Defra Research Project SP1010

Category 4 Screening Levels:
The Project and The Facts

Sarah Bull & Simon Firth

RICARDO-AEA

firth consultants
environmental risk assessment

SoBRA/SAGTA workshop, 8th April 2014

Environmental Health Sciences Limited

firth consultants
environmental risk assessment

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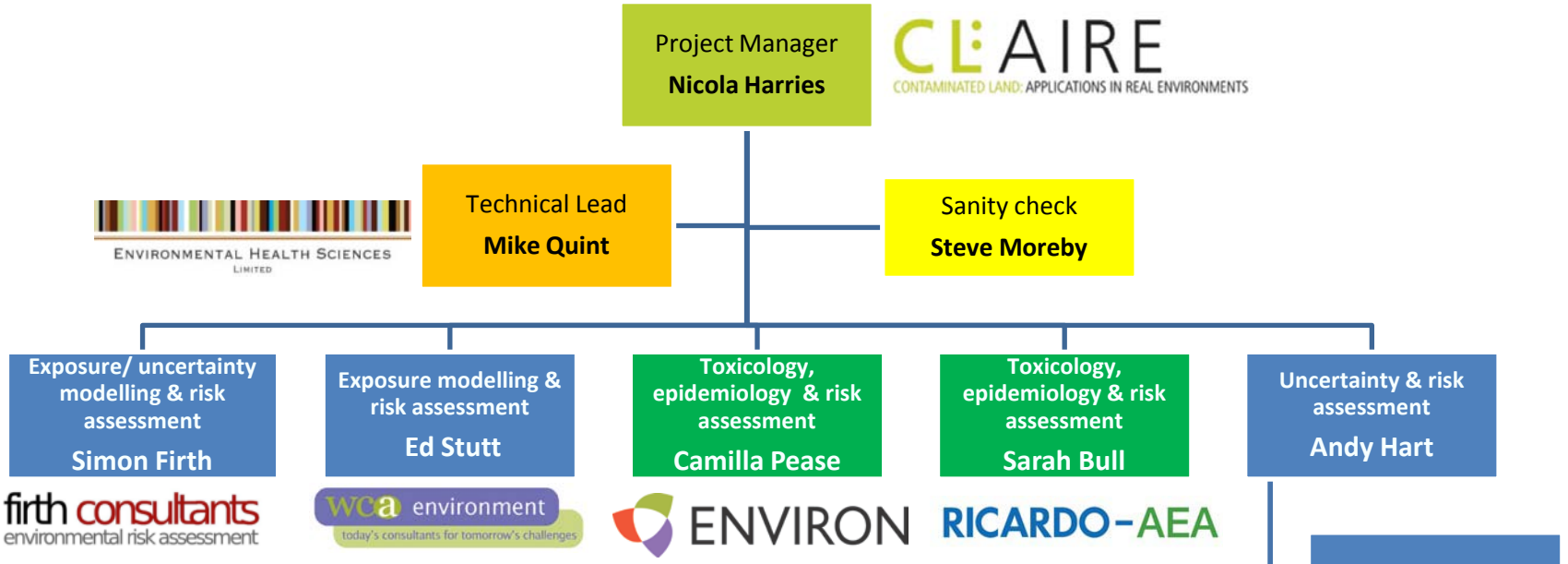
CONTAMINATED LAND: APPLICATIONS IN REAL ENVIRONMENTS

C4SLs Project Team



Cross-Government Agency Steering Group

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

Driver for C4SLs

Category 4 Screening Levels:

- **Revised Statutory Guidance (April 2012)** states that:
  - *"New technical tools and advice may be developed and used.... to help regulators and others conform to this Guidance."*
  - *"Tools might be developed to help assessors apply the Category 1-4 approach in relation to specific substances or situations. For example, this might include the development of generic screening levels to help assessors decide when land might be assumed to be in Category 4."*

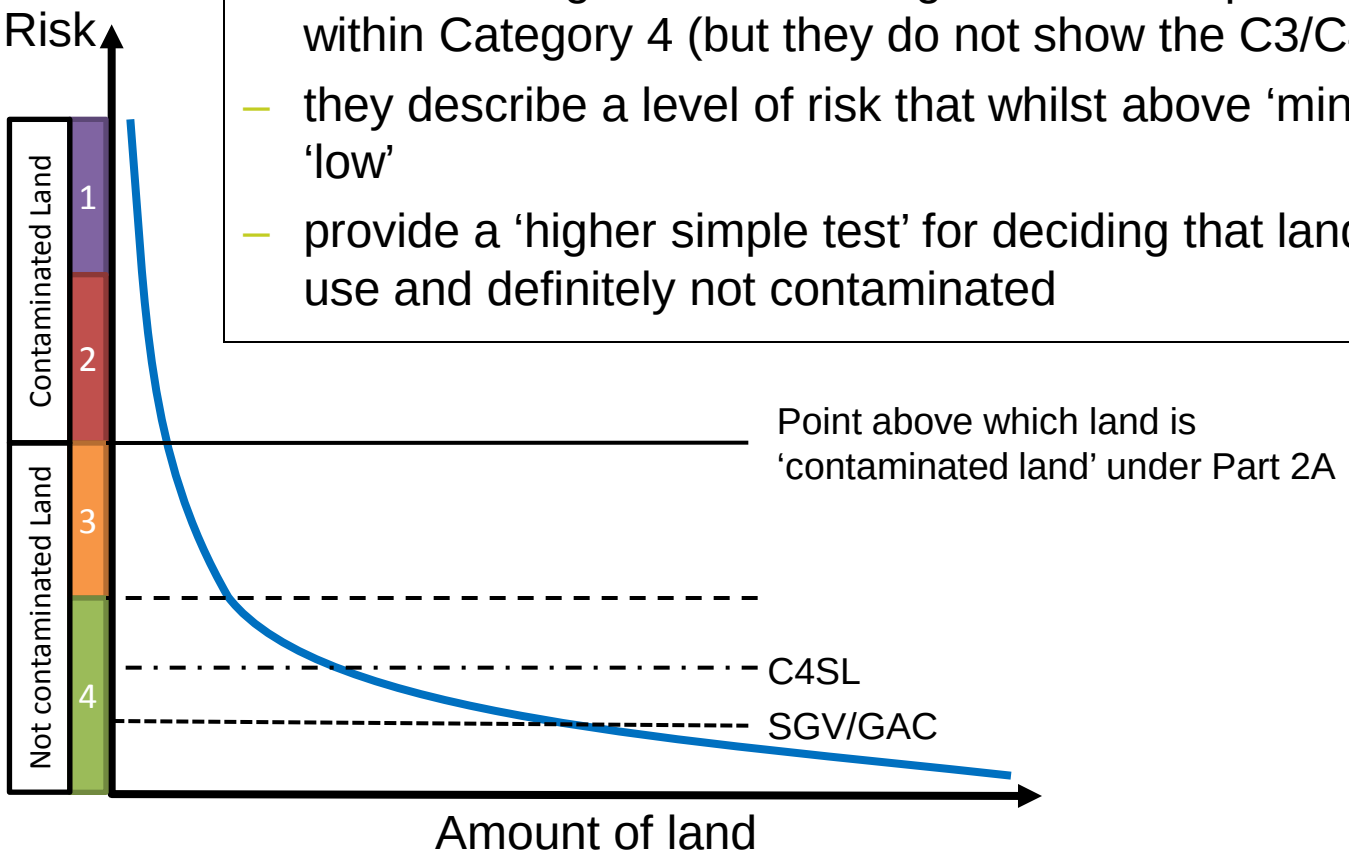
- **Impact assessment states that:**
  - *"The new statutory guidance will bring about a situation where the current SGV/GACs are replaced with more pragmatic (but still strongly precautionary) Category 4 screening levels (C4SLs) which will provide a higher simple test for deciding that land is suitable for use and definitely not contaminated land"*

What are C4SLs?

