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Category 4 Screening Levels: *cis*-1,2-Dichloroethene

CL:AIRE

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Foreword by Frank Evans, Chair of SAGTA

Looking back, the original Defra work from 2014 that developed the Category 4 Screening Levels (C4SL) was important in establishing the level at which risk from land contamination was considered to be acceptably low. It also provided a useful scientific framework for making this assessment of risk. I was also impressed by the delivery model used to create the Soil Generic Assessment Criteria in 2010 and in particular the strength that comes from the collective efforts of a group of experts and peers.

This report presents an output from a phase 2 project to develop a further set of C4SL. It is the result of a cross-industry collaboration brought together by seed funding from SAGTA, project management from CL:AIRE and a project team made up of a number of toxicologists and exposure modellers' who have given considerable time and expertise. This guidance document would not have been possible without everyone's collaborative working, determination, and enthusiasm. My deepest thanks go to them, and to the members of the Steering Group who have overseen the development of this guidance document.

I would also acknowledge the effort and commitment of Doug Laidler who was the long-standing secretary of SAGTA and who played an important role in initiating and coordinating the project. Sadly, Doug died in the autumn of 2019 and as with so many other matters in his life, was unable to see this work brought to conclusion. May he rest in peace.

Frank Evans
Chair of SAGTA

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CONTENTS

ABBREVIATIONS

ADE	Average Daily Exposure
AIC	Akaike's Information Criterion
ATSDR	Agency for Toxic Substances and Disease Registry
BMD	Benchmark Dose
BMDL	Lower Confidence Limit of BMD
$BMDL_{1SD}$	Lower Confidence Limit of the BMD for a BMR of 1SD
BMR	Benchmark Response
C4SL	Category Four Screening Level
CAS	Chemical Abstracts Service
CL:AIRE	Contaminated Land: Applications in Real Environments
CLEA	Contaminated Land Exposure Assessment
CSAF	Chemical specific adjustment factor
CSM	Chemical Specific Margin
ELCR	Excess Lifetime Cancer Risk
HBGV	Health based Guidance Value
LLTC	Low Levels of Toxicological Concern
$LLTC_{inhal}$	Low Levels of Toxicological Concern - Inhalation
$LLTC_{oral}$	Low Levels of Toxicological Concern - Oral
LOAEL	Lowest Observed Adverse Effect Level
MDI	Mean Daily Intake
NOAEL	No Observed Adverse Effect level
OEHHA	Office of Environmental Health Hazard Assessment
POD	Point of Departure
POS	Public Open Space
POS_{park}	Public Open Space - Park
POS_{resi}	Public Open Space – Residential
RIVM	National Institute of Public Health and the Environment (Netherlands)
SD	Standard Deviation
SOM	Soil Organic Matter
SR	Science Report
UF	Uncertainty Factor
UK	United Kingdom
US EPA	United States Environmental Protection Agency
WHO	World Health Organization

1. INTRODUCTION

This report presents Category 4 Screening Levels (C4SLs) for *cis*-1,2-dichloroethene based on the methodology described in Section 5 of CL:AIRE (2014) "SP1010 – Development of Category 4 Screening Levels for Assessment of Land Affected by Contamination". A separate C4SL report has been prepared for the trans isomer of 1,2-dichloroethene. Section 1.1 provides brief background information on *cis*-1,2-dichloroethene, while Section 2 summarises the toxicological review from which Low Levels of Toxicological Concern (LLTCs) are identified. Section 3 presents the exposure modelling aspects for the generic land-uses under consideration, while Section 4 presents the C4SLs.

1.1 BACKGROUND TO *CIS*-1,2-DICHLOROETHENE

cis-1,2-Dichloroethene (CAS No. 156-59-2), which is also commonly known as *cis*-1,2-dichloroethylene or 1,2-c-dichloroethene, has the chemical formula $C_2H_2Cl_2$. It is one of two isomers of 1,2-dichoroethene, the other being *trans*-1,2-dichloroethene.

cis-1,2-Dichloroethene is a highly flammable colourless liquid at room temperature, with a sharp harsh odour that can be detected (by humans) at low concentrations (above 17ppm) (ATSDR, 1996). It is a volatile compound (vapour pressure of approximately 13.7 kPa at 10˚C) and is soluble in water (7550 mg L^{-1} at 10˚C) (see Section 3.1). In the atmosphere *cis*-1,2-dichloroethene rapidly reacts with hydroxyl radicals and has an estimated lifetime of 12 days (ATSDR, 1996).

There are no known natural sources of *cis*-1,2-dichloroethene. It is mostly used in the synthesis of vinyl chloride monomer and to a lesser extent is used in the manufacture of a number of solvents (WHO, 2003).

ATSDR (1996) identifies that microbial degradation in soil of *cis*-1,2-dichloroethene is likely to be slow and that hydrolysis and oxidation (other potential breakdown pathways) are likely not environmentally important processes. Therefore, where found, *cis*-1,2-dichloroethene contamination has the potential to persist in the soil. However, as *cis*-1,2-dichloroethene also has a high volatility, it is not anticipated to remain in shallow soils. In groundwater, *cis*-1,2-dichloroethene undergoes slow reductive dechlorination under anaerobic conditions (ATSDR, 1996). Vinyl chloride is the main daughter product of microbial degradation of *cis*-1,2-dichloroethene.

2. DERIVATION OF LOW LEVEL OF TOXICOLOGICAL CONCERN FOR *CIS*-1,2-DICHLOROETHENE

A framework for evaluating chemical-specific toxicology data for the purposes of LLTC derivation is presented in the form of a flowchart in Figure 2.2 of SP1010 (CL:AIRE, 2014) and is reproduced in Figure 2.1. The remainder of this section demonstrates the application of this framework to *cis*-1,2-dichloroethene. A proforma summarising the pertinent information referred to in this section is included as Appendix A.

As indicated in Figure 2.1, the first task is to perform a review of existing health-based guidance values (HBGV) for all routes of exposure, collating information from authoritative bodies, as per the process in SR2 (Environment Agency, 2009a).

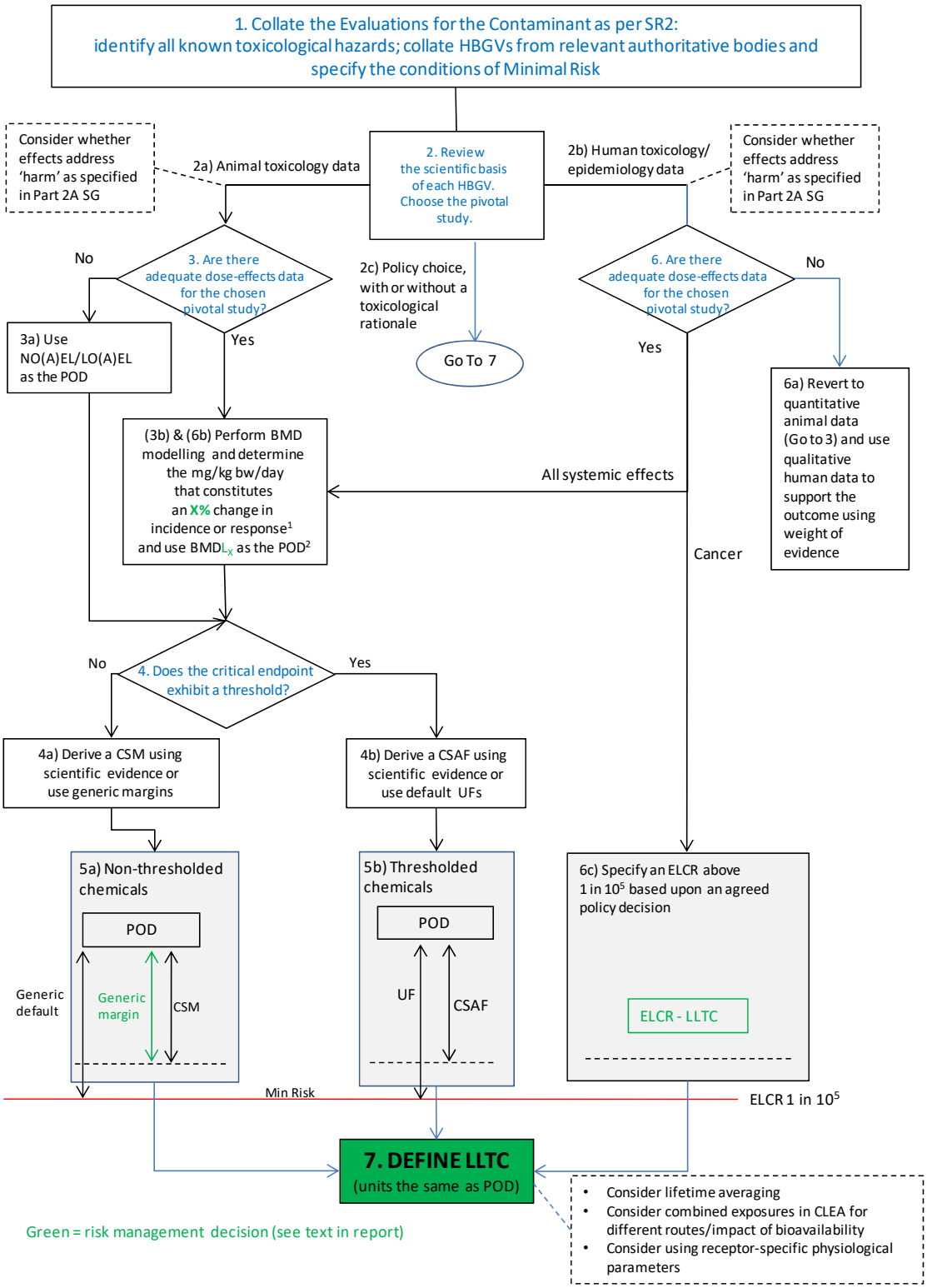

Figure 2.1: A framework for evaluating chemical-specific toxicology data for the purposes of LLTC derivation (reproduced from Figure 2.2 of SP1010 (CL:AIRE, 2014)).

