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Pentene, all isomers

CAS Registry Numbers:

1-pentene: 109-67-1

cis-2-pentene: 627-20-3

trans-2-pentene: 646-04-8

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TEXAS COMMISSION ON ENVIRONMENTAL QUALITY

Revision History

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Revised DSD August 4, 2014: The DSD was revised using an analog approach using the acute and chronic ESLs for 2-butene for all acute and chronic pentene isomers, respectively.

Revised DSD September 14, 2015: the chronic ReV was updated to use the chronic ReV of 2-butene as directed in the updated TCEQ guidelines (2015)

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Acronyms and Abbreviations

Acronyms and Abbreviations	Definition
ACGIH	American Conference of Governmental Industrial Hygienists
ADH	aldehyde dehydrogenase
AEGL	Acute Exposure Guideline Levels
ATSDR	Agency for Toxic Substances and Disease Registry
^{0} C	degrees centigrade
BMR	benchmark response
CNS	central nervous system
ConA	Concanavalin A
DSD	development support document
EC_{50}	Effective concentration at a 50% response level
ESL	Effects Screening Level
$^{acute}ESL$	acute health-based Effects Screening Level for chemicals meeting minimum database requirements
$^{acute}ESL_{odor}$	acute odor-based Effects Screening Level
$^{acute}ESL_{veg}$	acute vegetation-based Effects Screening Level
$^{chronic}ESL_{threshold(c)}$	chronic health-based Effects Screening Level for threshold dose response cancer effect
$^{chronic}ESL_{threshold(nc)}$	chronic health-based Effects Screening Level for threshold dose response noncancer effects
$^{chronic}ESL_{nonthreshold(c)}$	chronic health-based Effects Screening Level for nonthreshold dose response cancer effects
$^{chronic}ESL_{nonthreshold(nc)}$	chronic health-based Effects Screening Level for nonthreshold dose response noncancer effects
$^{chronic}ESL_{veg}$	chronic vegetation-based Effects Screening Level
EU	European Union
GC	gas chromatography
GLP	good laboratory practice

Acronyms and Abbreviations	Definition
h	hour
$H_{b/g}$	blood:gas partition coefficient
$(H_{b/g})_A$	blood:gas partition coefficient, animal
$(H_{b/g})_H$	blood:gas partition coefficient, human
HEC	human equivalent concentration
HQ	hazard quotient
HSDB	Hazardous Substance Data Base
IARC	International Agency for Research on Cancer
IC_{50}	Inhibitory concentration at a 50% response level
IL	interleukin
IOAEL	inhalation observed adverse effect level
IPCS	International Programme on Chemical Society
IRIS	USEPA Integrated Risk Information System
kg	kilogram
LC_{50}	concentration causing lethality in 50% of test animals
LD_{50}	dose causing lethality in 50% of test animals
LPS	lipopolysaccharide
LOAEL	lowest-observed-adverse-effect-level
LTD	Limited toxicity data
MW	molecular weight
µg	microgram
$µg/m^3$	micrograms per cubic meter of air
mg	milligrams
mg/m^3	milligrams per cubic meter of air
min	minute
MOA	mode of action
n	number

Acronyms and Abbreviations	Definition
NAC	National Advisory Committee
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no-observed-adverse-effect-level
NOEL	no-observed-effect-level
NRC	National Research Council
OECD	Organization for Economic Cooperation and Development
OSHA	Occupational Safety and Health Administration
PBPK	physiologically based pharmacokinetic
Phys/Chem	physical/chemical
POD	point of departure
POD_{ADJ}	point of departure adjusted for exposure duration
POD_{HEC}	point of departure adjusted for human equivalent concentration
ppb	parts per billion
ppm	parts per million
RD_{50}	50% reduction in respiration rate
ReV	reference value
RGDR	regional gas dose ratio
ROS	Reactive oxygen species
RP	Relative potency
RP_{GM}	Geometric mean of relative potency endpoints
SA	surface area
SD	Sprague-Dawley
SIDS	Screening Information Data Set
TCEQ	Texas Commission on Environmental Quality
TD	Toxicology Division
UF	uncertainty factor

Acronyms and Abbreviations	Definition
UF_H	interindividual or intraspecies human uncertainty factor
UF_A	animal to human uncertainty factor
UF_{Sub}	subchronic to chronic exposure uncertainty factor
UF_L	LOAEL to NOAEL uncertainty factor
UF_D	incomplete database uncertainty factor
USEPA	United States Environmental Protection Agency
V_E	minute volume

Chapter 1 Summary Tables

Table 1 for air monitoring and Table 2 for air permitting provide a summary of health- and welfare-based values from an acute and chronic evaluation of pentene isomers. Please refer to Section 1.6.2 of the TCEQ Guidelines to Develop Toxicity Factors (TCEQ 2012) for an explanation of air monitoring comparison values (AMCVs), reference values (ReVs) and effects screening levels (ESLs) used for review of ambient air monitoring data and air permitting. Table 3 provides summary information on pentene isomers' physical/chemical data.

