# 2,4-D

| CAS number: | 94-75-7 |
| --- | --- |
| Synonyms: | 2,4-Dichlorophenoxyacetic acid, hedonal, Weed‑B‑Gon |
| Chemical formula: | C8H6Cl2O3 |

Workplace exposure standard (retained)

| TWA: | **10 mg/m3 (1.11 ppm)** |
| --- | --- |
| STEL: | — |
| Peak limitation: | — |
| Notations: | **—** |
| IDLH: | **100 mg/m3** |
| | Sampling and analysis: | The recommended value is quantifiable through available sampling and analysis techniques. | | --- | --- | | |

## Recommendation and basis for workplace exposure standard

A TWA of 10 mg/m3 (1.11 ppm) is recommended to protect for effects in the kidney and thyroid in exposed workers.

## Discussion and conclusions

2,4-D is widely applied as a herbicide, fungicide and growth regulator (ACGIH, 2018; DFG, 1994).

Thyroid effects and damage to the kidneys are considered the critical effects. Several case studies report acute intoxications in humans and an association with incidences of Hodgkin’s disease, non‑Hodgkin’s lymphoma and soft tissue sarcoma. However, these studies do not support a recommendation for a TWA due to the difficulty in determining if toxic effects from 2,4-D act alone or if the effects are driven by other chemical agents (such as dioxins) in the mixtures tested. No studies with inhalation exposure are identified. Two studies, one in rats and one in mice, identified a chronic NOAEL of 5 mg/kg/day based on increased kidney and thyroid weights (ACGIH, 2018).

The current TWA of 10 mg/m3 is recommended to be retained. This value has been adopted directly from the ACGIH (2018) on the weight of evidence in animals. The TWA is considered protective of the critical effects in exposed workers.

## 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 recommended based on systemic effects in humans after dermal exposure.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 10 mg/m3 | |
|  |
| ACGIH 2017 TLV-TWA: 10 mg/m3 |
| TLV-TWA recommended to protect against effects in thyroid and kidney and is derived from chronic feeding studies in rats and mice and based on NOELs of 5 mg/kg/d.  No increases in mortality from non-Hodgkin’s lymphoma or soft tissue sarcoma; no significant increase in mortality incidence from chronic non-cancer disease; epidemiological studies in workers exposed to airborne particulates  Summary of data:  Human data   * + Limited evidence of carcinogenicity   + Burning sensation in throat and chest, weakness, loss of appetite and weight and slight albuminuria from field exposure   + Chlorinated dioxins found in 2,4-D products responsible for increased risk in mortality from neoplasms, non-Hodgkin’s lymphoma and lung cancer   + 69 cases of ingestion reported in literature up to 2003; 23 of which were fatal at average dose >300 mg/kg   + GIT irritation and sensory-motor peripheral neuropathy in substantial dermal exposure. Effects likely due to exposure to combined unidentified co-exposure agents   + Headache, pains to the cardiac region, weakness, hypertension, tachycardia, excessive perspiration and hepatomegaly in exposed woman * post exposure symptoms (3.5 y) included nausea, emesis, vegetative vascular paroxysm, stable hypertension, toxic encephalopathy, diffuse hepatomegaly and portal hypertension   + Acute poisoning symptoms including fatigue, period headache and vertigo, numbness, pain in leg, partial amnesia reported in a group of 11 female workers, 35–52 years of age: * post-exposure (followed for 2 yr) symptoms included persisting oligomenorrhea with development of chronic toxic hepatitis, encephalopolyneuritis, myocardial-dystrophy and vascular dystonia and chronic conjunctivitis in 2 women * all patients had statistically significant decreases in some oxidative enzymes of the peripheral blood leukocytes.   Animal Studies   * LC50 - rats (no deaths at ≤1.79 mg/L) * Oral LD50: 320–726 mg/kg (rats, males more sensitive). LD50: 100 mg/kg (dog),  318–346 mg/kg (mouse) and 800 mg/kg (rabbit) * Dermal LD50: 1,500 mg/kg (rats); 1,400 mg/kg and >2,000 mg/kg (rabbits). * Severe eye irritant for parent acid but not ester forms * Not a skin sensitiser * No sub-chronic repeated-dose inhalation exposure data available * Weight of evidence from 2 y feeding studies in rats and mice was used to identify chronic exposure NOELs of 5 mg/kg/d in both species used to derive the inhalational TWA; based on:   + increased absolute and relative thyroid weights in rats at 15 mg/kg/d (but not at 45 mg/kg/d);   + non statistically significant increase in kidney weights and proximal renal tubule effects at 15 mg/kg/d in both species * No oncogenic effect noted at NOEL of 1 mg/kg/d; LOEL 15 mg/kg/d; based on kidney effects; 104 wk diet in another study * No signs of neurotoxic effects in rats. Pregnant rabbits exhibited clinical signs of neurotoxicity * Not considered genotoxic although cytogenic effects reported:   + no developmental toxicity observed   + reproductive NOAEL: 17 mg/kg/d (male rats) and 21 mg/kg/d (female rats) and 75 mg/kg in rabbits.   Exposure of a 70 kg worker inhaling 10 m3 per 8 h shift to the TLV-TWA of 10 mg/m3 results in dose of ≈1.5 mg/kg/d; assuming 100% absorption (no further explanation provided).  Skin notation not recommended due to insufficient data to suggest systemic effects from skin absorption. |
| DFG 1994 MAK: 1 mg/m3 |
| MAK of 1 mg/m3 to protect against malignant lymphomas and reproductive toxic effects. Derived from NOEL of 0.3 mg/kg of the most sensitive species (dog) and need for further clarification due to the presence of impurities, limited case studies and uncertainties associated with extrapolations from a NOAEL derived from oral administration to inhalation. |
| 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 |
| --- | --- | --- | --- |
| US EPA |  | 1987 | * No Inhalation RfC * Oral RfD of 1.0E-02 for protection against hepatic and renal toxicity; derived on:   + NOAEL 1.0 mg/kg/d   + LOAEL 5.0 mg/kg/d for haematologic, hepatic and renal toxicity (rat, 90-d bioassay from a 2 y oral bioassay). |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | No |
| --- | --- |
| **The chemical is not a non-threshold based genotoxic carcinogen.** |  |

## Notations

| Source | Notations |
| --- | --- |
| SWA | NA |
| HCIS | NA |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | Carcinogenicity – A4 |
| DFG | NA |
| SCOEL | NA |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 2B |
| 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: | | | yes | 4.00 |  |
| Dermal LD50 ≤1000 mg/kg: | | |  |  |  |
| 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 warranted** | | | |

### IDLH

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

## Additional information

| Molecular weight: | 220.04 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 9.04 mg/m3; 1 mg/m3 = 0.11 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 |
| --- | --- |
| 1991 | 10 mg/m3 (1.1 ppm) |

## 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) (1998) 24‐Dichlorophenoxyacetic acid (2,4‐D) including Salts and Esters– MAK value documentation.

International Agency for Research on Cancer (IARC) (2018) 2,4-D (2,4-dichlorophenoxyacetic acid) (See also Chlorophenoxy herbicides). IARC Monographs on the evaluation of the carcinogenic risk to humans.

U.S. Environmental Protection Agency (US EPA). (1987). Chemical Assessment Summary – 2,4-Dichlorophenoxyacetic Acid (2,4-D); CASRN 94-75-7. Integrated Risk Information System (IRIS).

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – 2,4-D.