2.1 ORAL ROUTE

2.1.1 FLOWCHART ELEMENT 1: Collate the evaluations for the contaminant as per SR2: identify all known toxicological hazards; collate HBGVs from relevant authoritative bodies and specify the conditions of minimal risk

A review of toxicological hazards and available HBGVs presented by authoritative bodies for the oral route of exposure has been undertaken and is provided in Appendix A. This review indicates that liver and kidney effects are the most sensitive[1] toxicological effects following long-term exposure to *cis*-1,2-dichloroethene by the oral route. According to OEHHA (2018), there are no data on carcinogenicity in any species, including humans. Thus, its carcinogenic potential cannot be evaluated due to lack of information at this time.

2.1.2 FLOWCHART ELEMENT 2: Review the scientific basis of each HBGV. Choose the pivotal study

Three possible options are provided for the type of pivotal study that could be chosen at this point, i.e. in the form of: 1) animal toxicology data; 2) human toxicology/epidemiology data; and 3) a policy choice (i.e. based on an existing guideline from another regime, with or without a toxicological rationale).

2a) Animal Toxicology Data

The critical toxic endpoints selected from the toxicity studies available are increased kidney and liver weights in male rats.

Based on all the data available, the McCauley *et al*. (1990) study as presented in McCauley *et al*. (1995) has been selected as the pivotal study by the US EPA (2010), ATSDR (1996), OEHHA (2018) and by RIVM (2009).

cis-1,2-Dichloroethene was administered in corn oil by gavage to male and female Sprague-Dawley rats (10 rats/sex/group) for 90 days at doses of 0, 32, 97, 291, or 872 mg kg^{-1} bw day^{-1}.

Clinical observations during the study were reported by the authors as minimal and not compound-related. Terminal body weights in male rats at the two highest dose groups were lower than controls by 10−11%, but were not considered by the author as statistically significant; no treatment-related effects on body weight were reported in female rats.

Relative liver weights (i.e. liver weight as a percentage of body weight) were statistically significantly increased in a dose-related manner in males and females. Histopathological evaluation revealed no specific hepatic injury reflective of hypertrophy and hyperplasia. Likewise statistically significant increases in relative kidney weights were recorded in male rats in all dose groups. Histopathological findings for kidney effects were negative, leading the authors to hypothesise that the increases in relative kidney weight may be due at least in part to decreased body weight gain.

Decreased haemocrit levels were found in male rats exposed to 97 mg kg^{-1} bw day^{-1} and decreased haemoglobin levels were reported in both sexes at 291 mg kg^{-1} bw day^{-1}. However the observed changes in clinical chemistry and haematology parameters were considered by the authors to be marginal and of questionable biological significance. No

[1] In defining minimal or tolerable risk, it is only necessary to focus on the most sensitive of all effects in defining the HBGV. In order to choose a point on the dose-response curve that is higher than minimal or tolerable risk, it is important to note that the dose responses for the most sensitive effects may overlap with other effects. Therefore, in setting the LLTC, ALL endpoints must be borne in mind. This is an important principle in any of the toxicological evaluations where there are overlapping toxicological effects and is an important departure from the principles of evaluation of minimal or tolerable risk described in SR2.

noteworthy compound-related histopathological changes were observed in any dose group.

Dose-response data from McCauley *et al*. (1995), which presents the data from the unpublished 1990 report, are presented in Table 2.1.

Table 2.1: Relative kidney and liver weights of rats exposed to *cis*-1,2-dichloroethene by gavage for 90 days (McCauley *et al*., 1995) – from OEHHA (2018).

Dose[a] (mg kg^{-1} bw day^{-1})	0	32	97	291	872
Relative kidney weight[d]					
Males[b]	0.70 ± 0.06	0.80 ± 0.06[c]	0.83 ± 0.06[c]	0.83 ± 0.10[c]	0.89 ± 0.06[c]
Females[b]	0.69 ± 0.06	0.71 ± 0.05	0.82 ± 0.23	0.85 ± 0.21	0.85 ± 0.06
Relative liver weight[d]					
Males[b]	2.85 ± 0.26	3.15 ± 0.27	3.28 ± 0.18[c]	3.34 ± 0.44[c]	3.75 ± 0.20[c]
Females[b]	2.82 ± 0.19	2.91 ± 0.18	3.21 ± 0.22[c]	3.36 ± 0.18[c]	3.67 ± 0.27[c]

[a] Administered doses in McCauley *et al*. (1995) were reported as 0, 0.33, 1, 3, and 9 mmol/kg-day. These doses were incorrectly converted to 0, 10, 32, 198, and 206 mg/kg-day in the 1995 publication. The doses presented here are the correctly calculated doses reported by OEHHA (2018) and US EPA (2010).

[b] Values are mean ± standard deviation (SD)

[c] Significantly different from control group; p≤0.05, Tukey's multiple comparison test.

[d] Relative organ weight = organ weight as a percentage of body weight. Adjusted for early gavage-related deaths, N were 9 (control), 10 (32 mg kg^{-1} bw day^{-1}), 10 (97 mg kg^{-1} bw day^{-1}), 7 (291 mg kg^{-1} bw day^{-1}) and 6 (872 mg kg^{-1} bw day^{-1}) in males, and 10 (control), 9 (32 mg kg^{-1} bw day^{-1}), 9 (97 mg kg^{-1} bw day^{-1}), 10 (291 mg kg^{-1} bw day^{-1}) and 10 (872 mg kg^{-1} bw day^{-1}) in females (US EPA, 2010).

GO TO FLOWCHART ELEMENT 3

2b) Human Toxicology/Epidemiology Data

No human toxicological data were identified.

GO TO FLOWCHART ELEMENT 6

2c) Policy choice, with or without a toxicological rationale

Not applicable to the derivation of an oral LLTC for *cis*-1,2-dichloroethene.

GO TO FLOWCHART ELEMENT 7

2.1.3 FLOWCHART ELEMENT 3/6: Are there adequate dose-effects data for the chosen pivotal study – animal data?

Yes	No	Not applicable
X		

The data on increased relative kidney and liver weights from the McCauley *et al*. (1990) corn oil gavage study on rats will be considered as the pivotal study from which to derive an $LLTC_{oral}$. These data were used by US EPA (2010) and California EPA (OEHHA, 2018) on the basis that the increase in relative kidney and liver weight could represent an early indicator of toxicity to these target organs.

The Dutch National Institute of Public Health and the Environment (RIVM, 2009) (following the approach of ATSDR, 1996) used the same study but selected a higher endpoint, a No Observed Adverse Effect Level (NOAEL) of 32 mg kg^{-1} bw day^{-1} based on decreased haematocrit. As discussed above, McCauley *at al.* (1990 and 1995)

considered the observed changes in clinical chemistry and haematology parameters to be marginal and of questionable biological significance and so the approach used by the US EPA (2010) and OEHHA (2018) has been followed for derivation of the LLTC.

GO TO FLOWCHART ELEMENT 3a/b or 6a/b/c

2.1.4 FLOWCHART ELEMENT 3a: Use NOAEL/LOAEL as POD

Not applicable - A BMD_{1SD} has been derived by OEHHA (2018) using the McCauley *et al.* (1990) study (see below).

2.1.5 FLOWCHART ELEMENT 3b/6b: Perform BMD modelling

There are good quantitative data available from the McCauley *et al.* (1990) study that authoritative bodies have used to carry out benchmark dose (BMD) modelling.

OEHHA (2018) used the US EPA Benchmark Dose Software version 2.6 to estimate the Point of Departure (POD). Continuous models were run with default parameters and a benchmark response (BMR) of one standard deviation (SD) from the control mean[2].