Table 1. Air Monitoring Comparison Values (AMCVs) for Ambient Air

Short-Term Values	Concentration	Notes
Acute ReV	**Short-Term Health** **1-pentene** **c-2 and t-2-pentene** **34,000 µg/m^3 (12,000 ppb)**	The minimum database for development of an acute ReV was not met. The 2-butene acute ReV is used as a surrogate
$^{acute}ESL_{odor}$	**1-pentene** **Odor** **290 µg/m^3 (100 ppb)**	50% odor detection threshold for 1-pentene
$^{acute}ESL_{odor}$	**c-2 and t-2-pentene** **---**	No data found
$^{acute}ESL_{veg}$	---	No data found
Long-Term Values	**Concentration**	**Notes**
Chronic ReV	**Long-Term Health** **1,600 µg/m^3 (560 ppb)**	The minimum database for development of a chronic ReV was not met. The 2-butene chronic ReV is used as a surrogate
$^{chronic}ESL_{nonthreshold(c)}$ $^{chronic}ESL_{threshold(c)}$	- - -	No data found
$^{chronic}ESL_{veg}$	- - -	No data found

[a] Based on the acute ReV of 34,000 µg/m^3 for 2-butene (see Section 3.1).

[b] Based on the chronic ReV of 1,600 µg/m^3 for 2-butene (see Section 4.1).

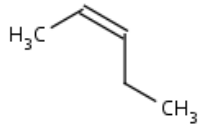
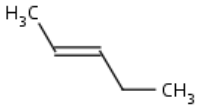
Table 2. Air Permitting Effects Screening Levels (ESLs)

Short-Term Values	Concentration	Notes
$^{acute}ESL$ [1 h]	**1-pentene** **10,000 µg/m^3 (3,500 ppb)**	The minimum database for development of an acute ESL was not met. The 2-butene acute ESL is used as a surrogate
$^{acute}ESL$ [1 h]	**c-2 and t-2-pentene** **Short-Term ESL for Air Permit Reviews** **10,000 µg/m^3 (3,500 ppb)**	The minimum database for development of an acute ESL was not met. The 2-butene acute ESL is used as a surrogate
$^{acute}ESL_{odor}$	**1-pentene** **Short-Term ESL for Air Permit Reviews** **290 µg/m^3 (100 ppb)**	Highly disagreeable 50% odor detection threshold for 1-pentene
$^{acute}ESL_{odor}$	**c-2 and t-2-pentene** - - -	No data found
$^{acute}ESL_{veg}$	- - -	No data found
Long-Term Values	**Concentration**	**Notes**
$^{chronic}ESL_{threshold(nc)}$	**Long-Term ESL for Air Permit Reviews** **480 µg/m^3 (170 ppb)**	The minimum database for development of a chronic ESL was not met. The 2-butene chronic ESL is used as a surrogate
$^{chronic}ESL_{nonthreshold(c)}$ $^{chronic}ESL_{threshold(c)}$	- - -	No data found
$^{chronic}ESL_{veg}$	- - -	No data found

[a] Based on the acute ESL of 10,000 µg/m^3 for 2-butene (see Section 3.1).

[b] Based on the chronic ESL of 480 µg/m^3 for 2-butene (see Section 4.1).

Table 3. Physical and Chemical Data

Parameter	**1-pentene**	**cis-2-pentene**	**trans-2-pentene**	**Reference**
Molecular Formula	C_5H_{10}	C_5H_{10}	C_5H_{10}	HSDB (2002)
Chemical Structure				ChemIDplus
Molecular Weight	70.13	70.13	70.13	HSDB (2002)
Physical State	Liquid	Liquid	Liquid	HSDB (2002)
Color	Colorless	---	---	HSDB (2002)
Odor	Highly disagreeable	---	---	HSDB (2002)
CAS Registry Number	109-67-1	627-20-3	646-04-8	HSDB (2002)
Synonyms	α-amylene; α-n-amylene; 1-pentalyene; propylethylene	β-amylene-cis; cis-β-amylene; cis-β-N-amylene; cis-pentene; (Z)-2-pentene	β-amylene-trans; trans-β-amylene; trans-β-N-amylene; (E)-2-pentene; 2-trans-pentene	HSDB (2002)
Water Solubility	148 mg/L @ 25°C	203 mg/L @ 25°C	203 mg/L @ 25°C	HSDB (2002)
Log K_{ow} or P_{ow}	---	---	---	---
Vapor Pressure	635 mm Hg @ 25°C	495 mm Hg @ 25°C	506 mm Hg @ 25°C	HSDB (2002)
Relative Vapor Density	2.42	2.4	---	HSDB (2002)
Density	0.6405 @ 25°C	0.6554 @ 20°C	0.6431 @ 25°C	HSDB (2002)
Melting Point	-165.2°C	-151.4°C	-140.2°C	HSDB (2002)
Boiling Point	29.9°C	36.9°C	36.3°C	HSDB (2002)
Conversion Factors @ 25°C	1 μg/m^3 = 0.35 ppb 1 ppb = 2.87 μg/m^3	1 μg/m^3 = 0.35 ppb 1 ppb = 2.87 μg/m^3	1 μg/m^3 = 0.35 ppb 1 ppb = 2.87 μg/m^3	Toxicology Division

Chapter 2 Major Uses or Sources and Ambient Air Concentrations

According to the Hazardous Substances Data Bank (HSDB 2002), 1-pentene is primarily used in organic synthesis as a blending agent for high octane motor fuel and in pesticide formulations. 2-pentene is used as a polymerization inhibitor in organic synthesis.

