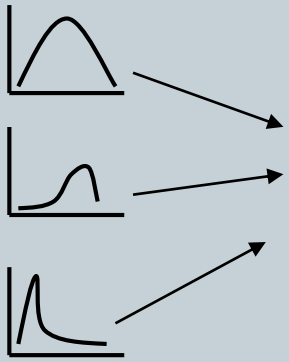
SUBSTANCE	TOXICOLOGICAL BASIS OF 2002/2009 ORAL HCV	TOXICOLOGICAL BASIS OF 2014 ORAL LLTC
Arsenic	Policy decision to equate HCV to the drinking water standard	Policy decision to equate HCV to the drinking water standard (LLTC = HCV), now supported by a scientific evaluation using BMD modelling from the WHO 2011 Evaluation. Calculated Risk at HCV/LLTC is 1 in 2000
Benzo[a]pyrene (as a surrogate marker for genotoxic PAHs)	WHO 1993 drinking water guideline using a study by Neal & Rigdon, 1967. Approach no longer endorsed by UK COC.	BMD modelling of the Culp et al 1998 PAH mixtures toxicology study
Benzene	Policy decision to equate HCV to the risk level of 1 in 100,000 Pliofilm cohort study (Rinksy 1981)	Policy decision to equate HCV to the risk level of 1 in 50,000 from the WHO drinking water guideline from 2011. Human excess lifetime cancer risk estimate.
Cadmium	TDI set by WHO expert committee on food additives in 1972. Then revised to minimal risk from EFSA 2009.	BMD modelling with kinetic modelling using EFSA 2009 evaluation
Chromium VI	Oral reference dose US EPA 1998 evaluation	BMD modelling of new NTP 2008 study, & US ATSDR 2012 evaluation.
Lead	WHO/JECFA Provisional tolerable weekly intake of 25 mg/kg equiv. to 10 µg/dL in blood. Withdrawn in 2010. EA withdrew SGV in 2011.	EFSA 2010 evaluation using the BMD modelling of Lanphear et al 2005, published by Budtz-Jorgensen 2013. Comparison with US CDC action level 2012

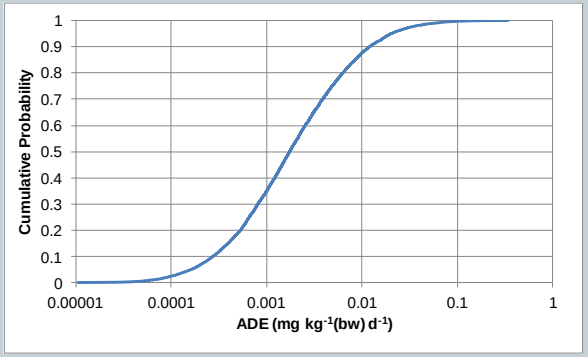
Toxicological Assessment (cont)

SUBSTANCE	TOXICOLOGICAL BASIS OF 2002/2009 INHALATION HCV	TOXICOLOGICAL BASIS OF 2014 INHALATION LLTC
Arsenic	ELCR estimates from a WHO 2001 evaluation (1 in 100,000 risk)	ELCR estimates from a WHO 2001 evaluation (1 in 50,000 risk) – as per 'low risk'
Benzo[a]pyrene (as a surrogate marker for genotoxic PAHs)	UK AQO (2002) based upon an EPAQS evaluation 0.25 ng/m³ (equivalent to 1 in 40,000)	Aligned with current UK AQO 1 ng/m3. This would equate to a 1 in 10,000 risk using the data in Armstrong et al 2004, on which the AQO is based. Policy choice to be higher than 1 in 50,000.
Benzene	UK AQO 5 µg/m³ Equivalent to an ELCR of 1 in 34,000 Policy choice to be higher than 1 in 100,000	UK AQO 5 µg/m3 Equivalent to an ELCR of 1 in 34,000 Policy choice to be higher than 1 in 50,000
Cadmium	EC working group definition of a limit value using LOEL & UF of 5.	BMD modelling renal effects using ATSDR 2012 evaluation of data, incorporating kinetic modelling. BMDL10 with CSAF of 9
Chromium VI	WHO AQG/UK AQO1 in 10,000	EPAQS evaluation of Park et al. 2004.
Lead	Blood lead level - Route independent, as per oral	Route independent, as per oral

