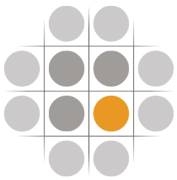
Supported by

SoBRA

The Society of Brownfield Risk Assessment



Category 4 Screening Levels: 1,2-Dichloroethane

CL:AIRE

ISBN: 978-1-905046-41-6

Published by Contaminated Land: Applications in Real Environments (CL:AIRE), Chiltern House, Haddenham Business Centre, Thame Road, Haddenham, Buckinghamshire HP17 8BY. 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, 2022. Category 4 Screening Levels: 1,2-Dichloroethane. CL:AIRE, Haddenham. ISBN 978-1-905046-41-6. 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.

Version Control Sheet

Version Number	Version Date	Description of Changes
1	May 2022	
1.1	January 2023	p12. Section 2.2.8. Amended “This LLTC value is lower than the previous Defra and Environment Agency (2004) minimal risk value of 6.2 µg kg^{-1} bw day^{-1}." to “This LLTC value is higher than the previous Defra and Environment Agency (2004) minimal risk value of 0.12 µg kg^{-1} bw day^{-1}.” Appendix A. Spreadsheet named “Reference checklist for sources of authoritative information” has been added.

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

Naomi Earl	
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	Advisian
Simon Cole	AECOM (formerly)
Meera Cush	Ramboll
Catherine Cussell	RSK
Melinda Evans	Soilfix
Andrew Fellows	Atkins (formerly)
Natasha Glynn	Atkins
Duncan Grew	Advisian
George Kowalczyk	GK Toxicology Consulting
James Lymer	
Barry Mitcheson	Wood
Rob Reuter	Wardell Armstrong LLP
Steve Ruckman	RSK (formerly)
Peter Sheppard	Advisian
Adam Symonds	Advisian
Sonja Trewavas	Atkins
Gareth Wills	WSP
Joanna Wilding	Cambridge Environmental Assessments, part of RSK ADAS Limited

Steering Group Members and Nominated Contact

AGS	Mike Plimmer
Blackburn with Darwen Borough Council (MAPAC)	David Johnson
Defra	Harriet Cooper and Rachel Boulderstone
Environment Agency	Ian Martin and Angela Haslam
EIC	Richard Puttock
EPUK	Karen Thornton
Food Standards Agency	Alan Dowding and Mark Willis
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
YALPAG	Lucie Watson

CONTENTS

1. INTRODUCTION 1

1.1 BACKGROUND TO 1,2-DICHLOROETHANE 1

2. DERIVATION OF LOW LEVEL OF TOXICOLOGICAL CONCERN FOR 1,2-DICHLOROETHANE 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? 6

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? 7

2.1.7 FLOWCHART ELEMENT 4a: Define a suitable chemical-specific margin 7

2.1.8 FLOWCHART ELEMENT 4b: Derive a chemical-specific assessment factor using scientific evidence 7

2.1.9 FLOWCHART ELEMENT 5a/b: Calculate the LLTC for non-thresholded / thresholded chemicals 7

2.1.10 FLOWCHART ELEMENT 7: Assess $LLTC_{oral}$ for 1,2-dichloroethane 8

2.2 INHALATION ROUTE 8

2.2.1 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 8

2.2.2 FLOWCHART ELEMENT 2: Review the scientific basis of each HBGV. Choose the pivotal study 9

2.2.3 FLOWCHART ELEMENT 3: Are there adequate dose-effects data for the chosen pivotal study to perform BMD modelling – animal data? 10

2.2.4 FLOWCHART ELEMENT 3b: Perform BMD modelling 10

2.2.5 FLOWCHART ELEMENT 4: Does the critical endpoint exhibit a threshold? 11

2.2.6 FLOWCHART ELEMENT 4a: Define a suitable chemical-specific margin 12

2.2.7 FLOWCHART ELEMENT 5a/b: Calculate the LLTC for non-thresholded / thresholded chemicals 12

2.2.8 FLOWCHART ELEMENT 7: Assess LLTC for 1,2-dichloroethane 12

2.3 DERMAL ROUTE 12

2.4 MEAN DAILY INTAKE 13

3. EXPOSURE MODELLING FOR 1,2-DICHLOROETHANE 14

3.1 CLEA PARAMETER INPUTS 14

4. C4SLs FOR 1,2-DICHLOROETHANE 17

4.1 C4SLs 17

4.2 OTHER CONSIDERATIONS 18

5. REFERENCES 20

APPENDICES

Appendix A - Human Toxicological Data Sheet for 1,2-Dichloroethane

Appendix B - Mean Daily Intake Data Sheet for 1,2-Dichloroethane

ABBREVIATIONS

ADE	Average Daily Exposure
AIC	Akaike Information Criteria
ALARP	As Low As Reasonably Practical
ATSDR	Agency for Toxic Substances and Disease Registry
BMC	Benchmark Concentration
BMCL	Lower Confidence Limit of BMC
BMD	Benchmark Dose
BMDL	Lower Confidence Limit of BMD
BMDS	Benchmark Dose Software
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 Assessment Factor
CSM	Chemical Specific Margin
Defra	Department for Environment, Food and Rural Affairs
DW	Dry Weight
ECHA	European Chemicals Agency
ELCR	Excess Lifetime Cancer Risk
HBGV	Health Based Guidance Value
HCV	Health Criteria Value
IPCS	International Programme on Chemical Safety
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
NCI	National Cancer Institute
NOAEL	No Observed Adverse Effect Level
NTP	National Toxicology Program
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
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SOM	Soil Organic Matter
SR	Science Report
$TD_{0.05}$	Dose associated with a 5% increase in tumour incidence
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 1,2-dichloroethane 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". Section 1.1 provides brief background information on 1,2-dichloroethane, 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 1,2-DICHLOROETHANE

1,2-Dichloroethane (CAS No. 107-06-2), which can also be referred to as Ethylene Dichloride, has the chemical formula $C_2H_4Cl_2$ and is present as a colourless, oily liquid at room temperature and pressure. It is primarily manufactured by the chlorination of ethylene and it is primarily used as a chemical intermediate in the production of vinyl chloride. It was used as a scavenger for tetraethyl lead in petrol.

1,2-Dichloroethane can also form through the degradation of other chlorinated hydrocarbons in the environment (Defra and Environment Agency, 2004). There are no known naturally occurring sources of 1,2-dichloroethane in the environment.

Releases of 1,2-dichloroethane to the environment mainly result from its manufacture, use, storage, distribution, and disposal of waste containing 1,2-dichloroethane. 1,2-Dichloroethane may also be released to the environment from the microbial degradation of other chlorinated alkanes. For example, 1,2-dichloroethane is a known product of the anaerobic biodegradation of 1,1,2,2-tetrachloroethane.

2. DERIVATION OF LOW LEVEL OF TOXICOLOGICAL CONCERN FOR 1,2-DICHLOROETHANE

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). The remainder of this section demonstrates the application of this framework to 1,2-dichloroethane. 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).

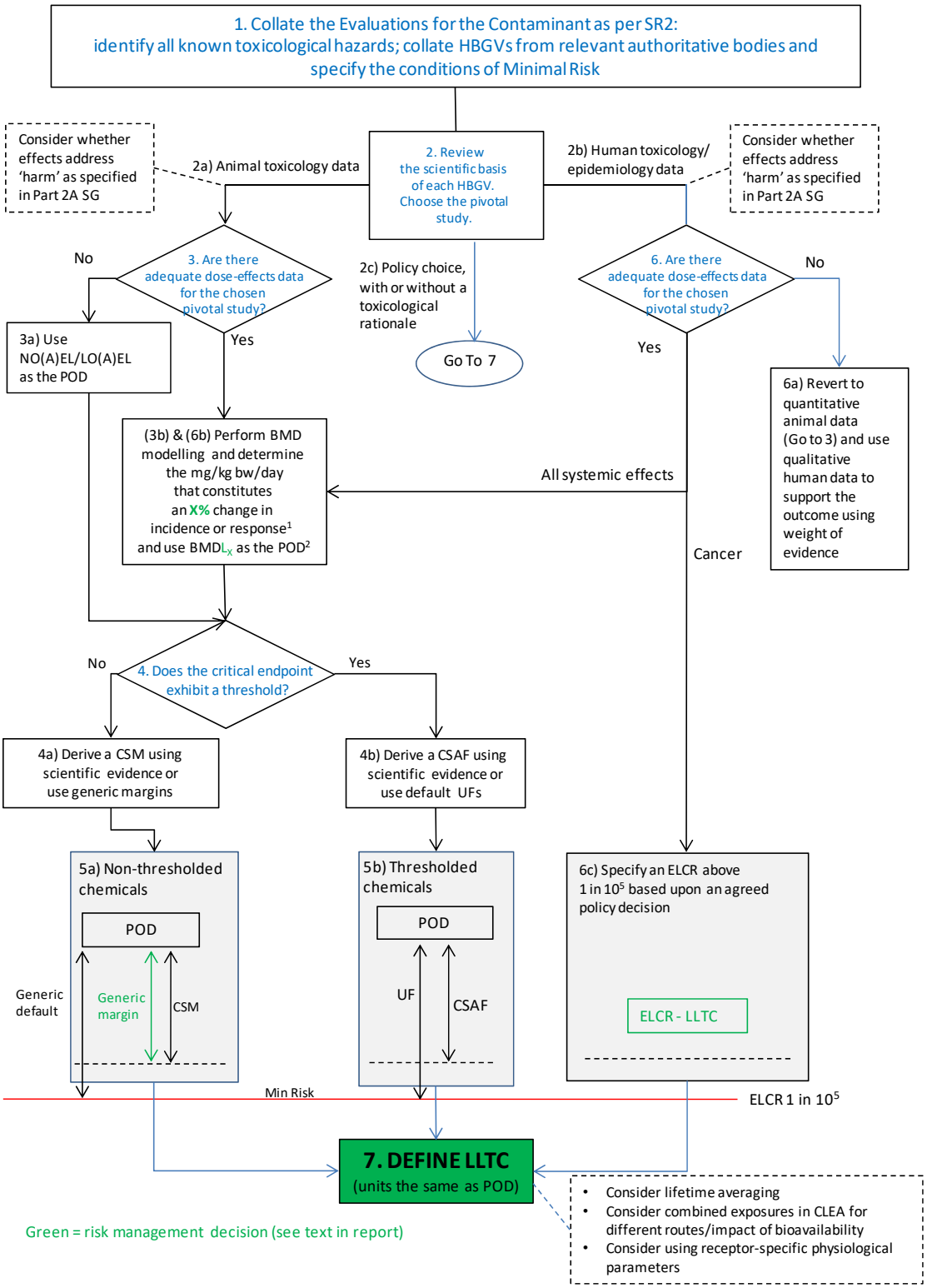


Figure 2.1: A framework for evaluating chemical-specific toxicology data for the purposes of LLTC derivation (reproduced from Figure 2.2 of SP1010 (CL:AIRE, 2014))

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 tumours at multiple sites, including squamous cell carcinomas of the stomach and haemangiosarcomas in male rats; adenocarcinomas of the mammary gland in female rats; alveolar/bronchiolar adenomas in male and female mice and mammary adenocarcinomas and endometrial stromal polyps or sarcomas (combined) in female mice are some of the most sensitive[1] toxicological effects following exposure to 1,2-dichloroethane by the oral route (WHO, 2003; IPCS, 1998; ECHA, 2015; Health Canada, 2014).

1,2-Dichloroethane also exerts threshold effects, with the kidneys being the primary target for non-cancer effects in animals. Renal effects include renal tubular regeneration, increased absolute and relative kidney weight and kidney lesions (ATSDR, 2001; Health Canada, 2014; OEHHA, 2005).

As a result, both a threshold and a non-threshold $LLTC_{oral}$ have been derived for 1,2-dichloroethane to ensure that the C4SL is suitably protective for both effects.

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

Non-threshold effects

The critical endpoint selected from the available studies is tumours at multiple sites. Based on all the data available, the 78 week National Cancer Institute (NCI) study (NCI, 1978) has been selected as the pivotal study.

Osborne-Mendel rats and B6C3F1 mice (50 per sex per dose) were administered 1,2-dichloroethane in corn oil via gavage, five days per week for 78 weeks followed by a 32-week observation period. Time-weighted doses for male and female rats were 47 or 95 mg kg^{-1} bw day^{-1}; for male mice were 97 or 195 mg kg^{-1} bw day^{-1} and for female mice were 149 or 299 mg kg^{-1} bw day^{-1}. Increases in the incidences of squamous cell carcinoma of the forestomach and haemangiosarcoma were observed in male rats; adenocarcinoma of the mammary gland was observed in female rats; mammary adenocarcinomas and endometrial stromal polyps or sarcomas were observed in female mice; and alveolar/bronchial adenomas were observed in male and female mice. (NOTE: some carcinomas may not be relevant to humans or may be very rare e.g. haemangiosarcoma).

NCI (1978) was selected by a number of authoritative bodies as the pivotal study for the derivation of their HBGVs including Defra and Environment Agency (2004), WHO (2003, 2017), IPCS (1998), Health Canada (1994), US EPA (1987) and OEHHA (1999, 2005). However, Health Canada (2014), ATSDR (2001) and US EPA (2010) noted the quality of the NCI (1978) study to be limited. This was due to reasons including: dosage adjustments

[1] In defining minimal/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/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 data, and is an important departure from the principles of evaluation of minimal or tolerable risk described in SR2.

throughout the course of the bioassay; potential for contamination by other volatile organic compounds; poor survival rates of treated animals; imprecise reporting of the purity of the 1,2-dichloroethane; the use of a corn oil vehicle which can alter the absorption of lipophilic compounds and induce spontaneous tumours; and small numbers of concurrent controls. As a result, Health Canada (2014) (and ECHA (2015)) carried out route to route extrapolation from inhalation to oral exposure using Nagano *et al.* (2006) as the pivotal study using physiologically based pharmacokinetic modelling. US EPA (2010) rejected the NCI (1978) study in favour of a 13 week (sub-chronic) duration study (NTP, 1991) as the basis for deriving a chronic oral provisional RfD.

