# 2-Ethylhexanoic acid

| CAS number: | 149-57-5 |
| --- | --- |
| Synonyms: | Butylethylacetic acid, 2-butylbutanoic acid,  clobuzarit alpha-ethylcaproic acid, 2-ethylcaproic acid, 2-EHA, ethylhexanoic acid, alpha-ethylhexanoic acid, 2-ethylhexoic acid, ethylhexoic acid, |
| Chemical formula: | C8H16O2 |

Workplace exposure standard (new)

| TWA: | **5 mg/m3** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **—** |
| 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 5 mg/m3 is recommended to protect for developmental effects in exposed workers.

## Discussion and conclusions

2-Ethylhexanoic acid (2-EHA) is used as an industrial intermediate for the preparation of metallic salts of lead, cobalt, manganese, zinc, calcium, iron and zirconium.

Limited data are available in humans. The critical effect of exposure is developmental toxicity including skeletal anomalies in foetuses as demonstrated in rat studies. A NOAEL of 100 mg/kg/day for skeletal anomalies is reported in rats dosed orally on gestation days six to fifteen. The hypothesised mechanism of toxicity is considered likely relevant to humans (ACGIH, 2018; ECHA, 2019; NICNAS 2013).

The recommended TWA of 5 mg/m3 is adopted from ACGIH (2018). It is derived by using the NOAEL of 100 mg/kg/day and applying conversion factors specific for female workers and extrapolated to a total daily dose of 1 mg/kg/d. The TWA provides a margin of safety of 100 when compared to the reported oral NOAEL andis considered to be sufficient to protect for developmental 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.

There are insufficient data to recommend a skin notation.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA NA NA | |
|  |
| ACGIH 2007 TLV-TWA: 5 mg/m3 |
| TLV-TWA recommended to reduce the risk of developmental toxicity in workers.  Summary of data:  Human data:   * Evidence of urea synthesis inhibition was reported in a study of sawmill workers exposed to 0.17 to 0.37 mg/m3 * toxicological significance unclear.   Animal data:   * Low acute oral toxicity * LD50:1,140 mg/kg (rabbits, dermal) * No clinical signs of toxicity in rats exposed *via* inhalation at 400 ppm for 6 h * NOEL: 61 mg/kg/d in male rat, liver enlargement * High-dose oral administration in rodent developmental and reproductive toxicity studies: * maternal toxicity – increased mortality, motor and respiratory depression, reduced weight gain and increased maternal liver weight * developmental toxicity – delayed ossification of bone and wavy ribs at doses absent of maternal toxicity * Rats exposed at 100 mg/kg/d in drinking water GD 6-19; foetal skeletal anomalies occurred; lowest dose, no NOAEL * NOAEL of 100 mg/kg/d for skeletal anomalies (rats oral dose GD 6–15) * hypothesised mechanism of toxicity potentially relevant to humans (induction of metallothionein with associated induction of foetal zinc deficiency) * Not developmentally toxic in rabbits * Recommended TLV-TWA of 5 mg/m3: * a 50 kg female worker inhaling 10 m3 of air with 5 mg/m3 2-EHA receives a total dose of 50 mg assuming 100% absorption; ≡1 mg/kg/d. |
| DFG 2015 Not assigned |
| Insufficient information to establish a MAK.  Summary of additional data:   * NOAEL for developmental toxicity cannot be derived from the available studies * Mechanisms of teratogenicity suggest existence of NOAEL but below doses tested to date * Severely irritating to the rabbit eye, causing corneal opacity, marked reddening and oedema, iritis and ocular discharge. |
| 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 |  | 2013 | * Did not induce dermal sensitisation in guinea pigs in a maximisation study * Maternal toxicity LOAEL of 600 mg/kg/d (highest dose) in rats; decreased maternal body weight gain * Developmental LOAEL of 100 mg/kg/d; rats administered GD 6–19 *via* drinking water; statistical increase in wavy ribs in the foetuses; malformation of the legs in foetuses. |
| ECHA |  | 2019 | * NOAEL in rats 100 mg/kg/d; adverse foetal effects included reduced bw; skeletal malformations and variations (same as NICNAS, 2013; ACGIH, 2018). |

### 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 | — |
| NICNAS | — |
| EU Annex | NA |
| ECHA | — |
| 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 |
| --- |
| Insufficient data to assign a skin notation. |

### IDLH

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

## Additional information

| Molecular weight: | 144.21 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 5.9 mg/m3; 1 mg/m3 = 0.17 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) (2015) 2-Ethylhexanoic acid – MAK value documentation.

European Chemicals Agency (ECHA) (2019) 2-Ethylhexanoic acid – REACH assessment.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) Hexanoic acid, 2-ethyl: Human health tier II assessment – IMAP report.