The dose-response models used by OEHHA (2018) to fit the data included:

- Exponential models (2 to 5)
- Linear model
- Hill model
- Polynomial models (2 and 3)
- Power model

The model selection criteria used for comparing outputs of different models for the same endpoint/dataset were: the lowest Akaike's Information Criterion (AIC), goodness of fit p-value ≥0.05, scaled residual ≤ the absolute value of 2, and visual inspection of the dose-response curve. From this, the Hill model was selected by OEHHA. OEHHA chose the $BMDL_{1SD}$[3] derived from the Hill model for changes in relative kidney weight in male rats as the POD because it was the lowest BMDL derived from a model that fit the data well, in addition to being the most sensitive endpoint. The outputs of the Hill model for kidney weight increases in male rats are shown in Table 2.2 and Figure 2.2 below.

For the purposes of deriving the LLTC, the OEHHA (2018) derived BMD_{1SD} of 16.4 mg kg^{-1} bw day^{-1} (rounded from 16.35 mg kg^{-1} bw day^{-1}) is proposed, based on effects on relative kidney weights in male rats from McCauley *et al.* (1990).

Table 2.2: BMD modelling results for kidney weight changes in male rats exposed to *cis*-1,2-dichloroethene by gavage for 90 days (from OEHHA, 2018).

Endpoint	Species/ sex	Model	AIC	BMD_{1SD} (mg kg^{-1} bw day^{-1})	$BMDL_{1SD}$ (mg kg^{-1} bw day^{-1})
Relative kidney weight	Male rat	Hill	-178	16.4	3.76*

* would be used for tolerable risk calculations

[2] US EPA guidance on benchmark dose modelling (US EPA, 2012) recommends use of a BMR of 1SD when there are no data to indicate what level of response is biologically significant. Note that for the relative kidney weight changes in male rats in the McCauley *et al.* (1990) study, 1SD equates to a change of approximately 9%.

[3] $BMDL_{1SD}$ = Lower Confidence Limit of the BMD for a BMR of 1SD

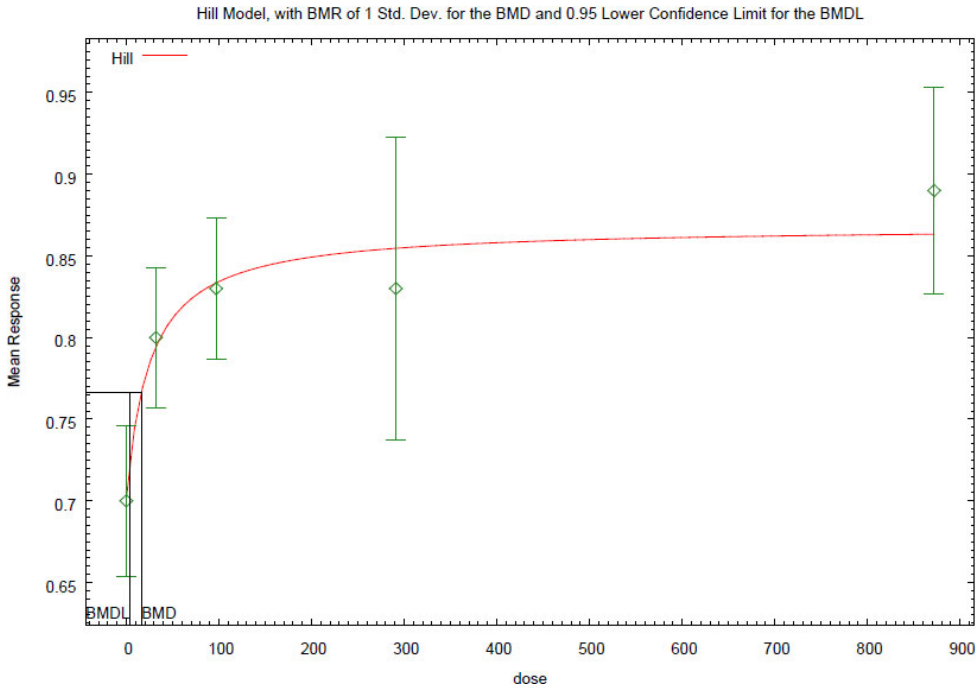

Figure 2.2: Hill model output for *cis*-1,2-dichloroethene; increased relative kidney weight in male rats (from OEHHA, 2018)

GO TO FLOWCHART ELEMENT 4a/b

2.1.6 FLOWCHART ELEMENT 4: Does the critical endpoint exhibit a threshold?

Yes	No	Not applicable
X		

2.1.7 FLOWCHART ELEMENT 4a: Define a suitable chemical-specific margin

Not applicable – threshold substance.

GO TO FLOWCHART ELEMENT 5a

2.1.8 FLOWCHART ELEMENT 4b: Derive a chemical-specific assessment factor using scientific evidence

For the derivation of the LLTC, a total uncertainty factor (UF) of 1000 is proposed based on the following:

- Intraspecies variability (x10);
- Interspecies differences (x10);
- Sub-chronic to chronic (x √10); and
- Database deficiencies (x √10):

The UFs applied are similar to those used by OEHHA. However, an UF of 10 was used for intraspecies variability, as used by US EPA (2010), rather than the UF of 30 (10 for toxicokinetics and √10 [rounded to 3] for toxicodynamics) used by OEHHA. The UF of 10 for intraspecies toxicokinetics is a default value used by OEHHA when there is no human kinetic data. In the UK, a default composite value of 10 (for both toxicokinetics and toxicodynamics) is used to account for intraspecies variability (Environment Agency, 2009a).

The standard default factor of 10 has been applied for interspecies differences and a factor of √10 has been used to account for use of a sub-chronic study.

There is limited toxicological information for *cis*-1,2-dichloroethene, and particularly there are virtually no inhalation toxicity studies. These data deficiencies, particularly in terms of lack of reproductive toxicity data, are considered by the application of an additional UF of √10.

GO TO FLOWCHART ELEMENT 5b

2.1.9 FLOWCHART ELEMENT 5a/b: Calculate the LLTC for non-thresholded / thresholded chemicals

For threshold chemicals, the POD is divided by the UF to derive the LLTC:

POD / UF = LLTC (units as per POD)

Table 2.3 presents the choice of POD, and the resultant LLTC.

Table 2.3: Proposed choice of oral LLTC value.

	POD	Value (mg kg^{-1} bw day^{-1})	CSM /UF	LLTC (µg kg^{-1} bw day^{-1})
LLTC (threshold) ADULT and CHILD	BMD_{1SD}	16.4	1000	16.4

GO TO FLOWCHART ELEMENT 7

2.1.10 FLOWCHART ELEMENT 7: Assess $LLTC_{oral}$ for *cis*-1,2-Dichloroethene

Based upon a scientific evaluation, an oral LLTC of **16.4 µg kg^{-1} bw day^{-1}** is proposed. This is based on a BMD_{1SD} as the POD from the OEHHA modelling of McCauley *et al.* (1990) data and an UF of 1000. There is no previous Health Criteria Value for comparison however, the LLTC is:

a) 13 times higher than the acceptable daily dose derived by the OEHHA (2018) of 1.25 µg kg^{-1} bw day^{-1} reflecting the use of the BMD_{1SD} rather than the $BMDL_{1SD}$ and use of a lower UF.

b) 8 times higher than the US EPA (2010) oral reference dose of 2 µg kg^{-1} bw day^{-1}.

This LLTC is a pragmatic level for setting a C4SL and is considered suitably protective of all health effects in the general population.

2.2 INHALATION ROUTE

No data were identified by RIVM, US EPA or OEHHA for any intermediate- or chronic-duration animal or human inhalation exposure studies.

In the absence of suitable inhalation toxicity data and in accordance with SR2 (Environment Agency, 2009a), inhalation exposure will be compared against the oral LLTC for the purposes of the derivation of the C4SL for *cis*-1,2-dichloroethene. The UFs used in the selection of the LLTC for oral exposure reflect the lack of inhalation toxicity data.

2.3 DERMAL ROUTE

No data were identified by RIVM, US EPA or OEHHA for any intermediate- or chronic-duration animal or human dermal exposure studies.

In the absence of suitable dermal toxicity data and in accordance with SR2 (Environment Agency, 2009a), dermal exposure will be compared against the oral LLTC for the purposes of the derivation of the C4SL for *cis*-1,2-dichloroethene.

2.4 MEAN DAILY INTAKE

The oral LLTC recommended for *cis*-1,2-dichloroethene is based on threshold effects. As such, in accordance with the C4SL SP1010 framework (CL:AIRE, 2014) and SR2 (Environment Agency, 2009a), the Mean Daily Intake (MDI) from non-soil sources is to be included in the exposure modelling for comparison with the oral LLTC.

Available oral and inhalation MDI data have been collated and reviewed and used to derive estimated adult MDIs for the oral and inhalation pathways (see Appendix B). The adult MDIs used to derive the C4SLs for *cis*-1,2-dichloroethene are shown in Table 2.4.