It is recognised that the NCI (1978) study is of poor quality. However, it was considered more appropriate to select an oral study as the basis of the C4SL for 1,2-dichloroethane than to carry out route to route extrapolation from an inhalation study (even if the latter is considered more robust). It is noted that most authoritative bodies have not updated their respective HBGVs since Nagano *et al.* (2006) was published. However, where updates have been made (e.g. Health Canada (2014)) route to route extrapolation has sometimes been used. Should further authoritative bodies choose this approach in favour of the NCI (1978) study in the future, then the C4SL for 1,2-dichloroethane may be reconsidered.

Threshold effects

The critical non-carcinogenic endpoints are renal tubular regeneration, increased absolute and relative kidney weight, and kidney lesions. Based on all the data available, the 13-week NTP study (NTP, 1991) has been selected as the pivotal study.

The 13-week oral study was conducted in groups of F344/N rats, Sprague-Dawley and Osborne-Mendel rats (20 males and 10 females per group), and B6C3F1 mice (10 males and females per group). The animals were administered doses of 0, 500, 1000, 2000, 4000 or 8000 ppm 1,2-dichloroethane in drinking water for 13 weeks. The intake for female F344/N rats (selected due to them being the most sensitive sex/strain) from drinking water was estimated as 58, 102, 182, 320 and 601 mg kg^{-1} bw day^{-1}, respectively.

Additional groups of F344/N rats (10 or 20 males and 10 females) were administered 1,2-dichloroethane in corn oil by gavage five days per week for 13 weeks. The doses for these groups were 0, 30, 60, 120, 240 or 480 mg kg^{-1} bw day^{-1} for males and 0, 18, 37, 75, 150 or 300 mg kg^{-1} bw day^{-1} for females. Kidney effects were observed even at the lowest dose, hence a No Observed Adverse Effect Level (NOAEL) could not be determined.

Most authoritative bodies selected NTP (1991) as the pivotal study for the derivation of non-cancer HBGVs, including OEHHA (1999), US EPA (2010), ATSDR (2001) and Health Canada (2014). There is general agreement between the authoritative bodies that the drinking water study was more representative of human exposure than the gavage study, although there were differences in the critical endpoint selected. ATSDR (2001) and US EPA (2010) considered increases in kidney weights of >10% to be the critical effect. ATSDR considered this effect represented an early-stage adverse effect as histopathological changes in the kidney were observed at higher doses. Health Canada (2014) selected renal tubular regeneration and OEHHA (1999) selected kidney lesions.

Confidence in the NTP study was considered to be medium by US EPA (2010) due to the fact that a NOAEL could not be identified for F344/N rats.

GO TO FLOWCHART ELEMENT 3

2b) Human Toxicology/Epidemiology Data

No suitable human or epidemiological data were located following oral exposure to 1,2-dichloroethane.

GO TO FLOWCHART ELEMENT 6

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

The UK drinking water standard for 1,2-dichloroethane is 3.0 µg L^{-1} which is equivalent to an intake of 0.086 µg kg^{-1} bw day^{-1} for a 70 kg adult drinking 2 L of water per day. This is lower than the $LLTC_{oral}$ derived from toxicological data (see Section 2.1.10) and therefore does not affect the final choice of $LLTC_{oral}$. This is consistent with the position that the C4SL should not disproportionately target exposure to soil compared to other media such as water or air (CL:AIRE, 2014).

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 (threshold)		
X (non-threshold)		

The data from the NCI (1978) on multi-site tumours and NTP (1991) on kidney toxicity are considered to be the pivotal studies for non-threshold and threshold effects, respectively. Such studies could form the basis of the $LLTC_{oral}$.

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

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

Not applicable. There are adequate quantitative data available to enable benchmark dose (BMD) modelling for both threshold and non-threshold effects.

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

Non-threshold effects

IPCS (1998) carried out benchmark dose modelling (multistage model) on the tumour data from the NCI (1978) study. The data were adjusted for continuous exposure for a standard duration of 104 weeks and corrected for the expected rate of increase in tumour formation in rodents. A scaling factor to account for differences in the body surface area in rodents and humans was not considered to be appropriate because carcinogenicity is likely to be due to a metabolite rather than the parent compound. Doses associated with a 5% increase in tumour incidence ($TD_{0.05}$ – equivalent to a BMD_5) were determined to be between 6.20 and 34.0 mg kg^{-1} bw day^{-1} across exposure groups (IPCS, 1998). For the purposes of deriving an LLTC, the lowest $TD_{0.05}$ i.e. 6.20 mg kg^{-1} bw day^{-1} is proposed as the point of departure (POD).

Threshold effects

US EPA (2010) undertook BMD modelling using US EPA Benchmark Dose Software (BMDS) (v2.0) on the data on absolute and relative kidney weights in female F344/N rats exposed to 1,2-dichloroethane via drinking water in the 13-week NTP study. A model fit was not achieved with any continuous data model even when high doses were sequentially excluded. As a result, US EPA (2010) reverted to using a lowest observed adverse effect level (LOAEL) of 58 mg/kg bw/day to calculate its reference dose.

However, Health Canada (2014) undertook BMD modelling, using BMDS (v2.2), on the data from the 13-week NTP study but considered tubular regeneration and thymal necrosis to be the critical effects. The report noted that significant increases in relative and absolute kidney weights occurred in most exposed females of all strains and species and in many male exposure groups, particularly those with highest levels of exposure. Renal tubular regeneration was present in male and female rats and mice in all drinking water studies. Health Canada noted that 'the endpoint was considered for the dose-response assessment

because dose-related increases in tubular regeneration occurred in female F344 rats and male B6C3F1 mice'.

Therefore, using the Weibull model and a benchmark response of 10% extra risk, Health Canada determined a BMD_{10} of 142 mg kg^{-1} bw day^{-1} in female rats and the corresponding 95th lower confidence limit ($BMDL_{10}$) of 78.0 mg kg^{-1} bw day^{-1}.

For the purposes of deriving an LLTC, the BMD_{10} of 142 mg kg^{-1} bw day^{-1} is proposed.

GO TO FLOWCHART ELEMENT 4a/b

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

1,2-Dichloroethane exhibits both non-threshold and threshold endpoints, namely multi-site tumours (non-threshold), and renal effects including increases in absolute and relative kidney weight, renal tubular regeneration and kidney lesions (threshold). Both threshold and non-threshold effects are evaluated in order to derive the most appropriate LLTC in accordance with the framework.

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

For the derivation of a non-threshold $LLTC_{oral}$ for 1,2-dichloroethane, a margin of 5,000 is proposed in conjunction with the $TD_{0.05}$. This relates to a notional minimal risk level of 1 in 100,000 as defined in SR2 (Environment Agency, 2009). Due to the poor quality of the NCI study (NCI, 1978) discussed in Section 2.1.2, the data were not sufficiently reliable to adequately model the dose response. In addition, IPCS (1998) does not provide information on how the $TD_{0.05}$ was derived including how the dose was corrected for the expected rate of increase in tumour formation in a standard 104-week study. Therefore, it was not considered appropriate to move away from minimal risk for the $LLTC_{oral}$ for 1,2-dichloroethane.

GO TO FLOWCHART ELEMENT 5a

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

For the derivation of a threshold $LLTC_{oral}$ for 1,2-dichloroethane, uncertainty factors (UF) are proposed as follows:

- Intraspecies variability: 10 (to account for toxicokinetic and toxicodynamic variability within the human population);
- Interspecies variability: 10 (to account for toxicokinetic and toxicodynamic variability between humans and rats); and
- Sub-chronic to chronic effects: 10.

Therefore, an UF of 1,000 is proposed.

This compares with a wide range of UFs used by authoritative bodies ranging from 300 to 10,000 and which reflect the poor quality of the study. Health Canada (2014) and OEHHA (2005) both selected UFs of 1,000.

GO TO FLOWCHART ELEMENT 5b

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

For non-thresholded chemicals, the LLTC is calculated by dividing the POD by the relevant margin (either a generic margin or a chemical specific margin (CSM)

POD/margin = LLTC (units as per POD)

For thresholded chemicals, the POD is divided by a chemical-specific assessment factor (CSAF) (or default UF);

POD/(CSAF or default UF) = LLTC (units as per POD)

Table 2.1 presents the choices of POD, choices of margin/UF and the resultant LLTCs.

Table 2.1: Proposed choices of oral LLTC values

	POD	Value (mg kg^{-1} bw day^{-1})	CSM/UF	LLTC (μg kg^{-1} bw day^{-1})
LLTC (non-threshold)	$TD_{0.05}$	6.20	5,000	1.24
LLTC (threshold)	BMD_{10}	142	1,000	142

GO TO FLOWCHART ELEMENT 7

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

Based upon a scientific evaluation of an oral study (by gavage) in rats and mice (NCI, 1978), an **oral LLTC of 1.24 μg kg^{-1} bw day^{-1}** is proposed for non-threshold effects, based on a $TD_{0.05}$ of 6.2 mg kg^{-1} bw day^{-1} and a margin of 5,000.

This LLTC value is two orders of magnitude lower than the LLTC calculated for threshold effects. It is an order of magnitude higher than the current Defra and Environment Agency (2004) value of 0.12 μg kg^{-1} bw day^{-1} which is based on an excess lifetime cancer risk (ELCR) of 1 in 1,000,000.

Due to the poor quality of the NCI study which was discussed in Section 2.1.2, it was decided that the LLTC should be based on an ELCR of 1 in 100,000, rather than an ELCR of 1 in 50,000 as described in Defra (2014) to represent low risk. Moreover, the LLTC value is based on tumours in rats that are extremely rare in humans.

Overall, this LLTC is considered to be a pragmatic level for setting a C4SL which is suitably protective of all health effects including cancer in the general population.

2.2 INHALATION ROUTE

2.2.1 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 inhalation route of exposure has been undertaken and is provided in Appendix A. This review indicates that tumours of the mammary glands including adenoma, fibroadenoma and adenocarcinoma are the most sensitive[2] carcinogenic effects following exposure to 1,2-dichloroethane by the inhalation route (IPCS, 1998; ECHA, 2015).

1,2-Dichloroethane also exerts threshold effects with the liver being the primary target for non-cancer effects in animals. Effects include fatty degeneration, cloudy swelling and necrosis of the liver.

[2] In defining minimal/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/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 data and is an important departure from the principles of evaluation of minimal or tolerable risk described in SR2.

2.2.2 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

Non-threshold effects

Based on all the data available, the study by Nagano *et al.* (2006) has been selected as the pivotal study for non-threshold effects. Combined adenoma, fibroadenoma and adenocarcinoma were considered to be the critical endpoints.

F344/DuCrj rats and Crj:BDF1 mice (50 per sex per dose) were exposed via whole body exposure to 1,2-dichloroethane vapour, six hours per day, five days per week for two years. The rats were exposed to 0, 10, 40 or 160 ppm (equivalent to 0, 41.1, 164.5 or 658.1 $mg.m^{-3}$) [3] and the mice were exposed to 0, 10, 30 or 90 ppm (equivalent to 0, 41.1, 123.4 and 370.2 $mg.m^{-3}$). Dose-dependent increases in incidences of benign and malignant tumours were observed, including: subcutaneous fibroma, mammary gland fibroadenoma and peritoneal mesothelioma in male rats; subcutaneous fibroma and mammary gland adenoma, fibroadenoma and adenocarcinoma in female rats; and broncho-alveolar adenoma and carcinoma, endometrial stromal polyp, mammary gland adenocarcinoma and hepatocellular adenoma in female mice. No overt toxic responses were produced other than tumour formation (Nagano *et al.,* 2006).

The Nagano *et al*. (2006) inhalation study was selected by Health Canada (2014) as the pivotal study from which to derive an oral HBGV for drinking water, using physiologically based pharmacokinetic modelling for route to route extrapolation. It was also used by ECHA (2015) and in the REACH dossier (ECHA, 2018) to discuss inhalation responses.

Since the Nagano *et al*. (2006) study was published, few authoritative bodies have updated their assessments of the inhalation effects of 1,2-dichloroethane and it has therefore not been widely used in the derivation of HBGVs to date. Prior to the publication of the Nagano *et al.* (2006) study, the available studies did not provide conclusive evidence that 1,2-dichloroethane was carcinogenic by the inhalation route. Authoritative bodies such as IPCS (1998) and US EPA (1987) which did choose to consider carcinogenicity undertook route to route extrapolation from the oral NCI (1978) study.

Threshold effects

A number of studies including Cheever *et al.* (1990), Spencer *et al*. (1951), Heppel *et al.* (1946), Hofmann *et al*. (1971) and Spreafico *et al.* (1980) were cited by other authoritative bodies such as WHO (2000, 2015), ATSDR (2001) and OEHHA (2000). However, all studies had methodological issues and were not considered to be appropriate as a basis of the LLTC.

GO TO FLOWCHART ELEMENT 3.

2b) Human Toxicology/Epidemiology Data

No suitable human/epidemiological data were located.

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

Not applicable to the derivation of an inhalation LLTC for 1,2-dichloroethane.

GO TO FLOWCHART ELEMENT 3

[3] Calculated from 1 ppm = 4.11 $mg.m^{-3}$ at 20^0C and 1 atm pressure

2.2.3 FLOWCHART ELEMENT 3: Are there adequate dose-effects data for the chosen pivotal study to perform BMD modelling – animal data?

Yes	No	Not applicable
X		

The data from Nagano *et al.* (2006) on combined mammary gland tumours (adenoma, adenocarcinoma and fibroadenoma) is considered to be the pivotal study from which to derive an $LLTC_{inhal}$.

GO TO FLOWCHART ELEMENT 3b

2.2.4 FLOWCHART ELEMENT 3b: Perform BMD modelling

For the non-threshold effects, there are good quantitative data available (Nagano *et al.,* 2006).

The REACH dossier (ECHA, 2018) calculated a benchmark concentration for a 10% increased incidence of cancer (BMC_{10}) of 160 mg m^{-3}. The study in the dossier was unnamed, but the details provided indicate that data from Nagano *et al.* (2006) were used. However, as the details of the modelling were not provided, the BMC_{10} was deemed inappropriate as the basis of the $LLTC_{inhal}$.

