# Cumene

| CAS number: | 98-82-8 |
| --- | --- |
| Synonyms: | Cumol, isopropylbenzene, 2-phenylpropane, benzene, (1-methylethyl) |
| Chemical formula: | C9H12 |
| Structural formula: | — |

Workplace exposure standard (interim)

| TWA: | 0.1 ppm (0.5 mg/m3) |
| --- | --- |
| STEL: | — |
| Peak limitation: | — |
| Notations: | Carc. 1B |
| IDLH: | — |
| Sampling and analysis: There is uncertainty regarding quantification of the recommended value with available sampling and/or analysis techniques. | |

## Recommendation and basis for workplace exposure standard

An interim TWA of 0.1 ppm (0.5 mg/m3) is recommended to protect for the risk of nasal and lung cancer in exposed workers.

The previous STEL of 75 ppm (375 mg/m3) is recommended to be withdrawn based on cumene’s characterisation as a non-threshold genotoxic carcinogen.

A priority review of the data for the chemical in the next scheduled review of the workplace exposure standards is recommended.

## Discussion and conclusions

Cumene is used commercially as a thinner for paints, enamels and in some petroleum products.

There is evidence to suggest carcinogenicity in experimental animals. However, human carcinogenicity is inconclusive (DFG, 2018). Although cumene is not considered to be genotoxic, there is evidence of genotoxicity for its metabolite *a-*methylstyrene oxide and a mutational mechanism is possible by which cumene could produce lung or nasal tumours in both rodents and humans (NICNAS, 2016; IARC, 2011). As such, it is characterised as a non-threshold genotoxic carcinogen.

Inhalation Unit Risk or Oral Slope Factors could not be identified. DFG (2018) derived the current MAK from a lower confidence limit of the benchmark dose of 42 ppm (BMDL05) for nasal adenoma in male rats in a two year inhalation study. By using the BMDL05 as a point of departure and dividing by 10,000 to provide an adequate margin of risk to obtain a value of 5 ppb (when rounded). Given the conflicting information about the chemical-specific genotoxicity in humans, this value is multiplied by 20 to arrive at a recommended TWA of 0.1 ppm. The recommended TWA of 0.1 ppm is considered sufficiently low to protect for cancer in exposed workers.

Based on the uncertainties associated with the data, investigation of additional data sources is recommended at the next scheduled review.

The previous STEL of 75 ppm is recommended to be withdrawn given the carcinogenic characterisation of cumene and genotoxic characteristics of its metabolite..

## Recommendation for notations

Classified as a category 1B carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). An examination of additional data sources is recommended at the next scheduled review due to the conflicting chemical-specific genotoxic information in the primary sources.