- Category 4
  - Describes land that is clearly not contaminated land
  - Land where there is '**no** risk or where the level of risk posed is **low'**

C4SLs are:

- intended as generic screening values to help show when land is within Category 4 (but they do not show the C3/C4 boundary)
- they describe a level of risk that whilst above 'minimal' is still 'low'
- provide a 'higher simple test' for deciding that land is suitable for use and definitely not contaminated



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Project Objectives

- To develop a methodology to derive C4SLs for 4 generic land-uses:
  - Residential
  - Allotments
  - Commercial
  - Public Open Space

WP1

- To derive C4SLs for 6 substances:
  - Benzo(a)pyrene
  - Cadmium

WP2

  - Arsenic
  - Benzene
  - Hexavalent chromium
  - Lead

WP3

Aug'12

Sep

Oct

Nov

Dec

Jan

Feb

Mar

Apr

May

Jun' 13

Stakeholder engagement

- Stakeholder engagement was built into the project specification, with stakeholder workshops being incorporated into each Work Package of the research
- Stakeholder workshops held on:
  - 6th November 2012
  - 4th February 2013
  - 2nd May 2013
- Feedback and comments from stakeholders were incorporated and taken into account in the development of the project

- COT, COC + peer reviews

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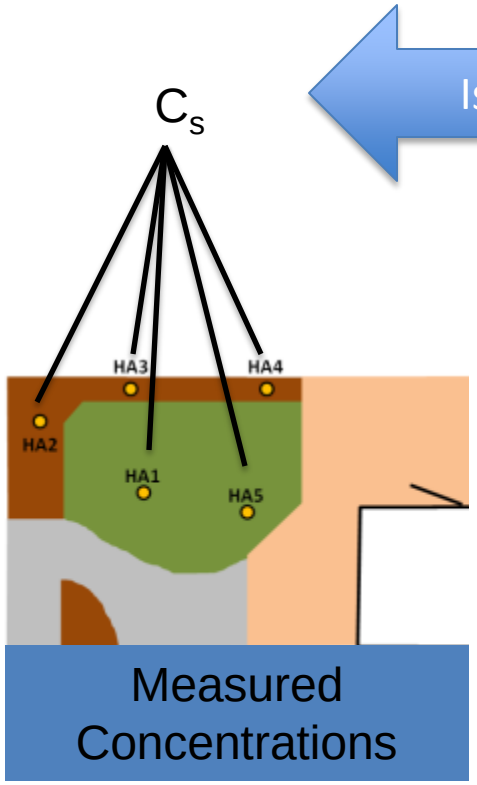
Development of framework

- Retained and used the CLEA framework, modified according to considerations of the underlying assumptions and science, within the context of Defra's policy background.

- Modifications relating to:
  - exposure modelling;
  - toxicological parameters and the setting of toxicological criteria at a higher than minimal risk (defined as a 'low level of toxicological concern' or LLTC);
  - consideration of uncertainty; and
  - considerations in the setting and use of C4SLs.

The CLEA paradigm for ‘minimal risk’



Is C_s > SGV?

SGV

- Review ‘authoritative’ human health/ tox guidance
- Follow the principles of defining minimal risk in SR2
- Take the lowest value for the most sensitive effect OR
- A ‘Policy’ decision is taken

e.g. to equate to an existing standard or objective

HCV

CLEA model

Environment Agency

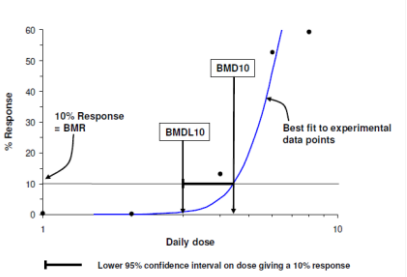
Exposure Parameters

- CLEA fit for purpose: to determine minimal risk values
- What modifications can be made to derive C4SL?

The CLEA paradigm for 'low risk'

Review 'authoritative' guidance
Follow the general principles in SR2
Review the dose response curve for the most sensitive effect(s)

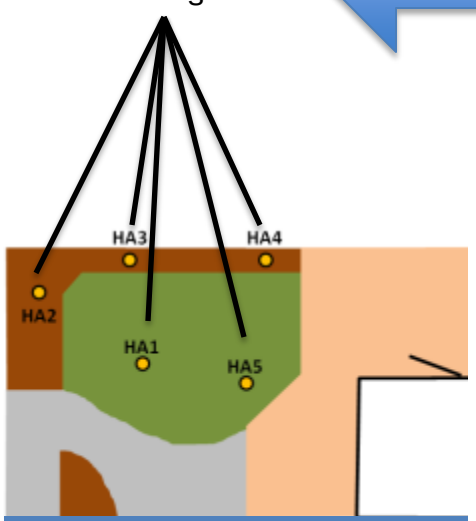
N.B. and consider ALL effects where dose-responses overlap)



Is C_s > C4SL?