BMDS version 2.7 was used to fit dichotomous models to incidence data for combined mammary tumours (adenoma, adenocarcinoma and fibroadenoma) in female F344 rats exposed to 1,2-dichloroethane from the two-year study by Nagano *et al.* (2006).

The dose-response models used to fit the data included:

- Gamma model
- Logistic model
- LogLogistic model
- LogProbit model
- Multistage model
- Multistage-Cancer model
- Probit model
- Weibull model
- Quantal-Linear model

The BMC_{10} and the corresponding 95th lower confidence limit ($BMCL_{10}$) were calculated associated with a benchmark response of 10% extra risk of the effect occurring. For the derivation of the LLTC, the BMC_{10} value is selected as the POD.

To assess the acceptability of the different models, various criteria were evaluated in accordance with good practice (US EPA, 2012). In general, model fit was assessed by a chi-square goodness of fit test (*i.e.* models with $p<0.1$ failed the goodness of fit criterion) and the Akaike Information Criteria (AIC) value. Smaller AIC values indicate a better fit of data. Of the models exhibiting adequate fit, the model with the lowest AIC value was selected as the best fit model as long as the BMCLs calculated from all models were 'sufficiently close' (US EPA, 2012).

Data from BMD modelling for non-thresholded effects are presented in Table 2.2 and the modelling output from BMDS is shown in Figure 2.2. The outputs from the BMD modelling were adjusted for continuous exposure and converted from mg m^{-3} to mg kg^{-1} bw day^{-1} assuming that a 70 kg adult breathes 20 m^3 day^{-1}.

Table 2.2: BMC_{10} and $BMCL_{10}$ calculations from the best fitting models for non-thresholded endpoints

POD	Endpoint	Species/ sex	Model	AIC	Adjusted BMC_{10} (mg m^{-3})	Adjusted BMC_{10} (mg kg^{-1} bw day^{-1})
BMC_{10}	*Adenoma, adenocarcinoma and fibroadenoma*	*Female F344 rats*	*Logistic*	*213.98*	*37.5*	*10.7*
$BMCL_{10}$	*Adenoma, adenocarcinoma and fibroadenoma*	*Female F344 rats*	*Logistic*	*213.98*	*29.4*	*8.40*

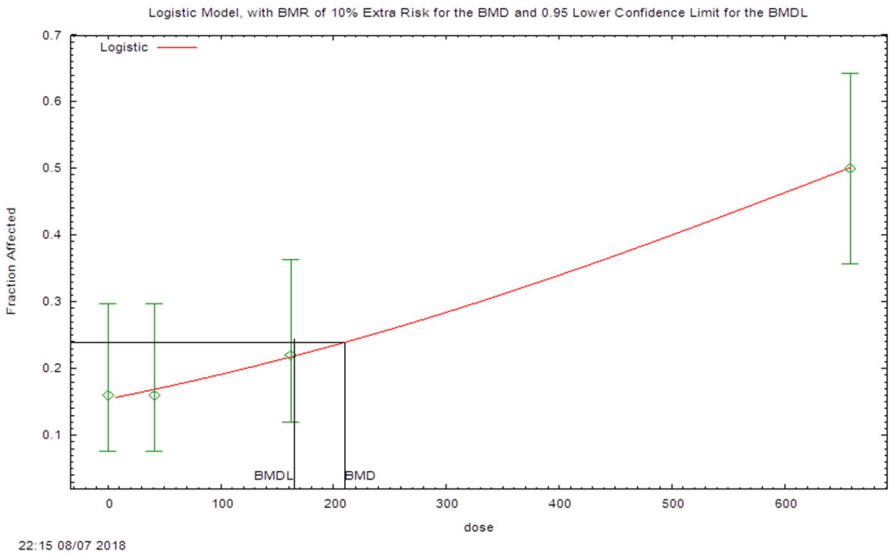


Figure 2.2: Multistage cancer model of combined mammary tumours (adenoma, adenocarcinoma and fibroadenoma) in female F344 rats

For the purposes of deriving an inhalation LLTC for non-threshold effects, a BMC_{10} of 10.7 mg kg^{-1} bw day^{-1} (equivalent to 37.5 mg m^{-3} assuming that a 70 kg adult breathes 20 m^3 day^{-1}) is proposed, based on combined mammary tumours (adenoma, adenocarcinoma and fibroadenoma) in female F344 rats.

GO TO FLOWCHART ELEMENT 4a/b

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

Yes	No	Not applicable
	X	

1,2-Dichloroethane exhibits both non-threshold and threshold endpoints, namely mammary tumours (non-threshold) and liver effects (threshold). However due to the poor quality of the studies reporting threshold effects, only carcinogenic (non-threshold effects) are evaluated to derive an LLTC.

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

For the derivation of a non-threshold $LLTC_{inhal}$ for 1,2-dichloroethane, a generic margin of 5,000 is proposed in conjunction with the BMC_{10}. This relates to a notional 'low' risk level of 1 in 50,000 as described in Defra (2014).

GO TO FLOWCHART ELEMENT 5a

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

For non-thresholded chemicals, the LLTC is calculated by dividing the POD by either a generic margin or a CSM.

POD/margin = LLTC (units as per POD)

Table 2.3 presents the choice of POD, choices of margin and the resultant LLTCs.

Table 2.3: Proposed choice of inhalation LLTC value

	POD	Value (mg kg^{-1} bw day^{-1})	CSM/CSAF	LLTC (μg kg^{-1} bw day^{-1})
LLTC (non-threshold)	BMC_{10}	10.7	5,000	2.14

GO TO FLOWCHART ELEMENT 7

2.2.8 FLOWCHART ELEMENT 7: Assess LLTC for 1,2-dichloroethane

Using the scientific evidence from the Nagano *et al.* (2006) inhalation study in female F344DuCrj rats, an **inhalation LLTC of 2.14 μg kg^{-1} bw day^{-1}** is proposed, based on a BMC_{10} of 10.7 mg kg^{-1} bw day^{-1} and a margin of 5,000 for non-threshold effects.

This LLTC value is higher than the previous Defra and Environment Agency (2004) minimal risk value of 0.12 μg kg^{-1} bw day^{-1}. However, it is based on a more recent, well conducted two year study that provided more robust evidence that 1,2-dichloroethane is carcinogenic via inhalation and is therefore a more appropriate study to use. Most authoritative bodies undertook their evaluations prior to the publication of Nagano *et al.* (2006). IPCS (1998) and Defra and Environment Agency (2004) selected non-threshold effects based on route to route extrapolation from oral animal studies (see NCI (1978) in Section 2.1.2).

Therefore, this LLTC is considered to be a pragmatic level for setting a C4SL and is suitably protective of all health effects including cancer in the general population.

2.3 DERMAL ROUTE

Few data were found on acute or chronic effects via the dermal route. Defra and Environment Agency (2004) report on one study (Van Duuren *et al.*, 1979) in which pulmonary papillomas were observed in mice treated with 126 mg 1,2-dichloroethane in acetone 3 times/week for 428-576 days. ATSDR stated that 'the results, which indicate a significant increase in benign tumours remote from the site of application, provide suggestive or supportive evidence that 1,2-dichloroethane is carcinogenic and that it can penetrate through the skin into the circulatory system' (ATSDR, 2001). It should be noted that such tumours are indeed benign in humans.

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 1,2-dichloroethane. This is considered to be appropriate because animal studies have determined 1,2-dichloroethane to be genotoxic via all routes and the oral LLTC is lower than the inhalation LLTC.

2.4 MEAN DAILY INTAKE

The oral and inhalation LLTC recommended for 1,2-dichloroethane are based on non-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 not to be included in the exposure modelling for comparison with the oral LLTC. For information purposes, a review of MDI data from food, air and drinking water sources is discussed in Section 4.2 below.

3. EXPOSURE MODELLING FOR 1,2-DICHLOROETHANE

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 and 2009b), the assessment criteria are normally integrated by CLEA to determine an overall assessment criterion 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.

In the case of 1,2-dichloroethane, the critical effects for the LLTC via both oral and inhalation routes of exposure are systemic and the integrated approach has been taken to determine the C4SLs for 1,2-dichloroethane.

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 1,2-dichloroethane are shown in Table 3.1.

Table 3.1: Contaminant specific parameter values used for derivation of C4SLs for 1,2-dichloroethane

Parameter	Units	Value	Source/Justification
Air-water partition coefficient	dimensionless	0.0238	CLEA SR7, Environment Agency, 2008
Diffusion coefficient in air	$m^2 s^{-1}$	8.60×10^{-06}	CLEA SR7, Environment Agency, 2008
Diffusion coefficient in water	$m^2 s^{-1}$	6.74×10^{-10}	CLEA SR7, Environment Agency, 2008
Relative molecular mass	$g\ mol^{-1}$	98.96	CLEA SR7, Environment Agency, 2008
Vapour pressure	Pa	4,920	CLEA SR7, Environment Agency, 2008
Water solubility	$mg\ L^{-1}$	8,680	CLEA SR7, Environment Agency, 2008
Log Koc	Log $cm^3\ g^{-1}$	1.30	CLEA SR7, Environment Agency, 2008
Log Kow	dimensionless	1.48	CLEA SR7, Environment Agency, 2008
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	CLEA SR3, Environment Agency, 2009b (Note that CLEA does not model soil-to-plant concentration factors for organic substances for herbaceous or shrub fruit)
Soil-to-plant concentration factor (root vegetables)		modelled	
Soil-to-plant concentration factor (tuber vegetables)		modelled	
Soil-to-plant concentration factor (herbaceous fruit)		-	
Soil-to-plant concentration factor (shrub fruit)		-	
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	CLEA SR3, Environment Agency, 2009b
Relative bioavailability soil	-	1	Conservative assumption made that bioavailability of 1,2-dichloroethane in soil and dust is the same as bioavailability of 1,2-dichloroethane 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 1,2-dichloroethane are discussed briefly below.

Soil to dust transport factor

The soil to dust transport factor should be contaminant specific, but where such data are not available the Environment Agency (2009b) recommends a default value of 0.5 g g^{-1} 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 used to calculate the C4SLs in this report.

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 1,2-dichloroethane has been modelled using the method for organic chemicals within the CLEA software.

CLEA predicts the greatest exposure to 1,2-dichloroethane from consumption of homegrown produce to be via root vegetables and tree fruit for both the residential and allotments scenarios. 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 1,2-dichloroethane and it is considered appropriately conservative to assume a relative bioavailability of 100% for the derivation of C4SLs.

4. C4SLs FOR 1,2-DICHLOROETHANE

4.1 C4SLS

The C4SLs for 1,2-dichloroethane 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 1,2-dichloroethane

Land-use	C4SLs (mg.kg^{-1})		
	SOM Content		
	1.0%	2.5%	6.0%
Residential with consumption of homegrown produce	0.11	0.18	0.31
Residential without consumption of homegrown produce	0.16	0.24	0.41
Allotments	0.054	0.10	0.19
Commercial	12	17	29
Public Open Space (residential)	300	310	310
Public Open Space (park)	300	330	380

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 C4SLs see Section 4.2 below.

The ADE:HCV[4] ratio at the C4SL (6% SOM) for both oral / dermal route and the inhalation routes of entry are shown in Table 4.2. The relative contribution of each exposure pathway contributing to the C4SL (6% SOM) is shown for each land-use in Table 4.3.

Table 4.2: ADE:HCV ratios at C4SLs derived at 6% SOM

Land-use	ADE:HCV Ratio Oral and dermal routes of entry	ADE:HCV Ratio Inhalation route of entry
Residential with consumption of homegrown produce	0.24	0.76
Residential without consumption of homegrown produce	0.00	1.00
Allotments	1.00	0.00
Commercial	0.01	0.99
Public Open Space (residential)	0.98	0.02
Public Open Space (park)	0.58	0.42

[4] "ADE:HCV ratio" is the term used within the CLEA model, referring to the ratio between the average daily exposure and the health criteria value. Although an LLTC is used in place of the HCV the terminology has been retained, reflecting the CLEA output.

Table 4.3: 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	0.12	0.14	0.03	0.62	90.94	40.18
Sum of consumption of homegrown produce and attached soil	15.26	0.00	99.92	0.00	0.00	0.00
Dermal contact (indoor)	0.00	0.00	0.00	0.04	2.75	0.00
Dermal contact (outdoor)	0.00	0.00	0.02	0.06	3.22	3.97
Inhalation of dust (indoor)	0.00	0.00	0.00	0.00	0.32	0.00
Inhalation of dust (outdoor)	0.00	0.00	0.00	0.00	0.00	0.01
Inhalation of vapour (indoor)	84.61	99.85	0.00	99.21	0.00	0.00
Inhalation of vapour (outdoor)	0.00	0.00	0.03	0.07	2.77	55.84
Oral background	0.00	0.00	0.00	0.00	0.00	0.00
Inhalation background	0.00	0.00	0.00	0.00	0.00	0.00

Based on the information in Tables 4.2 and 4.3, the principal risk driving pathways for 1,2-dichloroethane 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} 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 1,2-dichloroethane include the following:

- Since 1-2-dichloroethane is a potential human carcinogen (see above), it might be necessary to apply the "As Low as Reasonably Practicable" (ALARP) principle in relation to its remediation at specific sites (see Environment Agency, 2009a; 2009b for details). The principle of ALARP applies to the regulation and management of non-threshold chemicals in the UK. It is important to note that ALARP remains the overriding principle even when a margin of exposure or minimal risk level or LLTC suggests there is a minimal/low concern for human health. What is considered practicable is a remediation/risk management decision and could be lower or higher than the scientific values derived.
- Intake of 1,2-dichloroethane from non-soil sources (food, water and air) has been considered as follows:
    - The UK Drinking Water Inspectorate reports 99th percentile concentrations of 1,2-dichloroethane measured in tap water for all thirty water companies in England and Wales. The average of the reported 99th percentile concentrations for 2016 was 0.14 µg.L^{-1}. Assuming a 70 kg adult drinks 2 L of water per day, this equates to a daily intake of 0.28 µg kg^{-1} bw day^{-}

[1], which is approximately 23% of the oral LLTC. Given that this background exposure is based on 99th percentile concentrations, background oral exposure is likely to be typically much less.
    - Negligible concentrations are likely to be present in food and intake from food sources was not included in the oral MDI by Defra and Environment Agency (2004).
    - An MDI of 20 µg day^{-1} of 1,2-dichloroethane in air was estimated from an ambient air concentration of 1 µg m^{-3} (based on average measured concentrations in urban air (Defra and Environment Agency, 2004)) multiplied by an assumed adult respiration rate of 20 m^3 day^{-1}. This MDI equates to an intake of 0.29 µg kg^{-1} bw day^{-1}, which is approximately 14% of the inhalation LLTC.

