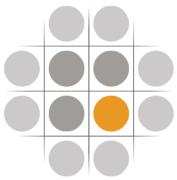
Supported by

SoBRA

The Society of Brownfield Risk Assessment



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

CL:AIRE

ISBN: 978-1-905046-45-4

Published by CL:AIRE, Reading Business Centre, Fountain House, Queens Walk, Reading, RG1 7QF.
Web: www.claire.co.uk Email: enquiries@claire.co.uk

Report Citation
It is recommended citation to this report is made as follows:
CL:AIRE, 2024. Category 4 Screening Levels: *trans*-1,2-Dichloroethene. CL:AIRE, Reading. ISBN 978-1-905046-45-4. Download at www.claire.co.uk/c4sl

Disclaimer
This and other documents in this C4SL Phase 2 project have been developed for the Soil and Groundwater Technology Association (SAGTA) by the following:

- C4SL Phase 2 Project Team – see page ii where the team members are listed.
- C4SL Phase 2 Steering Group – see page ii where the participants are listed.

The work reported herein together with other related documents was carried out on an agreed basis by the companies and organisations listed on page ii. However, any views expressed are not necessarily those of the members of the Phase 2 Project Team, SAGTA as the client, the Steering Group member organisations nor any individual's personal view.

Documents are intended to provide information on the risk that may be posed by particular potentially contaminative substances in soil, which readers may find relevant to the assessment of risk to human health by land affected by contamination.

However, it is emphasised that users must not refer to the Category 4 Screening Levels in isolation. The values are based on detailed exposure elements and toxicological opinions. As such, in referring to the documents it is emphasised that users:

- Must satisfy themselves that they fully understand their derivation and limitations as are described in the text
- Should undertake their own checks on accuracy to again satisfy themselves that the contents are appropriate for their intended use
- Take appropriate specific professional advice as may be necessary to fulfil these criteria

SAGTA is making outputs freely available to industry via downloading from the CL:AIRE website (www.claire.co.uk). As such, they may be reproduced free of charge in any format or medium. This is subject to them being reproduced accurately and not in a misleading context, as well as them being fully and appropriately referenced.

In making the documents available, it is on the basis that SAGTA, the Steering Group and the Project Team are not engaged in providing a specific professional service.

Whilst reasonable skill and care has been made to ensure the accuracy and completeness of the work and the content of the documents, no warranty as to fitness for purpose is provided or implied.

CL:AIRE, SAGTA, the Project Team or the Steering Group neither accept nor assume any responsibility for any loss or damage howsoever arising from the interpretation or use of the information within the documents, or reliance upon views as may have been included.

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

Acknowledgements

Project Management Team

Simon Firth	Firth Consultants Ltd
Nicola Harries	CL:AIRE

Project Team

Camilla Alexander-White	MK Tox & Co Ltd
Laura Aspinall	RSK
Kate Baker	Delta-Simons Ltd
Gareth Barns	Geosyntec
Dave Brooks	Sirius
Sarah Bull	TARA Consulting
Lucy Burn	Worley
Catherine Cussell	RSK
Melinda Evans	Soilfix
Natasha Glynn	AtkinsRéalis
Duncan Grew	Worley
George Kowalczyk	GK Toxicology Consulting
James Lymer	
Barry Mitcheson	WSP
Rob Reuter	Wardell Armstrong LLP
Adam Symonds	Worley
Gareth Wills	WSP
Joanna Wilding	Freelance

Steering Group Members and Nominated Contact

AGS	Mike Plimmer
Defra	Harriet Cooper and Rachel Boulderstone
Environment Agency	Ian Martin and Angela Haslam
EIC	Richard Puttock
EPUK	Karen Thornton
HBF	Frances Gregory
Homes England	Richard Boyle
Mole Valley District Council	Rob Ivens
Newport City Council	Steve Manning
NHBC	Steve Moreby
NRW	Matthew Llewhellin
UK Health Security Agency	Sarah Dack and Kerry Foxall
Public Health Wales	Andrew Kibble
Rochdale Borough Council (MAPAC)	Michael Moore
SAGTA	Daniel May and Hannah White
SoBRA	Rachel Dewhurst
Welsh Contaminated Land Group	Rachael Davies
Welsh Government	Andrew Williams and Richard Clark
Wyre Council	David Johnson
YALPAG	Lucie Watson

CONTENTS

1. **INTRODUCTION** 1

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

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

2.1 ORAL ROUTE 4

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 4

2.1.2 Flowchart element 2: Review the scientific basis of each HBGV. Choose the pivotal study 4

2.1.3 Flowchart element 3/6: Are there adequate dose-effects data for the chosen pivotal study to perform BMD modelling – animal data? 5