C4SL

C_s



Measured Concentrations

CLEA model

Environment Agency

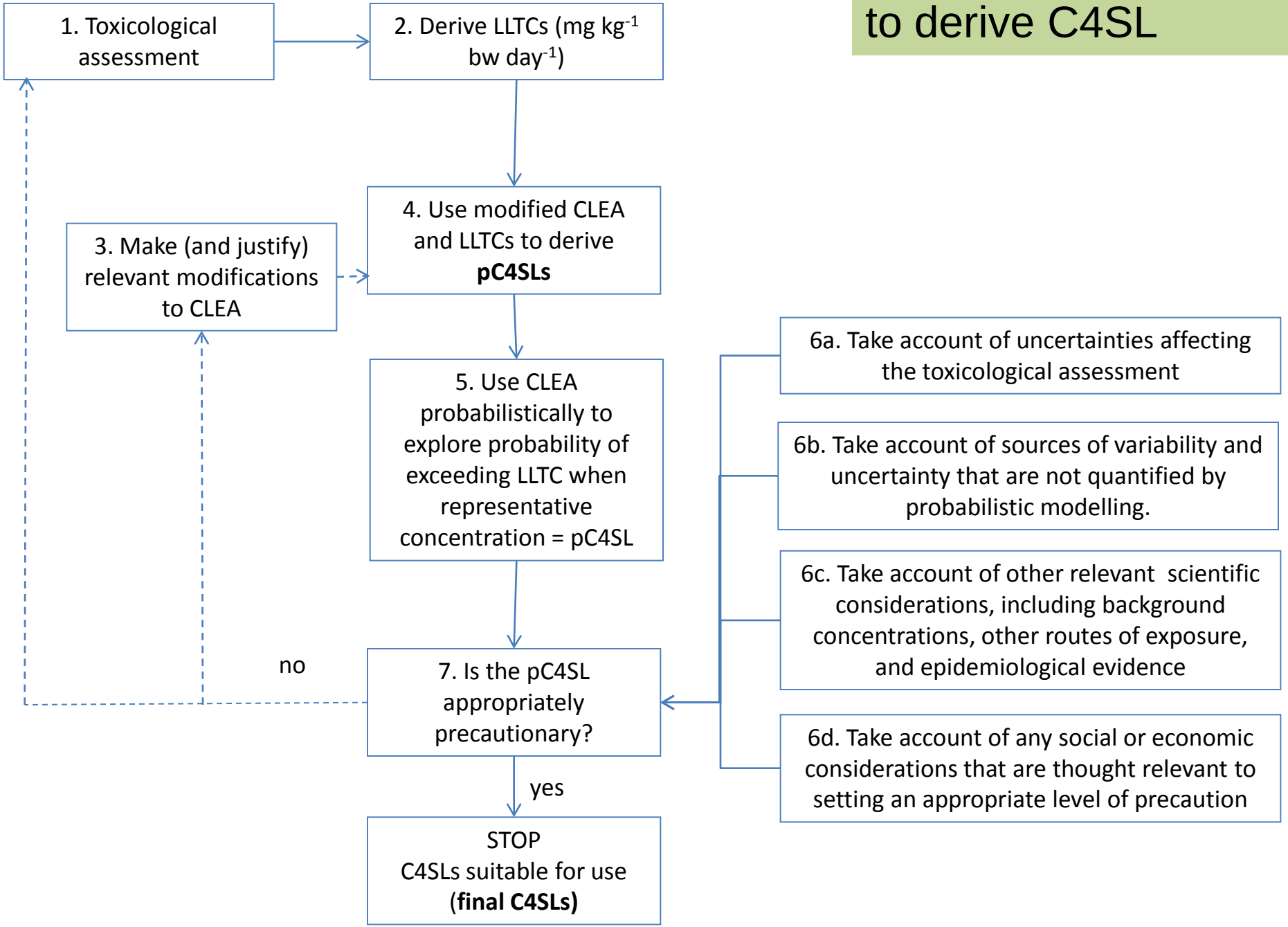
LLTC

'Policy' inputs/ Risk Management Decisions

Exposure Parameters

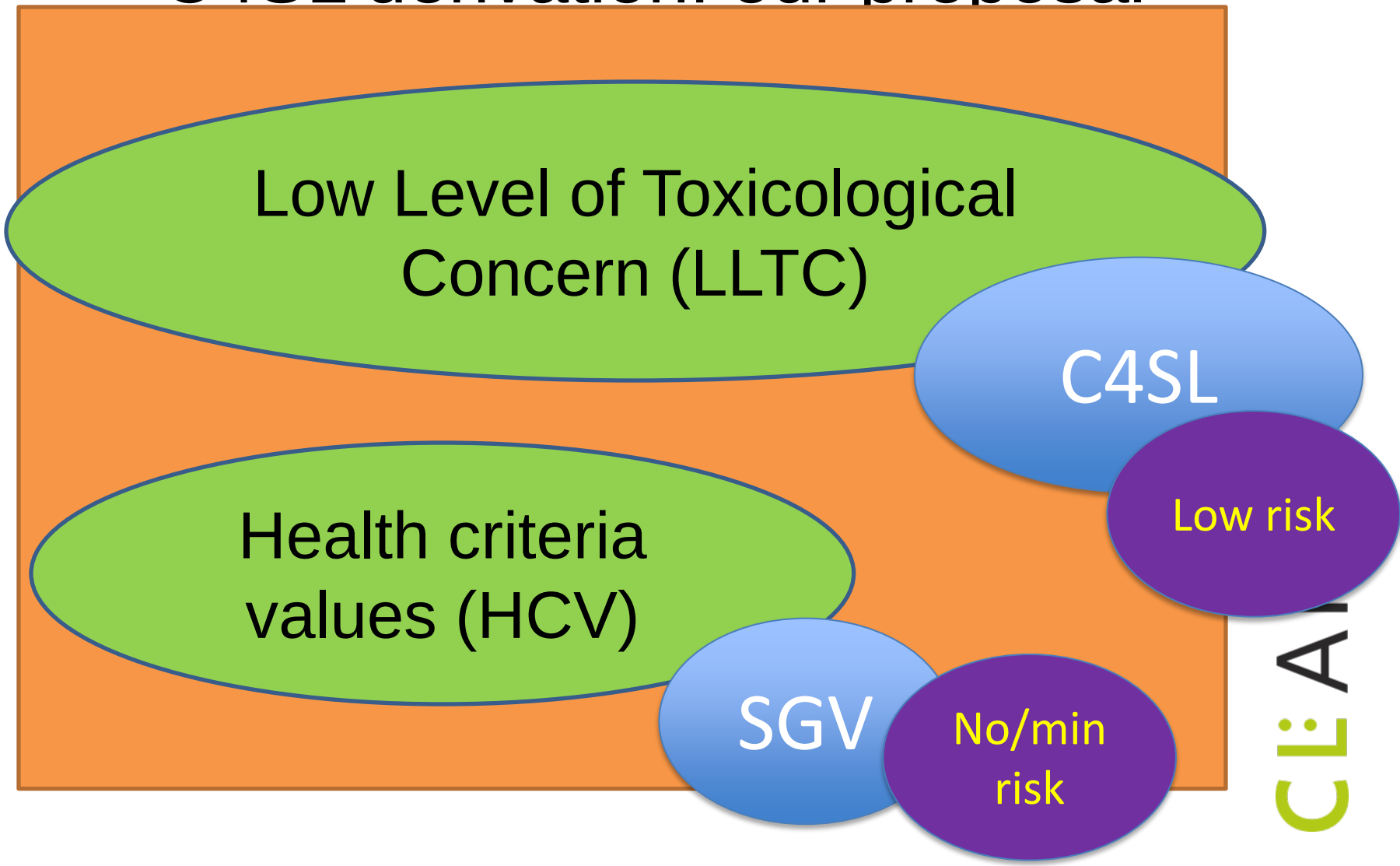
Consider modifications to exposure parameters

Developed framework to derive C4SL



Low Levels of Toxicological Concern (LLTCs)

Defining a new toxicology term for C4SL derivation: our proposal



A Suggested Framework for Deriving a LLTC

Perform hazard characterisation for each substance

Scientific approach that builds on SR2 and the principles of risk assessment

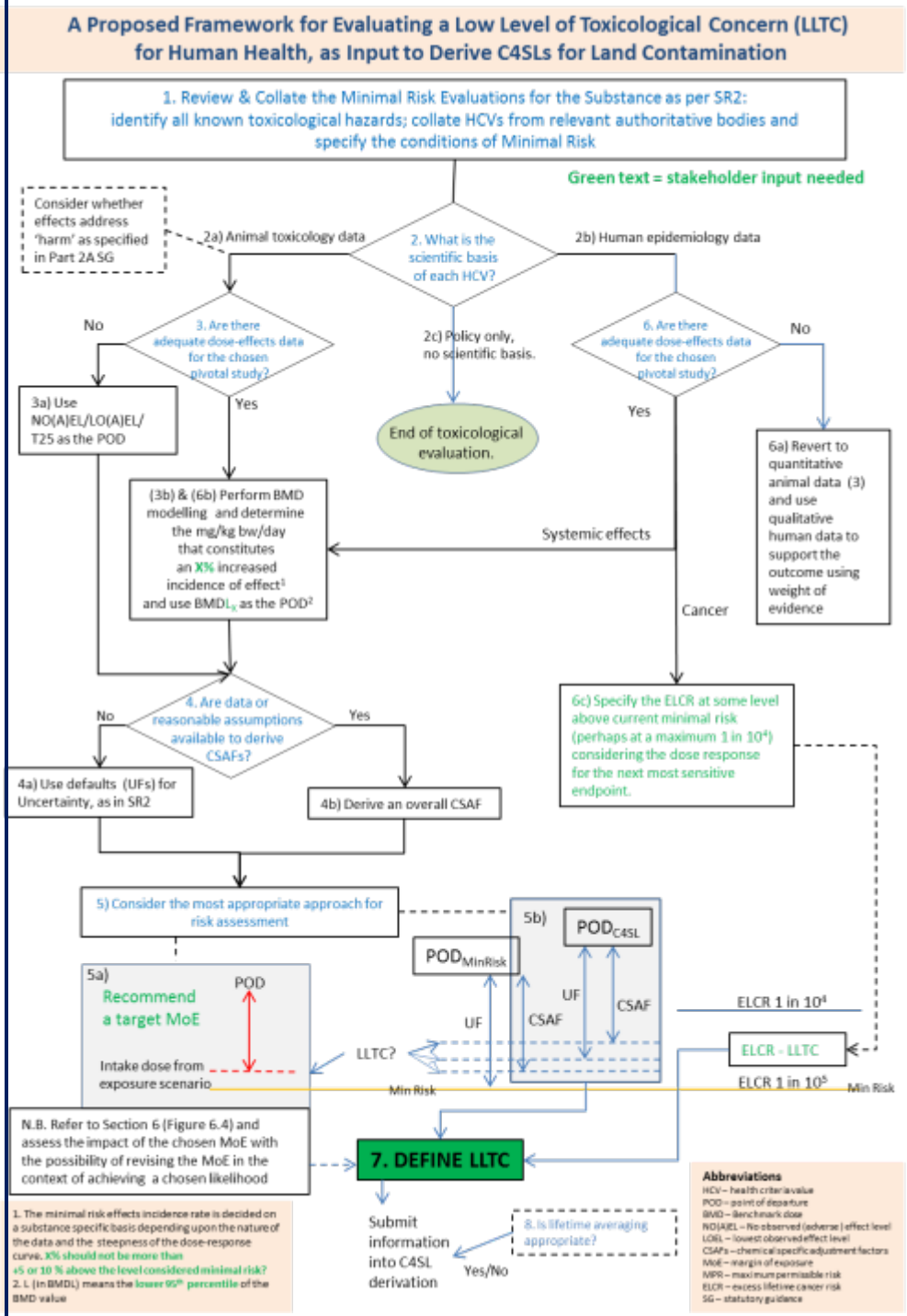
Review of all significant effects data

Use of the dose response information in the pivotal study where possible

Reinterpret the toxicology & epidemiology package
(incorporating any newly generated data if it exists)