- 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 1,2-dichloroethane 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 1,2-dichloroethane (Johnson *et al.*, 2012). 1,2-Dichloroethane 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 soils analytical data from two main commercial laboratories in the UK: Out of a total of approximately 6,100 soil samples analysed for 1,2-dichloroethane only 7.1% had a concentration above the limit of detection (1 to 10 µg kg^{-1}), with the vast majority of the detected concentrations being less than 50 µg kg^{-1}.
- Table 4.3 shows that for land-uses where the inhalation of vapour (indoor) exposure pathway is active (i.e. 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 1,2-dichloroethane and subsequent transport. Where exposure to soil vapour forms the principal risk driving pathway then further consideration should be given to supporting the assessment such as obtaining site specific empirical data for soil vapour and indoor air concentrations. The reader is referred to CIRIA (2009) and SoBRA (2018) for further guidance on this.
- The lowest derived C4SL in Table 4.1 of 0.054 mg kg^{-1} (54 µg kg^{-1}), which is for the Allotment land-use, is above the range of typical laboratory limits of detection for 1,2-dichloroethane in soil (typically circa 1 to 10 µg kg^{-1}).

5. REFERENCES

Agency for Toxic Substances and Disease Registry (ATSDR), 2001. Toxicological Profile for 1,2-Dicholoroethane.

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

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

Department for Environment Food and Rural Affairs (Defra) and Environment Agency, 2004. Contaminants in soil: Collation of toxicological data and intake values for humans. 1,2-Dichloroethane.

Defra, 2014. SP1010: Development of Category 4 Screening Levels for Assessment of Land Affected by Contamination – Policy Companion Document.

Environment Agency 2008. Compilation of Data for Priority Organic Pollutants for Derivation of Soil Guideline Values. Science Report SC050021/SR7. Environment Agency, Bristol, 2008.

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

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

European Chemicals Agency (ECHA), 2015. Application For Authorisation: Establishing A Reference Dose Response Relationship for Carcinogenicity Of 1,2-Dichloroethane' RAC/33/2015/09 Rev1 Final. 05 June 2015.

ECHA, 2018. REACH Registration Dossier: website https://echa.europa.eu/registration-dossier/-/registered-dossier/15430/1 (viewed April 2018).

Health Canada, 1994. Canadian Environmental Protection Act Priority Substances List Assessment Report: 1,2-Dichloroethane.

Health Canada, 2014. Guidelines for drinking water quality. Guideline technical document. February 2014.

International Programme on Chemical Safety (IPCS), 1998. World Health Organization (WHO). Concise International Chemical Assessment Document 1 (CICAD) 1,2-Dichloroethane.

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.

Nagano K., Umeda, Y., Senoh H,, Gotoh K., Arito, H., Yamamoto, S., and Matsushima, T., 2006. Carcinogenicity and Chronic Toxicity in Rats and Mice Exposed by Inhalation to 1,2-Dichloroethane for Two Years. J. Occup. Health 2006; 48: 424-436.

National Toxicology Program (NTP), 1991. Toxicity Studies of 1,2-Dichloroethane (Ethylene Bichloride) (CAS No. 107-06-2) in F334/N Rats, Sprague Dawley Rats, Osborne-Mendel Rats, and B5C3F1 Mice (Drinking Water and Gavage Studies). NIH Publication No. 91-3123.

National Cancer Institute (NCI), 1978. Bioassay of 1,2-dichloroethane for possible carcinogenicity. Technical Report Series, No. 55.

Office of Environmental Health Hazard Assessment, Californian Environmental Protection Agency (OEHHA), (1999). Public Health Goal for 1,2-Dichloroethane In Drinking Water.

OEHHA, 2000. Determination of Noncancer Chronic Reference Exposure Levels Batch 2A: Chronic Toxicity Summary Ethylene Dichloride (1,2-Dichloroethane).

OEHHA, 2005. Update of the Public Health Goal for 1,2-Dichloroethane' Memorandum, September 16 2005.

Society of Brownfield Risk Assessment (SoBRA), 2018. Vapour Intrusion to Support Sustainable Risk Based Decision Making. Summer Workshop 2017.

SoBRA, 2020. Development of Acute Generic Assessment Criteria for Assessing Risks to Human Health from Contaminants in Soil. Version 2.0. July 2020.

United States Environmental Protection Agency (US EPA), 1987. National Center for Environmental Assessment. Integrated Risk Information System (IRIS) Chemical Assessment Summary for 1,2-Dichloroethane (CASRN 107-06-2).

US EPA, 2010. National Center for Environmental Assessment. 'Provisional Peer-Reviewed Toxicity Values for 1,2-Dichloroethane (CASRN 107-06-2)' FINAL 10-1-2010.

US EPA, 2012. Benchmark Dose Technical Guidance. U.S. Environmental Protection Agency, Washington, DC 20460. EPA/100/R-12/001. June 2012.

Van Duuren B.L., Goldschmidt B.M., Loewengart G., Smith A.C., Melchionne S., Seidman I. and Roth D., 1979. Carcinogenicity of halogenated olefinic and aliphatic hydrocarbons. Journal of the National Cancer Institute 631433-1439.

WHO, 2000. Air Quality Guidelines for Europe, 2nd edition.

WHO, 2003. 1,2-Dichloroethane In Drinking Water: Background document for development of WHO Guidelines for Drinking-water Quality.

WHO, 2015. WHO Expert Consultation: Available evidence for the future update of the WHO Global Air Quality Guidelines (AQGs)', Meeting report Bonn, Germany 29 September - 1 October 2015.

APPENDIX A
HUMAN TOXICOLOGICAL DATA SHEET FOR 1,2-DICHLOROETHANE

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

Chemical: **1,2-Dichloroethane**

Human Health Hazard Profile - References

Authoritative bodies	Website	Checked (Y/N)	References
Environment Agency	hhttps://www.gov.uk/government/organisations/environment-agency	Y	Defra & EA *'Contaminants In Soil: Collation of Toxicological Data and Intake Values for Humans. 1,2-Dichloroethane'* Science Report Tox 22. August 2004.
Foods Standards Agency	http://www.food.gov.uk/	Y	None
Public Health England	https://www.gov.uk/government/organisations/public-health-england	Y	PHE *'1,2-Dichloroethane: General Information'* PHE publications gateway number 2014790. May 2017. PHE *'1,2-Dichloroethane: Incident Management'* PHE publications gateway number 2014790. January 2016.
Committee on Carcinogenicity	https://www.gov.uk/government/groups/committee-on-carcinogenicity-of-chemicals-in-food-consumer-products-and-the-environment-coc	Y	No statements, position papers or reports.
Committee on Mutagenicity	https://www.gov.uk/government/organisations/committee-on-mutagenicity-of-chemicals-in-food-consumer-products-and-the-environment	Y	No statements, position papers or reports.
Committee on Toxicity	http://cot.food.gov.uk/	Y	No statements, position papers or reports.
ECHA REACH - is there a dossier?	http://echa.europa.eu/information-on-chemicals	Y	https://echa.europa.eu/registration-dossier/-/registered-dossier/15430/1
EFSA - is there an opinion?	http://www.efsa.europa.eu/	Y	ECHA *'Application For Authorisation: Establishing A Reference Dose Response Relationship for Carcinogenicity Of 1,2-Dichloroethane'* RAC/33/2015/09 Rev1 Final. 05 June 2015.
		Y	No statements, position papers or reports.
JECFA	http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/en/?	Y	FAS 30-JECFA 39/89 Toxicological Monograph JECFA (1992) *'Evaluation of Certain Food Additives and Naturally Occurring Toxicants'* 39th report. WHO Technical Report Series 828.
WHO	http://www.who.int/en/	Y	WHO (2017) *'Guidelines for Drinking-water Quality'* Fourth Edition Incorporating the First Addendum WHO (2003) *'1,2-Dichloroethane In Drinking Water: Background document for development of WHO Guidelines for Drinking-water Quality.'* WHO(2000) *'Air Quality Guidelines for Europe'* 2nd edition. WHO *'WHO Expert Consultation: Available evidence for the future update of the WHO Global Air Quality Guidelines (AQGs)'* Meeting report Bonn, Germany 29 September - 1 October 2015 WHO (1999) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans *'Volume 71: Re-Evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide.'*
WHO IPCS	http://www.who.int/ipcs/en/	Y	WHO IPCS (1998) CICAD *'1,2-Dichloroethane'*
WHO EHC	http://www.who.int/ipcs/publications/ehc/en/	Y	WHO IPCS (1995) *'Environmental Health Criteria 176: 1,2-Dichloroethane'* 2nd edition
RIVM	https://www.rivm.nl/en	Y	RIVM (2001) *'Re-evaluation of human toxicological maximum permissible risk levels'* report 711701 025 A.J. Baars et al March 2001. RIVM (2017) *'Probit function technical support document'* 20170215 TSD probit 12-dichloorethaan_interim, 15 February 2017
US ATDSR	http://www.atsdr.cdc.gov/	Y	ATSDR *'Toxicological Profile for 1,2-Dicholoroethane'* September 2001
US EPA	http://www.epa.gov/	Y	USEPA National Center for Environmental Assessment *'Provisional Peer-Reviewed Toxicity Values for 1,2-Dichloroethane (CASRN 107-06-2)'* FINAL 10-1-2010 USEPA National Center for Environmental Assessment (1987) *'Integrated Risk Information System (IRIS) Chemical Assessment Summary for 1,2-Dichloroethane'* (CASRN 107-06-2)
US National Toxicology Program	https://ntp.niehs.nih.gov/	Y	NTP *'Toxicity Studies of 1,2-Dichloroethane In F344/N Rats, Sprague Dawley Rats, Osborne-Mendell Rats, and B6C3F1 Mice (Drinking Water and Gavage Studies'* NIH Publication No. 91-3123, January 1991. NCI (1978) *'Report n the Bioassay of 1,2-Dichloroethane for Possible Carcinogenicity'*
Health Canada	http://www.hc-sc.gc.ca/index-eng.php	Y	Health Canada (1994) *'Canadian Environmental Protection Act Priority Substances List Assessment Report: 1,2-Dichloroethane'* Health Canada (2014) *'Guidelines for drinking water quality'. Guideline technical document.*
Australia NICNAS	http://www.nicnas.gov.au/	Y	https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details?assessment_id=72#cas-A_107-06-2
Risk Assessment Information System	http://rais.ornl.gov	Y	https://rais.ornl.gov/tox/profiles/12dca.html#t45
Other scientific reviews	**Check for key reviews on pubmed**		
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment	https://oehha.ca.gov/	Y	OEHHA (1999) *'Public Health Goal for 1,2-Dichloroethane In Drinking Water'* OEHHA *'Update of the Public Health Goal for 1,2-Dichloroethane'* Memorandum September 16 2005 OEHHA (2000) *'Determination of Noncancer Chronic Reference Exposure Levels Batch 2A: Chronic Toxicity Summary Ethylene Dichloride (1,2-Dichloroethane)'*
Texas Commission on Environmental Quality	https://www.tceq.texas.gov/	Y	TCEQ (2016) *'Development Support Document: Ethylene Chloride CAS Reigstry Number: 107-06-2'*
EC Scientific Committee on Occupational Exposure Limits	http://ec.europa.eu/social/main.jsp?catId=148&intPageId=684&langId=en	Y	SCOEL (2016) *'SCOEL/REC/302 1,2-Dichloroethane (Ethylene dichloride)'*

NB. These weblinks were checked in March and April 2018, and may be subject to change at source.