2.1.4 Flowchart element 3a: Use NOAEL/LOAEL as PoD 6

2.1.5 Flowchart element 3b/6b: Perform BMD modelling 6

2.1.6 Flowchart element 4: Does the critical endpoint exhibit a threshold? 6

2.1.7 Flowchart element 4a: Define a suitable chemical-specific margin 6

2.1.8 Flowchart element 4b: Derive a chemical-specific assessment factor using scientific evidence 6

2.1.9 Flowchart element 5a/b: Calculate the LLTC for non-thresholded / thresholded chemicals 7

2.1.10 Flowchart element 7: Assess LLTCoral for *trans*-1,2-Dichloroethene 7

2.2 INHALATION ROUTE 7

2.3 DERMAL ROUTE 8

2.4 MEAN DAILY INTAKE 8

3. EXPOSURE MODELLING FOR *TRANS*-1,2-DICHLOROETHENE 9

3.1 CLEA PARAMETER INPUTS 9

4. C4SLs FOR *TRANS*-1,2-DICHLOROETHENE 12

4.1 C4SLs 12

4.2 OTHER CONSIDERATIONS 13

5. REFERENCES 15

APPENDICES

Appendix A - Human Toxicological Data Sheet for *trans*-1,2-Dichloroethene

Appendix B - Mean Daily Intake Data Sheet for *trans*-1,2-Dichloroethene

ABBREVIATIONS

ADE	Average Daily Exposure
AGS	Association of Geotechnical and Geoenvironmental Specialists
ATSDR	Agency for Toxic Substances and Disease Registry
BMD	Benchmark Dose
C4SL	Category Four Screening Level
CAS	Chemical Abstracts Service
CL:AIRE	Contaminated Land: Applications in Real Environments
CLEA	Contaminated Land Exposure Assessment
CSM	Chemical Specific Margin
EIC	Environmental Industries Commission
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
MRL	Minimum Risk Level
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)
SoBRA	Society of Brownfield Risk Assessment
SOM	Soil Organic Matter
SR	Science Report
TDI	Tolerable Daily Intake
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 *trans*-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 cis isomer of 1,2-dichloroethene. Section 1.1 provides brief background information on *trans*-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 *TRANS*-1,2-DICHLOROETHENE

trans-1,2-Dichloroethene (CAS No. 156-60-5), which is also commonly known as *trans*-1,2-dichloroethylene or (E)-1,2-dichloroethene, has the chemical formula $C_2H_2Cl_2$. It is one of two isomers of 1,2-dichoroethene, the other being *cis*-1,2-dichloroethene. *trans*-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 17 ppm) (ATSDR, 1996). It is a volatile compound (vapour pressure of approximately 22.6 kPa at 10˚C) and is soluble in water (5250 mg L^{-1} at 10˚C) (see Section 3.1). In the atmosphere, *trans*-1,2-dichloroethene rapidly reacts with hydroxyl radicals and has an estimated lifetime of 5 days (ATSDR, 1996).

There are no known natural sources of *trans*-1,2-dichloroethene (ATSDR, 1996). It is most commonly used in the synthesis of chlorinated solvents and the manufacture of solvents, perfumes, thermoplastics and lacquers (ATSDR, 1996; WHO, 2003). It is also generally used as a solvent and extractant and can be found in municipal wastewater and in effluents from a wide range of industries (ATSDR, 1996).

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

2. DERIVATION OF LOW LEVEL OF TOXICOLOGICAL CONCERN FOR *TRANS*-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 SP1010 (CL:AIRE, 2014) and is reproduced in Figure 2.1. The remainder of this section demonstrates the application of the LLTC framework to *trans*-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).

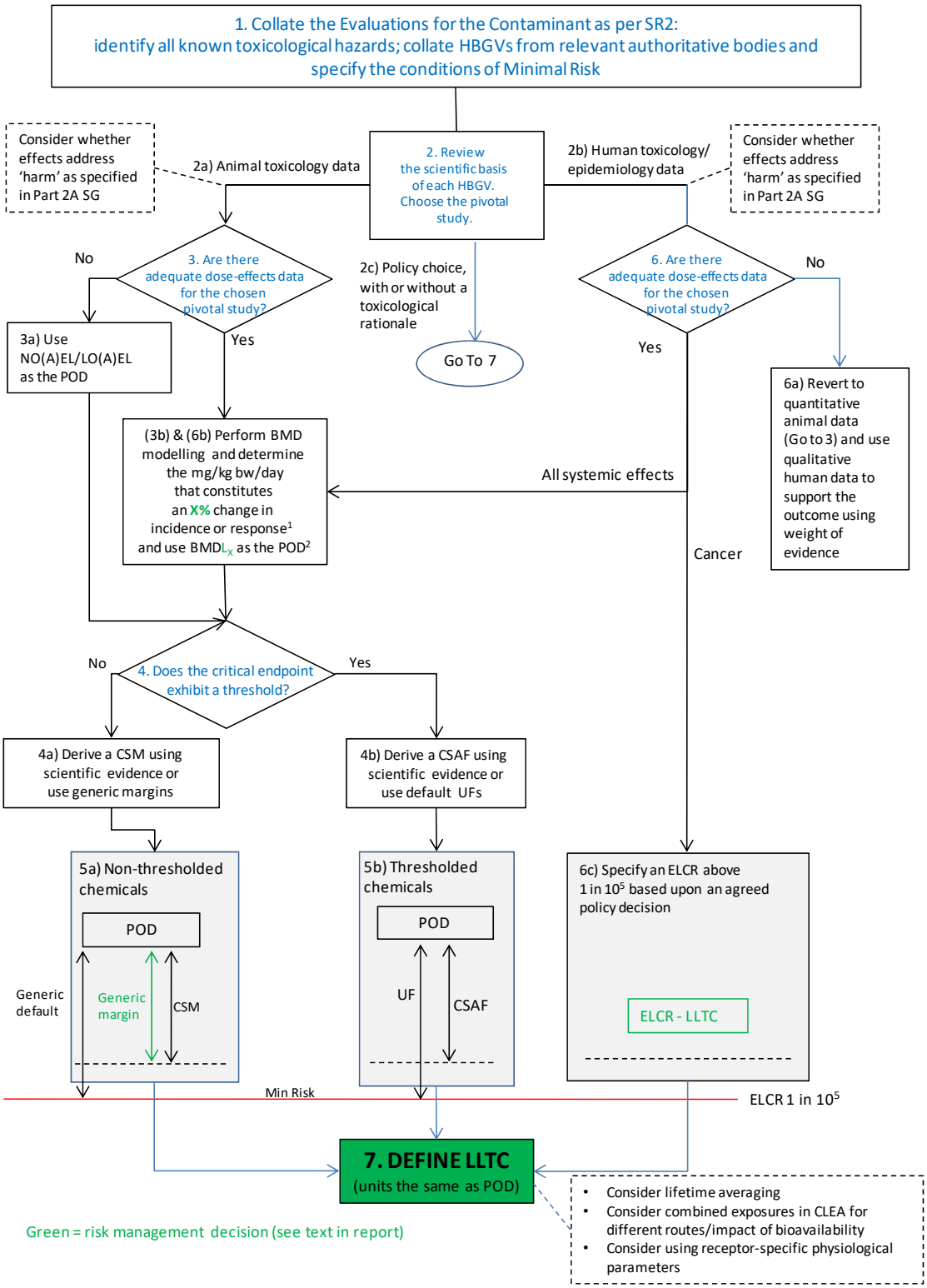


Figure 2.1: A framework for evaluating chemical-specific toxicology data for the purposes of LLTC derivation (reproduced from Figure 2.2 of SP1010 (CL:AIRE, 2014)).

