# 1,3-Butadiene

| CAS number: | 106-99-0 |
| --- | --- |
| Synonyms: | Biethylene, divinyl, erythrene, pyrrolylene, vinylethylene |
| Chemical formula: | C4H6 |

Workplace exposure standard (amended)

| TWA: | **0.01 ppm (2.7 µg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1A** |
| 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

A TWA of 0.01 ppm (2.7 µg/m3) is recommended to minimise the risk of cancer in exposed workers.

## Discussion and conclusions

1,3-Butadiene is primarily used as a chemical intermediate in manufacturing synthetic rubbers.

Evidence strongly suggests that 1,3-butadiene is a genotoxic carcinogen with a mutagenic mechanism of action. It is characterised as a non-threshold based genotoxic carcinogen (ACGIH, 2018; DFG 2001; HCTON, 2013; SCOEL 2007). The recommended TWA is calculated at a minimal cancer risk applying an inhalation unit risk value factor from human data identified in a high-quality study with exposure estimates for individual workers (USEPA, 2002).

## Recommendation for notations

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

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

There are insufficient data to recommend a skin notation.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1986 TWA: 10 ppm (22 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 2 ppm (4.4 mg/m3) |
| TLV-TWA recommended to reduce potential for cancer in exposed workers. Conflicting carcinogenicity data in animal and human studies.  Summary of data:  Human data:  Three prime epidemiological cohort studies in occupationally exposed workers:   * Study involving 29,000 workers identified significantly elevated cause of death as a result of lymphosarcoma and reticulosarcoma * estimated exposure concentrations of 25 ppm throughout the 1980s * Various other 2 styrene-butadiene rubber (SBR) plant studies also reported inconsistent and non-significant effects; although all these studies reported lymphopoietic cancer but not dose-response relationships * Potential human carcinogen of relatively low potency * Low acute toxicity.   Animal data:   * Evidence suggests low acute toxicity * LC50: 122,000 ppm (rats, inhalation) * Toxicity demonstrated to be species specific * Rats exposed at 1,000 and 8,000 ppm (6 h/d, 5 d/wk, for 2 yr) * increased common and uncommon tumours mainly in endocrine organs at both concentrations * increase in liver to bw ratio in males at both concentrations and females at 1,000 ppm * concluded weak oncogenic properties operating indirectly through the endocrine system * Mice exposed at 625 and 1,250 ppm for a planned 103 wk were sacrificed at 60 and 61 wk due to cancer related deaths in both sexes: * malignant lymphomas, haemangiosarcomas of the heart, alveolar-bronchiolar neoplasms, squamous cell neoplasms of the forestomach, acinar cell mammary carcinomas (females), granulosa cell neoplasms of the ovary, and hepatocellular neoplasms (females) * Mice exposed at 6.25, 20, 62.5, 200, and 625 ppm (6 h/d, 5 d/wk, for planned 2 yr): * 6.25 ppm: increased alveolar bronchiolar neoplasms in females * ≤200 ppm: neoplasms of the heart, lung, forestomach, Harderian gland, mammary gland, ovary, and liver (both sexes) * 625 ppm: significant early mortality from lymphocytic lymphomas (both sexes) * Evidence from *in vitro* data suggests mice may be more efficient converters of 1,3‑butadiene to the carcinogenic metabolites butadiene epoxide and diepoxide.   Genotoxicity:   * Evidence from *in vitro* assays indicates weak mutagenicity requiring metabolic activation in some bacterial strains * Negative in mouse lymphoma and *Drosophila melanogaster* assays. |
| DFG 2001 NA |
| No MAK due to carcinogenicity effects.  Summary of additional data:   * Occupational exposure suspected to lead to an increased risk in lymphosarcoma * 1,3-butadiene and intermediary metabolite shown to be mutagenic in *Salmonella typhimurium* * Metabolites positive in *Escherichia coli* * Germ cell mutagenicity demonstrated *in vivo.* |
| SCOEL 2007 NA |
| Provides a calculated excess cancer risk associated with exposure during a working life to various concentrations.  Summary of addition data:   * Increase in leukaemia mortality in butadiene rubber works related to cumulative exposure to butadiene (adjusting for styrene and dimethyldithiocarbamate exposure) * Possible human carcinogen operating *via* a genotoxic mechanism * Skin notation not considered necessary. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2013 NA |
| Derived risk values for concentrations to occupational exposure and in the general population.  Summary of additional data:   * Genotoxic carcinogen, expressing genotoxicity *via* its alkylating action of metabolites * Cited 8 epidemiological studies on leukaemia mortality among workers as of interest * Estimated cancer risk values *via* life-table analysis using exposure-response modelling from a study reviewing available data (2007) * Estimated the following excess risk of cancer mortality: * 4 excess deaths/1,000: 40 yr exposure to 4.7 ppm (10 mg/m3) * 4 excess deaths/100,000: 40 yr exposure to 0.047 ppm (0.1 mg/m3) * Skin absorption by direct contact not considered significant. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| US EPA |  | 2002 | * Sufficient evidence demonstrating genotoxicity in animals and humans; however, specific mechanism unknown * List same epidemiological studies as primary sources of evidence * Inhalation unit risk factor of 3 x 10-5 per 1 µg/m3 derived *via* life-table analysis with leukaemia incidence data as per US EPA risk assessment guidelines. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Yes |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Yes |
| **The chemical is a non-threshold based genotoxic carcinogen.** |  |
| Is a cancer slope factor or inhalation unit risk value available? | Yes |
| Inhalation unit risk value (1/(µg/m³)) | 3x10-5 |
| Calculated TWA value (µg/m3) | 2.7 |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Carc. 1A |
| HCIS | Carcinogenicity – category 1A |
| NICNAS | **—** |
| EU Annex | Carcinogenicity – category 1A |
| ECHA | Carcinogenicity – category 1A |
| ACGIH | Carcinogenicity – A2 |
| DFG | Carcinogenicity – 1 |
| SCOEL | Carcinogenicity – A |
| HCOTN | Carcinogenicity – category 1A |
| IARC | Carcinogenicity – Group 1 |
| US NIOSH | **—** |

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 |
| --- |
| Insufficient data to assign skin notation |

### IDLH

| Is there a suitable IDLH value available? | No, the chemical is a genotoxic carcinogen |
| --- | --- |

## Additional information

| Molecular weight: | 54.06 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 2.25 mg/m3; 1 mg/m3 = Number 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) 1,3-butadiene – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2007) Recommendation from the Scientific Committee on Occupational Exposure Limits for Risk assessment for 1,3-butadiene. SCOEL/SUM/75.

Health Council of the Netherlands (HCOTN) (2013) Antimony and antimony compounds. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2013/08.

International Agency for Research on Cancer (IARC) (2012) 1,3-butadiene. IARC Monographs on the evaluation of the carcinogenic risk to humans, volume 100F.

Tenth Adaptation to Technical Progress Commission Regulation (EU) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

US Environmental Protection Agency (US EPA) (2002) 1,3-Butadiene Integrated Risk Information System (IRIS) Chemical Assessment Summary.