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

Chemical: **1,2-Dichloroethane**

I) Human Health Hazard Profile - Toxicological Evidence

Most sensitive health effects:

Sensitive endpoints	Other information	Source of evidence
Carcinogenicity	Multiple tumours and sites (IARC Group 2B)	NCI 1978, Nagano et al 2006
Nephrotoxicity	Histological changes to kidneys	NTP 1991
Hepatotoxicity	Histological changes to liver	Cheever et al 1990

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
EXAMPLE: Draft USEPA 2010 RfD	*0.9*	*µg/kg bw/day*	*100*	*BMDL10*	*0.09*	*mg/kg bw/day*	*Epithelial hyperplasia*	*Based on epithelial hyperplasia in female mice (NTP 2008). NTP classified focal epithelial hyperplasia as a preneoplastic lesion so diffuse epithelial hyperplasia may also represent a preneoplastic lesion. However, although this lesion may progress to cancer (adenoma), EPA considered this to be a non-cancer endpoint because definitive data on the progression of this lesion does not exist. UF of 100 was applied (10 for inter and intraspecies differences; 1 to account for database deficiences).*	*USEPA, 2010. Toxicological Review of Contaminant X (CAS No. 00-00-0). In Support of Summary Information on the Integrated Risk Information System (IRIS). May 2010.*
WHO Drinking Water Guidelines ***Drinking Water Guideline***	0.86	µg/kg bw/day	NA	ELCR	1 in 100,000	NA	Squamous cell carcinoma of the stomach and hemangiocarcoma (male) and mammary adenocarcinoma (female)	WHO used data from NCI (1978) in which Osborne-Mendell rats and B6C3FI mice (50 per sex per dose), were administered 1,2-DCA in corn oil via gavage, 5 days/week for 78 weeks followed by 32 week observation. Time-weighted doses for rats were 47 or 95 mg/kg bw/day for males and females, respectively; for mice were 97 or 195 mg/kg bw/day (for male) and 149 or 299 mg/kg bw/day (for female). Increases in the incidences of squamous cell carcinoma of the forestomach and haemangiosarcoma were observed in male rats; adenocarcinoma of the mammary gland was observed in female rats; mammary adenocarcinomas and endometrial stromal polyps or sarcomas in female mice; and alveolar/bronchial adenomas in male and female mice. WHO applied the linearised multistage model to haemangiosarcomas observed in male rats and determined concentrations of 300, 30 and 3 µg/L corresponding to an ELCR of 10-4, 10-5 and 10-6. The HBGV was calculated based on an ELCR of 10-5, which correlates to 30 µg/L, assuming an adult weighing 70 kg drinks 2 L/day.	WHO (2017) *'Guidelines for Drinking-water Quality'* Fourth Edition Incorporating the First Addendum WHO (2003) *'1,2-Dichloroethane In Drinking Water: Background document for development of WHO Guidelines for Drinking-water Quality.'*
IPCS CICAD 1998 ***Guidance value***	0.12 - 0.68 to 1.2 - 6.8	µg/kg bw/day	5,000 to 50,000	$TD_{0.05}$	6.2 to 34	mg/kg bw/day	Squamous cell carcinoma of the stomach and hemangiocarcoma (male) and mammary adenocarcinoma (female)	IPCS used the study by NCI (1978) in which Osborne-Mendell rats and B6C3FI mice (50 per sex per dose), were administered 1,2-DCA in corn oil via gavage, 5 days/week for 78 weeks followed by 32 week observation. Time-weighted doses for rats were 47 or 95 mg/kg bw/day for males and femles, respectively; for mice were 97 or 195 mg/kg bw/day (for male) and 149 or 299 mg/kg bw/day (for female). Increases in the incidences of squamous cell carcinoma of the forestomach and haemangiosarcoma were observed in male rats; adenocarcinoma of the mammary gland was observed in female rats; mammary adenocarcinomas and endometrial stromal polyps or sarcomas in female mice; and alveolar/bronchial adenomas in male and female mice. NOTE: some carcinomas may not be relevant to humans e.g. forestomach. IPCS carried out multistage modelling adjusted for continuous exposure for a standard duration of 104 weeks and corrected for the expected rate of increase in tumour formation in rodents in a standard 104 week bioassay. Doses associated with a 5 % increase in tumour incidence (TD0.05) were between 6.2 and 34 mg/kg bw/day. Scaling factors to account for differences in body surface area between rodents and humans were not considered to be appropriate as carcinogenicity is likely to be due to a metabolite rather than the parent compound. The guidance value was derived by applying a margin of 5000 to 50,000 to the $TD_{0.05}$s, resulting in guideline values of between 1.2-6.8 µg/kg bw/day (6.2 or 34/5000) or 0.12-0.68 µg/kg bw/day(6.2 or 34/50,000).	WHO IPCS (1998) CICAD *'1,2-Dichloroethane'*
RIVM 2001 ***Provisional MPR***	1.4	µg/kg bw/day	N/A	ELCR	1 in 100,000	NA	Carcinogenicity	Using data from Vermeire et al (1991), a MPR of 14 µg/kg bw/day was set, which is associated with an ELCR of 10-4, calculated using linear extrapolation from the oral study in rats. 1.4 µg/kg bw/day is associated with an ELCR of 10-5. No other data on the study are available.	RIVM (2001) *'Re-evaluation of human toxicological maximum permissible risk levels'* report 711701 025 A.J. Baars et al March 2001.
ECHA 2015 ***Reference Dose Response T25*** *(oral, gen. pop)*	20,700	µg/kg bw/day	NA	T25	72.5	mg/m3	Combined mammary tumours - fibroadenomas, adenomas and adenocarcinomas	The inhalation study by Nagano et al 2006 was selected as the pivotal study and route to route extrapolation performed. The inhalation study was conducted in F33/DuCrj (SPF) rats, exposed to 1,2-DCA vapour (0, 10, 40 and 160 ppm / 0, 41, 164 and 658 mg/m3), 6 hours per day, 5 days per week for 2 years. A T25 was calculated using the combined frequency of mammary tumours, adenomas, fibroadenomas and adenocarcinomas. ECHA converted the T25 (inhalation, rat) of 98.8 ppm to a T25 (inhalation, gen. pop) of 17.6 ppm (72.5 mg/m3) to account for lifetime exposure for the general population (24 hours per day, 7 days per week). The T25 (inhalation, gen. pop) of 17.6 ppm (72.5 mg/m3) equates to a cancer risk of 3.45 x 10-6 per µg/m3. A HBGV (inhalation, gen. pop) of 20.7 mg/kg bw/day was calculated assuming a 70 kg adult breathes 20 m3 per day and 100 % absorption by the oral route compared to 100 % following inhalation exposure.	ECHA *'Application For Authorisation: Establishing A Reference Dose Response Relationship for Carcinogenicity Of 1,2-Dichloroethane'* RAC/33/2015/09 Rev1 Final. 05 June 2015. https://echa.europa.eu/registration-dossier/-/registered-dossier/15430/1

Health Canada 1994 ***Total daily intake***	0.43-0.7	µg/kg bw/day	NA	$TD_{0.05}$	6.2 to 297	mg/kg bw/day	Squamous cell carcinoma of the stomach and hemangiocarcoma (male) and mammary adenocarcinoma (female)	Health Canada used data from NCI (1978) as described by IPCS CICAD 1998. Based on multistage modelling, the TD0.05 ranged from 6.2-297 mg/kg bw/day. This differs from values cited by IPCS (who cited 6.2-34 mg/kg bw/day). The total daily intakes of 0.43-0.7 µg/kg bw/day equated to potency indices of 1.5x10-6 to 1.1x10-4. No information regarding UF used were given.	Health Canada (1994) *'Canadian Environmental Protection Act Priority Substances List Assessment Report: 1,2-Dichloroethane'*
Health Canada 2014 ***Drinking water guidelines - carcinogenic effects***	3	µg/kg bw/day	NA	ELCR	1 in 100,000	NA	Combined mammary adenoma, fibroadenoma, and adenocarcinoma	The Nagano (2006) chronic inhalation study in rats was selected as the pivotal study as Nagano exposed animals for a longer duration and maintained consistency in dosing levels and schedules. For information on the study see ECHA above. PBPK modelling was used to carry out route to route (inhalation to oral) extrapolation to estimate the relevant oral exposure levels. After estimating internal doses for each concentration, BMD modelling was carried out, using combined mammary adenoma, fibroadenoma, and adenocarcinoma in female rats as the most sensitive endpoint. As there are inadequate mode of action data for 1,2-DCA to discount the human relevance of mammary tumours, this was selected as the critical effect for the dose–response assessment. Using a multistage cancer slope factor for all combined tumours, the concentration of 1,2-DCA in drinking water associated with an ELCR of 10-4, 10–5 and 10−6 is 0.0027, 0.00027 and 0.000027 mg/l, respectively. To adjust from internal doses in animals to humans, allometric scaling was applied. Alternatively, a human PBPK model was used. Both approaches resulted in similar values but the PBPK modelling was used and gave an intake value of 0.003 mg/kg bw/day which was associated with an ELCR of 10-5.	Health Canada '*Guidelines for drinking water quality* '. Guideline technical document, 2014
IRIS 2008 ***Drinking Water Risk Concentration***	0.11	µg/kg bw/day	NA	ELCR	1 in 100,000	NA	Haemangiosarcoma Hepatocellular carcinoma	US EPA carried out linearised multistage modelling (LMS) on data on haemangiosarcomas in male Osbourne-Mendel rats following oral (gavage) exposure in a 78 week study (NCI, 1978). See above for information on the NCI, 1978 study. The oral slope factor was 9.1x10-2 per mg/kg bw/ day, which corresponds to a drinking water unit risk of 2.6x10-6 per µg/L, and 4 µg/L in drinking water associated with an ELCR of 10-5. The HBGV was calculated using an adult weighing 70 kg drinking 2 L/day.	USEPA National Center for Environmental Assessment (1987) '*Integrated Risk Information System (IRIS) Chemical Assessment Summary for 1,2-Dichloroethane* ' (CASRN 107-06-2) https://rais.ornl.gov/tox/profiles/12dca.html#t45
OEHHA ***Drinking Water public health goal (PHG)-carcinogenic effects***	0.11	µg/kg bw/day	NA	ELCR	1 in 100,000	mg/kg bw/day	Haemangiosarcoma	Public Health Goals (PHGs) were calculated based on carcinogenic and non-carcinogenic effects. For carcinogenic effects, the long term (78 week) gavage study in rats (NCI, 1978) was selected as the pivotal study, in which haemangiosarcomas were reported in male Osborne-Mendel rats. Based on these data, a cancer potency value of 0.047 per (mg/kg bw/day) was derived using both the benchmark dose approach and linearised multistage modelling. The PHG of 0.4 ug/l was calculated assuming 70 kg adult body weight drinks 2 L of water per day (an additional 2 L/day was included to account for inhalation exposure during bathing), and assuming an excess lifetime cancer risk of 10-6. An ELCR of 10-5 would equate to 4 ug/l. It should be noted that there is concern over the NCI (1978) study as described above. Moreover, other toxicity information and pharmacokinetic, metabolic and toxicity studies indicate that the high doses and gavage administration used in NCI (1978) may have augmented the carcinogenic potential of 1,2-DCA. Consequently, the cancer potencies were derived from the negative Maltoni et al (1980) and Cheever et al (1990) studies and were found to fall within the range of values based on NCI (1978).	OEHHA (1999) '*Public Health Goal for 1,2-Dichloroethane In Drinking Water*' OEHHA *'Update of the Public Health Goal for 1,2-Dichloroethane'* Memorandum September 16 2005
ATSDR ***Intermediate MRL***	200	µg/kg bw/day	300	LOAEL	58	mg/kg bw/day	Increased absolute and relative kidney weights	ATSDR calculated an intermediate-duration oral MRL of 0.2 mg/kg bw/day from a LOAEL of 58 mg/kg bw/day based on increased absolute and relative kidney weights in female F344/N rats, during a 13 week drinking water study (NTP, 1991). A NOAEL could not be determined as renal effects were observed at the lowest dose tested (58 mg/kg bw/day). Renal effects (increased absolute and relative kidney weights with renal tubular regeneration at higher doses) were considered to be an early-stage adverse effect because histopathological changes in the kidney were observed at higher doses. The MRL of 0.2 mg/kg bw/day was calculated by applying an uncertainty factor of 300 (10 for inter and intraspecies variation and 3 for use of a LOAEL) to the LOAEL of 58 mg/kg bw/day. No further details of the study were provided in ATSDR but the NTP (1991) original source document stated that F344/N rats, SD rats, Osborne-Mendel rats and B6C3F1 mice (20 males and 10 female rats and 10 male and female mice) were administered doses of 1,2-DCA of 0, 500, 1000, 2000, 4000 and 8000 ppm via drinking water, for 13 weeks. The estimated intake for female F344/N rats (selected due to them being the most sensitive sex/strain) from drinking water was 58, 102, 182, 320 and 601 mg/kg bw/day, respectively. In addition, F344/N rats (10 or 20 males and 10 females) were administered 1,2-DCA (0, 30, 60, 120, 240 or 480 mg/kg or 0, 18, 37, 75, 150 or 300 mg/kg, respectively) in corn oil by gavage for 5 days per week for 13 weeks.	ATSDR *'Toxicological Profile for 1,2-Dicholoroethane'* September 2001
Health Canada 2015 ***Drinking water guidelines - noncarcinogenic effects***	78	µg/kg bw/day	1000	BMDL10	78	mg/kg bw/day	Renal tubular regeneration	Health Canada selected the NTP (1991) study as the pivotal study (see above for study description). BMD modelling was applied by Health Canada to data on tubular regeneration and thymal necrosis. Although NOAELs could be derived, the BMD approach was used to derive the PoD as the whole dose response curve is used rather than a single dose group as with the NOAEL. Using the USEPA BMD software (2011), BMD and BMDL values were calculated for both tubular regeneration and thymal necrosis. The most conservative value was the BMDL10 of 78 mg/kg bw/day (BMD = 142 mg/kg bw/day) based on tubular regeneration in female F344/N rats, exposed via drinking water, calculated using the Weibull model. An UF of 1000 (10 for inter and intraspecies variation and 10 for database deficiencies due to lack of reproductive and developmental data and use of a subchronic study) was applied to the BMDL10 to give a TDI of 0.078 mg/kg bw/day.	Health Canada '*Guidelines for drinking water quality* '. Guideline technical document, 2014