Uncertainty Assessment

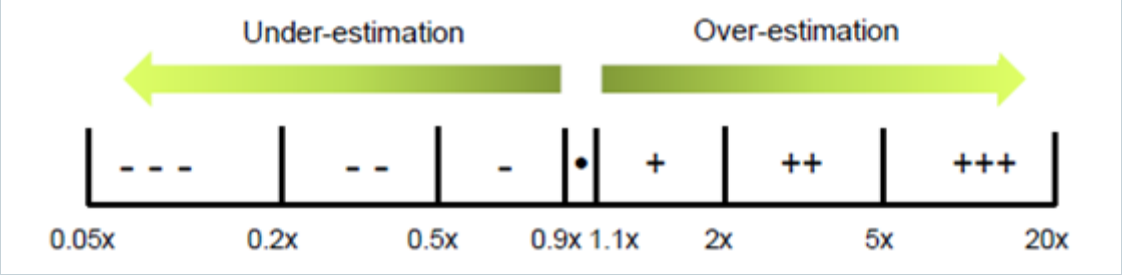
- How precautionary are the pC4SLs?
- How likely is the occurrence of significant harm at a given soil concentration (e.g. the SGV or pC4SL)?
  - How confident are we that significant harm would not occur at the health based guideline value (e.g. HCV or LLTC?)
  - How confident are we in our exposure estimates?
- Addressed using:
  - probabilistic modelling (Monte Carlo analysis) of CLEA exposure estimates
  - qualitative appraisal of uncertainties in the derivation of LLTCs and residual uncertainties in exposure modelling





Uncertainty Assessment (cont)

- Tables used to qualitatively assess residual uncertainties
- Qualitative evaluation of magnitude of uncertainty based on expert judgement



Uncertainty Assessment (cont)

- Example (for nickel)

INHALATION LLTC	
Choice of biomarker: In the ATSDR 2012 evaluation the most sensitive of biomarkers are evaluated, and it is not necessarily proven definitively that adverse effects would arise in the kidney at the low levels of biomarkers chosen. It is therefore considered likely that the $LLTC_{inhalation}$ is conservative (an underestimate).	-
Susceptibility of diabetics has already been taken into account in the CSAF.	●
Non-linearity of toxicokinetics: linearity has been assumed in the Nordberg-Kjelstrom model.	-/+
Overall evaluation of uncertainty for $LLTC_{inhalation}$: based on the above, the uncertainties affecting the LLTCs are mostly fairly limited (within a factor of two) with more tending to underestimation (conservative) than overestimation. The proposed $LLTC_{inhalation}$ is therefore considered a reasonable basis for setting the C4SL.	

Defra Companion Document

- General endorsement of the approach
- Clarifications:
  - Endorsement of a Benchmark Dose (BMD) approach to toxicological assessment and the use of a Benchmark Response (BMR) of 10% (generally).
  - Derivation of a Low Level of Toxicological Concern (LLTC) for non-threshold chemicals using a Chemical Specific Margin (where data allow) or a generic margin of 5,000 (when BMD10 used). Alternatively, if human data allow it, use an Excess Lifetime Cancer Risk (ELCR) of 1 in 50,000.
  - Where necessary, policy-based LLTCs should be used to avoid disproportionately targeting soil.
  - Lead LLTC = 3.5 µg/dl (blood).
  - Endorsement of use of US EPA's IEUBK model, and CLEA, for lead.
  - Changes to both exposure modelling and toxicological assessment should be used.
  - DCLG responsible for planning policy.
  - Fate of the SGVs lies with the Environment Agency (but CLEA, SR2 and SR3 should be retained).

