# 1,4-Dichloro-2-butene

| CAS number: | 764-41-0 |
| --- | --- |
| Synonyms: | 2-Butylene dichloride, DCB, 1,4-DCB, dichlorobutene, 1,4-dichlorobutene-2 |
| Chemical formula: | C4H6Cl2 |

Workplace exposure standard (interim)

| TWA: | **0.005 ppm (0.025 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc 1B; Sk.** |
| IDLH: | **—** |
| **Sampling and analysis:** The recommended value is likely to be below the current limit of detection for standard sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

An interim TWA of 0.005 ppm (0.025 mg/m3) is recommended to protect for the potential for significant eye and respiratory tract irritation in exposed workers.

Given the limited data available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

## Discussion and conclusions

1,4-Dichloro-2-butene (DCB) is a chemical intermediate for a range of industrial processes. It is identified as a severe irritant, mutagen and animal carcinogen.

Limited epidemiological data are available with exposure limit recommendations largely based on experimental animal studies. A NOAEC of 2 ppm for irritant effects is identified from a four week inhalation study in rats (ACGIH, 2018). It is considered a suspected human carcinogen (ACGIH, 2018). Animal carcinogenicity studies reported increased incidence of nasal tumours for all dosage scenarios with a LOAEC of 0.1 ppm (ACGIH, 2018). Information on the mechanism of carcinogenicity is not readily available and therefore it is not characterised as a non-threshold genotoxic carcinogen.

The recommended TWA is adopted directly from the current TLV-TWA of 0.005 ppm (0.025 mg/m3) by ACGIH (2018). Given the absence of suitable data about carcinogenicity a priority evaluation is recommended at the next scheduled review

## Recommendation for notations

Classified as a category 1B carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

A skin notation is recommended based on evidence suggesting potential dermal absorption and adverse systemic effects in animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA NA NA | |
|  |
| ACGIH 2001 TLV-TWA: 0.005 ppm (0.025 mg/m3) |
| TLV-TWA of 0.005 ppm (0.025 mg/m3) recommended to reported to minimise the potential for significant eye and respiratory tract irritation.  Summary of data:  No derivation of TLV-TWA provided  Human data:   * A study involving 525 male workers reported 7 deaths associated with malignant neoplasms * the study was unable to demonstrate a significant increase in cancer mortality as a result of exposure; considered inconclusive * Based on US EPA’s quantitative risk analysis of nasal tumours produced in male rats from a chronic inhalation study (US EPA, 2008), agency determined workers exposed to 8 h/d, 5 d/wk for 40 yr to 0.005 ppm would have an additional lifetime cancer risk of 8 x 10-3 with an upper bound of 1 x 10-2.   Animal data:   * LC50: 86 mg/kg (rats,4 h, inhalation) * LD50: 89 mg/kg (rats, oral) * LD50: 0.62 mL/kg (rabbits, dermal) * Acute inhalation by rats resulted in haemorrhaging in the lungs, liver and spleen * In a 2 wk inhalation study (6 h/d, 5 d/wk), no effects observed on hamsters and rats subjected to 0.1 ppm * under exposure concentrations of 10 ppm, rats exhibited retarded growth and respiratory tract inflammation * In another 4 wk inhalation study on rats, the NOAEL determined to be 2 ppm * 1 study designed to assess carcinogenicity determined incidence of animals with nasal tumours was dose-related (exposures ranged from 0–5 ppm) * A follow-up study confirmed rats exposed to concentrations ranging from 0–1 ppm for 599 d and after a 12 mo period, had slight basal cell flattening/hyperplasia and mucosal atrophy * benign nasal tumours appeared in all exposure groups (from 10–19 mo, depending on exposure concentration) * Multiple studies confirmed carcinogenicity on animals, with a tumour incidence and latency that is dose-dependent * Does not act as an embryotoxin or teratogen.   Genotoxicity   * Mutagenic in *S. typhimurium* and *Drosophila melanogaster*.   Recommended an A2 Suspected Human Carcinogen classification, but insufficient data available to assign a SEN notation or TLV-STEL. |
| DFG 2001 NA |
| No MAK recommended. Repeat inhalation exposure include irritant effects on the respiratory tract in additional to potential changes in organs.  Summary of additional data:   * 1 study subjected rats to concentrations of 1.7–7.9 mg/m3 for 1, 30 or 120 d and concluded all exposure groups developed significant chromosomal aberrations, the severity of which were time and concentration dependent * An *in vivo* study on rats determined that concentrations between 1.8–8.3 mg/m3 led to germ cell mutations and was therefore classified as a category 3A mutagen * LD50: 735 mg/kg (rabbits, dermal) * Undiluted application resulted in severe erythema and oedema and slight necrosis in 5 rabbits. Assumed significant absorption via the skin, as such designated a skin notation * Mutagenic in *S. typhimurium* and *E. coli*. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| IARC |  | 1999 | * Determined to be Carcinogenicity – Group 3 |
| OECD |  | 2006 | * Mutagenic to bacteria and yeast as well as mammalian cells *in vitro*. |
| US EPA |  | 2008 | * Mutagenicity is consistently demonstrated in bacterial and mammalian cell assays *in vitro* * Insufficient data exist to characterise the carcinogenic mode of action, but the available evidence is suggestive of carcinogenic potential * Inhalation unit risk factor is derived from dose-dependent incidences of nasal adenomas and carcinomas in a chronic inhalation study with treatment range: 0.1–1 ppm or 0.511‑5.11 mg/m3 (rats, 6 h/d, 5 d/wk, 19 mo, also (ACGIH, 2018); weaknesses in study introduced by complications due to infections and early mortality in some animals   + duration-adjusted lower bound for 10% increase in nasal tumour incidence in rats =0.098 mg/m3; allometric conversion to account for anatomical differences in the nasal cavities of humans affords a human equivalent concentration of 0.024 mg/m3   + linear extrapolation from this concentration to the origin provides an inhalation unit risk of 4.2 x 10-3 per µg/m3. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Yes |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Insufficient data |
| **Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.** | |