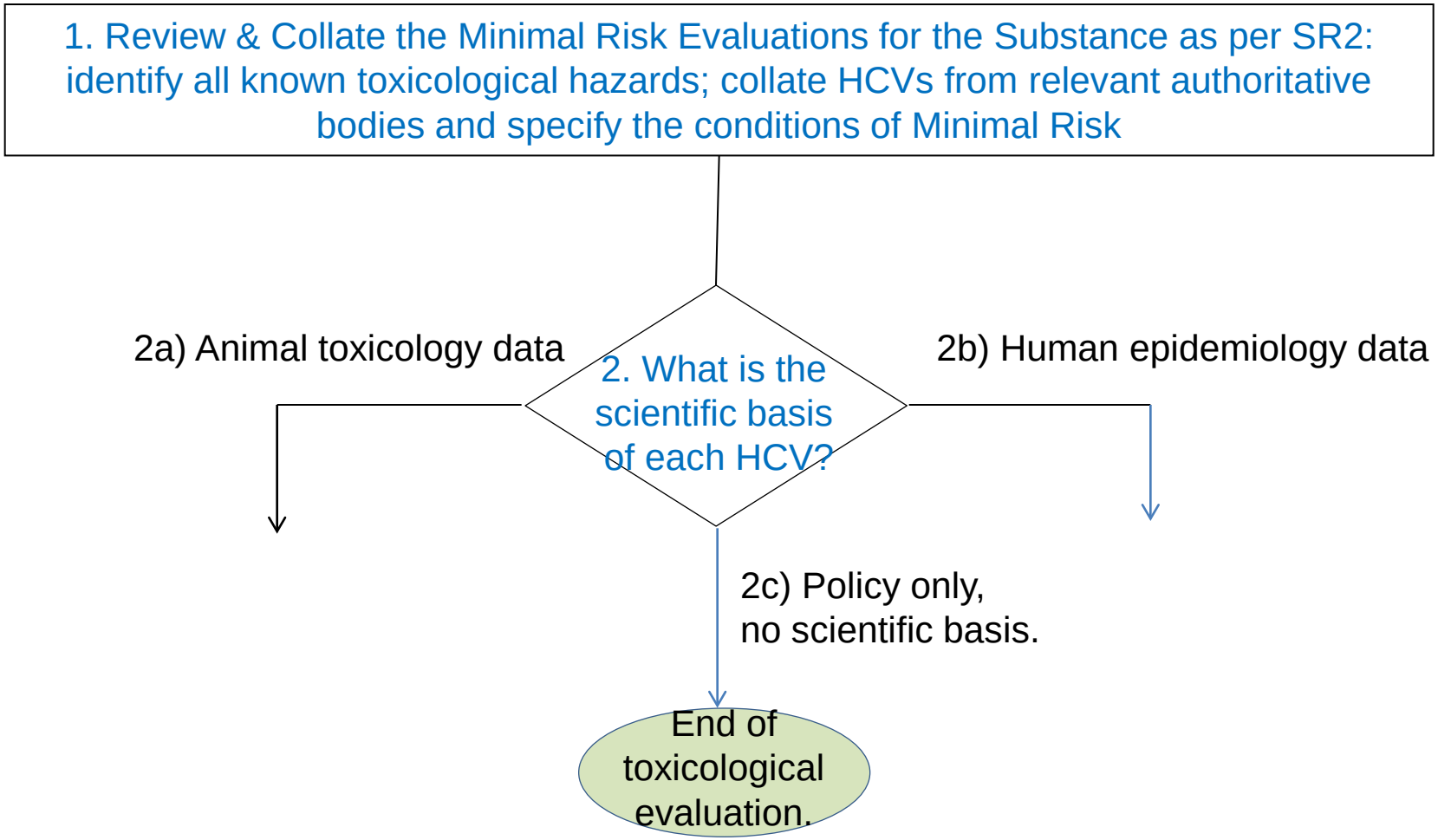
Stakeholder input – what level would society consider to be 'low'?

Low Level of Toxicological Concern



A Suggested Framework for Deriving a LLTC

Steps 1 & 2



Appendix 1 Current HCVs and MDIs for Arsenic

I) Human Health Hazard Profile - To be reviewed across all endpoints and com

a) Oral Route	POD	Units	Species	
b) Inhalation Route				
c) Dermal Ro				

Most Sensitiv

Key

II) Minimal Risk He . riteria Value (HCV) information (using the most sensitive effects data)

a) Oral Route	HCVoral	HCV units	UF used	PoD	Endpoint	Pivotal data used & Comments
WHO/JECFA PMTDI	2	µg kg^{-1} bw day^{-1}			Skin lesions	Provisional Maximum Tolerable Daily Intake (PMTDI) as a contaminant in food. Taiwan data on
RIVM TDI	1	µg kg^{-1} bw day^{-1}	2	PTWI; 15 µg kg^{-1} bw day^{-1}	Cancer	Additional UF of 2 applied to the JECFA PTWI (= TDI of 2.1 µg kg^{-1} bw), to account for uncertainty
EFSA 2009 BMDL01	0.3	µg kg^{-1} bw day^{-2}		$BMDL_1$; 0.3-8 µg kg^{-1} bw day^{-1}		2010 science based review. Concluded JECFA value no longer appropriate. Benchmark dose acc skin cancer.
CLEA 2009 HCV	0.3	µg kg^{-1} bw day^{-1}			Cancer	SC050021/Tox 1 Current published EA HCV recommendation. Policy based. Equivalent intake to water standard of 10 µg L^{-1} WHO - "practical quantification limit". Health Canada - "maximum ac drunk by a 70kg adult. An ELCR of 1 in 100000 would = 0.003 µg kg^{-1} bw day^{-1} as per USE EPA 2008
US ATSDR MRL	0.3	µg kg^{-1} bw day^{-1}	3	NOAEL; 0.8 µg kg^{-1} bw day^{-1}	Skin lesions	Taiwan study, human NOAEL and applying an UF of 3 (human interindividual variability)
US EPA 2011-2	0.21	(males) µg L^{-1}			Skin lesions	Water concentrations leading to a 10^{-4} cancer risk. Latest science on cancer risk estimates from Under consultation. EPA/635/R-10/001. Federal Register 2010, 75, 7477.
US EPA 2011-2	0.14	(females) µg L^{-1}				Under consultation. EPA/635/R-10/001. Federal Register 2010, 75, 7477.
US EPA 2008 HCV	0.003	µg kg^{-1} bw day^{-1}	N/A		Cancer	Index dose based upon evaluation of Tiawan drinking water studies & modelling an increased l

Step 3

Suggested C4SL CLEA Modification 10: Use BMD modelling rather than NOAELS and LOAELs to derive toxicological criteria where possible

Consider whether effects address 'harm' as specified in Part 2A SG

2a) Animal toxicology data

3. Are there adequate dose-effects data for the chosen pivotal study?

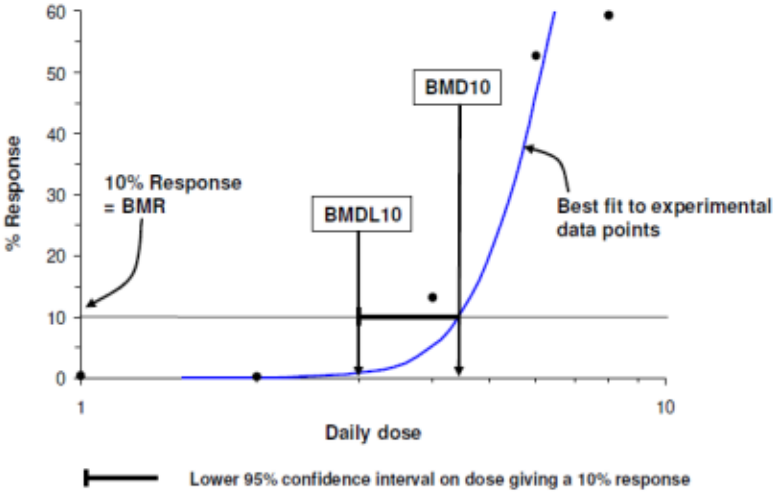
No

3a) Use NOAEL/LOAEL/ T25 as the POD

Yes

(3b) & (6b) Perform BMD modelling and determine the mg/kg bw/day that constitutes an **X%** increased incidence of effect and use $BMDL_X$ as the POD

The Principle of a Benchmark Dose



Choice of BMDLx

- One of the most important decisions in the derivation of LLTC
  - BMDL10 represents minimal risk
  - Cannot use a lower BMDL from cancer bioassay studies
  - Could use a higher BMR i.e. BMR15 or 20 indicating a 15 or 20% response above background
  - Could use lower BMDL from human studies (cadmium: BMDL5)
  - Could use BMD rather than the lower 95% CI