Chapter 3 Acute Evaluation

3.1 Health-Based ^{acute}ESL

At high concentrations, pentene causes respiratory and cardiac depression in animals whereas in humans, pentene causes primary excitation (Clayton 1994).

3.1.1 Physical/Chemical (Phys/Chem) Properties

The pentene category includes three isomers: 1-pentene (CASRN 109-67-1); cis-2-pentene (CASRN 627-20-3); and trans-2-pentene (CASRN 646-04-8). Pentene isomers are liquids with a high vapor pressure, moderate water solubility, and low molecular weight (70.13), which indicates the potential for pentene isomers to be absorbed via the lungs and widely distributed within the body. Other phys/chem properties of propene isomers can be found in Table 3.

3.1.2 Key Studies

Acute toxicity studies in animals or humans with adequate dose-response data are not available for the pentene isomers. Well-conducted studies are available for petroleum distillate blending streams (Bui et al. 1998; Lapin et al. 2001; Schreiner et al. 2000). However, the distillate is a mixture of compounds, making it impossible to differentiate the effects of specific chemicals. The only acute toxicity data for pentene is LC_{50} data, concentrations shown to be lethal to 50% of the study specimens: 4-hour (h) LC_{50} in rats = 175,000 mg/m^3 and 2-h LC_{50} in mice = 180,000 mg/m^3 (RTECS database 2006). These LC_{50} doses are relatively high and indicate that pentene has low acute lethal toxicity.

The minimum database for estimating an acute ReV was not met so procedures outlined in TCEQ Guidelines (2012) for limited toxicity data were followed to determine an acute generic ESL ($^{acute}ESL_{generic}$). Two methods were investigated: the NOAEL-to-LC_{50} ratio approach and an analog approach. An analog is defined as a chemical compound that is structurally similar to another compound but differs slightly in composition (as in the replacement of one atom by an atom of a different element or in the presence of a particular functional group). In order to use the analog approach, there should be unambiguous structural and metabolic relationships between the LTD chemical and the chemical with toxicity information. A comparison of these approaches is found in Section 3.1.4.5 Health-Based ^{acute}ESL.

3.1.3 NOAEL-to-LC_{50} Ratio Approach

As mentioned previously, the following acute toxicity data were reported in the RTECS database (2006):

4-h LC_{50} in rats = 175,000 mg/m^3
2-h LC_{50} in mice = 180,000 mg/m^3

Grant et al. (2007) determined a NOAEL-to-LC_{50} (N-L) ratio of 8.3 x 10^{-5}. This factor is multiplied by 4-h LC_{50} values to estimate a conservative $^{acute}ESL_{generic}$ (TCEQ 2012). As stated in Section 4.5.2.1 of the TCEQ guidelines (2012), a duration adjustment to 4 h is required for the 2-h LC_{50} data from mice (TCEQ 2012). Since the mode of action (MOA) is unknown, default procedures discussed in TCEQ (2012) with n=1 were used to adjust the exposure duration in the mouse study from 2 to 4 h as follows:

$C_1 \times T_1 = C_2 \times T_2$
180,000 mg/m^3 x 2 h = C_2 x 4 h
C_2 = 180,000 x (2/4)
C_2 = 90,000 mg/m^3

When the 4-h LC_{50} values for rats and mice are multiplied by 8.3 x 10^{-5}, the potential $^{acute}ESL_{generic}$ values are as follows:

- 7,500 $\mu g/m^3$ (2,600 ppb) based on the converted 4-h LC_{50} value in mice; and
- 14,500 $\mu g/m^3$ (5,060 ppb), based on the 4-hr LC_{50} value in rats.

Both of these potential $^{acute}ESL_{generic}$ values are conservative and estimate an acute value where no appreciable human health risks would be expected to occur. The lowest potential $^{acute}ESL_{generic}$ based on the mouse study to be considered further is 7,500 $\mu g/m^3$ (2,600 ppb).

3.1.4 Analog Approach

Since pentene isomers have limited acute toxicity data (LTD), an $^{acute}ESL$ for pentene was derived based on an analog approach using toxicity information on butene isomers (TCEQ a, b, and c).

The following procedures outlined in TCEQ (2012) are employed when similar chemical categories or an analog chemical approach is used, depending on data availability:

- Identify potential analog chemical(s) for which toxicity factors have been developed.
- Gather data on phys/chem properties, toxicity, etc. for the potential analog chemical and the LTD chemical.
- Perform an MOA analysis.

- Evaluate the data to determine the most appropriate health-based acute ESL for the LTD chemical, which in this case are the pentene isomers.

3.1.4.1 Identify Potential Analog Chemical(s)

Members of a chemical group or class share similar phys/chem properties, and can have similar MOAs. Therefore, they may behave in a similar toxicological manner (TCEQ 2012). The butene isomers were considered as analog chemicals to predict the chronic toxicity of pentene isomers for the following reasons:

- The TCEQ has developed acute toxicity factors for 1-butene (TCEQ 2014a), 2-butene (TCEQ 2014b), and isobutene (TCEQ 2014c).