US EPA 2010 **Sub-chronic *p-RfD***	20	µg/kg bw/day	3,000	LOAEL	58	mg/kg bw/day	Absolute kidney weight increase	The 13 week sub-chronic drinking water study by NTP (1991) was selected as the critical study, in which F344/N rats, Sprague-Dawley rats and Osborne-Mendell rats and B6C3F1 mice (20 males and 10 female rats and 10 male and female mice) were exposed to doses of 0, 500, 1000, 2000, 4000 and 8000 ppm in drinking water (daily doses estimated from consumption and average body weights). Additional groups of F344/N rats (10 or 20 males and 10 females) were administered 1,2-DCA (0, 30, 60, 120, 240 and 480 mg/kg bw/day for males and 0, 18, 37, 75, 150 and 300 mg/kg bw/day for females) by gavage 5 days per week for 13 weeks. A LOAEL of 58 and 54 mg/kg bw/day (500 ppm) was selected as the POD based on >10% absolute increase in kidney weight in female F344/N rats in the drinking water study and gavage study, respectively. Benchmark dose modelling of data on absolute and relative kidney weight in female F344/N rats exposed via drinking water was carried out. No model fit was achieved even when high dose groups were excluded from the analysis. Therefore the LOAEL of 58 mg/kg bw/day was selected. Although the LOAEL from the gavage study was similar, the LOAEL of 58 mg/kg bw/day from the drinking water study was selected as the route of exposure is more relevant to human exposure. The sub-chronic oral p-RfD of 0.02 mg/kg bw/day was calculated by applying a composite UF of 3,000 (10 for interspecies extrapolation, 10 for susceptible humans, 3 for database deficiencies and 10 for using a LOAEL as the POD) to the LOAEL.	USEPA National Center for Environmental Assessment *'Provisional Peer-Reviewed Toxicity Values for 1,2-Dichloroethane (CASRN 107-06-2)'* FINAL 10-1-2010
US EPA 2010 **Screening chronic *p-RfD***	6	µg/kg bw/day	10,000	LOAEL	58	mg/kg bw/day	Increased absolute kidney weights	The NCI (1978) chronic oral study and the Alumot et al 1976 study were considered to be of too poor a quality to be used to derive a chronic toxic oral provisional RfD. The Alumot study was poorly reported, had limitations in the toxicological evaluations and had uncertain dose levels. The NCI study had poor survival rate at the high dose and the dosing regime was variable. In addition, the clinical signs seen in rats were not seen in any of the subchronic studies in various rat strains exposed via drinking water or gavage at high concentrations. Therefore the 13 week sub-chronic drinking water study by NTP (1991) was selected as the critical study, as described above, from which a LOAEL of 58 mg/kg bw/day was determined, based >10% absolute increase in kidney weight in female F344/N rats. The screening chronic p-RfD of 0.006 mg/kg bw/day was calculated by applying an UF of 10,000 to the LOAEL. A composite UF of 30,000 (10 for interspecies extrapolation, 10 for susceptible humans, 3 for database deficiencies and 10 for using a LOAEL as the POD and 10 for using a sub-chronic study) was initially calculated but was thought to be unrealistic hence the UF was capped at 10,000 as there is evidence that the responses to chronic exposure are of a similar magnitude to subchronic responses.	USEPA National Center for Environmental Assessment *'Provisional Peer-Reviewed Toxicity Values for 1,2-Dichloroethane (CASRN 107-06-2)'* FINAL 10-1-2010
OEHHA ***Drinking Water public health goal (PHG)-non-carcinogenic effects***	45.3	µg/kg bw/day	1000	NOAEL	45.3	mg/kg bw/day	Kidney lesions	Public Health Goals (PHGs) were calculated based on carcinogenic and non-carcinogenic effects. For non-carcinogenic effects, the NTP (1991) sub-chronic drinking water study was used (as described above) from which a NOAEL of 45.3 mg/kg bw/day was determined. It is unclear how the NOAEL was determined as other authoritative bodies stated that a NOAEL could not be calcuated from the data. An UF of 1000 (10 for interspecies extrapolation, 10 for use of a subchronic study and 10 for sensitive human subpopulations) was applied to the NOAEL to calculate TDI, which formed the basis of the PHG.	OEHHA (1999) '*Public Health Goal for 1,2-Dichloroethane In Drinking Water* ' OEHHA *'Update of the Public Health Goal for 1,2-Dichloroethane'* Memorandum September 16 2005

COT/COC Opinion	No statements, position papers or reports 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
Defra/EA Tox22 (2004) ID	0.12	µg/kg bw/day	50,000	TD_5	6.2	mg/kg bw/day	Multi-site cancers	The HCV was based on a 78 week study conducted in 50 male and female rats and mice per group, administed 1,2-DCA by gavage 5 days per week (NCI, 1978). Rats received time-weighted average doses of 45 or 95 mg/kg bw/day, male mice received 97 or 195 mg/kg bw/day and female mice 149 or 299 mg/kg bw/day. Multi-site cancers developed (doses not stated). Adopted IPCS 1998 CICAD approach of extrapolation from a central estimate of the TD_5 value with a margin of safety of 50,000 applied to the TD_5 ranges on 6.2 to 34 mg/kg bw/day. Carcinogenicity of 1,2-DCA is probably due to a metabolite rather than the parent compound so not appropriate to incorporate a scaling factor from the differences in body surface area between rodents and humans. Based on the approach, estimated oral doses range from 0.12 to 0.68 µg/kg bw/day equated to an ELCR of 1 in 1,000,000.	Defra & EA '*Contaminants In Soil: Collation of Toxicological Data and Intake Values for Humans. 1,2-Dichloroethane*' Science Report Tox 22. August 2004.

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
EXAMPLE: ATSDR 2010 MRL	***1.43***	***ng/kg bw/day***	***5***	***ng/m^3***	***100***	***NOAEL***	***0.5***	***µg/m^3***	***Nasal toxicity***	**For chromium aerosols and mists. Based on occupational data from workers exposed to chromic acid (Lindberg & Hedenstierna 1983). LOAEL of 2 µg m-3 adjusted for continuous exposure (0.5 µg m-3), and UF of 10 used for interspecies variation and 10 for extrapolating from a LOAEL.**	***ATSDR, 2010. Toxicological Profile for Contaminant X. July 2010.***
IPCS CICAD 1998	1.02 - 5.71 to 0.1 - 0.57	µg/kg bw/day	0.36- 2.0 to 3.6 - 20	µg/m^3	5,000 to 50,000	$TD_{0.05}$	6.2 to 34	mg/kg bw/day	Multiple tumours and sites	IPCS used the study by NCI (1978) in which Osborne-Mendel rats and B6C3FI mice (50 per sex per dose), were administered 1,2-DCA in corn oil via gavage, 5 days/week for 78 weeks followed by 32 week observation. Time-weighted doses for rats were 47 or 95 mg/kg bw/day, for mice 97 or 195 mg/kg bw/day (male) and 149 or 299 mg/kg bw/day (female). Increases in the incidences of squamous cell carcinoma of the forestomach and haemangiosarcoma were observed in male rats; adenocarcinoma of the mammary gland was observed in female rats; mammary adenocarcinomas and endometrial stromal polyps or sarcomas in female mice; and alveolar/bronchial adenomas in male and female mice. The high doses in female mice and the high dose in both sexes of rat were excluded from the derivation of quantitative estimates of carcinogenic potency due to higher mortality at these doses. NOTE some carcinomas may not be relevant to humans e.g. forestomach. IPCS carried out multistage modelling adjusted for continuous exposure for a standard duration of 104 weeks and corrected for the expected rate of increase in tumour formation. Doses associated with a 5 % increase in tumour incidence (TD0.05) were 6.2-34 mg/kg bw/day. The guidance value for air was derived by applying a margin of 5000 to 50,000 to the TD0.05s, resulting in guideline values of 3.6-20 µg/m3 or 0.36-2 µg/m3, respectively. It should be noted that risk are overestimated on this bases as the available data indicate that 1,2-DCA is less potent when inhaled. Assuming a 70 kg adult inhales 20 m3 per day, the HBGV would be 1.02-5.71 or 0.1-0.57 µg/kg bw/day.	WHO IPCS (1998) CICAD *'1,2-Dichloroethane'*
RIVM 2001 *Provisional MPR*	1.37	µg/kg bw/day	4.8	µg/m^3	NA	ELCR	1 in 100,000	NA	Carcinogenicity	Using data from Vermeire et al (1991) and route to route extrapolation, a provisional MPR of 48 µg/m3 was set, which is associated with an ELCR of 10-4, calculated using linear extrapolation from the oral study in rats. 4.8 µg/m3 is associated with an ELCR of 10-5. No other data on the study are available. The air concentration was converted to a HBGV assuming a 70 kg adult inhales 20 m3/day. Vermiere et al (1991) selected route-to-route extrapolation from oral data due to a lack of inhalation carcinogenicity studies.	RIVM (2001) *'Re-evaluation of human toxicological maximum permissible risk levels'* report 711701 025 A.J. Baars et al March 2001.

REACH Dossier	-	-	-	-	-	NOAEL	658.1	mg/m^3	Combined fibroadenoma and adenoma	An unnamed study (presumed to be Nagano et al, 2006) was carried out following OECD 453 methodology. BDF1 mice and F344/DuCrj rats (50/sex/dose) were exposed to vapour (whole body exposure) for 104 weeks, 6 hours per day, 5 days per week. Mice were exposed to 0, 10, 30 and 90 ppm (v/v) equivalent to 0, 41.1, 123.4 and 370.2 mg/m3 and rats to 0, 10, 40 or 160 ppm equivalent to 0, 41.1, 164.5 or 658.1 mg/m3. Authors of the dossier cited that in rats, the NOAEL was 658.1 mg/m3 (160 ppm); a BMC10 of 160 mg/m3 (42 ppm) and a T25 of 99 ppm based on combined fibroadenoma and adenoma and combined fibroadenoma, adenoma and adenocarcinoma in females, respectively; and in mice, the NOAEL was 370.2 mg/m3 based on incidences of benign and malignant tumors, including bronchiolo-alveolar adenoma and carcinoma, endometrial stromal polyp, mammary gland adenocarcinoma and hepatocellular adenoma in female mice. No further details are available on the modelling carried out to derive the BMD10 values.	https://echa.europa.eu/registration-dossier/-/registered-dossier/15430/1
REACH Dossier	-	-	-	-	-	BMC10	160	mg/m^3	Combined fibroadenoma and adenoma		https://echa.europa.eu/registration-dossier/-/registered-dossier/15430/1
ECHA 2015 ***Reference Dose Response T25*** *(inhalation, gen. pop)*	0.8	µg/kg bw/day	2.8	$\mu g/m^3$	NA	ELCR	1 in 100,000	NA	Combined mammary tumours - fibroadenomas, adenomas and adenocarcinomas	Nagano et al 2006 was selected as the pivotal study. The inhalation study was conducted in F33/DuCrj (SPF) rats, exposed to 1,2-DCA vapour (0, 10, 40 and 160 ppm / 0, 41, 164 and 658 mg/m3), 6 hours per day, 5 days per week for 2 years. A T25 of 406 mg/m3 was calculated using the combined frequency of mammary tumours, adenomas, fibroadenomas and adenocarcinomas, where 658 mg/m3 was the lowest dose with a significantly increased frequency. 0.5 and 0.16 was the incidence of tumours in treated and controls at exposures of 6 hr/day, 5 days/week for 2 years. ECHA converted the T25 (inhalation, rat) to a T25 (inhalation, gen. pop) of 72.5 mg/m3 to account for lifetime exposure for the general population (24 hours per day, 7 days per week). The T25 (inhalation, gen. pop) of 17.6 ppm (72.5 mg/m3) equates to a cancer risk of 3.45 x 10-6 per µg/m3. Assuming linearity of reponse the ELCR following exposure to 1 ug/m3 is 3.45 x10-6 ELCR, hence 2.8 ug/m3 equates to an ELCR of 10-5. The air concentration was converted to a HBGV assuming a 70 kg adult inhales 20 m3/day.	ECHA *'Application For Authorisation: Establishing A Reference Dose Response Relationship for Carcinogenicity Of 1,2-Dichloroethane'* RAC/33/2015/09 Rev1 Final. 05 June 2015.
IRIS ***Inhalation Unit Risk Air Concentration***	0.11	µg/kg bw/day	0.4	µg/m3	NA	ELCR	1 in 100,000	NA	Haemangiosarcoma Hepatocellular carcinoma	The most reliable inhalation study by Maltoni et al (1980) was negative for carcinogenic effects hence route to route extrapolation from the oral pivotal study (NCI 1978) was carried out, assuming 100 % absorption and metabolism at low dose. US EPA carried out linearised multistage modelling (LMS) on data on haemangiosarcomas in male Osbourne-Mendel rats following oral (gavage) exposure in the 78 week study by NCI, 1978. A inhalation unit risk of 2.6x10-5 per µg/m3 was derived. 0.4 µg/m3 corresponds to an ELCR of 10-5. The air concentration was converted to a HBGV assuming a 70 kg adult inhales 20 m3/day.	USEPA National Center for Environmental Assessment (1987) '*Integrated Risk Information System (IRIS) Chemical Assessment Summary for 1,2-Dichloroethane* ' (CASRN 107-06-2) https://rais.ornl.gov/tox/profiles/12dca.html#t45
WHO European Air Quality Guideline 2000 ***AQG***	200	µg/kg bw/day	700	$\mu g/m^3$	1000	LOAEL	700	mg/m^3	Histological changes to liver	Long-term inhalation exposure studies (Spencer et al (1951), Heppel et al (1946), Hofmann et al (1971)) in rats, mice and guinea pigs exposed to DCE (at various exposure levels ranging from 400-3900 mg.m-3) for several weeks to 36 weeks indicate a NOAEL of ~ 400 mg/m3 and a LOAEL of ~700 mg/m3 based on fatty degeneration, cloudy swelling and necrosis of the liver. An uncertainty factor of 1000 (10 for inter and intraspecies variation and 10 for exposure time, limitations in the database and use of a LOAEL instead of a NOAEL) was applied to the LOAEL to give a guideline value of 0.7 mg/m3 based on continuous exposure (averaging time 24 hours). The air concentration was coverted to a HBGV assuming a 70 kg adult inhales 20 m3/day.	WHO (2000) *'Air Quality Guidelines for Europe'* 2nd edition. WHO *'WHO Expert Consultation: Available evidence for the future update of the WHO Global Air Quality Guidelines (AQGs)'* Meeting report Bonn, Germany 29 September - 1 October 2015
ATSDR ***Chronic MRL***	0.64	µg/kg bw/day	2.25	$\mu g/m^3$	90	NOAEL	202.37	mg/m^3	Kidney and liver lesions	Cheever et al 1990 was selected as the pivotal study, in which Sprague-Dawley rats (50/sex) were exposed to 50 ppm 1,2-DCA via inhalation 7 hours per day, 5 days per week for two years. Histopathology was conducted. A NOAEL of 50 ppm was determined based on histological changes to the liver in rats. A chronic exposure MRL of 0.6 ppm (2.25 mg/m3) was derived by applying an UF of 90 (3 for interspecies extrapolation, 10 for human variability and 3 for database deficiencies) to the NOAEL. The air concentration was converted to a HBGV assuming a 70 kg adult inhales 20 m3/day. The study was limited by the use of a single dose level of 50 ppm (which was determined to be the NOAEL), use of a single species and lack of sensitive immunotoxicity endpoints. 50 ppm = 202.37 mg/m3 based in a molecular weight of 98.96	ATSDR *'Toxicological Profile for 1,2-Dicholoroethane'* September 2001