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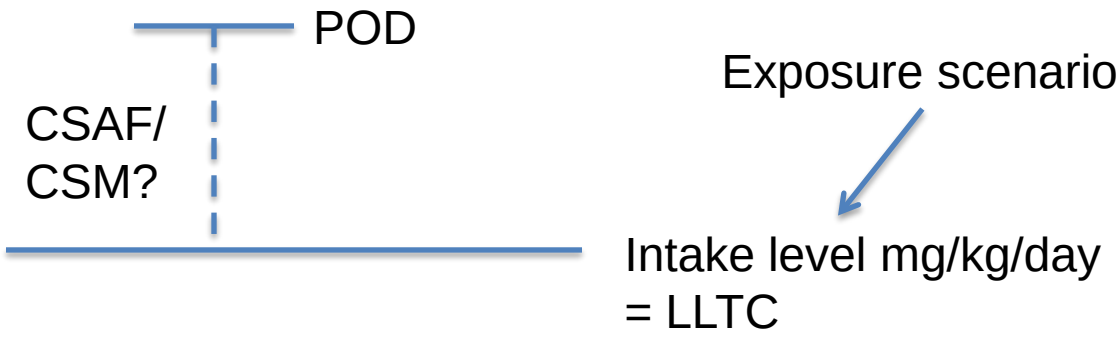
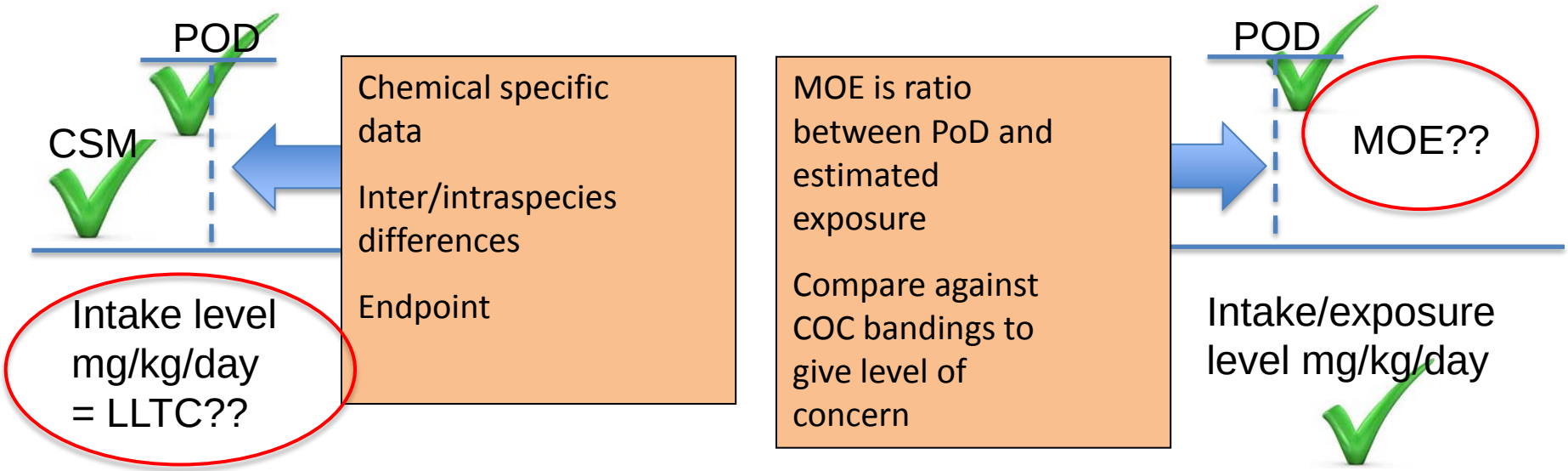
The Use of Chemical-Specific Adjustment Factors or Chemical Specific Margins



"The committee agreed that the use of a chemical-specific margin (CSM) approach, which paralleled the margin of exposure (MOE) approach, was appropriate to derive an LLTC for non-threshold chemicals. However, defining an acceptable margin entailed value judgements, and was not purely scientific."

Note of caution:
Do not mix up 'chemical specific margins' with 'margin of exposure'

Chemical-Specific Margins vs Margin of Exposure

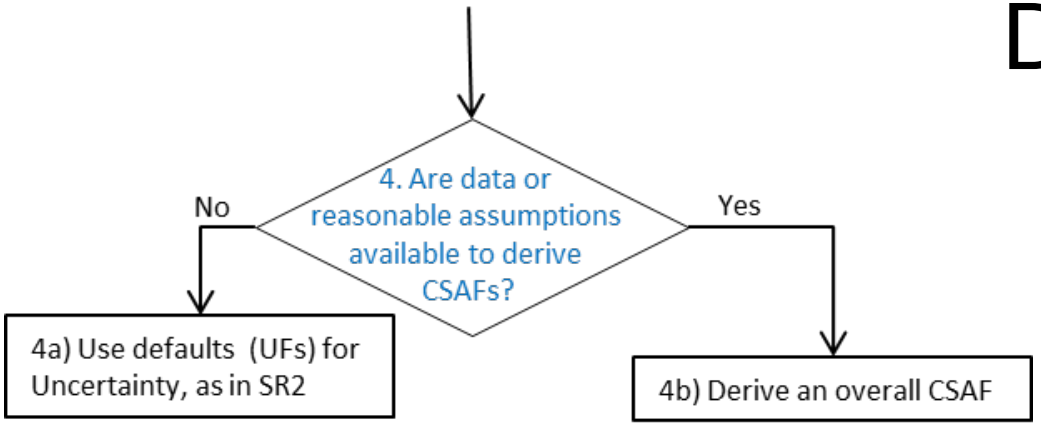


Risk assessment

Risk management/communication

The COC recommends that the Margin of Exposure (MOE) approach be adopted as a tool *to indicate the level of concern* in situations where exposure is unavoidable.
MOE can be compared against bandings suggested by COC during risk management and risk communication
MOE approach is useful when HBGVs are not available

Derivation of CSAF or CSM



Uncertainty Factors (UFs) and Chemical Specific Adjustment Factors (CSAFs)

IGHRC CR9 report on uncertainty factors in UK Government risk assessment	EFSA report on genotoxic carcinogens risk assessment	Default 'minimal risk' uncertainty factors	C4SL chemical specific adjustment factors	Justification for reducing from default values
Interspecies fate and behaviour differences (between mouse and human)	Interspecies fate and behaviour differences (between mouse and human)	10	1 to 10	e.g. toxicokinetics/dynamic differences are <10-fold different between mouse and man?
Intraspecies fate and behaviour differences (between human individuals)	Intraspecies fate and behaviour differences (between human individuals)	10	1 to 10	e.g. toxicokinetics/ toxicodynamics are <10-fold different between individuals.
Adequacy of study or database	The reference point on the dose-response curve	10	1 to 10	If the quality of the study is high, the UF could be less than 10, in terms of reliability of data points and NOEL/BMD etc.
Nature and severity of effect	Nature of carcinogenic process	10	1 to 10	Irreversibility of effect (e.g. use for carcinogens, reproductive toxins etc).
Total UF based on multiplication of individual factors		10,000	New value	

?

Suggested C4SL CLEA Modification 11: Use chemical-specific adjustment factors (CSAF) rather than default uncertainty factors to derive toxicological criteria, where possible

Generic margins – policy document

When data do not support the derivation of a CSM, use a generic margin

Policy companion document

*"Based on stakeholder engagement and the discussion within the final report, Defra recommends that **a generic margin of 5,000** be used for the purposes of deriving Low Levels of Toxicological Concern for non-threshold chemicals when a BMD10 from animal data is used as the Point of Departure."*

(USEPA, 2011; RIVM, 2001)

Potential LLTC values - BaP

	POD	Value (mg kg^{-1} bw day^{-1})	Margin /CSM	HCV/LLTC (µg kg^{-1} bw day^{-1})
Alternative	$BMDL_{10}$	0.1	10000*	0.01
Current HCV for BaP alone (EA 2002)	-	-	-	0.020
Alternative	$BMDL_{10}$	0.1	5000	0.020
Alternative	BMD_{10}	0.21	10000*	0.021
Proposed LLTC	**BMD_{10}**	**0.21**	**5000**	**0.042**

BMD data derived from Culp, using a multistage cancer model. BMDL10 data used by JECFA