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 immunotoxicity effects are the most sensitive[1] toxicological endpoints following long-term exposure to *trans*-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

Following a review of all available data, the Barnes *et al*. (1985) study in mice dosed with *trans*-1,2-dichloroethene in drinking water as described in ATSDR (1996), WHO (2003) and US EPA (2010) has been selected as the pivotal study for the oral exposure route. The 90-day study data are summarised in Table 4-6 of US EPA (2010). This study needs to be evaluated in the context of the later 90-day study reported by NTP (2002), which was also reviewed by US EPA (2010), where mice were dosed with microencapsulated *trans*-1,2-dichloroethene in feed. The drinking water study by Barnes *et al.* (1985) remains the most sensitive of these two studies due to greater absorption of the test substance from a water vehicle to that in food.

Barnes *et al.* (1985) reported a classical 90-day toxicology study in CD-1 mice. Male mice were administered doses of 0, 17, 175, or 387 mg kg^{-1} bw day^{-1}, with female mice administered doses of 0, 23, 224, or 452 mg kg^{-1} bw day^{-1}.

In male mice, the main effects were statistically significant reductions in glutathione levels and serum alkaline phosphatase enzymes, and an increase in liver weight, with a No Observed Adverse Effect Level (NOAEL) of 17 mg kg^{-1} bw day^{-1}. The liver observations are the most sensitive of all 'effects' observed in toxicological studies with *trans*-1,2-dichloroethene. US EPA (2010) note that in the absence of elevated liver enzymes or histopathology, the change in liver weight is difficult to interpret. It could be concluded that the liver observations are adaptive rather than adverse in nature, but for the purposes of setting the LLTC, these effects are considered relevant. However, it should also be noted that in the Barnes *et al.* (1985) study the changes in liver weight in males are variable with dose and do not follow a typical dose response. Hence, the selection of this NOAEL is a precautionary point of departure (POD).

In female mice, as well as reductions in some liver enzymes that could be considered adaptive, there was also an observed decrease in absolute thymus weight at the top dose and as a percentage of body weight at the middle and top doses. US EPA (2010) report the Lowest Observed Adverse Effect Level (LOAEL) in female mice (based on

[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.

reduced relative thymus weight) to be 224 mg kg^{-1} bw day^{-1} and the NOAEL to be 23 mg kg^{-1} bw day^{-1}.

ATSDR (1996), WHO (2003), and US EPA (2010) agreed on a NOAEL of 17 mg kg^{-1} bw day^{-1} from Barnes *et al.* (1985) for the purposes of risk assessment, principally based on the most sensitive observations in liver in male rodents.

A study from the same laboratory as reported by Shopp *et al.* (1985) was a supplementary investigation to see if the CD-1 random-bred mouse could be used in principle to look at immunotoxicity endpoints. However, the biological relevance to humans is questionable. It was a bespoke investigative study designed to see if the chemical could cause an effect via a modulated immune system in the mouse and the findings of this were equivocal, although a decrease in spleen cell antibody production directed against sheep red blood cells was observed in mice. The NOAEL from this study was also defined in males at 17 mg kg^{-1} bw day^{-1}.

The NOAEL from Barnes *et al*. (1985) is considered the POD from which to derive an $LLTC_{oral}$. It was also used by ATSDR (1996) to derive an intermediate duration oral Minimal Risk Level (MRL) and by WHO (2003) to derive a Tolerable Daily Intake (TDI).

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 *trans*-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 to perform BMD modelling – animal data?

Yes	No	Not applicable
	X	

US EPA (2010) did not consider the data on liver effects from Barnes *et al.* (1985) to be suitable for benchmark dose (BMD) modelling as a clear dose response across adequate doses was not seen for this effect.

It is worth noting that US EPA (2010) did perform BMD modelling on other endpoints, namely: the data from Shopp *et al*. (1985) on immunological response, the data from Barnes *et al.* (1985) on female thymus weight effects, and the data on relative liver weight from NTP (2002), and compared the outputs. The BMD values reported from the US EPA analysis ranged from a BMD_{1SD}[2] of 126 mg kg^{-1} bw day^{-1} for immunological effects to a

[2] BMD1SD = estimated benchmark dose at which change in the mean response is equal to one standard deviation from the control mean

BMD_{10}[3] of 3242 mg kg^{-1} bw day^{-1} for effects on relative liver weight. All were significantly higher than the NOAEL of 17 mg kg^{-1} bw day^{-1}.

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

2.1.4 Flowchart element 3a: Use NOAEL/LOAEL as PoD

The NOAEL for *trans*-1,2-dicholorethene of 17 mg kg^{-1} bw day^{-1} in male mice from a 90-day drinking water study (Barnes *et al.*, 1985), as identified by ATSDR (1996) and WHO (2003), has been selected as the POD. This is a precautionary choice for this substance, given the weight of evidence across several endpoints.

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

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

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.

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 oral LLTC, a total uncertainty factor (UF) of 300 is proposed based on the following:

- Intraspecies variability (x10);
- Interspecies differences (x10); and
- Extrapolation from sub-chronic to chronic duration (x3).