OEHHA ***Chronic Inhalation Reference Exposure Level (ChREL)***	114.28	µg/kg bw/day	400	µg/m^3	30	$NOAEL_{HEC}$	12.96	mg/m^3	Hepatoxicity (elevated liver enzyme levels in serum)	Spreafico et al (1980) was selected as the pivotal study, in which rats (8-10/sex/group) were exposed to 0, 5, 10, 50, 150-250 ppm 1,2-DCA via discontinuous whole body inhalation exposure, 7 hours per day, 5 days per week for one year. A NOAEL of 10 ppm was determined based on significant elevation of liver enzymes at 50 ppm. The average experimental exposure for the NOAEL group was 2.1 ppm (10 ppm x 7/24x5/7). This adjusted NOAEL of 2.1 ppm (8.505 mg/m3) was converted to a HEC of 3.2 ppm (12.96 mg/m3), based on a regional gas dose ratio (RGDR) of 1.5. The REL was determined by applying an UF 30 (3 for interspecies variation and 10 for intraspecies variation) to the NOAEL HEC, giving REL of 0.1 ppm (0.4 mg/m3; 400 µg/m3). The air concentration was converted to a HBGV assuming a 70 kg adult inhales 20 m3/day. 1 ppm = 4 mg/m3 This study should be selected with caution as the small number of animals per group may have resulted in false positives, false negatives and there was a lack of a clear dose response relationship.	OEHHA (2000) *'Determination of Noncancer Chronic Reference Exposure Levels Batch 2A: Chronic Toxicity Summary Ethylene Dichloride (1,2-Dichloroethane)'*
PPRTV 2010 ***pRfC***	2.1	µg/kg bw/day	7	µg/m3	3000	$LOAEL_{HEC}$	22	mg/m^3	Neurobehavioural effects	The occupational study by Kozik (1957) was selected as the pivotal study in which Russian aircraft employees were occupationally exposed to 1,2-DCA (no information about length of employment of duration of exposure reported). Neurobehavioural effects were selected as the POD largely due to to being the only endpoint being investigated in both exposed workers and controls. Therefore a LOAEL of 61 mg/m3 was determined which was adjusted for continuous exposure (assuming inhalation of 10 m3 per 8 hr and 20 m3 per 24 hours, 5 to 7 day per week), to derive a LOAEL HEC of 22 mg/m3. The UF of 3000 (1 for interspecies variability as human data were used, 10 for use of LOAEL, 10 for using a subchronic study, 10 to protect sensitive individuals and 3 for deficiencies in the database) was applied to the LOAEL HEC to derive the chronic provisional RfC of 0.007 mg/m3. The air concentration was converted to a HBGV assuming a 70 kg adult inhales 20 m3/day. Confidence in the study was very low due to poor reporting, a small number of subjects, poor quality of study and reporting, limited numbers of subjects, lack of control for confounders, lack of statistical analysis of data, no medical examination of unexposed workers and limited number of toxicity endpoints. Benchmark dose modelling was performed on Spreafico 1980 data as a comparison and a BMCL 1SD HEC of 27 mg/m3 was determined, based on ALT and GGT data. This was used to justify the validity of using Kozik 1957 as the pivotal study, which was considered to be protective of liver effects as well as the more sensitive human neurobehavioral effects.	USEPA National Center for Environmental Assessment *'Provisional Peer-Reviewed Toxicity Values for 1,2-Dichloroethane (CASRN 107-06-2)'* FINAL 10-1-2010
EC ***Occupational Exposure Limit***	Not assigned	Not assigned	Not assigned	Not assigned	N/A	BMD10	151.2	mg/m^3	Combined fibroadenoma and adenoma in the mammary gland	Nagano et al (2006) was selected as the pivotal study which was evaluated to be a well-conducted experiment which was performed according to OECD guideline and under GLP standards. Benchmark dose modelling was undertaken using the US EPA BMD software Version 2.6 which derived a BMD10 of 37.8 ppm (converted to 151.2 mg/m3 assuming 1 ppm = 4 mg/m3). This was adjusted for a workplace assessment which is not relevant for this assessment. Benign tumours were included in the BMD modelling as possible pre-stages of malignancy. The assumed mode of action is genotoxic and the dose-tumour response is probably non-linear. 1 ppm = 4 mg/m3 therefore 37.8 ppm = 151.2 mg/m3	SCOEL (2016) *'SCOEL/REC/302 1,2-Dichloroethane (Ethylene dichloride)'*

COT/COC Opinion	No statements, position papers or reports found.

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
Defra/EA Tox22 (2004) ID	0.12	µg/kg bw/day	50,000	TD_5	6.2	µg/kg bw/day	Multi-site cancers	Oral NCI study used for route-to-route extrapolation. A recent study (Nagano et al 1998) had indicated that 1,2-DCA was genotoxic by inhalation and the approach adopted followed the IPCS CICAD assumption of equal potency by both routes.	Defra & EA '*Contaminants In Soil: Collation of Toxicological Data and Intake Values for Humans. 1,2-Dichloroethane*' Science Report Tox 22. August 2004.

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
Defra/EA Tox22 (2004) ID	N/A	N/A	N/A		N/A	N/A	Benign lung papillomas	Van Duuren et al (1979), Incidence of benign lung papillomas significantly increased in mice that were treated three times weekly for 440-594 days with doses of 126 mg 1,2-DCA in an acetone vehicle.	Defra & EA '*Contaminants In Soil: Collation of Toxicological Data and Intake Values for Humans. 1,2-Dichloroethane*' Science Report Tox 22. August 2004.
ECHA 2015 ***Reference Dose Response T25*** ***(dermal, gen. pop)***	41.4	mg/kg bw/day	N/A	$T25_{(inhalation,rat)}$	98.8	ppm	Combined mammary tumours - fibroadenomas, adenomas and adenocarcinomas	Nagano et al 2006 was selected as the pivotal study. ECHA considered that 1,2-DCA was genotoxic and non-threshold, but that the assessment should be based on its genotoxic potential rather than the study's relevance to specific human cancers. 2 year inhalation study in F33/DuCrj (SPF) rats, exposed to vapour 6 hours per day, 5 days per week. Three dose levels (0, 10, 40 and 160 ppm / 0, 41, 164 and 658 mgm^{-3}). ECHA converted the $T25_{(inhalation,\ rat)}$ to account for lifetime exposure for the general population (24 hours per day, 7 days per week) to derive a $T25_{(inhalation,\ gen.\ pop)}$ of 17.6 ppm and equated this to a cancer risk of 3.45×10^{-6} per $\mu g.m^{-3}$. A further conversion to derive a $T25_{(dermal,\ gen.\ pop)}$ of 41.4 $mgkg^{-1}{}_{bw}day^{-1}$ was achieved by assuming $20m^3$ per day breathing rate, adult body weight of 70 kg and 50% dermal absorption.	ECHA *'Application For Authorisation: Establishing A Reference Dose Response Relationship for Carcinogenicity Of 1,2-Dichloroethane'* RAC/33/2015/09 Rev1 Final. 05 June 2015.

III) Current UK (WHO) regulatory values

	Value	Units	Refs
UK drinking water standard	3	μgL^{-1}	The Water Supply (Water Quality) Regulations 2016
WHO drinking water standard	30	μgL^{-1}	WHO (2017) *'Guidelines for Drinking-water Quality'* Fourth Edition Incorporating the First Addendum
UK air quality standard	N/A	N/A	The Air Quality Standards Regulations 2010
WHO air quality standard	0.7	$mg.m^{-3}$	WHO (2000) *'Air Quality Guidelines for Europe'* 2nd edition.

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
NTP 2008	*Drinking water*	*0.38, 0.91, 2.4 or 5.9 (m/m); 0.38, 1.4, 3.1 or 8.7 (f/m)*	*mg/kg bw/day*	*Mouse*	*2 year drinking water study*	*Endpoints based on non-neoplasic epithelial hyperplasia in female mice via a threshold MOA (BMDL 0.09) or oral carcinoma in male mice mg kg (BMDL 1.2) (IPCS 2011) .*
NTP 1991 for non-carcinogenic effects	Drinking water	18, 37, 75, 150 or 300 (f); 30, 60, 120, 240 or 480 (m)	mg/kg bw/day	Rat/Mouse	13 week oral gavage and drinking water study	NTP (1991) was selected as the pivotal study and was selected by most authoritative bodies to evaluate the non-carcinogenic effects of 1,2-DCA via ingestion. The sub-chronic oral study was conducted in F334/N rats, Sprague-Dawley rats, Osborne-Mendel rats and B6C3FI mice which were exposed to doses of 0, 500, 1000, 2000, 4000 or 8000 ppm in drinking water for 13 weeks. Additional groups of F334/N rats were administered 1,2-DCA by gavage 5 days per week for 13 weeks. The target organ is the kidney, although there are differences between authoritative bodies as to which effect is the critical endpoint and what the point of departure is. There is general agreement that the drinking water study is more representative than the gavage study. OEHHA selected a NOAEL of 45.3 mg/kg bw/day based on kidney lesions (other authoritative bodies concluded that a NOAEL could not be derived), USEPA and ATSDR selected a LOAEL based on increased absolute and relative kidney weights. Health Canada undertook benchmark dose modelling based on a critical endpoint of renal tubular regeneration and thymal necrosis. However, US EPA could not achieve a model fit even when high dose groups were excluded from the analysis.
NCI 1978 for carcinogenic effects	Gavage	47 or 95 (m/f rats); 97 or 195 (m. mice); 149 or 299 (f. mice)	mg/kg bw/day	Rat/Mouse	2 year carcinogenicity study	NCI (1978) was selected as the pivotal study to evaluate the carcinogenic effects of 1,2-DCA via ingestion. The 2 year study was conducted in Osborne-Mendel rats and B6C3F1 mice which were administered 1,2-DCA by gavage 5 days per week for 78 weeks followed by a 32 week observation period. The critical endpoint was multiple tumour types at multiple sites. The point of departure that was selected was the lowest $TD_{0.05}$ of 6.2 mg/kg bw/day which was modelled by IPCS (CICAD 1998).

Selection of POD

Published POD for ORAL LLTC: non-threshold (carcinogenic) effects		
Study	NCI 1978	
Are dose response data of adequate quality to derive a BMD	Yes	
Type of PoD	TD0.05	
Value selected	6.2	mg/kg bw/day

Note the TD0.05 is the dose that causes an 5% increase in tumours hence is equivalent to a BMD5

Derived POD for ORAL LLTC: threshold (non-carcinogenic) effects		
Study	NTP 1991	
Are dose response data of adequate	Yes	
Type of PoD	BMD10	
Value derived	142	mg/kg bw/day

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)			142	
	BMDL1	BMDL5	BMDL10	BMDL15
BMD modelling (value) (mg/kg bw/day)			78	

Comments: BMD modelling carried out by Health Canada using the US EPA BMD model. Data on renal tubular regeneration in female F344/N rats was modelled, and a BMDL10 of 78 mg/kg bw/day (BMD10 of 142 mg/kg bw/day) was calculated using the Weibull model.

Present benchmark dose graph here

Not available

Addressing uncertainty

Thresholded effects?	No
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 BMD) use generic margin of 5000 or (if data allows) calculate CSM	5,000
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 100,000

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	10
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		1000

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

Oral LLTC calculation:

	Value	Units	Justification
LLTC (Non-Thresholded chemical) using TD0.05 (equivalent to BMD5)	1.24	µg/kg bw/day	A TD0.05 of 6.2 mg/kg bw/day based on haemangiosarcoma, adenocarcinoma and fibroadenoma (combined) of the mammary gland in rats (NCI 1978) was used as a basis of the LLTC. A TD0.05 is a dose that induces cancers in 5% of animals. Due to the poor quality of the NCI 1978 study, it was decided to base the LLTC on a minimal risk ELCR of 1 in 100,000 as per Defra (2008) *Guidance on the legal definition of contaminated land* , rather that the C4SL Framework ELCR of 1 in 50,000. A margin of 5,000 is equivalent to an ELCR of 1 in 100,000 for a TD0.05 (or BMD5).
LLTC (Thresholded chemical) using BMD10	142	µg/kg bw/day	A BMD10 of 142 mg/kg bw/day based on kidney effects in rats was investigated as a basis of the LLTC. An UF of 1000 (10 for inter and intra species variation and 10 for the use of a sub-chronic study) was applied to the BMD10 to derive the LLTC. This LLTC based on threshold effects is higher than that based on non-threshold (carcinogenicity) effects hence will not be used to derive the C4SL.

Delete as appropriate

Sensitive Receptor		

b) INHALATION

Choice of Pivotal Data	Dosing vehicle	Doses	Units	Species	Study Type	Comments
Epidemiology study of lung cancer in workers in a chromate production (Gibb et al 2000)	*N/A*	*N/A*	*N/A*	*Human*	*Epidemiology study in chromate production workers*	*The ELCR for for lung cancer for 1, 0.1, 0.01 or 0.001 µg m-3 is equivalent to environmental exposure of 4 in 100, 4 in 1000, 4 in 10,000, or 4 in 100,000. Hence 1 in 100,000 would equate to 0.00025 mg m-3 (0.25 ng m-3).*
Nagano et al 2006 for carcinogenic effects	Whole body exposure	0, 41, 164 and 658	mg/m^3	Rat	2 year carcinogenicity and chronic toxicity study	Nagano et al (2006) was selected as the pivotal study. The inhalation study was conducted in F334 rats exposed to 1,2-DCA vapour (0, 10, 40 or 160 ppm / 0, 41, 164 or 658 mg/m3) and BDF1 mice (0, 10, 30 or 90 ppm) 6 hours per day, 5 days per week for 2 years. The critical endpoint was determined to be various mammary gland tumours in female rats (adenoma, fibroadenoma and adenocarcinoma) or combined adenoma, fibroadenoma and adenocarcinoma. A NOAEL of 164 mg/m3 (40 ppm) was determined based on a significantly increased frequency of mammary gland tumours and combined adenoma, fibroadenoma and adenocarcinoma in female rats at 160 ppm. Note: in the REACH dossier a NOAEL of 160 ppm (658.1 mg/m3) was determined. A BMC10 of approx. 160 mg/m^3 (42 ppm) was calculated in the REACH dossier, based on combined fibroadenoma and adenoma and combined fibroadenoma, adenoma and adenocarcinoma in female rats, respectively from data from an un-named study, presumed to be Nagano et al 2006 from the details of the study, the endpoint and the points of departure. Note: the BMC10 is very similar to the NOAEL identified by Nagano et al. However, no information about the BMD modelling is available. Consequently, BMD values were deemed unreliable to use, and hence modelling was carried out using the US EPA software.

