# 2,4-Pentanedione

| CAS number: | 123-54-6 |
| --- | --- |
| Synonyms: | Acetylacetone, acetoacetone, diacetylmethane, acetyl-2-propanone, 2,4-PD |
| Chemical formula: | C5H8O2 |
| Structural formula: | — |

Workplace exposure standard (new)

| TWA: | **25 ppm (102 mg/m3)** |
| --- | --- |
| STEL: | — |
| Peak limitation: | — |
| Notations: | **Sk.** |
| IDLH: | — |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 25 ppm (102 mg/m3) is recommended to protect for haematotoxicity, neurotoxicity and irritation of the nasal mucosa in exposed workers.

## Discussion and conclusions

2,4-pentanedione (PD) is used in a range of domestic cleaning and washing agents. It is also used as a metal chelator, lubricant additive and corrosion inhibitor and intermediate in the manufacture of pharmaceuticals and pesticides.

Critical effects of exposure are haematotoxicity, neurotoxicity and irritation of the nasal mucosa.

No relevant toxicological data are available in humans. A NOAEC of 101 ppm for systemic effects is reported in a 14-week inhalation study in rats based on minor, reversible changes in some haematological and clinical chemistry parameters. The same study reported a NOAEC of 307 ppm for local effects based on histological nasal findings (ACGIH, 2018; DFG, 2006). A NOAEC of 418 ppm for haematological effects is reported in a nine-day inhalation study in rats; a LOAEC of 197 ppm for nasal irritation is also reported in same study. This LOAEC is reported to be equivalent to a human NAEC of 100 ppm. A human equivalent workplace concentration of 35 ppm is derived using a reported LOAEL of 200 mg/kg/day for neurological effects in rats from a subcutaneous administration study (DFG, 2006). DFG maintained the MAK of 20 ppm as the lowest extrapolated concentration of 25 ppm (no derivation provided) for haematological effects is lower than the dose that causes local effects (35 ppm).

The lowest reported NOAEC is 101 ppm for minor systemic effects from rat inhalation studies. While a LOAEC of 197 ppm for nasal irritation equivalent to a human NAEL of 100 ppm is also reported. Based on the weight of evidence, the TWA of 25 ppm derived by ACGIH (2018) is recommended be adopted. The recommended TWA is expected to be protective of haematotoxicity, neurotoxicity and irritation of the nasal mucosa reported in animals.

## 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 evidence in animals of dermal uptake and systemic effects.

# Appendix

### Primary sources with reports

| **Source Year set Standard** |
| --- |
| SWA NA NA | |
|  |
| ACGIH 2011 TLV-TWA: 25 ppm (102 mg/m3) |
| TLV-TWA recommended to protect against degenerative changes in the central and possibly the peripheral nervous systems.  Summary of data:  TLV-TWA based on the observations in the 14-wk inhalation study in rats; no specific derivation provided but presumably the TLV-TWA of 25 ppm is derived by applying a factor of 4 (to account for interspecies differences) to the NOAEC of 101 ppm from the 14-wk inhalation study.  Data in humans:   * Skin patch test; weak urticaria in 2/12 and equivocal reactions in 7/12 human subjects.   Data in animals:   * LD50:790 mg/kg (female rabbits, dermal) * LC50:1,224 ppm (rats, 4 h); deaths from CNS depression and respiratory distress * May have some potential to accumulate in the body upon repeated exposure * No clinical signs observed in rats exposed at 628 ppm; acute exposure; no further information * 14-wk inhalation study in rats at 0, 101, 307 or 650 ppm 6 h/d, 5 d/wk: * 101 ppm: no changes; deemed NOAEC by authors * 307 ppm: no clinical signs or neurobehavioral anomalies or fatalities; minor, reversible changes in a few haematological and clinical chemistry parameters; deemed LOAEC by authors * 650 ppm: all females and 1/3 of the males died between the wk 2 and 6 of exposure; these animals showed acute degenerative changes in discrete areas of the brain and degeneration in the thymus; nuclear pyknosis (shrinking) and karyorrhexis (rupture); macrophages with vacuolated cytoplasm and gliosis prominent within these foci; no degenerative changes seen microscopically in the spinal cord or electron microscopically in the sciatic nerve; periodic neurobehavioral screening before the fatalities occurred revealed equilibrium disturbances in each animal with damaged cerebellar and vestibular nuclei; thymic lesions in these rats consisted of acute lymphoid degeneration and atrophy; no further information * Repeated cutaneous exposure produced dermal and systemic toxicity; 0, 244, 975 and 1,463 mg/kg on 9/11 d applied to backs of rabbits: * skin irritation and lesions * hypoactivity, tremors, uncoordinated movements, convulsions and prostration at 975 and 1,463 mg/kg.   No human or animal data were found to support a carcinogenicity notation.  Insufficient data to recommend a sensitiser notation or TLV-STEL. |
| DFG 2006 MAK: 20 ppm (83 mg/m3) |
| MAK recommended to protect for critical effects of haematotoxicity, neurotoxicity and irritation of the nasal mucosa.  Summary of additional data:   * 14-wk inhalation study in the rats; 0, 101, 307 or 650 ppm (cited by ACGIH, 2018): * NOAEC of 307 ppm for local effects; histological nasal findings * NOAEC of 101 ppm; LOAEC of 307 ppm for minimal effects on the blood and reduced body weight * 650 ppm resulted in severe brain damage * human equivalent NAEC of 200 ppm based on LOAEC of 307 for minor systemic effects; no derivation provided * 9-d inhalation study in the rat; 0, 197, 418 or 805 ppm (99% pure): * LOAEC 197 ppm for nasal irritation; assumed human NAEC of 100 ppm; no derivation provided * necrosis in the nasal mucosa at 418 ppm; more frequently observed at 805 ppm * sensory irritation at 805 ppm * NOAEC of 418 ppm for haematological effects * The derivation of the MAK of 20 ppm based on the following explanation; no further information to explain its function: * based on 40-wk subcutaneous administration study; LOAEL of 200 mg/kg/d changed nerve conduction speeds; toxicokinetic conversion to human equivalent workplace airborne concentration: * rat to human-specific correction 1:4 * assumed 100% absorption * body weight 70 kg, respiratory volume 10 m3/8-h * 40% inhalation absorption * derivation factor for NAEC 1:3 * transmission of animal test data to humans 1:2 * ≡35 ppm. * Concludes that the MAK of 20 ppm can be maintained as the lowest extrapolated concentration for haematological effects of 25 ppm (derivation not presented; no further information) is lower than that for local effects (35 ppm). |
| 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** |
| --- | --- | --- | --- |
| NICNAS |  | 2018 | * Mild eye irritant in animal studies; mild, reversible dermal and ocular irritation in humans * Inhalational exposure to vapour in humans reported to cause non-specific effects such as dizziness, headache, nausea, vomiting and loss of consciousness * No additional toxicological information. |

### 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 | Skin |
| DFG | H (skin) |
| 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: |  |  |  | | Dermal LD50 ≤1000 mg/kg: | yes | 3.00 |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  | 3 | **consider assigning a skin notation** | |

### IDLH

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

## Additional information

| Molecular weight: | 100.13 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 4.1 mg/m3; 1 mg/m3 = 0.244 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) (2019) Acetylaceton (2,4-Pentandion) – MAK value documentation.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) 2,4-Pentanedione: Human health tier II assessment – IMAP report.