# Butyl acetate (all isomers)

| CAS number: | 123-86-4 (*n*-butyl acetate)110-19-0 (isobutyl acetate)105-46-4 (*sec*- butyl acetate)540-88-5 (*tert*-butyl acetate) |
| --- | --- |
| Synonyms: | Butyl ethanoate |
| Chemical formula: | C6H12O2 |

 Workplace exposure standard (amended)

| TWA: | **50 ppm (270 mg/m3)** |
| --- | --- |
| STEL: | **100 ppm (541 mg/m3)** |
| Peak limitation: | **—** |
|  Notations: | **—** |
| IDLH: | **1,300 ppm (10% LEL)** |
| Sampling and analysis: | There is uncertainty regarding quantification of the recommended value with currently available sampling and/or analysis techniques. |

## Recommendation and basis for workplace exposure standard

A TWA of 50 ppm (270 mg/m3) is recommended to protect for reversible eye and upper respiratory tract irritation in exposed workers.

A STEL of 100 ppm (541 mg/m3) is recommended to protect for more intense irritation and potential breathing difficulties.

## Discussion and conclusions

Butyl acetates are encountered as solvents in the production of photographic films, lacquers and cosmetics. Simultaneous exposures to mixtures of these substances occur frequently (ACGIH, 2018; NICNAS, 2014). Due to commonalities in their structures and critical effects, all butyl isomers have been grouped for the purposes of this assessment.

The substances have been shown to be non-carcinogenic in animals. Critical effects in humans following exposure are irritation of the eyes and upper respiratory tract (ACGIH, 2018). Other effects noted include hyperactivity, possible reproductive effects and liver dysfunction in animals (ACGIH, 2018). Irritation thresholds in humans are inconsistent (DFG, 2000), but have been reported to occur at concentrations above 113 ppm and 177 ppm for the n- and tert-butyl isomers, respectively (ACGIH, 2018). Few studies involving the iso- and sec-butyl isomers exist; sec-butyl acetate was reported to have a similar nasal irritation threshold to n‑butyl acetate (ACGIH, 2018).

The recommended TWA is derived from a NOAEL of 74 ppm for eye and throat irritation in a human chamber study with n-butyl acetate (ACGIH, 2018). Due to the reversibility of the irritation effects, the STEL is similarly derived from a LOAEL of 147 ppm from the same human chamber study (ACGIH, 2018, DFG, 2000).

Due to their common occurrence as mixtures, the IDLH value is based on 10% of the lowest LEL of these compounds, isobutyl acetate.

## Recommendation for notations

Not classified as carcinogens 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. Repeat dermal exposure studies in both animals and humans indicate that a dermal sensitiser notation is not warranted.

A skin notation not recommended due to low potential for skin penetration.

# Appendix

### Primary sources with reports

| Source Year set Standard  |
| --- |
| SWA | Year | n-Butyl acetate | TWA: 150 ppm (713 mg/m3); STEL: 200 ppm (950 mg/m3) |
|  |  | Isobutyl acetate | TWA: 200 ppm (950 mg/m3) |
|  |  | sec-Butyl acetate | TWA: 200 ppm (950 mg/m3) |
|  |  | tert-Butyl acetate | TWA: 150 ppm (713 mg/m3) |
|  |
| ACGIH 2016 TLV-TWA: 50 ppm (238 mg/m3), TLV-STEL: 150 ppm (712 mg/m3) |
| Based on similar nasal pungency and irritation, all butyl acetate isomers are assessed together. TLV‑TWA intended to minimise reversible irritation of the eyes and upper respiratory tract in exposed workers. TLV-TWA should also protect against transient hyperactivity, possible reproductive effects and hepatic effects observed in animal models. TLV-STEL is recommended to protect against mucous membrane irritation reported in humans above 200 ppm. Skin notation not warranted based on animal experiments. Insufficient data to recommend a sensitiser or carcinogenicity notation.Summary of data:Substances are hydrolysed to corresponding alcohol *in vitro* and *in vivo.*Human data:* Odour threshold 0.01–0.19 ppm
* Eye irritation thresholds for *n*- and *tert*-butyl isomers 113 ppm and 177 ppm, respectively (10 s)
* Inhalation NOAEL of 74 ppm for eye/throat irritation and breathing function in series of chamber studies (n=24, 20 min, *n*-butyl acetate)
* LOAEL of 147 ppm for objection to odour (20 min) and throat irritation/breathing difficulty (4 h)
* Throat irritation at 200 ppm
* eye, nose and severe throat irritation at 300 ppm (n=10, 2–5 min, chamber study, isomer not specified)
* Median exposure of 1.9 ppm and range of 0–354 ppm in paint/coating industry
* 1–10 ppm in breathing zone of furniture factory workers
* Severe exposure causes drowsiness and narcosis (concentration not specified)
* No sensitisation in patch test or maximisation studies:
* *n*-butyl acetate (n=50, induction with 0.5 mL neat, 24 h for 3 wk, challenge after 10–14 d)
* isobutyl acetate (n=28, 2% in petrolatum, 48 h)
* Epidemiologic data difficult to evaluate due to mixed exposures, e.g. xylenes and toluene.