Selection of POD

Published POD for INHALATION LLTC: non-threshold (carcinogenic) effects		
Study	Nagano 2006	
Are dose response data of adequate quality to derive a BMD	Yes	
Type of PoD	BMC10	
Value selected	10.7	mg/kg bw/day

Derived POD for INHALATION LLTC: threshold (non-carcinogenic) effects		
Study		
Are dose response data of adequate quality to derive a	Yes	
Type of PoD	NOAEL	
Value selected		mg/kg bw/day

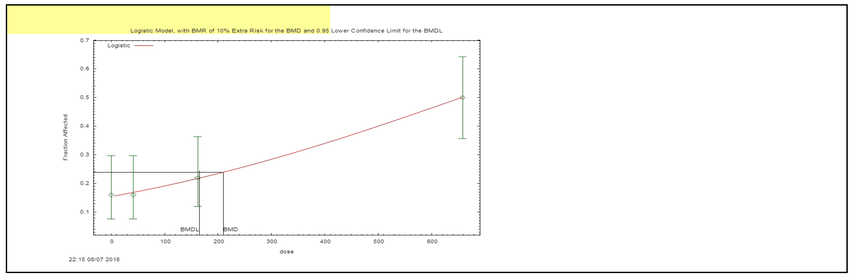
BMD Modelling (if answered 'Yes' to question above - see worksheet BMD modelling pivotal study)

Software used **US EPA BMDS 2.7**

	BMD1	BMD5	BMD10	BMD15
BMD modelling (value) (mg/m3)			37.45	
	BMDL1	BMDL5	BMDL10	BMDL15
BMD modelling (value) (mg/m3)			29.41	

Comments:

Logistic model used for cancer effects from Nagano.
Calculated using both the dose in mg/m3 and ppm as the dose metric.
BMD and BMDL above given in mg/m3. These were converted to mg/kg bw/day by assuming a 70 kg adult breathes 20 m3 per day.



Thresholded effects?	No
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	5000
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	1
Interspecies	1 - 10	1
Sub-chronic to chronic	1-10	1
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		1

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 (Non-Thresholded chemical) using BMC10	2.14	µg/kg bw/day	A BMC10 (adjusted) of 10.7 mg/kg bw/day based on various mammary gland tumours in female rats (adenoma, fibroadenoma and adenocarcinoma) or combined adenoma, fibroadenoma and adenocarcinoma was used as a basis of the LLTC . The default margin of 5000 was applied to the BMC10 to calculate the LLTC.
LLTC (Thresholded chemical) using NOAEL		µg/kg bw/day	

Delete as appropriate

Sensitive Receptor	Female	

IV A) BMD modelling

ARE DATA OF SUFFICIENT QUALITY **YES**

Toxicological data	Inhalation
Endpoint	Mammary gland tumours
Level of modelled response	10%
Chemical used in study	1,2-DCA

Dose (mg/kg bw/day)	Species	Sex	n	Incidence of endpoint
0	Rat	F	50	8
41.1	Rat	F	50	8
161.88	Rat	F	50	11
658.1	Rat	F	50	25

Model Name	Maximum number of iterations	AIC	Chi squared value	p value	Accept	BMD (mg/m3)	BMD adjusted (mg/m3)	BMDL (mg/m3)	BMDL adjusted (mg/m3)
Gamma	250	215.95		0.9027	y	204.2	36.47	92.7	16.55
Logistic	250	213.98		0.9793	y	209.7	37.45	164.7	29.41
LogLogistic	250	215.95		0.9101	y	201.8	36.04	51.5	9.20
LogProbit	250	215.94		0.9623	y	197.9	35.35	54.9	9.81
Multistage	250	215.98		0.8459	y	209.9	37.49	65.4	11.68
Multistage-Cancer	250	215.98		0.8459	y	209.9	37.49	92.5	16.52
Probit	250	213.99		0.9777	y	199.5	35.62	156.0	27.85
Weibull	250	215.96		0.89	y	205.5	36.69	92.7	16.55
Quantal-Linear	250	214.29		0.8386	y	135.1	24.12	90.6	16.17

Range (mg/m3)	BMD1	BMD5	BMD10	BMD15
BMD modelling (value)			37.45	
	BMDL1	BMDL5	BMDL10	BMDL15
BMD modelling (value)			29.4	

USE DATA TO COMPLETE BMD MODELLING SECTION ON 'LLTC DERIVATION AND EVIDENCE' WORKSHEET

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

APPENDIX B
MEAN DAILY INTAKE DATA
SHEET FOR 1,2-DICHLOROETHANE

Substance: **Substance name** 1,2 Dichloroethane

MDI Oral			**Recommended adult oral MDI**	**Units**	**Justification:** Adult MDI for water estimated from average 99th percentile concentration in tapwater in England and Wales from DWI (2016) multiplied by assumed adult water consumption rate of 2 L.d-1		
			0.28	ug day-1			
Organisation/Source	**Date**	**Media**	**Value**	**Units**	**Description**	**Reference**	**Web link**
DWI	Jul-17	Tap water	0.14	µg L-1	99th percentile concentrations of 1,2-dichlroethane measured in 2016 averaged across all 30 water companies in England & Wales	Data summary tables from Drinking Water Inspectorate annual report Drinking water 2016	http://www.dwi.gov.uk/about/annual-report/2016/index.html
Defra & Environment Agency	2004	Food	0	ug day-1	TOX report suggests concentrations of 1,2-dichloroethane in food are likley to be negligible	Contaminants in Soil: Collation of Toxicological Data and Intake Values for Humans. 1,2-Dichloroethane. Science Report TOX22.	http://webarchive.nationalarchives.gov.uk/20140328084622/http://www.environment-agency.gov.uk/static/documents/Research/dceoldapproach_2029062.pdf
WHO CICAD	1998	Food			1,2-Dichloroethane has only rarely been detected in foodstuffs in extensive surveys in Canada and the USA. Also, as 1,2-dichloroethane has low potential for bioaccumulation, food is unlikely to be a major source of exposure.	WHO (1998). Concise International Chemical Assessment Document 1: 1,2-Dichloroethane.	https://www.who.int/ipcs/publications/cicad/en/cicad01.pdf?ua=1

MDI Inhalation			**Recommended adult inhalation MDI**	**Units**	**Justification:** 1,2-Dichloroethane is not monitored by the Defra UK AIR Netwo rk. The available data suggests that the outdoor air concentration selected by Defra and the Environment Agency (2004) of 1 µg m-3 remains reasonably conservative, and indoor air concentrations are in the same range. Ambient air concentrations likely to be reducing over time due to the cessation of the use of leaded petrol although no recent European or UK measurements were sourced.		
			20	ug day-1	1 µg m-3 is converted to 20 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**
DEFRA & Environment Agency Report	2004	Urban ambient air	1	µg m-3	Cites IPCS (1995) stating that the most recent UK data found was Clark et al (1984 a&b) with an average rural concentration of 0.08 µg m-3 and average urban concentration of 1.2 µg m-3. WHO (2000) reported the average levels in cities to range from 0.4 to 1 µg m-3. Up to 6 µg m-3 was recorded around petrol stations (1,2-DCA was an anti-knock agent). US data from ATSDR (2001) quoted similar urban values with some indication of declining concentrations more recently with the cessation of the use of leaded petrol. Given the lack of recent UK data, a conservative estimate of 1 µg m-3 was selected.	Defra and Environment Agency (2004). Contaminants in Soil: Collation of Toxicological Data and Intake Values for Humans.1,2 Dichloroethane.	http://webarchive.nationalarchives.gov.uk/20140328111046/http://www.environment-agency.gov.uk/research/planning/64002.aspx
WHO Air Quality Guidelines	2000	Urban ambient air	0.4 to 1.0	µg m-3	Average concentrations in cities range from 0.4 - 1.0 µg m-3, increasing to 6.1 µg m-3 near petrol stations, parking garages and production facilities. Rural/background concentrations in western Europe and N. America are around 0.2 µg m-3.	WHO (2000) ' *Air Quality Guidelines for Europe'* WHO Regional Publications, European Series, No. 91. Second edition	http://www.euro.who.int/__data/assets/pdf_file/0005/74732/E71922.pdf?ua=1
WHO Background for Drinking Water	2003	Urban ambient air	1.2	µg m-3	Reports mean concentrations from surveys of ambient air in non-source dominated areas in cities including: 0.07–0.28 µg m-3 in Canada, <0.004–3.8 µg m-3 in Japan and 1.2 µg/m3 in the United Kingdom and the Netherlands. Earlier surveys in the USA reported mean levels of 0.33–6.05 µg m3.	WHO (2003). 1,2-Dichloroethane in Drinking-water: Background document for development of WHO Guidelines for Drinking-water Quality. WHO/SDE/WSH/03.04/67	https://www.who.int/water_sanitation_health/water-quality/guidelines/chemicals/12-Dichloroethane.pdf?ua=1
WHO Background for Drinking Water	2003	Indoor air	<0.1 to 3.4	µg m-3	Reports mean concentrations from surveys of ambient air in non-source dominated areas in cities including: <0.1 µg m-3 in Canada, 0.1–0.5 µg m-3 in the USA, and 3.4 µg m-3 in the Netherlands.	WHO (2003). 1,2-Dichloroethane in Drinking-water: Background document for development of WHO Guidelines for Drinking-water Quality. WHO/SDE/WSH/03.04/67	https://www.who.int/water_sanitation_health/water-quality/guidelines/chemicals/12-Dichloroethane.pdf?ua=1
IPCS EHC	1995	Urban ambient air	1.2	µg m-3	Reports mean concentrations from a range of countries including Clark et al (1984 a&b) with an average rural concentration of 0.08 µg m-3 and average urban concentration of 1.2 µg m-3.	IPCS (1995). 1,2-Dichloroethane, Environmental Health Criteria 176 2nd. ed.	http://www.inchem.org/documents/ehc/ehc/ehc176.htm
IPCS EHC	1995	Indoor air	1.2	µg m-3	Reports mean concentrations from a range of countries from 0.1 to 3.4 µg m-3.	IPCS (1995). 1,2-Dichloroethane, Environmental Health Criteria 176 2nd. ed.	http://www.inchem.org/documents/ehc/ehc/ehc176.htm
WHO CICAD	1998	Urban ambient air	1.2	µg m-3	Reports mean concentrations from a range of countries including Clark et al (1984 a&b) with an average rural concentration of 0.08 µg m-3 and average urban concentration of 1.2 µg m-3.	WHO (1998). Concise International Chemical Assessment Document 1: 1,2-Dichloroethane.	https://www.who.int/ipcs/publications/cicad/en/cicad01.pdf?ua=1
WHO CICAD	1998	Indoor air	1.2	µg m-3	Reports mean concentrations from a range of countries from 0.1 to 3.4 µg m-3.	WHO (1998). Concise International Chemical Assessment Document 1: 1,2-Dichloroethane.	https://www.who.int/ipcs/publications/cicad/en/cicad01.pdf?ua=1
OECD SIDS	2002	Ambient air	21.4	µg m-3	Mean concentrations measured near Hamburg in 1986 were 21.4 µg m-3 including industrial locations and 12.4 µg m-3 without industrial locations. Background data range for Japan (1988) was 45 to 2,200 ng m-3.	OECD (2002). 1,2-Dichloroethane. SIDS Initial Assessment Report for 14th SIAM.	http://inchem.org/documents/sids/sids/95501.pdf
US ATSDR	2001	Urban ambient air	0.049 to 0.28	µg m-3	The median daily urban air concentrations in the US between 1970 and 1987 was 0.049 µg m-3 and the mean from 12 Canadian cities between 1988 and 1990 was 0.07 to 0.28 µg m-3.	ATSDR (2001). Toxicological Profile For 1,2-Dichloroethane	https://www.atsdr.cdc.gov/ToxProfiles/tp38.pdf
Health Canada	2013	Ambient air	2.882	µg m-3	Ambient air data from 2004 to 2006 (urban and rural) mean concentration range of 0.027 to 2.882 µg m-3.	Health Canada (2013). Guidelines for Canadian Drinking Water Quality: Guideline Technical Document - 1,2-Dichloroethane	https://www.canada.ca/content/dam/canada/health-canada/migration/healthy-canadians/publications/healthy-living-vie-saine/water-dichloroethane-eau/alt/water-dichloroethane-eau-eng.pdf
Health Canada	2013	Indoor air		µg m-3	Indoor personal air monitoring data is available for 2005-2006. The ranges are within those quoted in the CICAD and EHC.	Health Canada (2013). Guidelines for Canadian Drinking Water Quality: Guideline Technical Document - 1,2-Dichloroethane	https://www.canada.ca/content/dam/canada/health-canada/migration/healthy-canadians/publications/healthy-living-vie-saine/water-dichloroethane-eau/alt/water-dichloroethane-eau-eng.pdf
Rotterdam Convention	2002	Urban ambient air	8.10E-01	µg m-3	1,2-DCA commonly occurs in the air of urban and suburban areas at concentrations less than 0.2 ppb. Using a conversion factor of 4.05 this equates to 0.81 µg m-3.	FAO and UNEP (2002). Decision Guidance Document. Ethylene dichloride.	http://www.pic.int/Portals/5/DGDs/DGD_Ethylene%20dichloride_EN.pdf