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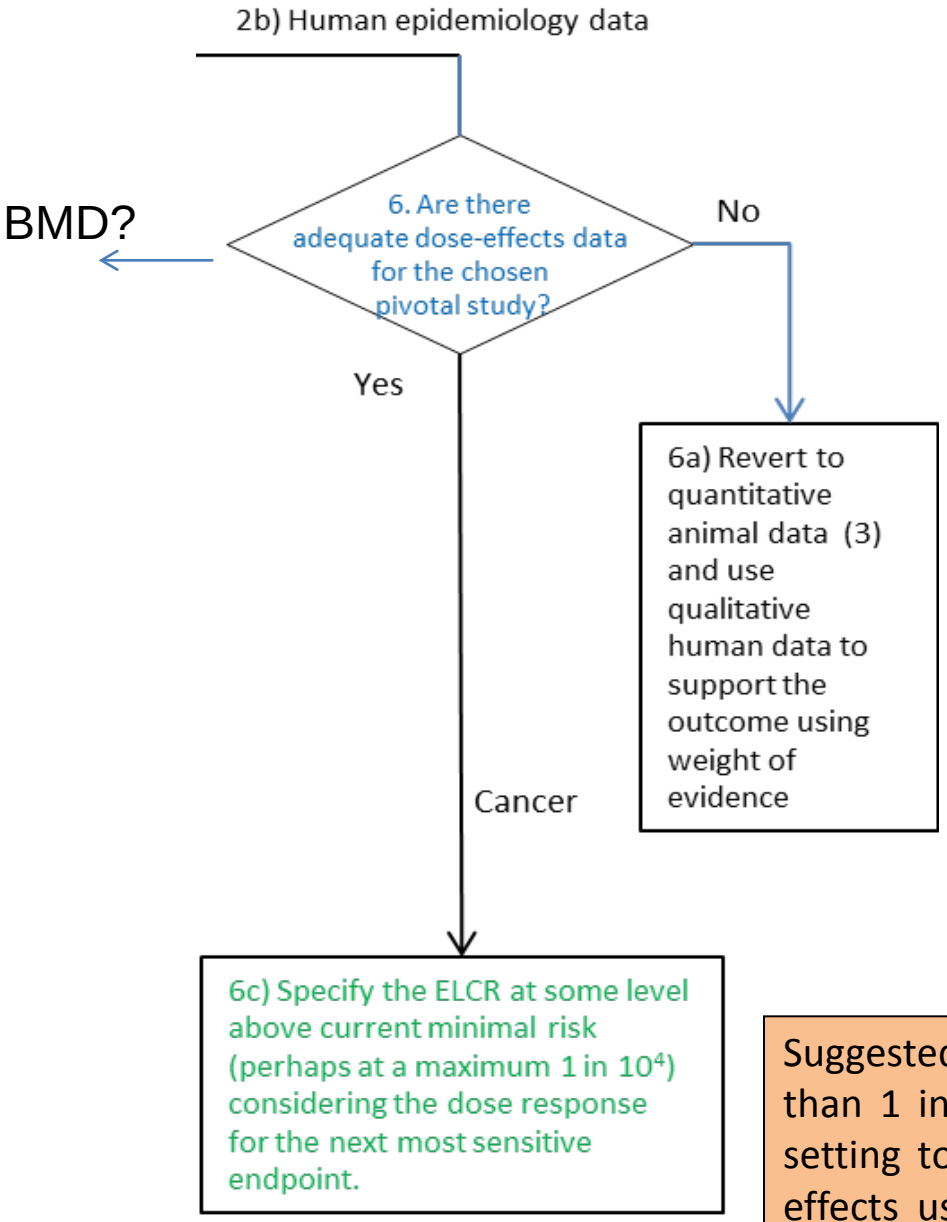
Step 6



Suggested C4SL CLEA Modification 12: Use of higher ELCR than 1 in 100,000 (e.g. a maximum of 1 in 10,000) when setting toxicological criteria for non-threshold carcinogenic effects using quantitative dose-response modelling (based on human data).

ELCR used in different scenarios

- US EPA - ELCR of 1 in 10,000 to 1 in 1,000,000
- Exposures causing more than 1 in 10,000 excess cancers are of concern
- ‘0.3 per 10,000 falls within the USEPA acceptable risk range of 1 in 10,000 and 1 in 1,000,000’
- RIVM based the maximum permissible risk levels on 1 in 10,000

(USEPA, 2011; RIVM, 2001)

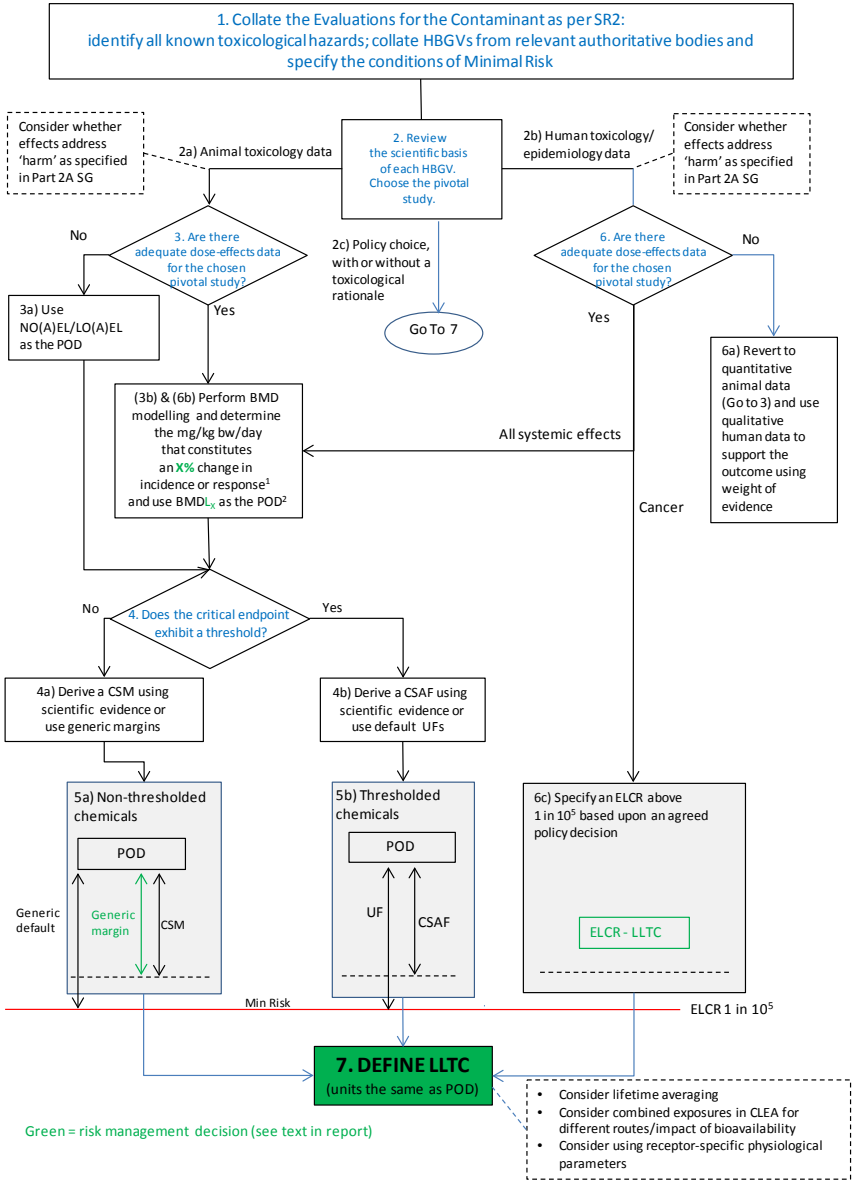
ELCR - policy document

"Defra recommends that for the purposes of deriving Category 4 Screening Levels, a risk estimate of 1 in 50,000 could be specified as 'low risk' and this would be a ***generic level used for all human genotoxic carcinogens*****."**

- Arsenic – ELCR of 1 in 2,000 used by WHO (water guideline values)
- BaP - ELCR of 1 in 10,000 was used by EPAQS
- Benzene – ELCR of 34,000 used for UK AQO

(USEPA, 2011; RIVM, 2001)

Overall choices



Potential differences to SR2

- Take account of all critical health effects – not just the most sensitive
- Use of BMD modelling to set POD where possible
- Use BMD rather than BMDL
- Use scientifically based chemical specific adjustment factors/margins, where possible rather than default UFs
- Consider moving above ELCR of 1 in 100,000 (e.g. 2 in 100,000) for carcinogens with human epidemiological data

Epidemiology studies

…. more pragmatic (but still strongly precautionary)

- Shipham / Belgium – high levels of cadmium
  - … was no clear evidence of health effects from possible exposure to cadmium in Shipham despite the extremely high concentrations of cadmium in the soil (Elliott *et al*., 2000).
  - …all-cause mortality rates in Shipham was similar to the control group and well below national average (Inskip *et al*., 1982).

