# 1,1,2,2-Tetrachloro-1,2-difluoroethane

| CAS number: | 76-12-0 |
| --- | --- |
| Synonyms: | CFC-112, 1,2-difluoro-1,1,2,2-tetrachloroethane, halocarbon 112, refrigerant 112 |
| Chemical formula: | C2Cl4F2 |

Workplace exposure standard (retained)

| TWA: | **500 ppm (4,170 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **—** |
| IDLH: | **2,000 ppm** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 500 ppm (4,170 mg/m3) is recommended to protect for liver damage and effects on the central nervous system (CNS) in exposed workers.

## Discussion and conclusions

1,1,2,2-Tetrachloro-1,2-difluoroethane is used primarily as a refrigerant, in dry-cleaning, as a blowing or foaming agent, a solvent extractant, and a corrosion inhibitor.

The critical effect of exposure is liver damage; subsequent CNS effects occurs at higher exposures.

Limited toxicological data in humans are available. Intentional inhalation of aerosols containing fluorocarbons for intoxication is reported to produce cardiac arrhythmia, bone marrow depression, cerebral degradation and damage to liver, kidneys and peripheral nerves following prolonged exposure at undocumented concentrations (ACGIH, 2018). Exposure of guinea pigs at 500 ppm for six months resulted in necrosis and regenerative changes in the liver; a NOAEC for this endpoint is not determined in this study (ACGIH, 2018). Shorter sub-chronic inhalational exposures at 1,000 ppm are associated with the onset of liver damage in rats (DFG, 2007). Sub-chronic exposure at 3,000 ppm caused CNS depression and respiratory tract irritation in rats (ACGIH, 2018). Minor changes in biomarkers for liver function measured as urinary enzyme activity are observed in rats following gavage at 125 mg/kg; an inhalational equivalent concentration of this oral dose is estimated at 110 ppm (ACGIH, 2018).

Changes in the liver of guinea pigs identified at 500 ppm are characteristic of adaptation processes and is not considered sufficient evidence to amend the TWA. The ACGIH (2018) extrapolation of an estimated inhalation dose from an oral study associated with minor liver and kidney changes in rats also does not provide sufficient evidence. Given the absence of robust toxicological evidence, particularly in humans, the current SWA TWA of 500 ppm (4,170 mg/m3) is recommended to be retained. The substance is currently prohibited for use in Australia, however, some residual use or storage may occur in industry.

## Recommendation for notations

Not classified as a 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 not recommended based on the available evidence.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 500 ppm (4,170 mg/m3) | |
|  |
| ACGIH 2008 TLV-TWA: 50 ppm (417 mg/m3) |
| TLV-TWA recommended to minimise the risk of liver and kidney damage and CNS impairment in exposed workers.  Summary of data:  TLV-TWA based on kidney and liver effects reported at a LOAEC of 500 ppm in a sub-chronic inhalation study in guinea pigs and minor changes in urinary enzyme activities at 125 mg/kg reported in repeat gavage study with rats; agency estimates an equivalent inhalational dose at ≈110 ppm (no further details on derivation provided).  Human data:   * Aerosol spray containing fluorocarbon propellant are a source of solvent intoxication (no details on exposure provided): * symptoms due to prolonged exposure include cardiac arrhythmia, bone marrow depression, cerebral degradation and damage to liver, kidneys and peripheral nerves * deaths attributed to inhalation abuse *via* cardiac arrhythmia.   Animal data:   * LD50 of >25,000 mg/kg (rats, oral) * No fatalities in rabbits exposed to 7,500 mg/kg dermally * LC50 of 15,000 ppm (mice, 2 h) * Rats exposed *via* inhalation for 7 h/d, 5 d/wk, 6 mo, inhalation at 500 and 1,000 ppm: * irritation of the bronchiolar passages noted at 1,000 ppm, but not 500 ppm * Group of 16 guinea pigs and 4 rabbits exposed at 500 ppm for 7 h/d, 5 d/wk, 6 mo: * fatty degeneration, necrosis, and regenerative changes of liver noted in guinea pigs * No significant toxic response, other than reduction in weight gain, in 10 rats exposed at 3,000 ppm for 6 h/d, 5 d/wk, 4 wk (inhalation) * CNS depression and respiratory irritation reported in rats exposed 4 h/d for 10 d at 3,000 ppm; all animals survived * A slight increase in liver function biomarkers measured as urinary aspartate aminotransferase activity at both doses in male rats reported in a 3 wk gavage study in rats (0, 125 and 250 mg/kg/d; dose estimated at an inhalation equivalent of 110 and 220 ppm assuming air exchange rate of 10 m3 per workday for a 70-kg person): * an increase in urinary N-acetyl-β-D-glucosaminidase activity at 250 mg/kg in male rats reported * No evidence of a carcinogenic potential observed in 56 neonatal mice given SC injections of CFC-112 for one year * 1% sarcomas and 5% hepatomas reported in a second study in newborn mice given SC injections of CFC-112 (dosage not stated) for 365 d., but not statistically significant difference from controls * Neither of the 2 carcinogenicity studies were conducted according to standard (bioassay) protocols; thus, the limited data and lack of reliability of these studies do not support carcinogenicity in mice * A weak positive in genotoxicity study when tested in *S. typhimurium*.   Insufficient data to recommend a carcinogen notation. A skin or sensitiser notation not warranted. |
| DFG 2007 MAK: 200 ppm (1,700 mg/m3) |
| MAK established in 1989 is retained based on the onset of liver damage at 1,000 ppm in rats but needs to be safeguarded by studies on long-term exposure.  Summary of additional data:   * Exposure at 1,000 ppm (rats, mice, guinea pigs, rabbits, 6 h/d, 5 d/wk, 6 wk, inhalation) symptoms included: * statistically significantly reduction of leukocytes in female rats only * enlarged cells reported in liver of male animals, with vacuolisation of the cytoplasm and different sizes of cell nuclei * some fatty liver cells and an increased cytoplasmic density of liver cells found in female animals * the authors regard these liver findings as "typical of liver adaptation processes when foreign substances toxic to the liver are administered and not as a specific finding”. |
| 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 |
| --- | --- | --- | --- |
| ECHA |  | 2013 | * Negative results *in vivo* mammalian germ cell study for chromosome aberration. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Insufficient data |
| --- | --- |
| 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 | — |
| HCIS | NA |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | — |
| DFG | — |
| SCOEL | NA |
| HCOTN | NA |
| IARC | NA |
| 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 |
| --- |
| |  |  |  |  | | --- | --- | --- | --- | | Adverse effects in human case study: | no |  |  | | Dermal LD50 ≤1000 mg/kg: | no |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  |  | **a skin notation is not warranted** | |

### IDLH

| Is there a suitable IDLH value available? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 203.8 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 8.30 mg/m3; 1 mg/m3 = 0.120 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) (2007) 1,1,2,2-Tetrachlor-1,2- difluorethan – MAK value documentation.

European Chemicals Agency (ECHA) (2013) Tetrachloro-1,2-difluoroethane – REACH assessment.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – 1,1,2,2-Tetrachloro-1,2-difluoroethane.