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

There are insufficient data to recommend retaining the skin notation as there is no indication of systemic effects resulting from skin absorption. Therefore, a skin notation is not recommended.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 2001 TWA: 25 ppm (125 mg/m3); STEL: 75 ppm (375 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 50 ppm (246 mg/m3) |
| TLV-TWA of 50 ppm recommended to minimise potential for dermal, ocular and respiratory tract irritation as well as CNS depression in exposed workers.  Summary of data:  Human data:   * No reports regarding toxicity available * 50% inhalation uptake (three doses from 49 ppm up to 147 ppm) with excretion of the metabolite (2-phenylpropan-2-ol) in urine proportional to concentration.   Animal data:   * LD50: 1,400–8,620 mg/kg (rats); effects included sluggishness, prostration, narcosis with autopsy indicating pneumonitis, pulmonary oedema and haemorrhage, gastrointestinal inflammation and liver discoloration. * Dermal LD50: 10.6 g/kg (rats) and >3.16 g/kg (albino rabbits). * LC50: 2,000 ppm (albino mice, 7 h inhalation) * Acute exposures can result in CNS depression * Sub-chronic inhalation ≥500 ppm and oral ≥462 ppm resulted in mild to moderate toxicity * Slight and moderate increase in kidney weight in rats from oral administration of 462 mg/kg/d and 740 mg/kg/d, respectively; hyperaemia and congestion in liver, lungs and kidney at 500 ppm (rats and rabbits, inhalation, 8 h/d for 6 d/wk for 150 d) * No toxic effects on rats, dogs, guinea pigs or monkeys in similar inhalation study up to 244 ppm * Decreased startle response, blepharospasm, increased water consumption, periocular swelling and increase in leukocytes, lymphocytes, platelets, protein and liver, kidney and adrenal weights up to 1,200 ppm (rats, inhalation, 6 h/d, 5 d/wk for 13 wk) * No carcinogenic studies available * No evidence of reproductive/developmental or genotoxic effects in studies reported.   There are inadequate data to recommend a Skin, SEN or carcinogenic notations or a TLV-STEL. |
| DFG 2018 MAK: 10 ppm (50 mg/m3) |
| Summary of additional data:  Human data:   * No data on sensitisation reported * Negative effects on adaptation to darkness, optical chronaxie and electrocortical reflexes reported for inhalation ≥0.028 mg/m3. No other details provided * Eye and nose irritation threshold values of 1,800–4,000 ppm is reported with effects of painful eye and pain in the upper respiratory tract after exposure to 300–400 ppm.   Animal data:   * Slight skin, eye and respiratory tract irritation reported with tumour-inducing effects on the lungs of mice and nose of rats after repeated inhalation * LD50: >3,160 mg/kg (rabbits); effects included weight loss with pulmonary haemorrhage discoloration of liver, kidney, spleen, enlarged gallbladder and inflammation of gastrointestinal tract reported in some of the animals * NOAEC: 100 ppm (rats, 90 d inhalation study) * No fetotoxic or teratogenic effects in rats and rabbits up to 1,200 and 2,300 ppm for 6 h/d from gestation days 6–15 and 16–18, respectively. Maternal toxicity reported for concentrations >100 and >500 ppm in rats and rabbits, respectively * Not considered genotoxic and no data on germ cell mutagenicity is available. However, the prevalence of mutations in *K-ras* and *p5*3 mutations have been observed, although inconclusive. Carcinomas, adenomas, metaplasia and hyperplasia in the lungs and hyperplasia and adenomas in the nose have been reported in exposed rats.   MAK derived from a lower confidence limit of the benchmark dose of 42 ppm for nasal adenoma in male rats in a 2 yr inhalation study. |
| SCOEL 1993 Not assigned |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| US EPA |  | 1988 | * Inadequate human or animal data to assign carcinogenicity classification * Inhalation Reference Concentration (RfC) of 0.4 mg/m3 was derived based on NOAEL of 2,438 mg/m3 (496 ppm) and LOAEL of 5,909 mg/m3 (1202 ppm) for increased kidney and adrenal weights (rats, 13 wk inhalation study). |
| IARC |  | 2011 | * Not mutagenic in *Salmonella*; some metabolites are mutagenic * Mutational mechanism possible to produce lung or nasal tumours in both rodents and humans * Dose related increase in the incidence of nasal tumours in male and female rats exposed via inhalation to 0, 250, 500 or 1,000 ppm; 12 min/d, 5 d/wk for 105 wk. |
| NICNAS |  | 2016 | * Critical health effect is carcinogenicity * Can also cause respiratory irritation and reversible neurotoxic effects * Evidence of genotoxicity for the metabolite  a-methylstyrene oxide * Although irritating, the chemical does not cause severe toxic effects following repeated dermal application. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Yes |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Yes |
| **The chemical is a non-threshold based genotoxic carcinogen.** |  |
| Is a cancer slope factor or inhalation unit risk value available? | No |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Skin |
| HCIS | Carcinogenicity – category 1B |
| NICNAS | Carc. Cat. 2 |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | NA |
| 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 |
| --- |
| Insufficient data to assign a skin notation |

### IDLH

| Is there a suitable IDLH value available? | No, the chemical is a genotoxic carcinogen |
| --- | --- |

## Additional information

| Molecular weight: | 120.19 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 4.92 mg/m3; 1 mg/m3 = 0.2 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) (2018) Isopropyl benzene (Cumene) – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (1993) Recommendation from the Scientific Committee on Occupational Exposure Limits for Cumene. SCOEL/SUM/29.

International Agency for Research on Cancer (IARC) (2013) Some chemicals present in industrial and consumer products, food and drinking-water. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Benzene, (1-methylethyl): Human health tier II assessment – IMAP report.

US Environmental Protection Agency (US EPA). (1988). Chemical Assessment Summary – Cumene; CASRN 98-82-8. Integrated Risk Information System (IRIS).