The uncertainty factors for interspecies variability and interspecies differences are as selected by ATSDR (1996) for derivation of their **intermediate** duration MRL. An additional factor of √10 (rounded to 3) has been used to account for use of a sub-chronic duration (90 day) toxicological study which is broadly consistent with ATSDR (1996).

GO TO FLOWCHART ELEMENT 5b

[3] BMD_{10} = estimated benchmark dose at which change in the mean response is equal to 10% of the control mean

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 2.2 presents the choice of POD, and the resultant LLTC.

Table 2.2: 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	NOAEL	17	300	56.7

GO TO FLOWCHART ELEMENT 7

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

Based upon a scientific evaluation, an oral LLTC of **56.7 µg kg^{-1} bw day^{-1}** is proposed. This is based on a NOAEL of 17 mg kg^{-1} bw day^{-1} as the POD from a study by Barnes *et al.* (1985) and an UF of 300. This LLTC value is:

a) 2.8 times higher than the US EPA (2010) Reference Dose of 20 µg kg^{-1} bw day^{-1}.

b) 3.5 times lower than the intermediate duration MRL[4] of 200 µg kg^{-1} bw day^{-1} (ATSDR, 1996)[5] which was also based on Barnes *et al.* (1985). A chronic MRL was not derived.

This LLTC is considered to be a pragmatic level for setting a C4SL and is considered suitably protective of all health effects in the general population given the limited data available.

2.2 INHALATION ROUTE

A review from authoritative bodies of inhalation HBGVs indicates that liver and lung effects may be sensitive[6] toxicological endpoints following long-term exposure to *trans*-1,2-dichloroethene by inhalation. However, the data available are of poor quality and are insufficient to perform a quantitative assessment via the inhalation route.

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.

---

[4] Intermediate MRL is used to assess exposures >14 – 364 days

[5] ATSDR rounded up MRL from 170 to 200 µg kg^{-1} bw day^{-1}

[6] 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 minimal or tolerable risk described in SR2.

2.3 DERMAL ROUTE

No data were identified by RIVM (2009), US EPA (2010) or OEHHA (2018) 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.

2.4 MEAN DAILY INTAKE

The oral LLTC recommended for *trans*-1,2-dichloroethene is based on a threshold effect. 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 *trans*-1,2-dichloroethene are shown in Table 2.3.

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 concentration of mixed isomers of 2 µg L-1. Few data are available relating to exposure to *trans*-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 *trans*-1,2-dichloroethene in the UK and Europe. *trans*-1,2-Dichloroethene was below the relatively high detection limit of 1 ppb (3.96 µg m-3) in 13 air samples taken from US cities (Mohamed *et al.*, 2002). A single measurement from downwind of an industrial facility in Edison, New Jersey (Brodzinsky and Singh, 1982) recorded a *trans*-1,2-dichloroethene concentration of 0.93 ppb (3.68 µg m^{-3}). Urban air concentrations of the other 1,2-dichloroethene isomer, *cis*-1,2-dichloroethene, are better characterised. 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} (0.01 to 0.76 ppb). These data are taken from a 1983 study by the US EPA detailed in ATSDR (1996). Values are consistent with a median value of 0.27 µg m^{-3} (0.068 ppb) for *cis*-1,2-dichloroethene reported by Brodzinsky and Singh (1982). ATSDR (1996) report that the median concentration of 1,2-dichloroethene (cis and trans) in outdoor air (based on 161 data points from the 1983 US EPA study) was 0.037 ppb (0.15 µg m^{-3}). Based on the available information it is considered reasonable to use the *cis*-1,2-dichloroethene isomer as a proxy for *trans*-1,2-dichloroethene for urban air concentrations.

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

Table 2.3: 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 *TRANS*-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 for *trans*-1,2-dichlorothene is based upon a scientific evaluation of liver toxicity observed in animal studies (mice) administered via drinking water (Barnes et al. 1985), 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. using 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 *trans*-1,2-dichloroethene are shown in Table 3.1.

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

Parameter	Units	Value	Source/Justification
Air-water partition coefficient	dimensionless	$1.77x10^{-1}$	CL:AIRE, EIC & AGS, 2010
Diffusion coefficient in air	$m^2\ s^{-1}$	$9.09\ x10^{-6}$	CL:AIRE, EIC & AGS, 2010
Diffusion coefficient in water	$m^2\ s^{-1}$	$7.08\ x10^{-10}$	CL:AIRE, EIC & AGS, 2010
Relative molecular mass	$g\ mol^{-1}$	96.94	CL:AIRE, EIC & AGS, 2010
Vapour pressure	Pa	$2.26\ x10^{4}$	CL:AIRE, EIC & AGS, 2010
Water solubility	$mg\ L^{-1}$	5250	CL:AIRE, EIC & AGS, 2010
Log K_{oc}	Log $cm^3\ g^{-1}$	1.78	CL:AIRE, EIC & AGS, 2010
Log K_{ow}	dimensionless	2.08	CL:AIRE, EIC & AGS, 2010
Dermal absorption fraction	dimensionless	0.1	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 *trans*-1,2-dichloroethene in soil and dust is the same as bioavailability of *trans*-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 *trans*-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 the 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 *trans*-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 *trans*-1,2-dichloroethene has been modelled using the method for organic chemicals within the CLEA software.

CLEA predicts the greatest exposure to *trans*-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, 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 *trans*-1,2-dichloroethene and it is considered appropriately conservative to assume a relative bioavailability of 100% for the derivation of C4SLs.

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

4.1 C4SLS

The C4SLs for *trans*-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 *trans*-1,2-dichloroethene.