The oral MDI is based upon a value of 4 µg day-1 for background exposure through drinking water proposed within the WHO background document for development of the WHO Guideline Values for Drinking Water Quality (WHO, 2003). This value is based on a study in the USA that found 1,2-dichloroethene (mixed isomers) detected in 8% of drinking supplies derived from groundwater, with detected concentrations ranging from 2 to 120 µg L-1. WHO calculated the background exposure on the assumption that a person consumes 2 L water per day with an average of 2 µg L-1 1,2-dichloroethene. Few data are available relating to exposure to *cis*-1,2-dichloroethene via food consumption, however WHO (2003) concluded that exposure in most cases via the diet was likely to be negligible.

There are limited air monitoring data for *cis*-1,2-dichloroethene in the UK and Europe. WHO (2003) concluded that the mean concentration of *cis*-1,2-dichloroethene in urban air ranged from 0.04 to 0.3 µg m-3. ATSDR (1996), WHO (2003), and RIVM (2001) all cited a maximum urban air concentration of 0.076 ppb (0.3 µg m-3) from a 1983 study by the US EPA, which was consistent with a median value reported by Brodzinsky and Singh (1982).

The inhalation MDI of 6 µg day-1 has been calculated from the maximum concentration of 0.3 µg m-3 from the US EPA 1983 study cited in ATSDR (1996), by multiplying by an assumed adult respiration rate of 20 m^3 day^{-1}.

Table 2.4: Adult mean daily intake values for input to CLEA.

Adult Mean Daily Intake	Value (µg day^{-1})
Oral MDI	4
Inhalation MDI	6

3. EXPOSURE MODELLING FOR *CIS*-1,2-DICHLOROETHENE

As described in the C4SL SP1010 report (CL:AIRE, 2014), the CLEA model has been used deterministically with the above LLTCs to derive C4SLs for the following six land-uses for a sandy loam soil type:

- Residential with consumption of homegrown produce;
- Residential without consumption of homegrown produce;
- Allotments;
- Commercial;
- Public open space (POS):
    - The scenario of open space close to housing that includes tracking back of soil (POS_{resi}); and
    - A park-type scenario where the park is considered to be at a sufficient distance from the home that there is negligible tracking back of soil (POS_{park}).

3.1 CLEA PARAMETER INPUTS

CLEA derives an estimate of average daily exposure (ADE) for each exposure pathway. ADEs are then summed for some or all exposure pathways for comparison with the LLTC. The pathways considered in the summation are dependent on the critical toxicological effects that the LLTC is based on. CLEA uses iteration to find the soil concentrations at which the summed ADEs equal the respective LLTC values and these are termed 'assessment criteria'. As described in the CLEA SR2 and SR3 documents (Environment Agency, 2009a,b), the assessment criteria are normally integrated by CLEA to determine an overall value where the critical toxicological effects via both routes of exposure are systemic. Where the critical toxicological effect is localised for either the oral or inhalation routes of exposure, the assessment criteria are not integrated and the lowest of the two criteria is chosen as the overall assessment criterion.

The LLTCoral is based upon a scientific evaluation of kidney toxicity observed in animal studies (rats) administered via corn oil (McCauley et al., 1990), which is a threshold effect.

Insufficient toxicological data were identified in order to derive an LLTCinhal, therefore the C4SLs have been calculated by adding systemic inhalation exposure to exposure from all other routes. Total systemic exposure was then evaluated against the LLTCoral (i.e. simple route-to-route extrapolation).

CLEA requires a number of contaminant and non-contaminant specific parameter values for modelling exposure. The description of these parameters is provided within the C4SL SP1010 report (CL:AIRE, 2014) and the SR3 report (Environment Agency, 2009b). Contaminant-specific parameter values used for *cis*-1,2-dichloroethene are shown in Table 3.1.

Table 3.1: Contaminant-specific parameter values used for derivation of C4SLs for *cis*-1,2-dichloroethene.

Parameter	Units	Value	Source/Justification
Air-water partition coefficient	dimensionless	7.46×10^{-2}	CL:AIRE, EIC & AGS, 2010
Diffusion coefficient in air	$m^2\ s^{-1}$	9.02×10^{-6}	CL:AIRE, EIC & AGS, 2010
Diffusion coefficient in water	$m^2\ s^{-1}$	7.08×10^{-10}	CL:AIRE, EIC & AGS, 2010
Relative molecular mass	$g\ mol^{-1}$	96.94	CL:AIRE, EIC & AGS, 2010
Vapour pressure	Pa	1.37×10^{4}	CL:AIRE, EIC & AGS, 2010
Water solubility	$mg\ L^{-1}$	7550	CL:AIRE, EIC & AGS, 2010
Log K_{oc}	Log $cm^3\ g^{-1}$	1.61	CL:AIRE, EIC & AGS, 2010
Log K_{ow}	dimensionless	1.86	CL:AIRE, EIC & AGS, 2010
Dermal absorption fraction	dimensionless	0.1	Default value from CLEA SR3, Environment Agency, 2009b
Soil-to-plant concentration factor (green vegetables)	mg g^{-1} FW plant over mg g^{-1} DW soil	modelled	Environment Agency, 2009b
Soil-to-plant concentration factor (root vegetables)		modelled	
Soil-to-plant concentration factor (tuber vegetables)		modelled	
Soil-to-plant concentration factor (herbaceous fruit)		not considered	
Soil-to-plant concentration factor (shrub fruit)		not considered	
Soil-to-plant concentration factor (tree fruit)		modelled	
Soil-to-dust transport factor	g g^{-1} DW	0.5	Default value from CLEA SR3, Environment Agency 2009b
Sub-surface soil to indoor air correction factor	-	1	Environment Agency, 2009b
Relative bioavailability soil	-	1	Conservative assumption made that bioavailability of *cis*-1,2-dichloroethene in soil and dust is the same as bioavailability of *cis*-1,2-dichloroethene in critical toxicological studies used to derive the LLTC
Relative bioavailability dust	-	1	

The key contaminant specific parameter values used for derivation of the C4SLs for *cis*-1,2-dichloroethene are discussed briefly below.

Soil to dust transport factor

The soil to dust transport factor should be ideally contaminant specific but where contaminant specific data are not available Environment Agency (2009b) recommends a default value of 0.5 g g^{-1} dry weight (DW), meaning that the concentration of contaminant in respirable dust is assumed to be 50% of the concentration of contaminant in outdoor soil. This default value has been assumed for *cis*-1,2-dichloroethene.

Soil to plant concentration factors

No reliable information was found in the literature to support the use of contaminant specific plant uptake factors. Consequently, plant uptake for *cis*-1,2-dichloroethene has been modelled using the method for organic chemicals within the CLEA software.

CLEA predicts the greatest exposure to *cis*-1,2-dichloroethene from root vegetables and tree fruit for both the residential and allotments scenarios (via the consumption of homegrown produce pathways). Therefore, in accordance with the "top two" approach (as described in CL:AIRE, 2014), 90th percentile consumption rates have been used for these two produce types and mean consumption rates have been used for the remaining produce types.

Relative bioavailability

There are few data available on the relative bioavailability of *cis*-1,2-dichloroethene and it is considered appropriately conservative to assume a relative bioavailability of 100% for the derivation of C4SLs.

4. C4SLs FOR *CIS*-1,2-DICHLOROETHENE

4.1 C4SLS

The C4SLs for *cis*-1,2-dichloroethene derived using a Soil Organic Matter (SOM) content of 1%, 2.5% and 6% are presented in Table 4.1 below.

Table 4.1: C4SLs for *cis*-1,2-dichloroethene.

Land-use	C4SLs (mg.kg^{-1})		
	SOM Content		
	1.0%	2.5%	6.0%
Residential with consumption of homegrown produce	0.46	0.78	1.5
Residential without consumption of homegrown produce	0.50	0.84	1.6
Allotments	0.89	1.7	3.6
Commercial	38	64	120
Public Open Space (residential)	3800	3800	3900
Public Open Space (park)	2000	2400	3100

N.B. These C4SLs are based on chronic risk only. For further discussion of acute risks and other factors that should be considered when using these C4SL see section 4.2 below.

The relative contribution of each exposure pathway contributing to the C4SL (6% SOM) is shown for each land-use in Table 4.2.

Table 4.2: Relative contributions of exposure pathways to overall exposure at 6% SOM.

Exposure pathway	Relative contribution to total exposure (%)					
	Residential		Allotments	Commercial	POS_{resi}	POS_{park}
	With home grown produce	Without home grown produce				
Direct soil & dust ingestion	0.07	0.07	0.04	0.34	88.01	32.23
Sum of consumption of homegrown produce and attached soil	6.10	0.00	96.28	0.00	0.00	0.00
Dermal contact (indoor)	0.00	0.00	0.00	0.02	2.67	0.00
Dermal contact (outdoor)	0.00	0.00	0.02	0.03	3.12	3.19
Inhalation of dust (indoor)	0.00	0.00	0.00	0.00	0.31	0.00
Inhalation of dust (outdoor)	0.00	0.00	0.00	0.00	0.00	0.01
Inhalation of vapour (indoor)	90.23	96.33	0.00	98.68	0.00	0.00
Inhalation of vapour (outdoor)	0.00	0.00	0.06	0.05	3.65	60.98
Oral background	1.37	1.37	1.37	0.35	0.89	1.37
Inhalation background	2.22	2.22	2.22	0.52	1.36	2.22

Based on the information in Table 4.2, the principal risk driving pathways for *cis*-1,2-dichloroethene are expected to be:

- Consumption of homegrown produce for Allotments land-use;
- Indoor inhalation of vapours for Residential and Commercial land-uses;
- Ingestion of soil and soil derived dust for the POS_{resi} and POS_{park} land-uses; and,
- Outdoor inhalation of vapours for POS_{park} land-use.