Animal data:* All isomers considered non-sensitising based on negative maximisation trial results (mouse, guinea pigs)
* no data available for *sec*-butyl acetate
* All isomers non-mutagenic based on negative bacterial *in vitro* studies. No data available for isobutyl acetate.

*n-Butyl acetate*:* LC50: 67,000 ppm (guinea pigs, 4 h), 68,000 ppm (cats, 17 min)
* 16,000 ppm causes death in all animals after 8 h, no deaths after 4 h (rats)
* LC50: 156–2000 ppm (rats, 4 h)
* large variance and relatively low rat LC50 values possibly due to mixed exposure to mist and vapour
* Inhalation LOAEL of 1,500 ppm for decreased activity and response to stimuli (rats, 6 h)
* Eye irritation at 3,300 ppm, upper respiratory irritation and narcosis at 7,000 ppm, death at 14,000 ppm (guinea pigs, up to 13.5 h)
* Inhalation NOAEL of 500 ppm for olfactory degeneration (rats, 6 h/d, 5 d/wk, 13 wk)
* 50% decrease in respiratory rate (RD50) at 730 ppm (mice, no further information)
* LD50: >5,000 mg/kg (rabbits, dermal)
* Oral LD50: 1,413 mg/kg (rats), 7,100 mg/kg (mice), 7,400 mg/kg (rabbits), 4,700 mg/kg (guinea pigs)
* 6,100 ppm causes eye irritation and salivation but no narcosis (cats, 6 h)
* Low hepatotoxicity based on intraperitoneal injection study (guinea pigs), toxic responses occurred at dose >500 mg/kg. First toxic responses reported at 750 mg/kg.

*Isobutyl acetate*:* LC50: 2,946–8,188 ppm (rats, 4 h)
* RD50: 817 ppm (mice, no further information)
* LD50: 13,400–15,000 mg/kg (rats, oral).

*sec-Butyl acetate*:* LC50:468 to >3,570 ppm (rats, 4–6 h), inconsistency in data noted but not discussed
* LD50:>2,000 mg/kg (rabbits, dermal)*.*