## Notations

| Source | Notations |
| --- | --- |
| SWA | NA |
| HCIS | NA |
| NICNAS | Carc. Cat. 2 |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | Carcinogenicity – A2; Skin |
| DFG | Carcinogenicity category – 2; H (skin) |
| SCOEL | NA |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 3 |
| US NIOSH | NA |

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

### Skin notation assessment

| Calculation |
| --- |
| |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Conclusion:** |  |  |  |  |  |  | |  | Adverse effects in human case study: |  |  |  |  |  | |  | Dermal LD50 ≤1000 mg/kg: | yes |  |  |  |  | |  | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  |  |  | |  | Dermal LD50/Inhalation LD50 <10: |  |  |  |  |  | |  | *In vivo* dermal absorption rate >10%: |  |  |  |  |  | |  | Estimated dermal exposure at WES >10%: |  |  |  |  |  | |  |  |  | **consider assigning a skin notation** | | | | |  |  |  |  |  |  |  | | |

### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

| Molecular weight: | 125.0 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 5.11 mg/m3; 1 mg/m3 = 0.20 ppm |
| This chemical is used as a pesticide: |  |
| This chemical is a biological product: |  |
| This chemical is a by-product of a process: |  |
| A biological exposure index has been recommended by these agencies: | ACGIH  DFG  SCOEL |

## Workplace exposure standard history

| Year | Standard |
| --- | --- |
| Click here to enter year |  |

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [*TLVs® and BEIs® Guidelines section*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2001) 1,4‐Dichlor‐2‐buten (cis‐ und trans‐) – MAK value documentation.

International Agency for Research on Cancer (IARC) (1999) Volume 71, Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) 2-Butene, 1,4-dichloro-: Human health tier II assessment – IMAP Report.

Organisation for Economic Co-operation and Development (OECD) (2006) SIDS initial assessment profile – 1,4-Dichlorobut-2-ene.

US Environmental Protection Authority (US EPA) (2008) Integrated Risk Information System (IRIS) Provisional Peer Reviewed Toxicity Values for (mixed isomers) 1,4-Dichloro-2-butene.