- Glasgow – high levels of chromium VI
  - 25 mg/kg in Glasgow (C4SL - 21 mg/kg)
  - Exposure at LLTC is lower than intake from ambient air
  - LLTC based on ELCR of 1 in 50,000 (AQO 1 in 10,000)

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Exposure modelling

Exposure Modelling

- Critical review of uncertainties in CLEA model
  - CSM
  - Algorithms
  - Parameter values
- Sensitivity analysis
  - To identify key areas of uncertainty
- Probabilistic CLEA modelling
  - To further explore impacts of uncertainty

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Key pathways

Sensitivity analysis identified the key pathways/parameters causing greatest uncertainty in CLEA model results

- Soil + dust ingestion
- Consumption of homegrown produce
- Consumption of soil attached to homegrown produce
- Dermal contact indoors
- Dermal contact outdoors
- Inhalation dust indoors
- Inhalation dust outdoors
- Inhalation vapours indoors
- Inhalation vapours outdoors

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Evaluation of parameter values

- Are these suitably precautionary for derivation of C4SL?
- E.g. Dermal contact
  - Child assumed to wear shorts + T shirt and get filthy in garden 365 d/yr
  - Propose to use CT estimate for soil adherence in combination with worst case skin area, 170 d/yr

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Proposed modifications to exposure parameter values

Proposed change in draft WP1 report	Change invoked?		
	Res	Allo	Comm
Reduce soil ingestion rates for residential and commercial land-uses	×		×
Halve exposure frequencies for children on allotments		×	
Reduce soil adherence factors in children for residential land-use from 1 to 0.1 mg cm^{-2}	✓		
Reduce exposure frequency for dermal contact outdoors for residential land-use from 365 to 170 days per year	✓		
Update vapour inhalation rates to the mean values recommended in USEPA, 2011	✓		✓
Reduce indoor dust loading factors for residential and commercial land-uses to better reflect likely concentration of PM2.5	×		×
Use of central tendency estimates of fruit and vegetable ingestion rates rather than 90th percentiles	½	½	
Reduce the fraction of homegrown produce for residential land-use	×		
Exclude the quantitative consideration of background exposure from the derivation of C4SLs	×	×	×

Public Open Space

- Scenario 2, POS_{resi} - Grassed Area Close to Housing

- Scenario 2, POS_{park} – Park Type Open Space

POS_{resi}

- Assumptions:
  - Grassed area of up to 0.05 ha and a considerable proportion of this (up to 50%) may be bare soil
  - Predominantly used by children for playing and may be used for activities such as a football kickabout
  - Sufficiently close proximity to home for tracking back of soil to occur, thus indoor exposure pathways apply
- Adaptations to CLEA ‘resi without h/g produce’
  - ingestion rate 75 $mg.day^{-1}$ (approximately 50:50 ratio between ingestion of soil and soil-derived dust (USEPA, 2011 & EA, 2009c).)
  - older children as the critical receptor on basis that they will use site most frequently (AC 4-9)

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POS_{park}

- Assumptions:
  - Public park (>0.5 ha), predominantly grassed and may also contain children's play equipment and border areas of soil containing flowers or shrubs (75% cover)
  - Outdoor exposure pathways only (no tracking back)
- Based on adaptation of the CLEA allotment land use scenario for receptor characteristics:
  - Female child age classes 1-6
  - Soil ingestion rate of 50 $mg.day^{-1}$ [based on proportion (~50%) of daily ingestion rate (100 $mg.day^{-1}$) assigned to ingestion of soil outdoors (USEPA, 2011)]
  - Occupancy period outdoors = 2 $hours.day^{-1}$
  - Exposure frequency of 170 $days.year^{-1}$ for age classes 2-18 and 85 $days.year^{-1}$ for age class 1

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Uncertainty and other considerations

Uncertainty

- How precautionary are the C4SL?
- How likely is the occurrence of significant harm at a given soil concentration (e.g. the SGV or C4SL)?
  - 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?
- We have addressed this using:
  - Probabilistic modelling (Monte Carlo analysis) of CLEA exposure estimates
  - Qualitative appraisal of uncertainties in derivation of LLTC and residual uncertainties in exposure modelling

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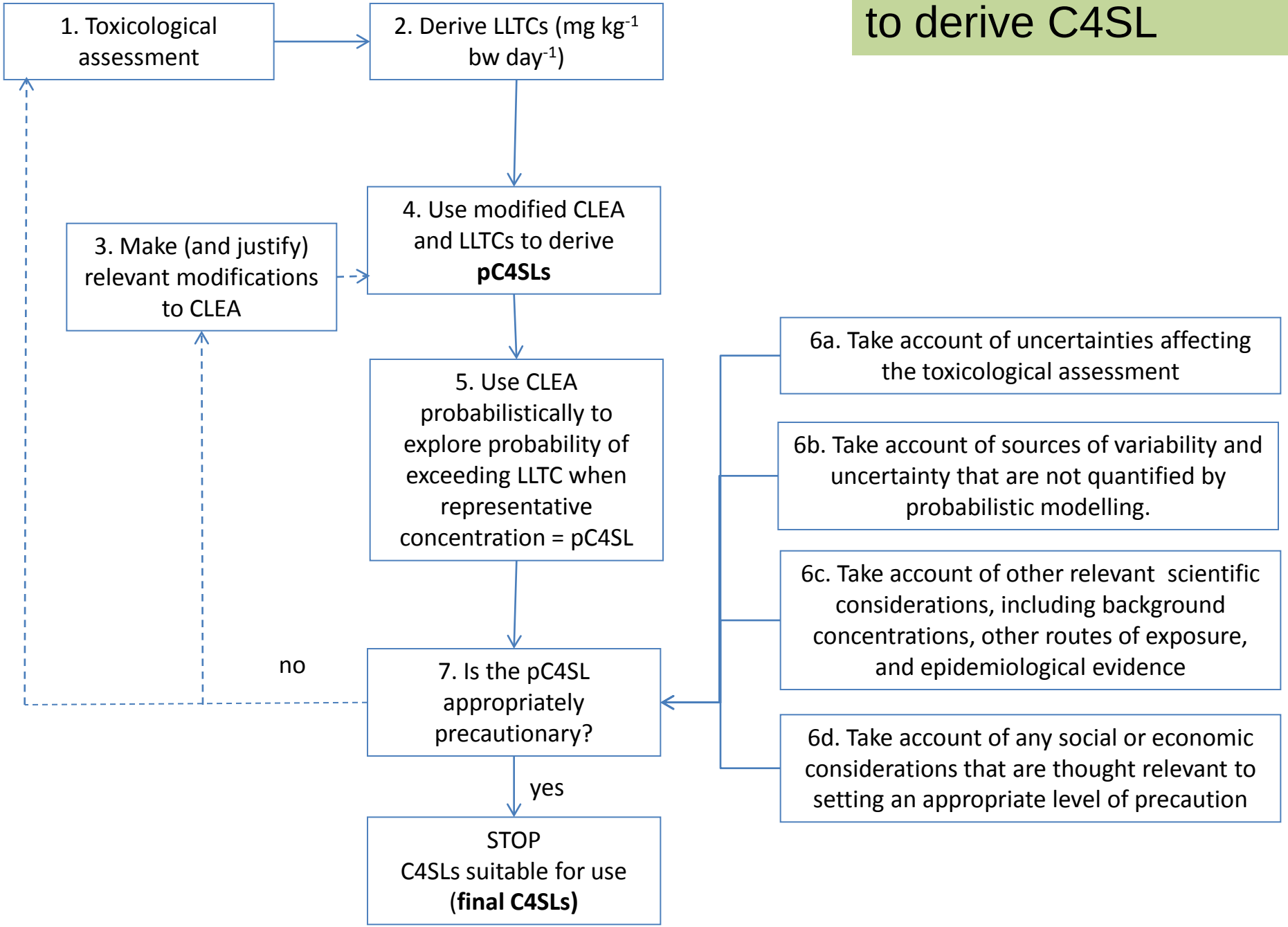
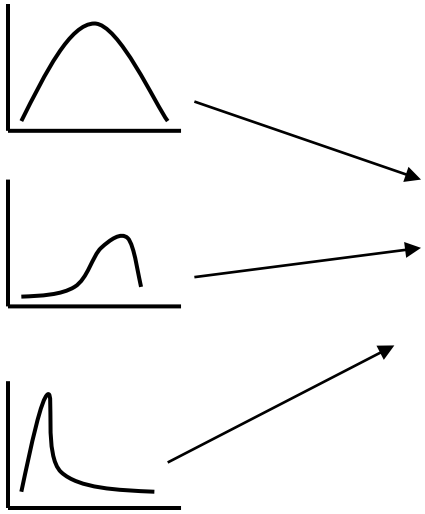
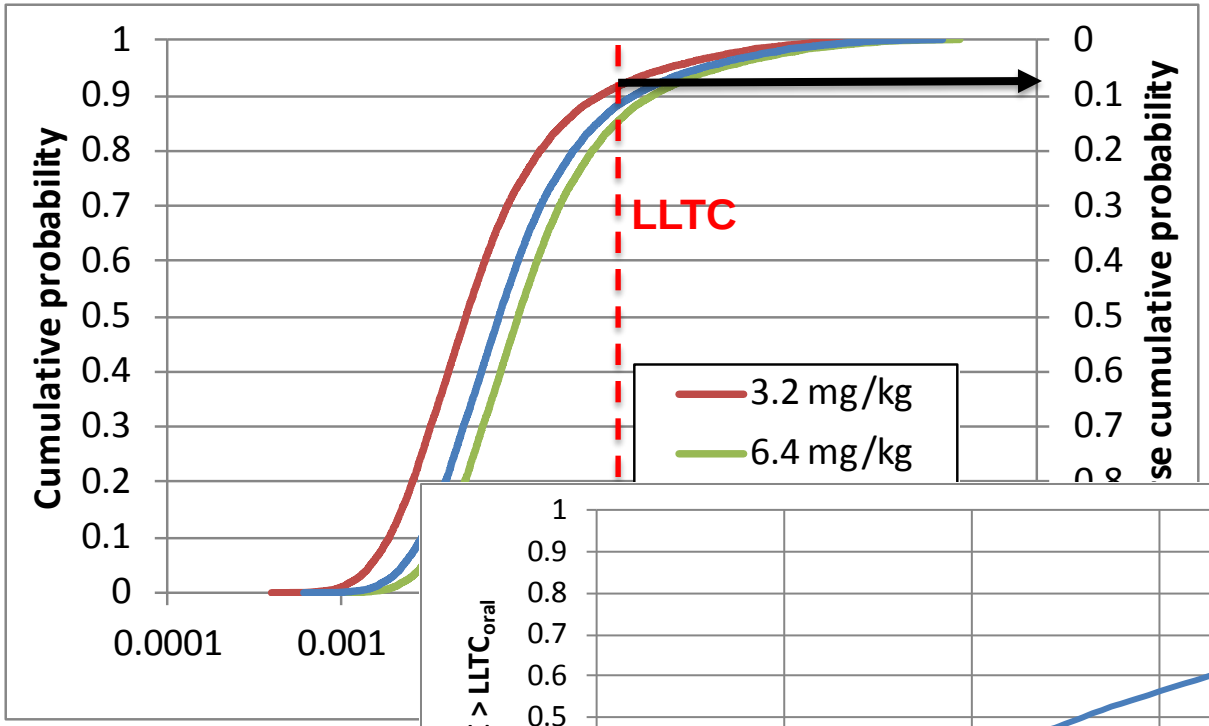
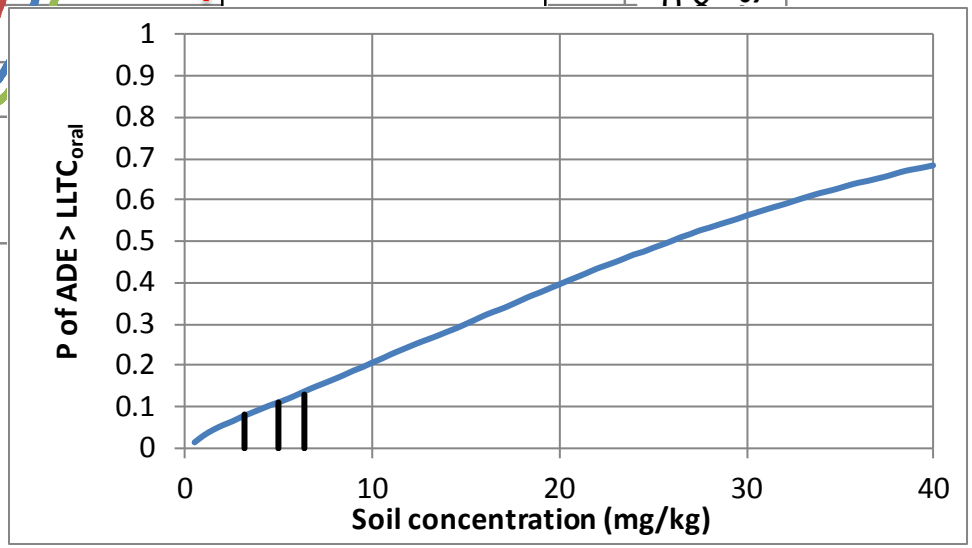
Developed framework to derive C4SL