4.2 OTHER CONSIDERATIONS

Other considerations that were relevant when setting the C4SLs for *cis*-1,2-dichloroethene include the following:

- Background intake of *cis*-1,2-dichloroethene from non-soil sources (food, water and air) compares to the oral LLTC as follows:
    - Dividing the adult oral MDI of 4 µg day^{-1} (which is likely to be a high-end estimate) by an adult body weight of 70 kg results in an estimated background exposure of 0.0571 µg kg^{-1} bw day^{-1}, which is approximately 0.4% of the $LLTC_{oral}$.
    - Dividing the adult inhalation MDI of 6 µg day^{-1} (which is likely to be a high-end estimate) by an adult body weight of 70 kg results in an estimated background exposure of 0.0857 µg kg^{-1} bw day^{-1}, which is approximately 0.5% of the $LLTC_{oral}$, in the absence of an $LLTC_{inhal}$.
- C4SLs have been derived on the basis of chronic exposure and risks to human health, and do not explicitly account for acute risks (e.g. due to one-off ingestion of a significant amount of soil by a young child). It is noted here that the C4SLs derived for POS_{resi} and POS_{park} are significantly higher than values for the Residential land-use, where inhalation of vapour (indoor) is the principal risk driving pathway in deriving the C4SL. Therefore, further consideration of the possibility of acute risk due to ingestion of soil at the *cis*-1,2-dichloroethene concentrations equal to the POS_{resi} and POS_{park} C4SLs may be necessary. The reader is referred to the Society of Brownfield Risk Assessment (SoBRA) "Development of Acute Generic Assessment Criteria for Assessing Risks to Human Health from Contaminants in Soil" (SoBRA, 2020) for further guidance on this.
- The British Geological Survey has not derived normal background concentrations for *cis*-1,2-dichloroethene (Johnson *et al.*, 2012). *cis*-1,2-Dichloroethene is not expected to occur above typical laboratory limits of detection in soil away from a source and background soil concentrations are therefore expected to be negligible. This is supported by soil analytical data from two main commercial laboratories in the UK: out of a total of approximately 16,800 soil samples analysed for *cis*-1,2-dichloroethene only 2.7% had a concentration above the limit of detection (1 to 13 µg kg^{-1}), with most detected concentrations less than 50 µg kg^{-1}.
- Table 4.2 shows that when the inhalation of vapour (indoor) exposure pathway is active (for both Residential and the Commercial land-use scenarios), it is the principal risk driving pathway. In applying the C4SL, the risk assessor should consider that generic modelling of this pathway is based on general assumptions and published data regarding vapour partitioning of *cis*-1,2-dichloroethene and subsequent transport. Where exposure to soil vapour forms the principal risk driving pathway then further consideration should be given to supporting the assessment. For example, through obtaining site-specific empirical data for soil vapour concentrations. The reader is referred to CIRIA (2009) and SoBRA (2018) for further guidance on this.
- When considering the risk from vapour inhalation, it is also worth noting that there were insufficient data to derive an inhalation LLTC and that the C4SL are therefore based on comparison of exposure via all routes of exposure to the oral LLTC.

- The lowest derived C4SL in Table 4.1 of 0.46 mg kg^{-1} (460 µg kg^{-1}), which is for the Residential with Consumption of Homegrown Produce land-use, is above typical laboratory limits of detection for *cis*-1,2-dichloroethene in soil (typically circa 1 to 10 µg kg^{-1}).

5. REFERENCES

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APPENDIX A
HUMAN TOXICOLOGICAL DATA SHEET FOR *CIS*-1,2-DICHLOROETHENE

Human Toxicological Data Sheet for C4SL derivation: Reference checklist for sources of authoritative information

Chemical: **cis 1, 2 dichloroethene (CAS 156-59-2) - cis DCE**

Human Health Hazard Profile - References

Authoritative bodies	Website	Checked (Y/N)	References
Environment Agency	hhttps://www.gov.uk/government/organisations/environment-agency	Y	None found
Foods Standards Agency	http://www.food.gov.uk/	Y	None found
Public Health England	https://www.gov.uk/government/organisations/public-health-england	Y	
Committee on Carcinogenicity	https://www.gov.uk/government/groups/committee-on-carcinogenicity-of-chemic	Y	
Committee on Mutagenicity	https://www.gov.uk/government/organisations/committee-on-mutagenicity-of-ch	Y	
Committee on Toxicity	http://cot.food.gov.uk/	Y	
ECHA REACH - is there a dossier?	http://echa.europa.eu/information-on-chemicals	Y	No REACH Dossier found. ECHA CLP database checked for classifications.
EFSA - is there an opinion?	http://www.efsa.europa.eu/	Y	No opinion identified
JECFA	http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/en/?	Y	No JECFA report found
WHO	http://www.who.int/en/	Y	Drinking Water Guideline combined for both stereoisomers of 1,2 dichloroethene based on trans form
WHO IPCS	http://www.who.int/ipcs/en/	Y	No IPCS report
WHO EHC	http://www.who.int/ipcs/publications/ehc/en/	Y	No EHC report found
RIVM	https://www.rivm.nl/en	Y	Reviewed
US ATDSR	http://www.atsdr.cdc.gov/	Y	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service Agency for Toxic Substances and Disease Registry TOXICOLOGICAL PROFILE FOR 1,2-DICHLOROETHENE,August 1996
US EPA	http://www.epa.gov/	Y	U.S. Environmental Protection Agency 2010 TOXICOLOGICAL REVIEW OF cis-1,2-DICHLOROETHYLENE and trans-1,2-DICHLOROETHYLENE (CAS Nos. cis: 156-59-2; trans: 156-60-5; mixture: 540-59-0) In Support of Summary Information on the Integrated Risk Information System (IRIS) September 2010
US National Toxicology Program	https://ntp.niehs.nih.gov/	Y	
Health Canada	http://www.hc-sc.gc.ca/index-eng.php	Y	No toxicology data found
Australia NICNAS	http://www.nicnas.gov.au/	Y	
Risk Assessment Information System	http://rais.ornl.gov	Y	Not reviewed - latest report superceded by 3 later US reports included in review TOXICITY SUMMARY FOR CIS- AND TRANS-1,2-DICHLOROETHYLENE DECEMBER 1994, Prepared by Prepared by Tim Borges, Ph.D.,, Chemical Hazard Evaluation Group, Biomedical and Environmental Information Analysis Section,, Health Sciences Research Division,, Oak Ridge National Laboratory*, Oak Ridge, Tennessee.Prepared for OAK RIDGE RESERVATION ENVIRONMENTAL RESTORATION PROGRAM
Other scientific reviews	**Check for key reviews on pubmed**		
Office of Environmental Health Hazard Assessment California Environmental Protection Agency	https://oehha.ca.gov/water/chemicals/12-dichloroethylene-cis	Y	OEHHA 2018 OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT Public Health Goals,.Cis-/Trans-1,2-Dichloroethylene in Drinking Water. Pesticide and Environmental Toxicology Branch Office of Environmental Health Hazard Assessment California Environmental Protection Agency.July 2018

NB. These weblinks were checked on 6 Mar 2018, and may be subject to change at source.