- Hexene was considered as an analog chemical for pentene, but a DSD for hexene has not been developed.

- Butenes and pentenes have similar phys/chem properties and have similar structures (i.e., both are straight-chain alkenes) (Section 3.1.4.2)

- Butenes and pentenes are considered to have low acute toxicity (Section 3.1.4.3.1)

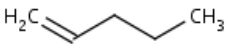
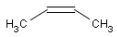
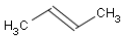
- Butenes and pentenes are expected to produce CNS effects after acute exposure to high concentrations.

- The MOA for CNS effects are expected to be similar based on phys/chem properties (Section 3.1.4.4).

3.1.4.2 Phys/Chem Properties

For a complete listing of phys/chem properties of the butene isomers, refer to Table 3 of TCEQ (2014a, b, and c). For a complete listing for the pentene isomers, refer to Table 3 of this document. Table 4 shows a comparison of key phys/chem properties for 1-pentene to 2-butene (cis and trans). Data for 2-butene are shown since the phys/chem properties of other butene isomers (1-butene and isobutene) are similar. Pentene and butene have similar chemical structures both being straight-chain alkenes, differing by one carbon. Pentene is a liquid and butene is a gas so the vapor pressure for pentene is lower than butene by a factor of 2. Both pentene and butene are moderately soluble in water and have a moderately low K_{ow}.

Table 4. Physical/Chemical Parameters for Pentene and 2-Butene

Parameter	1-pentene	Cis-2-butene [a]	Trans-2-butene [a]
Molecular Formula	C_5H_{10} HSDB 2002	$CH_3HC{=}CHCH_3$ ChemIDplus	$CH_3HC{=}CHCH_3$ ChemIDplus
Chemical Structure	 ChemIDplus	 ChemIDplus	 ChemIDplus
Molecular Weight	70.13 HSDB 2002	56.11 TRRP 2006	56.11 TRRP 2006
Physical State	Liquid HSDB 2002	Gas TRRP 2006	Gas TRRP 2006
Water Solubility mg/L	148 HSDB 2002	347.58 TRRP 2006	347.58 TRRP 2006
Log K_{ow} or P_{ow}	2.93 TRRP 2011	2.37 TRRP 2006	2.37 TRRP 2006
Vapor Pressure mm Hg	635 HSDB 2002	1460.14 TRRP 2006	1460.14 TRRP 2006
Relative Vapor Density	2.42 HSDB 2002	0.6042 OECD 2004	0.6042 OECD 2004
Conversion Factors @ 25°C	1 ppb = 2.87 µg/m^3 1 µg/m^3 = 0.35 ppb Toxicology Division (TD)	1 ppb = 2.29 µg/m^3 1µg/m^3 = 0.437 ppb TD	1 ppb = 2.29 µg/m^3 1µg/m^3 = 0.437 ppb TD

[a] Refer to the 2-Butene DSD (TCEQ 2014b) for references for phys/chem parameters for cis- and trans-2- butene.

3.1.4.3 LC_{50} data for Pentene and Isobutene

LC_{50} data are only available for isobutene and pentene. LC_{50} data indicate these alkenes have low acute toxicity:

- Mice and rats were exposed to varying concentrations of isobutene vapors in order to determine the LC_{50} for each species (Shugaev 1969; TCEQ 2014c): the 4-h LC_{50} in rats was 270,000 ppm and the 2-h LC_{50} in mice was 180,000 ppm.

- LC_{50} data reported in the RTECS database (2006) for pentene are as follows: 4-h LC_{50} in rats = 61,000 ppm and 2-h LC_{50} in mice = 63,000 ppm.

LC_{50} data indicate pentene is more toxic than isobutene. This may relate to the proposed MOA for CNS effects and lethality and differences in toxicokinetics, as discussed below.

3.1.4.4 MOA Information

3.1.4.4.1 Toxicokinetics

Eide et al. (1995) investigated the toxicokinetics of individual C2-C8 1-alkenes as well as measuring hemoglobin and DNA adducts to evaluate genotoxicity and reactivity. Male SD rats were exposed to 300 ppm of the individual 1-alkenes for 12 h/day for three consecutive days. Chamber concentrations were evaluated by gas chromatography.

Immediately after exposure after each of the three exposures, concentrations of the 1-alkenes in blood and tissues (liver, lung, brain, kidneys, and fat) were measured to investigate toxicokinetics. Steady state for all C2-C8 1-alkenes was reached after the first 12-h exposure. Concentrations in blood and tissues were similar when measured on day 1, 2, or 3, so only data from day 3 were provided. Table 5 shows the concentrations of 1-butene and 1-pentene in different tissues. Refer to Eide et al. (1995) for data for ethene, propene, 1- hexane,1-heptene and 1-octene. Concentrations of 1-alkenes in blood and different tissues increased with increasing number of carbon atoms.