Quantitative appraisal of uncertainty in exposure modelling



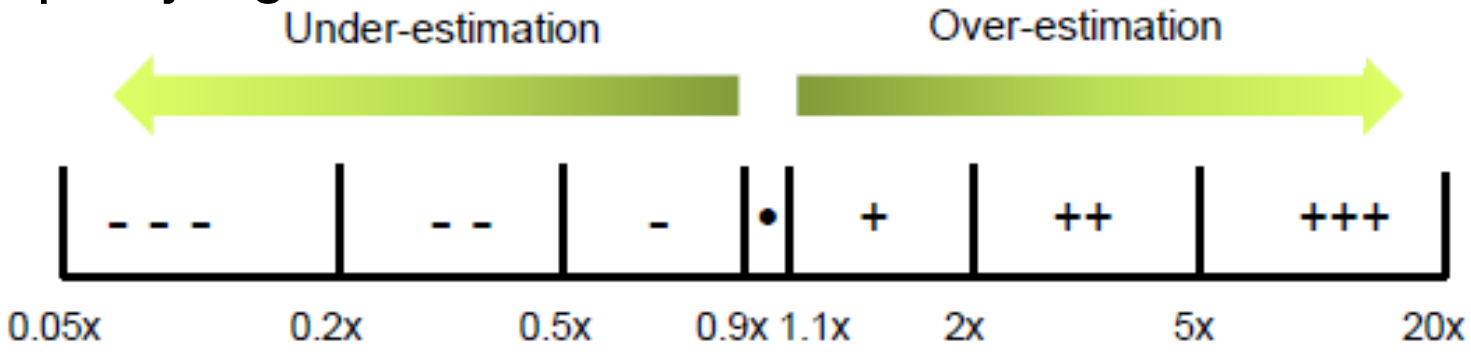




- Monte Carlo analysis using probability distributions for key exposure parameters

Qualitative appraisal of uncertainty

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



- Example (for benzene):

Parameter	Evaluation
Estimation of indoor air concentrations using Johnson and Ettinger model for UK building stock. The CLEA model uses the J&E model which is likely to over-estimate the indoor air concentration of benzene in a large proportion of UK building stock. The extent of over-estimation is anticipated to be up to several orders of magnitude.	● / **+++**

Further considerations

- May need to consider wider context when setting the C4SL for a particular substance, e.g.:
  - Background soil concentrations
  - Background exposure from non soil sources
  - Epidemiological evidence
  - Socio-economic considerations, e.g. the cost and proportionality in setting C4SLs so low as to always be exceeded

- Sense check on whether there could be odour, phytotoxicity or visual acceptability issues or acute risks at the C4SL

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Provisional C4SL

- Research derived a range of possible C4SL values:
  - Just making changes to exposure parameters
  - Just making changes to tox
  - Making changes to both exposure parameters and tox
- In addition, range of LLTC derived for lead:
  - 1.6 ug/dL blood lead
  - 3.5 ug/dL blood lead
  - 5.0 ug/dL blood lead
- Defra then used the evidence presented to make a policy decision on which values to choose as C4SL

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C4SLs

Substance	C4SL with changes to exposure parameters and LLTC ($mg.kg^{-1}$) (SGV or GAC shown in brackets for comparison)					
	Residential		Allotments	Commercial	POS_{resi}	POS_{park}
	With home grown prod.	Without home grown prod.				
Arsenic	37 (32)	40	49 (43)	640 (640)	79	168
Benzene	0.87 (0.33)	3.3	0.18 (0.07)	98 (95)	140	230
Benzo(a)pyrene (as a surrogate marker for genotoxic PAHs)	5.0 (1.0)	5.3	5.7 (2.1)	76 (14)	10	21
Cadmium	26 (10)	149	4.9 (1.8)	410 (230)	220	880
Chromium (VI)	21 (4.3)	21	170 (2.1)	49 (35)	23	250
Lead	200 (450*)	310 (450*)	80 (450*)	2330 (750*)	630	1300

GAC from Nathanail et al., 2009 shown

* Former SGV now withdrawn

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Using C4SLs (1)

- Like SGVs, C4SLs are generic screening values and should be used in the same way:
  - Must understand their derivation and limitations before using
  - They apply to a wide range of, but not all, sites
  - They 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
  - They can be used to help determine whether a site is within Category 4 for human health
  - They are below the Cat 3/4 boundary. DQRA may show that a site with soil concentrations > C4SL is still within Category 4, i.e. risk is low

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Using C4SLs (2)

- Relationship to normal background concentrations
  - Part 2A SG - ‘normal’ background concentrations should not be considered to cause a site to be determined as contaminated under Part 2A unless there is a reason to consider otherwise
  - Defra envisage that C4SL used as initial screen but where concentrations exceed C4SL, site concentrations could be compared with ‘normal’ background concentrations for that area
  - If concentrations are higher than the relevant Category 4 Screening Level but within ‘normal’ background concentrations for that area, it is not envisaged that a site would be determined as contaminated under Part 2A (unless there was a reason to consider otherwise)
  - Specific advise provided on C4SL and NBCs for lead in Defra policy document

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Thank you

CONTAMINATED LAND: APPLICATIONS IN REAL ENVIRONMENTS

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