# Cresol, all isomers

| CAS number: | 1319-77-3 (mixture)  108-39-4 (*m*-cresol  95-48-7 (*o*-cresol)  106-44-5 (*p*-cresol) |
| --- | --- |
| Synonyms: | Mixture:  Coal tar or coal tar phenols, acede cresylique, Bacillol, cresol - mixed isomers, cresoli, cresols, cresylic acid  *m*-Cresol:  1-hydroxy-3-methylbenzene, 3-cresol, 3-hydroxytoluene, 3-methylphenol, m-cresole, m-cresylic acid  *o*-Cresol:  1-Hydroxy-2-methylbenzene, 2-cresol, 2-hydroxytoluene, 2-methylphenol, orthocresol, phenol,2-methyl, o-cresylic acid  *p*-Cresol:  4-cresol, p-cresylic acid, 1-hydroxy-4-methylbenzene, p-hydroxytoluene, p-kresol, p-methylhydroxybenzene, p-methylphenol |
| Chemical formula: | C7H8O |
| Structural formula: | — |

Workplace exposure standard (interim)

| TWA: | **5 ppm (22 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Sk.** |
| IDLH: | **250 ppm** |
| Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

An interim TWA of 5 ppm (22 mg/m3) is recommended to protect for irritation of the respiratory tract in exposed workers.

Given the limited data available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

## Discussion and conclusions

Cresols are found in plant oils, tobacco smoke and formed in fuel combustion processes and are derived from coal tar or petroleum synthesis or oxidation from toluene. Mixtures are used as solvents, disinfectants and particularly wood preservatives with additional use as lubricants and air filter oil additives.

The critical effect from exposure to airborne concentrations is irritation of the upper respiratory tract. There are inadequate inhalation studies and no available data demonstrating a no effect concentration. SCOEL (2002) suggests a TWA of 5 ppm (22 mg/m3) may be too high to protect for adverse effects. However, ACGIH (2018) note there is limited evidence to support reducing the value based on irritant effects.

Systemic toxicity of the cresol isomers has been adequately studied in animal oral experiments, resulting in a NOAEL of 50 mg/kg/day for rats. However, this is not considered sufficiently protective of the local irritation critical effect in humans associated with exposure to vapours (SCOEL, 2002).

In the absence of adequate inhalation studies and no clear suitable NOAEL it is recommended that the current TWA be retained as an interim value with a review of additional sources at the next scheduled review. It is recommended that a review of additional sources be conducted at the next scheduled review to provide further weight of evidence to support or recommend changes to current exposure standard.

## 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 as evidence indicates rapid absorption through the skin and reports of acute irritant effects in the workplace. There is sufficient evidence to recommend the skin notation based on human and animal data of systemic toxicity on nervous system, respiratory tract and gastrointestinal organs (DFG; 2000).