Table 5 Tissue Concentrations of 1-Butene and 1-Pentene (Eide et al. 1995)

Tissue	1-Butene	1-Pentene
Blood	1.9 ± 0.1	8.6 ±1.4
Brain	3.0 ± 0.3	41.0 ± 4.9
Liver	0.8 ± 0.3	51.6 ± 12.9
Lung	4.9 ± 1.1	31.4 ± 10.6
Kidneys	5.7 ± 1.4	105.7 ± 13.7
Fat	70 ± 8	368 ± 79
Fat after 12 h elimination	0.3 ± 0.1	19 ± 9

3.1.4.4.2 MOA for CNS Effects and Lethality

Anesthesia, narcosis, and other CNS effects were observed for the butene isomers after acute exposure at high concentrations greater than 150,000 ppm (TCEQ 2014 a, b, c). High concentrations in the brain may cause solvent effects on lipid and fatty acid compositions of membranes. Eide et al. (1995) showed that concentrations of 1-pentene in brain were 14-times higher than for 1-butene (Table 5). This indicates that 1-pentene may cause greater CNS effects and lethality due to higher concentrations in the brain compared to 1-butene. This may also explain the lower LC_{50} data for pentene when compared to isobutene (Section 3.1.4.3), although this relates more to lethality than critical effects that would occur at lower concentrations.

3.1.4.4.3 MOA for Decrease Body Weight

For 2-butene, a decrease in body weight after exposure for one week was observed (TCEQ 2014 b). The MOA for the decrease in body weight due to 2-butene exposure is unknown.

3.1.4.5 Health-Based ^{acute}ESL

Although the acute health effects for pentene isomers are unknown, based on their similar structures, phys/chem properties, their toxicity would be similar and the toxicity values for butene isomers would be appropriate to use for pentene isomers. Table 6 provides acute ReVs and ^{acute}ESLs for 1-butene, 2-butene, and isobutene.

Table 6 Comparison of ^{acute}ESLs for Butene Isomers

Chemical	Acute ReV	^{acute}ESL	Critical Effect(s)
1-butene	62,000 µg/m^3 (27,000 ppb)	19,000 µg/m^3 (8,100 ppb)	**Critical Effect(s):** Based on free-standing NOAEL, no adverse effects observed in SD rats in a repeat dose, subacute study. At much higher concentrations, CNS effects were observed.
2-butene	34,000 µg/m^3 (15,000 ppb)	10,000 µg/m^3 (4,500 ppb)	**Critical Effect(s):** Decreased body weight in female Wistar rats observed after seven days in a reproductive/developmental study. At much higher concentrations, CNS effects were observed.
isobutene	620,000 µg/m^3 (270,000 ppb)	180,000 µg/m^3 (81,000 ppb)	**Critical Effect(s):** Based on free-standing NOAEL, no adverse effects observed in Wistar rats in a reproductive/developmental study. At much higher concentrations, CNS effects were observed.

2-Butene has the most conservative acute ReV and ^{acute}ESL based on decreased body weight as the critical effect after a multiple day exposure. The TCEQ Guidelines (2012) state "the lowest, most conservative toxicity factor for a series of structurally-similar compounds can be used as a generic value for other structurally-similar compounds with limited toxicity information." Therefore, the acute ReV of 34,000 µg/m^3 and the ^{acute}ESL of 10,000 µg/m^3 for 2-butene will be used as an analog for all pentene isomers until toxicity data for pentene isomers become available.

The lowest potential $^{acute}ESL_{generic}$ based on the mouse study using the N-L ratio approach was 7,500 µg/m^3 (2,600 ppb) (Section 3.1.3). The N-L ratio approach is considered a conservative approach for deriving generic ESLs for LTD chemicals. The ^{acute}ESL of 10,000 µg/m^3 (4,500 ppb) based on the structural/analog approach is slightly higher compared to the value derived using the N-L ratio approach (less than two times higher). The structural/analog approach is preferred and will be used for the pentene isomers.

Table 7 is a summary of the derivation of the ReV and ^{acute}ESL for 2-butene based on the Waalkens-Brendsen and Arts (1992) study. Refer to TCEQ (2014b) for a detailed description of this study. The acute ReV of 34,000 µg/m^3 and the ^{acute}ESL of 10,000 µg/m^3 for 2-butene will be used as a toxicity factor analog for all pentene isomers (TCEQ 2012).

Table 7 Derivation of the Acute ReV and ^{acute}ESL for 2-Butene [(a)]

Parameter	**Summary**
2-Butene	ReV and ^{acute}ESL
Study	OECD Guideline 422 combined repeated-exposure, reproduction and screening study (Waalkens-Brendsen and Arts 1992 in OECD 2004)
Study population	Male and female Wistar rats (12/sex/concentration)
Study quality	High
Exposure methods	Exposures via inhalation at 0, 2,500 and 5,000 ppm (0, 2,476 ± 68 ppm, and 5,009 ± 88 ppm analytical)
Critical effects	NOAEL based on decreased body weight in female rats after 7 days of exposure
POD	2,476 ppm (NOAEL)
Exposure duration	6 h/day for 7 days
Extrapolation to 1 h	6 h to 1 h (TCEQ 2012 with n = 3)
POD_{ADJ} (1 h)	4,499 ppm
POD_{HEC}	4,499 ppm (gas with systemic effects, based on default RGDR = 1.0)
Total uncertainty factors (UFs)	300
Interspecies UF	3
Intraspecies UF	10
LOAEL UF	Not applicable
Incomplete Database UF *Database Quality*	10 Medium
acute ReV [1 h] (HQ = 1)	34,000 µg/m^3 (15,000 ppb)
^{acute}ESL [1 h] (HQ = 0.3)	10,000 µg/m^3 (4,500 ppb)
Pentene isomers	**ReV and ^{acute}ESL**
Acute ReV	**34,000 µg/m^3 (12,000 ppb) [(b)]**
^{acute}ESL	**10,000 µg/m^3 (3,500 ppb) [(b)]**