Human Toxicological Data Sheet for C4SL derivation: Toxicological Evidence, HBGVs, MDIs and LLTC derivation

Chemical: **cis 1, 2 dichloroethene (CAS 156-59-2) - cis DCE**

I) Human Health Hazard Profile - Toxicological Evidence

Most sensitive health effects:

Sensitive endpoints	Other information	Source of evidence
Nephrotoxicity	Liver and Kidney effects in two studies	EPA 2010
Hepatotoxicity	Liver and Kidney effects in two studies	EPA 2010
Neurotoxicity	CNS effects (acute exposure)	EPA 2010

II) Health Based Guidance Values (HBGVs) from Authoritative Bodies (in descending order of magnitude)

A) Oral route

Authoritative body (date) and HBGV type	HBGV value	Unit	UF used	PoD	POD value	Unit	Endpoint	Pivotal data used & Comments	Full Reference
USEPA (2010) RfD	0.002	mg/kg bw/day	3000	BMDL10	5.1	mg/kg bw/day	Relative kidney weights in Male rats	EPA (2010), considered the data of McCauley et al (1995, 1990) as the pivotal study. Cis-1,2-DCE was administered by corn oil by gavage to male and female Sprague-Dawley rats (10 rats/sex/group) for 90 days at doses of 0, 32, 97, 291, or 872 mg/kg bw/day. Clinical observations during the study were reported by the authors as minimal and not compound-related. Terminal body weights in male rats at the two highest dose groups were lower than controls by 10–11%, but were not considered by the author as statistically significant; no treatment-related effects on body weight were reported in female rats. Relative liver weights were statistically significantly increased in a dose-related manner in males and females. Histopathological evaluation revealed no specific hepatic injury reflective of hypertrophy and hyperplasia. Likewise statistically significant increases in relative kidney weights were recorded in male rats in all dose groups. Histopathological findings for kidney effects were negative, leading the authors to hypothesize that the increases in relative kidney weight may be due at least in part to decreased body weight gain. Observed changes in clinical chemistry and haematology parameters were considered by the authors to be marginal and of questionable biological significance. No noteworthy compound-related histopathological changes were observed in any dose group. Benchmark dose (BMD) modelling methodology (U.S. EPA, 2000) was used to determine the point of departure (POD. A 10% change in relative kidney weight compared with the control was selected as the benchmark response (BMR) level. For the male rat, BMDS modelling of relative kidney weight data showed that only the Hill model adequately fitted the data (test 4 $\chi 2$ p > 0.1). This predicted a BMD10 and BMDL10 of 19.8 and 5.1 mg/kg-day, respectively, provided the best fit (lowest Akaike Information Criteria (AIC) value and adequate visual fit of the data). The POD for the RfD for cis-1,2-DCE was selected as 5.1 mg/kg-day based on male rat relative kidney weight, Uncertainty factors of 3000 comprising factors an interspecies differences (10), human variability (10), use of a sub chronic study (10) and data base deficiencies (3) including lack of reproductive and developmental toxicity data for the cis- isomer.	**USEPA 2010** TOXICOLOGICAL REVIEW OF cis-1,2-DICHLOROETHYLENE and trans-1,2-DICHLOROETHYLENE (CAS Nos. cis: 156-59-2; trans: 156-60-5; mixture: 540-59-0) In Support of Summary Information on the Integrated Risk Information System (IRIS) September 2010 U.S. Environmental Protection Agency **McCauley, PT; Robinson, M; Daniel, FB; et al. (1990)** The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in rats. Health Effects Research Laboratory, U.S. Environmental Protection Agency, Cincinnati, OH and Toxic Hazards Division, Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH; unpublished report. **McCauley, PT; Robinson, M; Daniel, FB; et al. (1995)** The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug Chem Toxicol 18:171–184.
California EPA (OEHHA 2018) ADD (Acceptable Daily Dose) (Draft value)	0.00125	mg/kg bw/day	3000	BMDL 1SD	3.76	mg/kg bw/day	Relative kidney weights in Male rats	A recent review by California EPA (OEHHA 2018) to derive a Public Health Goal (PHG) in Drinking water for cis DCE, also uses data of Mc Cauley et al (1990 , 1995) to derive a PoD. Benchmark dose modelling was conducted and continuous models were run with a "benchmark response (BMR) of one standard deviation (SD) from the control mean, which is typically used when there are no data to indicate what level of response is biologically significant (US EPA, 2012)". BMDL 1SD for relative kidney weight increase in male rats of 3.76 mg/kg bw/day was chosen as the PoD to derive an Acceptable Daily Dose (ADD) by applying a total uncertainty factor of 3000 comprising 10 for interspecies extrapolation, 30 for intraspecies variability (10 for toxicokinetics and √10 for toxicodynamics), √10 for extrapolation from a subchronic study, and √10 for deficiencies in toxicity data. (Note the BMD1SD was 16.35 mg/kg bw/day)	**OEHHA 2018** OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT Public Health Goals Cis-/Trans-1,2-Dichloroethylene in Drinking Water July 2018 Pesticide and Environmental Toxicology Branch Office of Environmental Health Hazard Assessment California Environmental Protection Agency
ATSDR (1996) Intermediate MRL (subchronic)	0.3	mg/kg bw/day	100	NOAEL	32	mg/kg bw/d	Decreased heamatoctit and haemoglobin	ATSDR (1996) derived an intermediate MRL for cis DCE based on the McCauley et al (1990) study described above, based on the NOAEL of 32 mg/kg bw/day. This was based on decreased haematocrit in females at doses of 97 mg/kg bw/day and above. A total UF of 100 (covering interspecies differences and human variability) was applied as this was an intermediate duration MRL based on a 90 day study. There was no factor applied for database deficiencies	TOXICOLOGICAL PROFILE FOR 1,2-DICHLOROETHENE **ATSDR (1996)** U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service Agency for Toxic Substances and Disease Registry August 1996
RIVM (2009) Tolerable Daily intake	0.03	mg/kg bw/day	1000	NOAEL	32	mg/kg bw/d	Decreased heamatoctit and haemoglobin	RIVM 2009 derived a TDI for cis DCE based on the McCauley et al (1995) study described above, based on the NOAEL of 32 mg/kg bw/day. This was based on decreased haematocrit in females at doses of 97 mg/kg bw/day and above. A total UF of 1000 (covering interspecies differences and human variability and a further factor of 10 for use of a sub-chronic (i.e. 90 day) study. The previous factor applied for database deficiencies was removed in the light of the genotoxicity studies newly performed by NTP with each isomer and with the mixture of both isomers which contradicted a similar study that was previously evaluated by RIVM. No effects were observed in vivo for cis-1,2-dichloroethene in a mouse bone marrow micronucleus test. **NOTE : TDI WAS APPLIED TO SUM OF *cis* and trans-1,2-Dichloroethene**	RIVM 2009 Report 601782013/2009 R.H.L.J. Fleuren | P.J.C.M. Janssen | L.R.M. de Poorter Environmental risk limits for twelve volatile aliphatic hydrocarbons An update considering human-toxicological data

COT/COC Opinion

No CoT nor CoC opinion for cis DCE has been found

Current UK oral HCV

Authoritative body (date) and HBGV type	HBGV value	Unit	UF used	PoD	POD value	Unit	Endpoint	Pivotal data used & Comments	Full Reference
NONE									

B) Inhalation Route

Authoratative body (date) and HBGV type	Converted HBGVinh	Unit	HBGVinh	Unit	UF used	POD	POD value	Unit	Endpoint	Pivotal Study used & Comments	Full Reference
NONE										No studies of the effects of cis-1,2-DCE by inhalation exposure in humans were identified. There are no inhalation studies of subchronic, chronic, reproductive, or developmental toxicity of cis-1,2-DCE. Investigation of the inhalation toxicity of cis-1,2-DCE is limited to an acute 4-hour inhalation LC50 study in rats (DuPont, 1999) (EPA 2010)	USEPA 2010 (see above for full reference)

COT/COC Opinion

Current UK inhalation HCV

Authoratative body (date) and HBGV type	HBGV value	Unit	UF used	PoD	POD value	Unit	Endpoint	Pivotal data used & Comments	Full Reference
NONE									

C) Dermal Route

Authoratative body (date) and HBGV type	HBGV value	Unit	UF used	POD	POD value	Unit	Endpoint	Pivotal Study used & Comments	Full Reference
NO INFORMATION									

III) Current UK (WHO) regulatory values

	Value	Units	Refs
UK drinking water standard	NONE		
WHO drinking water standard	50	µg/L	WHO drinking water guideline for cis and trans 1,2-DCE combined but is based on toxicological study of trans 1,2-DCE. WHO, 2011, Guidelines for Drinking Water Quality. 4th Edition. ISBN 978 92 4 154815 1
UK air quality standard	NONE		
WHO air quality standard	NONE		

IV) Mean Daily Intakes from Other Sources (e.g. Diet)

	Pathways	Units	Adults	Children	Refs
Food (average)	Oral				
Food (average)	Oral				
Water	Oral				
Air	Inhalation				
Smoking	Inhalation				

V) LLTC derivation

A) ORAL

Choice of Pivotal Data	Dosing vehicle	Doses	Units	Species	Study Type	Comments
McCauley et al., 1990 & 1995	Gavage -corn oil	0, 32, 97, 291, or 872	mg/kg bw/day	Rat	90 day oral	Increased relative kidney weights in male rats. Study sumarised in the above sections. BMD modelling was conducted on these data by OEHHA in 2017 and the BMD_{1SD} of 16.35 mg/kg bw/day was selected as the POD

Selection of POD

Published POD for ORAL LLTC:		
Are dose response data of adequate quality to derive a BMD	Yes	
Type of PoD	Other BMD1SD	
Value selected	16.4	mg/kg bw/day

Provided in Appendix B of EPA 2010

Derived POD for ORAL LLTC: (from data below)		
Type of PoD		
Value derived		
AIC value		
P value		

BMD Modelling (if answered 'Yes' to question above - see worksheet BMD modelling pivotal study)

Software used: US EPA BMDS Version [to be specified]