Land-use	C4SLs (mg.kg^{-1})		
	SOM Content		
	1.0%	2.5%	6.0%
Residential with consumption of homegrown produce	0.90	1.6	3.3
Residential without consumption of homegrown produce	0.93	1.7	3.4
Allotments	3.7	7.5	16
Commercial	69	120	260
Public Open Space (residential)	13000	13000	13000
Public Open Space (park)	5600	7000	9100

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	0.04	0.04	0.06	0.20	88.46	27.81
Sum of consumption of homegrown produce and attached soil	3.06	0.00	98.77	0.00	0.00	0.00
Dermal contact (indoor)	0.00	0.00	0.00	0.01	2.68	0.00
Dermal contact (outdoor)	0.00	0.00	0.03	0.02	3.14	2.75
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)	95.86	98.91	0.00	99.47	0.00	0.00
Inhalation of vapour (outdoor)	0.00	0.00	0.11	0.04	4.76	68.40
Oral background	0.40	0.40	0.40	0.10	0.26	0.40
Inhalation background	0.64	0.64	0.64	0.15	0.39	0.64

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

- Consumption of homegrown produce for Allotments land-use;
- Indoor inhalation of vapours for Residential with Homegrown Produce, Residential without Homegrown Produce and Commercial land-uses;
- Ingestion of soil and soil derived dust for the POS_{resi} land-use; and,
- Outdoor inhalation of vapours for POS_{park} land-use.

4.2 OTHER CONSIDERATIONS

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

- Background intake of *trans*-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 0.1% 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 0.15% 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 *trans*-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 *trans*-1,2-dichloroethene (Johnson *et al.*, 2012). *trans*-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 *trans*-1,2-dichloroethene only 0.8% had a concentration above the limit of detection (1 to 10 µg kg^{-1}), with most of the 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 *trans*-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 0.9 mg kg^{-1} (900 µg kg^{-1}), which is for the Residential with Consumption of Homegrown Produce land-use, is above typical laboratory limits of detection for *trans*-1,2-dichloroethene in soil (typically circa 1 to 10 µg kg^{-1}).

5. REFERENCES

Agency for Toxic Substances and Disease Registry (ATSDR), 1996. Toxicological Profile for 1,2-Dichloroethene (Update). August. Atlanta, GA.

Barnes, D.W., Sanders, V.M., White, K.L., Jr., Shopp, G.M., Jr. and Munson, A.E., 1985. Toxicology of trans-1,2-Dichloroethylene in the Mouse. Drug and Chemical Toxicology 8(5):373-392.

Brodzinsky, R. and Singh, H.B., 1982. Volatile organic chemicals in the atmosphere: An assessment of available data. Menlo Park, CA: Atmospheric Science Center, SRI International. Contract 68-02-3452.

CIRIA, 2009. The VOCs Handbook. Investigating, assessing and managing risks from inhalation of VOCs at land affected by contamination. CIRIA report C682.

CL:AIRE, 2014. SP1010 – Development of Category 4 Screening Levels for Assessment of Land Affected by Contamination. Final Project Report (revision 2). FINAL. Contaminated Land: Applications in Real Environments.

CL:AIRE, EIC & AGS, 2010. The Soil Generic Assessment Criteria for Human Health Risk Assessment. CL:AIRE, London, UK.

Environment Agency, 2009a. Human health toxicological assessment of contaminants in soil. Science Report – SC050021/SR2, Environment Agency, Bristol, UK.

Environment Agency, 2009b. Updated technical background to the CLEA model. Science Report – SC050021/SR3, Environment Agency, Bristol, UK.

Johnson, C.C., Ander, E.L., Cave, M.R. and Palumbo-Roe, B., 2012. Normal background concentrations (NBCs) of contaminants in English soils: Final project report. British Geological Survey Commissioned Report, CR/12/035.

Mohamed, M.F., Kang, D. and Aneja, V.P., 2002. Volatile organic compounds in some urban locations in United States. Chemosphere 47(8): 863-882.

National Institute for Public Health and the Environment (RIVM), 2009. Environmental risk limits for twelve volatile aliphatic hydrocarbons - An update considering human-toxicological data. Report 601782013/2009. National Institute for Public Health and the Environment.

National Toxicology Program (NTP), 2002. NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Public Health Service, U.S. Department of Health and Human Services; NTP TR 55.

Office of Environmental Health Hazard Assessment (OEHHA), 2018. Public Health Goals for Cis-/Trans-1,2-Dichloroethylene in Drinking Water. California Environmental Protection Agency.

Shopp, G.M., Jr., Sanders, V.M., White, K.L., Jr. and Munson, A.E., 1985. Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug Chem Toxicol 8:393-407.

Society of Brownfield Risk Assessment (SoBRA), 2020. Development of Acute Generic Assessment Criteria for Assessing Risks to Human Health from Contaminants in Soil. V2.0. July 2020.

SoBRA, 2018. Vapour Intrusion to Support Sustainable Risk Based Decision Making Summer Workshop 2017.

United States Environmental Protection Agency (US EPA), 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).

World Health Organization (WHO), 2003. 1,2-Dichloroethene in Drinking-water. Background document for development of WHO Guidelines for Drinking-water Quality. Originally published in Guidelines for drinking-water quality, 2nd ed. Vol.2. Health criteria and other supporting information. World Health Organization, Geneva, 1996.