[(a)] Refer to TCEQ (2014b) for details on critical study for 2-butene

[(b)] after adjustment of concentration in µg/m^3 to ppb based on different molecular weights for 2-butene and pentene

3.2 Welfare-Based Acute ESLs

3.2.1 Odor Perception

The Japanese Ministry of the Environment is listed as a Level 1 source of information for odor thresholds (TCEQ 2012). The 50% odor detection threshold for 1-pentene determined by the triangular odor bag method was 0.10 ppm (Nagata 2003). Therefore, the $^{acute}ESL_{odor}$ for 1-pentene is 100 ppb (290 µg/m^3).

Odor data are unavailable for other isomers of pentene. Nagata et al. (2003) describe wide variation in the odor threshold between isomers of other substances. Therefore, unlike a health-based ^{acute}ESL, which may be applied to all isomers, the odor threshold determined by Nagata (2003) is specific for 1-pentene.

3.2.2 Vegetation Effects

No acute vegetative studies were identified for any isomers of pentene.

3.3 Short-Term ESLs and Values for Air Monitoring Evaluation

Toxicity data are unavailable for other isomers of pentene. However, the phys/chem properties of these isomers are quite similar to 1-pentene. Therefore, the health-based acute ReV and ^{acute}ESL will be applied to all isomers.

3.3.1 Values for 1-Pentene

For 1-pentene, the acute evaluation resulted in the derivation of the following acute values:

- Acute ReV = 34,000 µg/m^3 (12,000 ppb)
- $^{acute}ESL_{odor}$ = 290 µg/m^3 (100 ppb)
- ^{acute}ESL = 10,000 µg/m^3 (3,500 ppb)

For evaluation of air monitoring data, the $^{acute}ESL_{odor}$ of 290 µg/m^3 (100 ppb) and the health-based acute ReV = 34,000 µg/m^3 (12,000 ppb) may be used (Table 1).The short-term ESL for air permit evaluations of 1-pentene is based on odor potential and is 290 µg/m^3 (100 ppb) as this value is lower than the ^{acute}ESL (Table 2).

3.3.2 Values for c-2-Pentene and t-2-Pentene

For c-2-pentene and t-2-pentene, the acute evaluation resulted in the derivation of the following acute value:

- Acute ReV = 34,000 µg/m^3 (12,000 ppb)
- ^{acute}ESL = 10,000 µg/m^3 (3,500 ppb)

For evaluation of air monitoring data, the health-based acute ReV = 34,000 µg/m^3 (12,000 ppb)

may be used (Table 1). The short-term ESL for air permit evaluations of c-2- and t-2-pentene is the health-based ^{acute}ESL of 10,000 µg/m^3 (3,500 ppb) (Table 2).

3.4 Acute Inhalation Observed Adverse Effect Level

An acute inhalation observed adverse effect level was not determined for pentene isomers since an approach for limited toxicity data was used to determine the ^{acute}ESL.

Chapter 4 Chronic Evaluation

4.1 Noncarcinogenic Potential

No studies were available describing the potential chronic toxicity of any isomer of pentene. Since pentene isomers have limited chronic toxicity data (LTD), a ^{chronic}ESL for pentene was derived based on an analog chemical approach using toxicity information on butene isomers (TCEQ 2014 a, b, and c), similar to the approach to develop an ^{acute}ESL for pentene isomers.

Procedures outlined in TCEQ (2012) were employed for an analog chemical approach. These procedures have been previously discussed in Section 3.1.4.

4.1.1 Identify Potential Analog Chemical(s)

Members of a chemical group or class that share similar phys/chem properties can have similar MOAs. Therefore, they may behave in a similar toxicological manner (TCEQ 2012). The butene isomers were considered as analog chemicals to predict the chronic toxicity of pentene isomers for the following reasons:

- The TCEQ has developed chronic toxicity factors for 1-butene (TCEQ 2014a), 2-butene (TCEQ 2014b), and isobutene (TCEQ 2014c).
- Hexene was considered for use as an analog chemical for pentene, but was not used because a DSD for hexene has not been developed.
- Butenes and pentenes have similar phys/chem properties and have similar structures (i.e., both are straight-chain alkenes differing by only one carbon) (Section 4.1.2)
- Butenes and pentenes, as well as other alkenes, are metabolized by cytochrome P450 to epoxides. The MOA for effects after chronic exposure may relate to the similar metabolism of butenes and pentenes (Section 4.1.4).