*tert-Butyl acetate*:* Inhalation LOAEL of 400 ppm for hyperactivity (mice, rats, 6 h/d, 7 d/wk, 13 wk)
* adverse renal and liver effects but no clinical signs of toxicity at 1,600 ppm (rats) in same study
* renal/liver effects not deemed relevant to humans due to rat-specific metabolism of the compound
* LC50: 4,200 ppm (rats, 6 h), >3,000 ppm (mice, 6 h)
* deceased rats showed signs of lung congestion
* *tert*-Butyl alcohol, major metabolite, may be weakly carcinogenic in rats
* relevance to humans is not known.
 |
| DFG | 1997 | n-Butyl acetate |  MAK: 100 ppm (480 mg/m3) |
|  |  2003 | Isobutyl acetate | MAK: 100 ppm (480 mg/m3) |
|  | 1999 | sec-Butyl acetate | MAK: not yet established |
|  | 2013 | tert-Butyl acetate | MAK: 50 ppm (238 mg/m3) |
| Summary of additional data:Isomers are assessed separately but based on ACGIH, 1997 assessments.*n-Butyl acetate*:* Previous MAK of 200 ppm considered unprotective and lowered to 100 ppm based on same series of chamber studies as ACGIH, 1997/2016
* Irritative effects may be caused by hydrolysis to acetic acid
* Does not readily penetrate human skin based on *in vitro* permeability study
* Results of human threshold limit studies considered inconsistent
* MAK of 100 ppm considered protective of long-term exposure based on metabolism of substance to corresponding alcohol, for which MAK is also 100 ppm.

*Isobutyl acetate*:* No significant difference in the irritation potency of *n*- and isobutyl acetate
* Based on MAK for *n*-butyl acetate and major metabolite, isobutyl alcohol.

*sec-Butyl acetate*:* No MAK established due to lack of toxicological data for substance and its metabolite, sec-butyl alcohol.

*tert-Butyl acetate*:* MAK derived from inhalation NOAEL of 100 ppm for hyperactivity and, assuming 100% metabolism to tert-butyl alcohol
* A NOAEL of 1,600 ppm for foetal toxicity (mice, rats, 6 h/d, 7 d/wk, 13 wk) due to insufficient substance-specific data in humans (same study as in ACGIH, 2016)
* Renal toxicity observed in highest exposure groups (1,600 ppm) not considered relevant for humans due to species-specific metabolism.
 |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2001 — |
| Summary of additional data:* Additional studies recommended for all four isomers:
	+ kinetic studies
	+ 28 d inhalation toxicity studies (except for n-butyl acetate)
	+ reproduction toxicity studies
	+ human respiratory and eye irritation tests suitable for determining a NOAEL.
 |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2014 | * All isomers grouped for assessment, also grouped with other related alkyl acetates.
* Similar hazard profiles expected due to similar absorption, metabolism, distribution and excretion
* Data gaps filled with exposure data from corresponding alcohols, which are the major metabolites
* The substances have similar uses.
 |
| US NIOSH |  | 1994 | * IDLH for n-butyl acetate and sec-butyl acetate is 1,700 ppm and 1,500 for tert-butyl acetate based on 10% of the lower explosive limit (LEL)
* IDLH for isobutyl acetate is 1,300 ppm based on 10% of the LEL.
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### 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 | — |
| HCIS | — |
| NICNAS | — |
| EU Annex | — |
| 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** |

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### IDLH

| Is there a suitable IDLH value available? | Yes, based on LEL. |
| --- | --- |

## Additional information

| Molecular weight: | 116.16 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa:  | 1 ppm = Number mg/m3; 1 mg/m3 = Number ppm |
| This chemical is used as a pesticide: |[ ]
| This chemical is a biological product: |[x]
| This chemical is a by-product of a process: |[x]
| 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) (2000) n-Butyl acetate – MAK value documentation.

Deutsche Forschungsgemeinschaft (DFG) (1999) sec-Butyl acetate – MAK value documentation.

Deutsche Forschungsgemeinschaft (DFG) (2000) sec-Butyl acetate – MAK value documentation.

Deutsche Forschungsgemeinschaft (DFG) (2003) Isobutyl acetate – MAK value documentation.

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Deutsche Forschungsgemeinschaft (DFG) (2018) tert‐Butylacetat – MAK value documentation, German language edition.

Health Council of the Netherlands (HCOTN) (2001) n-, iso-, sec-, and tert-Butyl acetate. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2001/03OSH.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Acetate esters (C2-C4): Human health tier II assessment: Human health tier II assessment – IMAP report.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – n-butyl acetate.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – isobutyl acetate.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – sec-butyl acetate.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – tert-butyl acetate.