	BMD1SD	BMD5	BMD10	BMD15
BMD modelling (value) (mg/kg bw/day)	16.35			
	BMDL1SD	BMDL5	BMDL10	BMDL15
BMD modelling (value) (mg/kg bw/day)	3.76			

Comments:

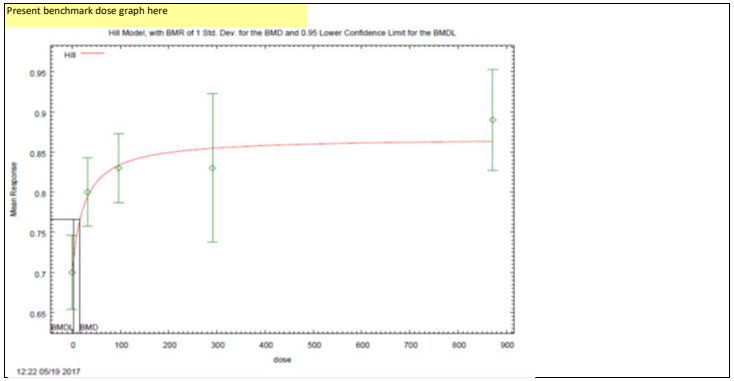
From OEHHA, 2018:

Table 2. Summary of BMD modeling results for organ weight changes in rats exposed to cis-1,2-DCE by gavage for 90 days (McCauley et al., 1995)

Sex/ Species	Endpoint	Model[a]	p-Value	BMD_{1SD} (mg/kg-day)	$BMDL_{1SD}$ (mg/kg-day)
Male rat	Relative kidney weight	Hill	0.3423[b]	16.35[b]	**3.76[b]**
	Relative liver weight	Hill	0.1092	63.34	18.70
Female rat	Relative liver weight	Hill	0.3208	53.20	28.76

[a] All models were run with default parameters and set with adverse direction up, based on data.
[b] US EPA analysis used N=10 for this endpoint and produced different values: p=0.2257, BMD_{1SD}=16.35 mg/kg-day, $BMDL_{1SD}$=5.14 mg/kg-day; OEHHA used early gavage death-adjusted N values for consistency, as described in the footnote in Table 1.

Present benchmark dose graph here



Addressing uncertainty

Thresholded effects?	Yes
If yes - use generic UF of 100 or (if data allow) calculate CSAF	1000
If no : see below for non-thresholded effects	
If animal data are used as POD (NO(A)EL or BDM) use generic margin of 5000 or (if data allows) calculate CSM	
If human data are used to derive a BMD use the margin that relates to a notional risk of 1 in 50000 based on the BMR (using the table opposite). The same margin can also be applied to a NO(A)EL, but not to a LO(A)EL.	
ELCR =	1 in 50000

BMR	Margin	Corresponding ELCR estimate
0.50%	250	1 in 50000
1%	500	1 in 50000
5%	2500	1 in 50000
10%	5000	1 in 50000

Chemical Specific Adjustment Factor/Chemical Specific Margin to account for uncertainties in the data		
	Range	Selected value
Intraspecies	1 - 10	10
Interspecies	1 - 10	10
Sub-chronic to chronic	1-10	3.16
Database deficiencies	1-3	3.16
Quality of study	1 - 10	1
Use of LOAEL as POD	1-10	1
Other	1 - 10	1
Total CSAF/CSM		1000

Is the LLTC based on systemic or localised toxicological effects?	Systemic
Lifetime averaging to be applied in CLEA (Yes/No)	No

Oral LLTC calculation:

	Value	Units	Justification
LLTC (Thresholded chemical) using NOAEL/LOAEL		µg/kg bw/day	
LLTC (Thresholded chemical) using BMD	16.4	µg/kg bw/day	The POD is based on BMD Modelling carried out by California EPA in 2017 (OEHHA 2018) for changes in kidney weights in male rats in 90day study. Uncertainty factors account for database deficiencies (√10), use of sub-chronic study (√10) and inter and intraspecies variability (10 x 10). There is limited toxicological information for cis 1,2 DCE, and particularly there are virtually no inhalation toxicity studies. These data deficiencies, particularly in terms of lack of reproductive toxicity data, are considered by the application of an additional uncertainty factor of √10 to the selected PoD. An uncertainty factor of √10 is applied for subchronic to chronic extrapolation based on OEHHA use of a factor of √10 for extrapolation from a subchronic study which is less than 12% of the animal lifespan (see Appendix III of OEHHA 2018) and also in consideration of the nature of the end point (kidney weight gain with no evidence of histopathology at any of the dose level). Available data indicate that cis 1,2 DCE is of relatively low toxic potency.

LLTC (Non Thresholded chemical) using NOAEL/LOAEL	µg/kg bw/day	
LLTC (Non Thresholded chemical) using BMD	µg/kg bw/day	

Delete as appropriate

Sensitive Receptor		

b) INHALATION

Choice of Pivotal Data	Dosing vehicle	Doses	Units	Species	Study Type	Comments
No studies available						There are no suitable inhalation data for cis 1,2 dichloroethene and no inhalation LLTC is proposed. Modelled systemic Inhalation exposure will be added to exposure from other routes and total systemic exposure will be evaluated agai

Selection of POD

Published POD for INHALATION LLTC:		
Are dose response data of adequate quality to derive a BMD	No	
Type of PoD		
Value selected		mg/kg bw/day

Derived POD for INHALATION LLTC: (from data below)		
Type of PoD		
Value derived		mg/kg bw/day
AIC value		
P value		

BMD Modelling (if answered 'Yes' to question above - see worksheet BMD modelleing pivotal study)

Software used: US EPA BMDS 2.3.1

	BMD1	BMD5	BMD10	BMD15
BMD modelling (value) (mg/kg bw/day)				
	BMDL1	BMDL5	BMDL10	BMDL15
BMD modelling (value) (mg/kg bw/day)				

Present benchmark dose graph here

Comments:

Thresholded effects?	
If yes - use generic UF of 100 or (if data allow) calculate CSAF	
If no : see below for non-thresholded effects	
If animal data are used as POD (NO(A)EL or BDM) use generic margin of 5000 or (if data allows) calculate CSM	
If human data are used to derive a BMD use the margin that relates to a notional risk of 1 in 50000 based on the BMR (using the table opposite). The same margin can also be applied to a NO(A)EL, but not to a LO(A)EL.	
ELCR =	1 in 50000

BMR	Margin	Corresopnding ELCR estimate
0.50%	250	1 in 50000
1%	500	1 in 50000
5%	2500	1 in 50000
10%	5000	1 in 50000

Chemical Specific Adjustment Factor/Chemical Specific Margin to account for uncertainties in the data		
	Range	Selected value
Intraspecies	1 - 10	
Interspecies	1 - 10	
Sub-chronic to chronic	1-10	
Database deficiencies	1-3	
Quality of study	1 - 10	
Use of LOAEL as POD	1-10	
Other	1 - 10	
Total CSAF/CSM		

Is the LLTC based on systemic or localised toxicological effects?	
Lifetime averaging to be applied in CLEA (Yes/No)	

Inhalation LLTC calculation:

	Value	Units	Justification
LLTC (Thresholded chemical) using NOAEC/LOAEC		µg/kg bw/day	
LLTC (Thresholded chemical) using BMD		µg/kg bw/day	
LLTC (Non Thresholded chemical) using NOAEL/LOAEL		µg/kg bw/day	
LLTC (Non Thresholded chemical) using BMD		µg/kg bw/day	

Delete as appropriate

Sensitive Receptor		

Any Additional Comments: There is limited toxicological information for cis 1,2 DCE, and particularly there are virtually no inhalation toxicity studies. These data deficiencies, particularly in terms of lack of reproductive toxicity data, are considered by the application of an additional uncertainty factor of 3 to the selected PoD. Available data indicate that cis 1,2 DCE is of relatively low toxic potency.