4.1.2 Phys/Chem Properties

Please refer to Section 3.1.4.2 and Table 4 for a comparison of the phys/chem properties of 1-pentene to 2-butene. As stated previously, pentene and butene have similar chemical structures (i.e., straight-chain alkenes), differing by one carbon.

4.1.3 Critical Effects after Chronic Exposure

The critical effects after acute exposure for the butene isomers observed at high concentration (> 150,000 ppm) were CNS effects and respiratory depression. CNS effects were due to high concentrations and would not be expected at lower concentrations: (1) free-standing NOAELs of 8,000 ppm for 1-butene (subacute study) and isobutene (chronic study) were observed and (2) the critical health effect observed for 2-butene was decreased body weight (NOAEL of 2,500 ppm observed in a subacute study)(TCEQ 2014 a, b, c). Based on their similar structures, similar phys/chem properties and reactivities (Section 4.1.5), critical effects after chronic exposure would be expected to be similar.

4.1.4 MOA Information

The MOA for CNS effects after high, acute exposures (Section 3.1.2) is not relevant to low level, chronic exposure. The MOA after chronic exposure to the pentenes and butenes is unknown, but may be related to the metabolism of 1-alkenes to epoxides.

4.1.4.1 Metabolism of Alkenes

The presence of the double bond makes alkenes optimal substrates for the cytochrome P450 enzymes that convert them to the respective reactive epoxides that possess alkylating capacity towards nucleophilic sites in proteins and DNA. Epoxides may be rapidly metabolized by epoxide hydrolase (EH) and glutathione-S-transferase (GST) and detoxified.

Information on the metabolism of isobutene has been studied (TCEQ 2014c). Isobutene is metabolized in the liver by the CYP2E1 cytochrome P-450 isoform to 2-methyl-1,2-epoxypropane (MEP) (1,1-dimethyloxirane), a reactive epoxide. The epoxide is rapidly metabolized by epoxide hydrolase (EH) and glutathione-S-transferase (GST), converting the epoxide to 2-methyl-1,2-propanediol and to a glutathione conjugate, respectively. Detailed information on metabolism of 1- and 2-butene and the pentene isomers is not available.

The epoxides for C4 and C8 alkenes may be less reactive when compared to other chemicals with double bonds that undergo metabolism to epoxides. Fabiani et al. (2012) investigated the reactivity for different epoxides for 1,3-butadiene, isoprene, styrene, propylene and 1-butene *in vitro* using the comet assay in human peripheral blood mononuclear cells and promyelocytic leukaemia cells. He showed that 1-butene had a low capacity for binding to proteins and DNA when compared to the other investigated chemicals.

Hemminki et al. (1994) investigated the reaction kinetics of alky epoxides with DNA and other nucleophiles *in vitro*. He found that the reaction rates with DNA for the C3 to C8 1,2-epoxy alkanes were inversely related to the chain lengths of the epoxide (i.e., reaction rates decreased with increasing chain length).

Eide et al. (1995) investigated the toxicokinetics of individual C2-C8 1-alkenes (discussed in Section 3.1.4.4) as well as measuring hemoglobin adducts in blood (N-(2-hydroxyalkyl)valine)

and DNA adducts in lymphocytes and liver (7-alkyguanine) to evaluate potential genotoxicity and reactivity of C2-C8 alkenes. Male SD rats were exposed to 300 ppm of the individual 1-alkenes for 12 h/day for three consecutive days. Chamber concentrations were evaluated by gas chromatography.

Concentrations of 1-alkenes in blood and different tissues increased with increasing number of carbon atoms (refer to Section 3.1.4.4 for additional information). However, levels of hemoglobin and DNA adducts, a measure of reactivity, decreased with increasing number of carbon atoms. This agrees with the *in vitro* results of Hemminki et al. (1994) who found the levels of DNA adducts decreased with increasing number of carbon atoms.

Table 5 provides data on hemoglobin and DNA adducts from Eide et al. (1995). All 1-alkenes caused formation of detectable levels of hemoglobin and DNA adducts, although the levels of hemoglobin adducts after C4-C8 exposure were low when compared to ethene and propene. The hemoglobin and DNA adducts measured for 1-pentene were in the same range compared to levels measured for 1-butene. If the MOA for butene and pentene were based on reactivity as evaluated with hemoglobin and DNA adducts, it would suggest 1-butene would be an adequate analog for the pentene isomers (i.e., indicates the toxicity of 1-pentene and 1-butene may be similar).

Table 8 Hemoglobin and DNA Adducts for C2-C5 Alkenes [a]

1-Alkene	Hemoglobin [b]	Lymphocytes [c]	Liver [c]
ethene	2730 ± 100	5.8 ± 2.2	7.4 ± 1.0
propene	740 ± 50	1.8 ± 0.9	2.8 ± 0.9
1-butene	20 ± 1	0.8 ± 0.4	2.1 ± 0.5
1-pentene	51 ± 3	0.5 ± 0.2	1.8 ± 0.6

[a] Levels (mean ± SD) of N-(2-hydroxyalkyl)valine in hemoglobin (pmol/g) and 7-alkyguanine in lymphocytes and liver (adducts/ 10^7 normal nucleotides). Background values have been subtracted.