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

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

Chemical: **Trans-1,2 Dichloroethene**

Human Health Hazard Profile - References

Authoritative bodies	Website	Checked (Y/N)	References
Environment Agency	hhttps://www.gov.uk/government/organisations/environment-agency	Y	
Foods Standards Agency	http://www.food.gov.uk/	Y	
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-chemicals-in-food-consumer-	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	
EFSA - is there an opinion?	http://www.efsa.europa.eu/	Y	
JECFA	http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/en/?	Y	
WHO	http://www.who.int/en/	Y	
WHO IPCS	http://www.who.int/ipcs/en/	Y	
WHO EHC	http://www.who.int/ipcs/publications/ehc/en/	Y	
RIVM	https://www.rivm.nl/en	Y	
US ATDSR	http://www.atsdr.cdc.gov/	Y	https://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=82
US EPA	http://www.epa.gov/	Y	
US National Toxicology Program	https://ntp.niehs.nih.gov/	Y	
Health Canada	http://www.hc-sc.gc.ca/index-eng.php	Y	
Australia NICNAS	http://www.nicnas.gov.au/	Y	
Risk Assessment Information System	http://rais.ornl.gov	Y	https://rais.ornl.gov/tox/profiles/12dce_c.html
Other scientific reviews	**Check for key reviews on pubmed**		

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: **Trans-1,2 Dichloroethene**

I) Human Health Hazard Profile - Toxicological Evidence

Most sensitive health effects:

Sensitive endpoints	Other information	Source of evidence
Immunotoxicity	Decreased ability to produce antibodies	Shopp et al 1985
Hepatotoxicity	Liver tissue pathology, significant increase in serum alkaline phosphatase and relative liver weight	Barnes et al 1985
Other	Local lung tissue pathology	Freundt et al 1997

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 IRIS Tox Review, 2010 Reference Dose (RfD)	0.02	mg/kg bw/day	3000	BMDL1SD	65	mg/kg bw/day	decreased ability to produce antibodies against sheep RBCs in male spleen cells	Shopp et al. (1985). This 90-day drinking water study in CD-1 mice investigates immune responses to trans 1,2-DCE. Supression of the humoral immune system was observed although there was not a strong dose-response; other changes of the immune system were not pronounced as adverse. The humoral response was as measured by suppressed spleen cell antibody production directed against sRBCs (sheep red blood cells). 12 mice in control group, 8 mice in treatment group. The authors concluded that the randomly bred CD-1 mouse immune system 'does not appear to be overly sensitive to the effects of DCE. The few effects which were seen were probably the result of general toxicity as opposed to specific target organ toxicity.' A control and 3 doses were used for male mice (17, 175 and 387 mg.kg-day) and a control and 3 doses for female (23, 224 and 452 mg.kg-day). The EPA used the Schopp data to derive a POD as determined using a BMD approach. The BMDL1SD of 65 mg.kg-day was selected as the POD for deriving the RfD for trans 1,2-DCE. UF of 3,000 applied based on 10 to protect sensitive individuals, 10 to extrapolate from animals to humans, 10 for study subchronic duration and 3 for database deficiences. This resulted in a RfD of 0.02 mg.kg-day. Note that the BMDL1SD is the 95% lower confidence limit on the benchmark dose (BMD1SD) corresponding to a change in mean response equal to one standard deviation from the control mean number of AFCs. However, it should be noted that the study authors did not consider their data showed an adverse effect, the animal numbers were small and the dose response was not convincing.	Toxicological review of cis-1,2-Dicholoroethylene and trans-1,2-Dicholorethylene; In Support of Summary Information on the Integrated Risk Information System (IRIS); September 2010; U.S. Environmental Protection Agency, Washington, DC
ATSDR, 1996, Intermediate Minimal Risk Level (MRL)	0.2	mg/kg bw/day	100	NOAEL	17	mg/kg bw/day	reduced glutathione levels (males); increase in serum alkaline phosphatase (females)	Study based on: Barnes DW, Sanders VM, White KL Jr, Shopp GM, and Munson AE. 1985. Toxicology of trans-1,2-Dichloroethylene in the Mouse. Drug and Chemical Toxicology 8(5):373-392. 90-day study with 260 male and 260 female mice in the control group and 140 mice of each sex in groups exposed to drinking water with 0.1, 1.0, or 2.0 mg trans-1,2-dichloroethene/mL (males: 0, 17, 175, 387 mg/kg/day; females: 0,23, 224,452 mg/kg/day). Exposure was averaged over the 90 days. Trans-1,2-dichloroethene was maintained in solution using a 1% emulphor (vegetable oil) and deionized water. Male mice showed reduced glutathione and an increase in relative liver weights (8%) at the highest dose and increased serum alkaline phosphatase at 175 mg/kg/day. Effects were seen in females on serum alkaline phosphatase at all doses. ATSDR selected the POD as the NOEL from the study in males at 17 mg/kg/day. UF of 10 for extrapolation from animals to humans and 10 for inter human variability, and value rounded up for an intermediate MRL. A chronic MRL was not derived by ATDSR.	TOXICOLOGICAL PROFILE FOR 1,2-DICHLOROETHENE, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service Agency for Toxic Substances and Disease Registry, August 1996