Defra Companion Document (cont)

Final Category 4 Screening Levels based on the risk management decisions outlined above[9]

Substance	Residential (with home-grown produce)	Residential (without home-grown produce)	Allotments	Commercial	Public Open Space 1	Public Open Space 2
Arsenic	37 mg/kg	40 mg/kg	49 mg/kg	640 mg/kg	79 mg/kg	170 mg/kg
Benzene	0.87 mg/kg	3.3 mg/kg	0.18 mg/kg	98 mg/kg	140 mg/kg	230 mg/kg
Benzo(a)pyrene	5.0 mg/kg	5.3 mg/kg	5.7 mg/kg	77 mg/kg	10 mg/kg	21 mg/kg
Cadmium	22 mg/kg	150 mg/kg	3.9 mg/kg	410 mg/kg	220 mg/kg	880 mg/kg
Chromium VI	21 mg/kg	21 mg/kg	170 mg/kg	49 mg/kg	21 mg/kg	250 mg/kg
Lead	200 mg/kg	310 mg/kg	80 mg/kg	2300 mg/kg	630 mg/kg	1300 mg/kg

This table should be read in conjunction with the Final C4SL R&D report.

Using C4SLs

- Like SGVs, C4SLs are generic screening values and should be used in the same way:
  - understand their derivation and limitations before using
  - apply to a wide range of, but not all, sites
  - can be used as part of a GQRA for assessing risks to human health from long-term exposure to soil contamination for common scenarios / pathways
  - can be used to help determine whether a site is within Category 4 for human health
  - Detailed Quantitative Risk Assessment (DQRA) may show that a site with soil concentrations > C4SL is still within Category 4 (ie, risk is low)

DQRA

- Human health DQRA can involve any or all of the following:
  - Site-specific changes to the conceptual model
  - Advanced statistical treatment of environmental data
  - Adjustments to exposure assumptions
  - Modified modelling approaches
  - Bioaccessibility measurements
  - Sampling and analysis of environmental exposure media
  - Site-specific media uptake factors
  - Human bio-monitoring (HBM) studies
  - Medical and/or epidemiology studies
  - Adjustment of toxicological criteria and benchmarks
  - Consideration of toxicological mixture effects
  - “Margin of exposure” (MOE) approaches
  - Consideration of acute risks
  - Sensitivity analysis
  - Uncertainty analysis (eg, Monte Carlo simulation)

Expert Review

- Toxicological aspects submitted to the Committee on Toxicity (COT) on 14 May 2013, by Defra, for consideration, along with five specific questions.
- Minutes from this meeting (including answers to the questions) are available online (http://cot.food.gov.uk/cotmtgs/cotmeets/).
- Selected exerpts from the minutes:
  - *"One Committee Member, who was familiar with contaminated land policy, commented that the broad approach was reasonable."* (para 24)
  - *"Members agreed that the report was good"* (para 28)
- Defra's responses to the COT's answers are provided in the Policy Companion Document

Expert Review (cont)

- Toxicological aspects (and especially the approach to dealing with non-threshold carcinogens) were also submitted to the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) on 19 September 2013, by Defra, for consideration.
- Minutes from this meeting also available online (see http://www.iacoc.org.uk/meetings/index.htm).

Expert Review (cont)

- Defra received comments from two peer reviewers.
- Selected comments from Peer Reviewer 1 (Dr Robert Scofield, Director of the Center for Exposure Assessment and Dose Reconstruction, Exponent, USA):

> *"In summary, I think it must be recognized that the challenge of balancing the competing goals of being "strongly precautionary" while avoiding being "over cautious" is substantial. Because such a balance requires technical and policy considerations, identification of the optimal balance point is highly subjective and it is safe to say that it would be impossible to develop screening levels that would have unanimous support."*
>
> *"The project team accepted a substantial challenge and provided a very well thought out and well documented approach, and they clearly identified the scientific uncertainties, as well as the fact that policy considerations are important in the derivation of any soil screening levels. Because the approach proposed by the project team is based on conservative human health risk assessment methods and acceptable risk policies, the provisional screening values produced by the proposed process are virtually certain to be "strongly precautionary.""*

Expert Review (cont)

- Selected comments from Peer Reviewer 2 (Professor Alan Boobis, Director of Toxicology Unit, Imperial College):

  "Given the policy requirements and context, this appears to be a reasonable approach to the development of Category 4 Screening Levels (C4SLs)"

  "Probabilistic approaches have been used effectively to explore exceedences of the average daily exposure at the LLTC and the soil concentration at the provisional C4SL."

Thanks for listening!

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