[b] n = 3-8 for hemoglobin adduct analyses

[c] n = 4 for DNA adduct analyses

4.1.5 Health-Based ^{chronic}ESL for Pentene Isomers

The toxicity data for pentene isomers are limited although the toxicity data for butene isomers were adequate to develop isomer-specific $^{chronic}ESL_{threshold(nc)}$ (TCEQ 2014 a, b, c). Table 6 provides $^{chronic}ESL_{threshold(nc)}$ for 1-butene, 2-butene, and isobutene. 2-Butene has the most conservative chronic ReV of 1,600 µg/m^3 (690 ppb) and $^{chronic}ESL_{threshold(nc)}$ of 480 µg/m^3 (210 ppb) (Table 9).

The TCEQ Guidelines (2012) state "the lowest, most conservative toxicity factor for a series of structurally-similar compounds can be used as a generic value for other structurally-similar compounds with limited toxicity information." The chronic ReV of 1,600 µg/m^3 and the $^{chronic}ESL_{threshold(nc)}$ of 480 µg/m^3 for 2-butene will be used for all pentene isomers. Table 10 is a summary of the derivation of the $^{chronic}ESL_{threshold(nc)}$ for 2-butene based on the Waalkens-Brendsen and Arts (1992) study (refer toTCEQ 2014b for a detailed description) and shows the chronic ReV and ^{chronic}ESL for all pentene isomers

Table 9 Comparison of $^{chronic}ESL_{threshold(nc)}$ for Butene Isomers

Chemical	Chronic ReV	$^{chronic}ESL_{threshold(nc)}$	Critical Effect(s)
1-butene	5,300 µg/m^3 (2,300 ppb)	1,600 µg/m^3 (690 ppb)	**Critical Effect(s):** Based on free-standing NOAEL, no adverse effects observed in SD rats in a repeat dose, subacute study
2-butene	1,600 µg/m^3 (690 ppb)	480 µg/m^3 (210 ppb)	**Critical Effect(s):** Decreased body weight in Wistar rats observed in a subacute reproductive/developmental study
isobutene	110,000 µg/m^3 (47,000 ppb)	32,000 µg/m^3 (14,000 ppb)	**Critical Effect(s):** Based on free-standing NOAEL in a chronic study, no adverse effects observed in F344/N rats and B6C3F1 mice

Table 10 Derivation of the Chronic ReV and $^{chronic}ESL_{threshold(nc)}$ for 2-Butene

Parameter	Summary
2-Butene	**ReV and $^{chronic}ESL_{threshold(nc)}$**
Study	OECD Guideline 422 combined repeated-exposure, reproduction and screening study (Waalkens-Brendsen and Arts 1992 in OECD 2004) [(a)]
Study population	Male and female Wistar rats (12/sex/concentration)
Study quality	High
Exposure methods	Exposures via inhalation at 0, 2,500 and 5,000 ppm (0, 2,476 ± 68 ppm, and 5,009 ± 88 ppm analytical)
Critical effects	NOAEL based on decreased body weight in rats
POD	2,476 ppm (NOAEL)
Exposure duration	6 h/day for 7 days
POD_{ADJ} to continuous exposure	619
POD_{HEC}	619 ppm (gas with systemic effects, based on default RGDR = 1.0)
Total uncertainty factors (UFs)	900
Interspecies UF	3
Intraspecies UF	10
LOAEL UF	Not applicable
Subchronic UF	3
Incomplete Database UF *Database Quality*	10 low
chronic ReV (HQ = 1)	**1,600 µg/m^3 (690 ppb)**
$^{chronic}ESL_{threshold(nc)}$ (HQ = 0.3)	**480 µg/m^3 (210 ppb)**
Pentene isomers	**$^{chronic}ESL$**
chronic ReV	**1,600 µg/m^3 (560 ppb)** [(b)]
$^{chronic}ESL_{threshold(nc)}$	**480 µg/m^3 (170 ppb)** [(b)]

[(a)] refer to TCEQ (2014b) for details on key study for 2-butene.
[(b)] after adjustment of concentration in µg/m^3 to ppb based on different molecular weights for 2-butene and pentene

4.2 Carcinogenic Potential

There are no studies indicating that pentene isomers have carcinogenic potential.

4.3 Welfare-Based Chronic ESL- Vegetation Effects

No chronic vegetative studies were identified for any isomers of pentene.

4.4 Long-Term ESLand Values for Air Monitoring Evaluation

The chronic evaluation resulted in the derivation of the following values:

- Chronic ReV = 1,600 µg/m^3 (560 ppb)
- $^{chronic}ESL_{threshold(nc)}$ = 480 µg/m^3 (170 ppb)

The long-term ESL for air permit evaluations is the $^{chronic}ESL_{threshold(nc)}$ of 480 µg/m^3 (170 ppb) (Table 2). The chronic ReV of 1,600 µg/m^3 (560 ppb) be utilized during evaluation of air monitoring data (Table 1).

4.5 Chronic Inhalation Observed Adverse Effect Level

A chronic inhalation observed adverse effect level was not determined for pentene isomers since an approach for limited toxicity data was used to determine the $^{chronic}ESL$.

Chapter 5 References

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