WHO, 2003, Tolerable Daily Intake (TDI)	0.017	mg/kg bw/day	1000	NOAEL	17	mg/kg bw/day	reduced glutathione levels (males); increase in serum alkaline phosphatase (females)	Also based on Barnes DW et al. (1985) Toxicology of trans-1,2-dichloroethylene in the mouse. Drug chemistry and toxicology, 1985, 8:373-392. As per ATSDR, the same NOEL of 17 mg/kg of body weight per day was used, but for derivation of a chronic drinking water value with defined intake, a higher uncertainty factor of 1000 was used (100 for intra- and interspecies variation and 10 for the short duration of the study) to derive a TDI of 17 µg/kg of body weight per day. This gives a guideline value of 50 µg/litre (rounded figure) for an allocation of 10% of the TDI to drinking-water.	1,2-Dichloroethene in Drinking-water, Background document for development of WHO Guidelines for Drinking-water Quality, WHO 2003
EPA Health Advisory on Drinking Water, 1987	0.002	mg/kg bw/day	1000	NOAEL	200	ppm	Hepatic and pulmonary effects	Extrapolated from inhalation data: Same pivotal study as the US EPA p-RfC. Freund et al. (1977). Study exposed Wistar rats to air containing trans-1,2-dichloroethylene at 0, 200, 1000 or 2000 ppm. Brief (8hrs) or prolonged (8 hrs/day, 5 days/week for 1, 2, 8 or 16 weeks) exposure. Exposure at 200ppm produced slight degeneration of liver lobule and lipid accumulation in kupffer cells. At 8 and 16 weeks exposure, severe pnemonic infiltration was observed. Exposure at 1000ppm for 8hrs resulted in significant reductions in sreum albumin, urea nitrogen and alkaline phosphatase. 8hrs exposures at both 200 and 1000 ppm prduced a significant decrease in number of leucocytes. POD for an inhalation study applied to derive longer term health advisory level. NOAEL of 200ppm used to derive a total absorbed dose using 200 ppm x 3.97 to convert to mg/m3. 794 x 0.006 (conversion factor to achieve m3.hr) x 8hrs = 38 mg/m3. The value is divided by 0.19 kg (rat weight) to derived 200mg/kg total absorbed dose (TAD). 200 mg/kg/day x (5/7 correction factor for 5 day study) / 70kg = 2.04 mg.kg/ bw day. UF of 1000 applied to give 0.002 mg.kg/bw day. Lifetime exposure assessment based on study on 1,1-DCE and therefore not considered applicable for 1,2 DCE	Trans-1,2-Dicholoroethylene; Health Advisory, Office of Drinking Water, U.S. Environmental Protection Agency, March 31st 1987

COT/COC Opinion	No published opinion from either COC or COT

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
US EPA Peer Review tox values for RfC, 2006	**0.02**	mg.kg bw-day	0.06	mg.m3	3000	LOAEL	189	mg.m3	adverse effects on liver and lungs	Freundt et al. (1977) applied as the critical study - 8hr exposure study on rats. Freundt et al. (1997) exposed groups of six female Wistar rats by inhalation to 0 or 200 ppm (0 or 794 mg.m3) of trans-1,2-DCE for 8hrs a day for 1 day only and for 8hrs a day for 5 days a week for prolonged periods 1, 2, 8 and 16 weeks. Additional studies were done at higher concs (1000 and 3000 ppm) for 8hrs in a single day. No narcosis reported and no fatalities. Histopathological effects were observed only in the liver (fatty accumulation in liver lobule and Kupffer cells) and lungs (capillary hyperemia and alveolar septum sitension). Only slight changes in 1-2 weeks, with more severe change in 8 to 16 weeks. Study identified a LOAEL of 200ppm (794 mg.m-3) for hepatic and pulmonary lesions in rats subchronically exposed to trans 1,2-DCE. This was adjusted for continuous exposure by multiplying by 8hrs/24hrs x 5days/7day to give an adjusted LOAEL of 189 mg.m-3. This was divided by a composite uncertainty factor of 3000 reflecting the following areas of uncertainty: use of a LOAEL, use of a less than chronic study, extrapolation from rats to humans using the dosimetric adjustments, protection of sensitive individuals, and database deficiencies (including lack of a multigeneration reproduction study). The individual uncertainty factors are not provided.	Provisional Peer Reviewed Toxicity Values for Trans-1,2-Dichloroethylene, Derivation of a Chronic Inhalation RfC, U.S. Environmental Protection Agency, March 2006
US EPA Toxicological Review of Cis ,1,2-DCE and Trans 1,2-DCE, 2010										The available inhalation data for trans-1,2-DCE were considered insufficient to support reference value derivation. An RfC for trans-1,2-DCE was not derived. EPA concluded that the available inhalation toxicity database for trans-1,2-DCE, including DuPont (1998) and Freundt et al. (1977), was insufficient for derivation of an RfC for this isomer.	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 Washington, DC &EPA
ATSDR, 1996, Intermediate Minimal Risk Level (MRL)	**0.227**		0.2	ppm	1000	LOAEL	200 (794)	ppm (mg/m3)	fatty degeneration of liver cells	Freundt et al. (1977). Freundt et al. (1997) exposed groups of six female Wistar rats by inhalation to 0 or 200 ppm (0 or 794 mg.m3) of trans-1,2-DCE for 8hrs a day for 1 day only and for 8hrs a day for 5 days a week for prolonged periods 1, 2, 8 and 16 weeks. Additional studies were done at higher concs (1000 and 3000 ppm) for 8hrs in a single day. In the 8-week experiment, slight fatty degeneration of the hepatic lobules was observed in 316 exposed rats and severe fatty accumulation in the Kupffer cells was seen in 3/6 exposed rats (200 ppm). In the16-week experiment, slight (2/6 exposed) and severe (3/6 exposed) fatty accumulation in the liver lobule was seen and slight fatty accumulation in the Kupffer cells was seen in 5/6 exposed rats (200 ppm).	TOXICOLOGICAL PROFILE FOR 1,2-DICHLOROETHENE, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service Agency for Toxic Substances and Disease Registry, August 1996

COT/COC Opinion	No published opinion from either COC or COT

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 data

III) Current UK (WHO) regulatory values

	Value	Units	Refs
UK drinking water standard			N/A
WHO drinking water standard	0.05	mg/L	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)
UK air quality standard			N/A
WHO air quality standard			N/A

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
Barnes et al (1985)	Drinking water	Male: 0, 17, 175, or 387 Female: 0, 23, 224, or 452	mg/kg day	Mouse	90 day drinking water study	Barnes et al (1985) was a 90-day drinking water study in CD-1 mice. The POD was a NOEL of 17 mg/kg/day in males; at higher doses a reduction in glutathione levels, increased liver weights (8% at high dose) and increased serum alkaline phosphatase was seen. In females increased serum alkaline phosphatase was seen at all doses.

