

CYCLOHEXANONE

CAS number: 108-94-1

Synonyms: Anone, cyclohexyl ketone, ketoexamethylene, pimelic ketone

Chemical formula: $C_6H_{10}O$

Structural formula: —

Workplace exposure standard (amended)

TWA: 10 ppm (40 mg/m³)

STEL: 20 ppm (80 mg/m³)

Peak limitation: —

Notations: Sk.

IDLH: 700 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 10 ppm (40 mg/m³) is recommended to protect for systemic effects on the central nervous system (CNS) and irritation in exposed workers.

A STEL of 20 ppm (80 mg/m³) is recommended to protect for CNS effects in acutely exposed workers.

Discussion and conclusions

Cyclohexanone is predominantly used in the production of nylon. It is also used as a solvent in insecticides, paints, paint and varnish removers, natural and vinyl rubbers and in the textile and tanning industries.

Critical effects of exposure are localised irritation and effects on the CNS in human studies and systemic effects on the liver and kidneys in animal studies (ACGIH, 2018; DFG, 2003). A study in human volunteers reported throat irritation at 50 ppm after three to five minutes of exposure. A NOAEL of 25 ppm was identified in the same study. A LOAEL of 190 ppm is reported for liver and kidney effects in rabbits exposed for six hours a day for 50 days. However, these effects were reported as barely demonstrable and it is unclear if these effects were adaptive and relevant for humans. A NOAEL of 100 mg/kg/day was reported in rats for no adverse effects after exposure *via* intravenous administration, corresponding to a concentration of 700 mg/m³ (175 ppm) (ACGIH, 2018; DFG, 1998; SCOEL, 1992).

The recommended TWA is derived from the NOAEL of 25 ppm in humans with an uncertainty factor of two is applied based on study limitations (SCOEL, 1992). The STEL is recommended based on pronounced irritation at 75 ppm and this effect being within ten times of the TWA.

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 of dermal absorption contributing to total body burden in animals.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 25 ppm (100 mg/m³)
ACGIH	2003	TLV-TWA: 20 ppm (80 mg/m³); TLV-STEL: 50 ppm (200 mg/m³)
<p>TLV-TWA and TLV-STEL recommended to protect for the potential for eye, nasal and throat irritation, effects on the CNS and possible effects on the liver and kidneys.</p> <p>Summary of data:</p> <p>Human data:</p> <ul style="list-style-type: none"> Human volunteers in chamber study exposed for 3–5 min: <ul style="list-style-type: none"> 25 ppm not uncomfortable 50 ppm irritating to the throat 75 ppm pronounced irritation to eyes, nose and throat Habituation possibility identified in another volunteer study Increased eye and respiratory irritation, headache, mood disorders, memory difficulties, bone pain and other symptoms in workers exposed to 41–92 ppm (no further information) 2 case reports of human sensitisation cyclohexanone resin <ul style="list-style-type: none"> patch test showed sensitisation to cyclohexanone resin and not the compound itself 1 case report of sensitisation to cyclohexanone confirmed with patch testing. <p>Animal data:</p> <ul style="list-style-type: none"> 4 h LC₅₀: >1,400 ppm and 2,450 ppm (rats) RD₅₀: 756 ppm (mice) LD₅₀: 950 mg/kg (rabbits, dermal) LOAEL of 190 ppm reported in rabbits for barely demonstrable degenerative changes in the liver and kidneys (50 daily exposures for 6 h) CNS effects (pupil dilation, lacrimation, stupor, ataxia) and increased liver weights, plasma-cell infiltrates in hepatic veins, bone marrow hyperplasia and metabolic acidosis reported in dogs (IV; 284 mg/kg/d) NOEL of 100 mg/kg in rats (28 d IV) reported no adverse pathological, histopathological or serum chemistry effects NOEL of 686 ppm for maternal and foetal toxicity in rats Irritating to the eyes and skin of rabbits Not a sensitiser in guinea pig maximiser test and mice ear swelling test No mutagenic evidence. <p>TLV-TWA validated via comparison with the translation of the oral NOEL of 100 mg/kg to an air concentration of 700 mg/m³ (175 ppm); derived with 10 m³ volume of air over 8 h shift, 70 kg body weight.</p>		
DFG	1998	NA
<p>No MAK recommended due to the unclear genesis of the thyroid gland tumours in the rat.</p> <p>Summary of additional data:</p> <ul style="list-style-type: none"> NOEL of 25 ppm reported in humans (same study as ACGIH) 		

Source	Year set	Standard
<ul style="list-style-type: none"> Refers to the NOEL of 100 mg/kg in rabbits (ACGIH, 2018) In a long-term drinking water study with rats, an increase in follicular thyroid gland tumours was observed in the high dose group. <p>Systemic effects at concentrations markedly higher than NOEL for irritative effects.</p>		
SCOEL	1992	TWA: 10 ppm (40.8 mg/m³); STEL: 20 ppm (81.6 mg/m³)
<p>Summary of additional data:</p> <ul style="list-style-type: none"> TWA is based on the NOAEL of 25 ppm in human volunteers for irritation to the throat and eyes (DFG, 1998) with an uncertainty factor of 2 applied Justified by comparison with systemic effects NOAEL of 100 mg/kg. <p>A skin notation is also recommended as dermal absorption could contribute substantially to the total body burden.</p>		
OARS/AIHA	NA	NA
No report.		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓	<ul style="list-style-type: none"> Human health tier I assessment – not considered to pose an unreasonable risk to the health of workers based on the Tier I IMAP assessment.
ECHA	✓ 2017	<ul style="list-style-type: none"> Workers – hazard <i>via</i> inhalation route: <ul style="list-style-type: none"> long term DNEL of 40 mg/m³ for repeat dose and skin irritation; modified starting point NOAEC acute/short-term DNEL of 80 mg/m³ for repeat dose and skin irritation; modified starting point NOAEC as described, no further information provided.

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	Skin
HCIS	NA
NICNAS	NA

Source	Notations
EU Annex	NA
ECHA	NA
ACGIH	Skin, Carcinogenicity – A3
DFG	—
SCOEL	Skin
HCOTN	NA
IARC	Carcinogenicity – Group 3
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**

Dermal repeat-dose NOAEL ≤ 200 mg/kg:

Dermal LD₅₀/Inhalation LD₅₀ < 10:

In vivo dermal absorption rate > 10%:

Estimated dermal exposure at WES > 10%:

consider assigning a skin notation

IDLH

Is there a suitable IDLH value available? **Yes**

Additional information

Molecular weight:	98.15
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m ³ ; 1 mg/m ³ = Number ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input checked="" type="checkbox"/> DFG <input type="checkbox"/> 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](#) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2006) Cyclohexanone – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (1992) Recommendation from the Scientific Committee on Occupational Exposure Limits for Cyclohexanone. SCOEL/SUM/17.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

International Agency for Research on Cancer (IARC) (1999) Cyclohexanone. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (N.D) Cyclohexanone: Human health tier II assessment – IMAP report.

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