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 2016 TWA: 5 ppm (22 mg/m3) | |
| No documentation. |
| ACGIH 2010 TLV-TWA: 20 mg/m3 (Inhalable fraction and vapor) |
| TLV-TWA recommended to minimise acute upper respiratory tract irritant effects. It is not clear how the assigned TLV value was determined.  The toxicity of cresol isomers appears to differ slightly; however, the general effects are noted to be similar suggesting a common TLV is appropriate.  Isomers often found as a mixture sometimes known as cresylic acid (cresol isomers - 20% ortho-, 40% meta- and 30% para). Recommended that the common TLV not apply to creosote mixture because of the higher concentrations of PAHs from coal tar fractionation.  Sampling methodology is complicated by the particulate mass and vapor phase concentrations at temperature and total airborne concentration should be considered.  Summary of data:   * *In vitro* studies suggest *p-*cresol is more toxic than *o-* or *m-*cresols * Not classifiable as a human carcinogen * No mutagenic activity from *o-*, *m-* and *p-*cresols tested separately in *Salmonella* strains * Metabolites are excreted by the kidney and in bile with trace amounts via lungs * Limited evidence of mutagenicity; may have tumour-promoting activity * Highly irritating to skin as observed in animal studies * Insufficient data to recommend sensitiser notation; however, there are suggestions of contact allergy and dermatitis in sensitive persons to *o-* and *m-*cresols.   Human data:   * Limited human studies * Evidence of chronic poisoning via oral or skin absorption * Digestive and nervous disorders, faintness, vertigo, skin eruptions and systemic jaundice effects observed following accidental dermal contact and poisonings.   Animal data:   * LC50: 178 mg/m3 (mice, duration not specified) * Lower LC50 values identified in rats; however, minimal study information available * LD50 (dermal) in female albino New Zealand rabbits were 2,000, 890, 2,380, 300 mg/kg body weight for mixed isomers, *o-*, *p-* and *m-*cresols, respectively * *In vitro* testing indicated inhibition of DNA in rat testis (*p*-cresol) * *In vitro* unscheduled DNA synthesis observed in Syrian hamster cells (*m*-cresol) * *o-*, *m-* and *p-*cresols showed tumour promoting activity in the skin of albino mice exposed to DMBA (dimethylbenzanthracene) in acetone. |
| DFG 2000 Not assigned |
| Toxic effect of the cresols is the local irritation of skin and mucous membranes.  Evidence of weak genotoxic effects and of tumour-promoting activity prevent derivation of a MAK value, therefore the cresol isomers were classified provisionally as Carcinogen Category 3.  Toxic levels may be taken up through the skin and therefore designated with an “H” (skin) notation.  Insufficient evidence to designate a sensitiser notation; *p-*cresol and mixtures of both *m-* and *p-*cresol do not appear to cause sensitisation.  Summary of additional data:   * *In vivo* studies — no genotoxic effects noted * Suggestions of genotoxic effects on mammalian cells *in vitro.*   Human data:   * Limited human studies or poorly documented * Undiluted cresol is corrosive and can cause dermatitis * Limited evidence of brief exposures (time not stated) to *o-*cresol (6 mg/m3) caused irritation of the upper respiratory tract.   Animal data:   * NOAEL 50 mg/kg (rats, oral) * *m-*cresol is less acutely toxic in dermal application (than the other 2 isomers). * Undiluted cresol applied to rabbit eyes caused extreme irritation. |
| SCOEL 2002 Not assigned |
| Inadequate inhalation studies and no available data demonstrating a “no-effect concentration”, is insufficient evidence to determine scientifically based occupational exposure limits.  It is noted that the previous TWA of 5 ppm (22 mg/m3) may be too high.  Systemic toxicity of cresol isomers adequately studied in oral animal experiments, resulting in a NOAEL for rats of 50 mg/kg/d; may not be protective for local irritation; the noted critical effect of cresol vapour exposure  A skin notation recommended based on evidence of dermal absorption contributing substantially to total body burden was available.  Summary of data:   * Cresol isomers are strong eye and skin irritating compounds * No adequate inhalation studies are available * Repeated-dose oral toxicity studies do not indicate significant differences to the toxicity of the separate isomers. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| US EPA |  | 2003 | * No further 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 | Carcinogenicity – A4, Skin |
| DFG | Carcinogenicity – 3, H (skin) |
| SCOEL | Skin |
| 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: | yes | 4.00 |  | | Dermal LD50 ≤1000 mg/kg: | yes | 3.00 |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: | yes | 3.00 |  | | Dermal LD50/Inhalation LD50 <10: | yes | 3.00 |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  | 3 | **a skin notation is warranted** | |

### IDLH

| Is there a suitable IDLH value available? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 108.14 |
| --- | --- |
| 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: |  |
| 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) (2000) Cresol (all isomers) – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2002) Recommendation from the Scientific Committee on Occupational Exposure Limits for cresol (all isomers). SCOEL/SUM/96.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Cresol (*o-,m-,p-*, isomers).