Selection of POD

Published POD for ORAL LLTC:		
Are dose response data of adequate quality to derive a BMD		
Type of PoD	NOEL	
Value selected	17	mg/kg bw/day

Derived POD for ORAL 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 modelling pivotal study)

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

	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: *Example: Multistage model used for cancer effects. Gamma etc used for non-cancer effects (diffuse epithelial hyperplasia)*

Addressing uncertainty

Thresholded effects?	Yes
If yes - use generic UF of 100 or (if data allow) calculate CSAF	300
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 =	

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
Database deficiencies	1-3	1
Quality of study	1 - 10	1
Use of LOAEL as POD	1-10	1
Other	1 - 10	1
Total CSAF/CSM		300

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	56.7	µg/kg bw/day	Barnes et al 1985. General thresholded toxicity effects on liver. POD = 17 mg/kg/day. UF = 10 (intraspecies) x 10 (interindividual) x root 10 (sub-chronic to chronic).
LLTC (Thresholded chemical) using BMD		mg/kg bw/day	

LLTC (Non Thresholded chemical) using NOAEL/LOAEL		µg/kg bw/day	N/A
LLTC (Non Thresholded chemical) using BMD		mg/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 trans 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

Selection of POD

Published POD for INHALATION LLTC:		
Are dose response data of adequate quality to derive a BMD		
Type of PoD		
Value selected		mg/kg/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: *Example: Multistage model used for cancer effects. Gamma etc used for non-cancer effects (diffuse epithelial hyperplasia)*

Thresholded effects?	Yes
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 =	

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?	Systemic
Lifetime averaging to be applied in CLEA (Yes/No)	No

Inhalation LLTC calculation:

	Value	Units	Justification
LLTC (Thresholded chemical) using NOAEL/LOAEL		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:

The Shopp et al 1985 and Barnes et al 1985 studies are effectively the same study and reported back to back. Barnes et al 1985 describes the full 90-day study, and in both papers the authors state 'the target of toxicity appeared to be the liver as measured by glutathione levels and aniline hydroxylase activity'. The Shopp paper was a pilot piece of investigative work to see if the CD-1 random bred mouse could be used to look at immunotoxicity, and the findings of this were equivocal. The biological significance of any results was doubted by the authors; dose responses were not apparent. The Barnes et al 1985 paper (from the same group) describes the critical effects on the liver, and hence these data should be used for the POD as the pivotal study. The quantitative measures in male mice were significant reductions in glutathione levels and serum alkaline phosphatase enzymes. The authors state "The most noteworthy changes occurred in the males exposed to the highest level of DCE, where there was a significant decrease in glutathione levels, and in the females exposed to all three DCE levels, where there was a significant decrease in aniline hydroxylase activity." So effects in both males and females on liver metabolism observed.

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

Substance: **Substance name** Trans 1,2 - Dichloroethene

MDI Oral			**Recommended adult MDIoral**	**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

MDI Inhalation			**Recommended adult MDIoral**	**Units**	**Justification: trans-1,2-Dichloroethene is not monitored by the Defra UK AIR Network and features in very few reports produced by authoritative bodies.** No data available for urban/ suburban areas for trans 1,2 - dichloroethene. Use of single value from source dominated area not considered appropriate. Cis 1,2 - dichloroethene isomer considered to be well characterised. Considered appropriate to use cis isomer as proxy for the trans isomer. Considered conservative to use highest recorded median in urban areas for cis 1,2 - dichloroethene of 0.076ppb (0.3ug m-3). Multiplied by an assumed adult respiration rate of 20 m3.d-1, this is equal to 6 ug m-3. This is the same as used in the CL:AIRE 2010 GAC report.		
			6	ug 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. Values taken from EPA 1983a general urban atmosphere values for US cities.	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 1,2-DCE (isomer not stated) up to 32.2 µg m-3 have been measured in indoor air. Valueconverted from Gupta et al 1984 study	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
US ATSDR	1996	Ambient air	0.147	µg m-3	Most of the US data for total 1,2-DCE cited is old (1970s and early 1980s) or the sampling dates are not stated. Data from 1986 (Shah and Singh (1988)) recorded an average ambient air concentration of total 1,2-DCE to be 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 median 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
Brodzinsky and Singh in ATSDR	Brodzinsky and Singh 1982, ATSDR 1996	Air	0.93	ppb	trans 1,2- DCE Concentration recorded in Edison, New Jersey . Only value provided in document. Value is for a source dominated sample. Single recording. Equal to 3.68 µg m-3.	Toxicological Profile for 1,2 - Dichloroethene	https://www.atsdr.cdc.gov/toxprofiles/tp87-c5.pdf
Gupta et al in ATSDR	Gupta et al 1984, ATSDR 1996	Air	8.1	ppb	From Knoxville TN, Winter 1982 from 16 samples for indoor air. Equal to 32 ug m-3. This is value in CL:AIRE GAC report quoted from WHO guidelines for drinking water quality document. Limited data on indoor air available. Other value present in ATSDR is 0.015 ppb (Barkley et al 1980). Isomer not stated.	Toxicological Profile for 1,2 - Dichloroethene	https://www.atsdr.cdc.gov/toxprofiles/tp87-c5.pdf
EPA in ATSDR	EPA 1983, ATSDR 1996	Air	0.076	ppb	Highest recorded mean in general urban atmosphere for cis isomer . From Denver Colarado. Trans isomer not included in study.	Toxicological Profile for 1,2 - Dichloroethene	https://www.atsdr.cdc.gov/toxprofiles/tp87-c5.pdf
Mohamed MF et al	2002	Air	<1	ppb	Not detected, <1ppb (<3.96 µg m-3) in 13 US cities. Data for trans DCE.	PubChem. Mohamed MF et al; Chemosphere 47: 863-82 (2002)	https://pubchem.ncbi.nlm.nih.gov/compound/trans-1_2-Dichloroethylene#section=Atmospheric-Concentrations