The oral PoD is derived from the BMD1SD of 16.35 mg/kg bw/day generated by OEHHA in 2017 from the 90 day oral toxicity data of McCauley et al (1990, 1995), using USEPA BMDS modelling software. A BMR of 1SD difference from control values is considered by USEPA (2012) to be a more reliable indicator of adversity rather than a BMR 10 when this is based on a relative organ weight increases in the absence of clinical or histopathological evidence, where the biological significance of this finding is uncertain. A total uncertainty factor of 1000 was applied to the POD including a value of 3 for use of a sub chronic study following the approach used by OEHHA (2018). The resulting oral LLTC of 16.4 µg/kg bw/day is of the same magnitude as the proposed LLTC for trans 1,2-DCE. This is consistent wih the known metabolism of these two isomers to a common metabolite. The oral LLTC is an order of magnitude higher that the EPA RfD of 0.002mg/kg/d (based on BMDL10 and total UF of 3000) and the Acceptable Daily Dose (ADD) of 0.00125 mg/kg/d calculated by California EPA (Based on BMDL1SD and total UF of 3000 - although using different UF sub factors to those chosen by USEPA)

There are no suitable inhalation data for cis 1,2 dichloroethene and no inhalation LLTC is proposed. Modelled systemic Inhalation exposure will be added to exposure from other routes and total systemic exposure will be evaluated against the oral LLTC

APPENDIX B
MEAN DAILY INTAKE DATA
SHEET FOR *CIS*-1,2-DICHLOROETHENE

Substance: **cis-1,2-Dichloroethene**

MDI Oral			**Recommended adult oral MDI**	**Units**	**Justification:** Only US Data has been identified. In the majority of cases exposure through drinking water and food is likely to be negligible however sources in drinking water have been identified. A value of 4ug day-1 for background exposure through drinking water is tentatively proposed within the WHO Background document for development of WHO Guidelines for Drinking Water Quality. This value appears to be based on the US study that identified detectable concentrations in 8% of drinking water sources with detectable concentrations ranging between 2-120ug/l. In conjunction with the MDI Inhalation (6ug day-1 see below) this equates to a total of 10ug/day background exposure which conforms reasonably well with the RIVM estimate of total background exposure to the mixed isomers of 0.13ug/kg-bw/day (9.1ug/day for a 70kg adult). The same value has also been selected for the trans isomer since the primary study does not distinguish between the two isomers.		
			4	ug day-1			
Organisation/Source	**Date**	**Media**	**Value**	**Units**	**Description**	**Reference**	**Web link**
WHO Guidelines for Drinking Water Quality	Apr-09	Drinking water	4	ug/day	1,2 dichloroethene (mixed isomers) detected in 8% of drinking supplies derived from groundwater, at concentrations between 2-120ug/l. The high end value is therefore greatly atypical with the majority of drinking water containing concentrations less than detection levels. Estimated 4ug/l MDI is based on a concentration of 2ug/l in drinking water.	WHO (2003) 1,2-Dichloroethene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality. Geneva, World Health Organization, (WHO/SDE/WSH/03.04/72)	http://www.who.int/water_sanitation_health/dwq/1,2-Dichloroethene.pdf
Dutch National Institute for Public Health and the Environment (RIVM) Maximum Permissible Risk (MPR) Levels	14/04/2009	Drinking water	0-120	ug/l	Dutch data not available. 1,2 dichloroethene (mixed isomers) detected in 8% of drinking supplies derived from groundwater, at concentrations between 2-120ug/l.. RIVM estimated background exposure of 0.13ug/kg-bw/day for the mixed isomers via inhalation and oral intake.	RIVM Report 711701 025. Re-evaluation of human toxicological maximum permissible risk levels A.J. Bars, R.M.C Theelan, P.J.C.M. Janssen, J.M. Hesse, M.E. van Apeldoorn, M.C.M. Meijerink, L.Verdam, M.J.Zeilmaker March 2001	http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf
US Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles and Minimal Risk Levels	14/04/2009	Drinking water	0-120	ug/l	1,2 dichloroethene (mixed isomers) detected in 8% of drinking supplies derived from groundwater, at concentrations between 2-120ug/l. The high end value is atypical with the majority of drinking water containing concentrations less than detection levels.	Toxicological Profile for 1,2-Dichloroethene, ATSDR, 1996	http://www.atsdr.cdc.gov/toxprofiles/tp87.pdf
USEPA Health Advisories	14/04/2009	DW	0.07	mg/l	MCLG & MCL		www.epa.gov/waterscience/criteria/drinking/
Toxicological Data Network (TOXNET)	14/04/2009		ND to 408	ug/l	ADI from water in HSDB Database (Cis isomer specific)	(3) EPA; National Contaminant Occurrence Database. cis-1,2-Dichloroethylene. Available from the Database Query page at http://www.epa.gov/safewater/data/ncod.html as of Apr 12, 2001.	http://toxnet.nlm.nih.gov/

MDI Inhalation			**Recommended adult inhalation MDI**	**Units**	**Justification:** cis-1,2-Dichloroethene is not monitored by the Defra UK AIR Network and features in very few reports produced by authoritative bodies. The ATSDR toxicological profile (1996) reports a maximum recorded urban air concentrations of cis-1,2,-Dichloroethene of 0.076 ppb (0.3 µg m-3) in the EPA 1983 study. This maximum is quoted in the WHO 2003 and RIVM 2001 documents. This value is similar to the median value recorded in the earlier Brodzinky and Singh 1982 urban air study. There is limited data available from Europe. The location of monitoring points from the Shah and Singh 1988 ambient air study is unknown.		
			6	ug day-1	0.3 µg m-3 is converted to 6 µg day-1 by multiplying by an assumed adult respiration rate of 20 m3 day-1.		
Organisation/Source	**Date**	**Media**	**Value**	**Units**	**Description**	**Reference**	**Web link**
WHO Background for Drinking Water	2003	Urban & industrial ambient air	0.3	µg m-3	Cites ATSDR (1990). Mean concentrations of cis 1,2-DCE in urban and industrial areas range from 0.04 - 0.3 µg m-3. *Reviewer note: Original source of data is likely EPA 1983 study discussed in the US ATSDR Toxicological profile (1996). 0.3 µg m-3 equals 0.076 ppb.*	WHO (2003). 1,2-Dichloroethene in Drinking-water: Background document for development of WHO Guidelines for Drinking-water Quality. WHO/SDE/WSH/03.04/21	https://www.who.int/water_sanitation_health/water-quality/guidelines/chemicals/1-2-dichloroethene-background.pdf?ua=1
WHO Background for Drinking Water	2003	Indoor air	32.2	µg m-3	Cites ATSDR (1990). Mean concentrations of total 1,2-DCE up to 32.2 µg m-3 have been measured in indoor air.	WHO (2003). 1,2-Dichloroethene in Drinking-water: Background document for development of WHO Guidelines for Drinking-water Quality. WHO/SDE/WSH/03.04/21	https://www.who.int/water_sanitation_health/water-quality/guidelines/chemicals/1-2-dichloroethene-background.pdf?ua=1
RIVM	2001	Urban air	0.3	ug m-3	Value for cis-DCE. Average concentration of 0.27µg m-3 in US urban and suburban areas. Range of 0.04 to 0.3µg m-3. *Reviewer note: Original source of data is likely EPA 1983 study discussed in the US ATSDR Toxicological profile (1996). 0.3 µg m-3 equals 0.076 ppb.*	RIVM Report 711701 025 Re-evaluation of human-toxicological maxi-mum permissible risk levels	https://www.rivm.nl/bibliotheek/rapporten/711701025.pdf
Shah and Singh in ATSDR	Shah and Singh 1988, ATSDR 1996	Outdoor ambient air	0.147	µg m-3	National database. Average (mean) ambient air concentration of 0.326 ppb across 161 data points with a median of 0.037 ppb (75% of values fell below 0.113 ppb). The location and spread of urban to rural was not stated. Using a conversion factor of 3.96 the average concentration of 0.037 ppb equates to 0.147 µg m-3.	ATSDR (1996). Toxicological Profile For 1,2-Dichloroethene.	https://www.atsdr.cdc.gov/ToxProfiles/tp87.pdf
EPA in ATSDR	EPA 1983, ATSDR 1996	Urban air	0.076	ppb	Value for cis-DCE. Highest recorded mean in general urban atmosphere was 0.076ppb, from Denver Colarado. Equal to 0.3 µg m-3. Mean concentrations from 7 locations vary from 0.013 to 0.076ppb (0.04 to 0.3 µg m-3)	ATSDR (1996). Toxicological Profile For 1,2-Dichloroethene.	https://www.atsdr.cdc.gov/ToxProfiles/tp87.pdf
Brodzinsky and Singh in ATSDR	Brodzinsky and Singh 1982, ATSDR 1996	Urban air	0.068	ppb	Value for cis-DCE. Median from 669 urban/suburban sites. Equal to 0.27 ug m-3. Maximum of 3.5ppb. Location of samples unknown, considered innappropriate to use maximum value in case it relates to a source zone.	ATSDR (1996). Toxicological Profile For 1,2-Dichloroethene.	https://www.atsdr.cdc.gov/ToxProfiles/tp87.pdf
Brodzinsky and Singh in ATSDR	Brodzinsky and Singh 1982, ATSDR 1996	Source Sites	0.3	ppb	Value for cis-DCE. Median from 101 source areas. Maximum of 6.7ppb	ATSDR (1996). Toxicological Profile For 1,2-Dichloroethene.	https://www.atsdr.cdc.gov/ToxProfiles/tp87.pdf
Clark et al in WHO	Clark et al 1984, WHO 1998	Air	1.2	g m-3	Isomer not stated. Mean concentration from UK ambient air. WHO document is a first draft. *Reviewers note: Potential errors in document. Values are very different to other sources. Source documents not freely available to check.*	Concise International Chemical Assessment Document 1 : 1,2 Dichloroethene	http://www.who.int/ipcs/publications/cicad/en/cicad01.pdf