# Workplace Exposure Standard (WES) review

***PHENOL***
***(CAS NO: 108-95-2)***

March 2020

New Zealand Government

WORKSAFE
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## appendices



## tables

# 1.0
# Introduction

# This WorkSafe New Zealand (WorkSafe) review considers whether the **WES** for phenol should be changed.

The WES review considers the potential for exposures to phenol in New Zealand, the health effects and risks, exposure standards from other jurisdictions around the world, and the practicability of measuring exposures given currently available analytical methods.

The review includes a recommendation to change the WorkSafe WES for phenol, which is currently set at a **WES-TWA** of 5**ppm** with a ***skin*** *notation*, as published in the special guide *Workplace Exposure Standards and Biological Exposure Indices*, 11th Ed., November 2019 (WorkSafe, 2019).

Terms that are **bold** (first occurrence only) are further defined in the Glossary. Synonyms: Carbolic acid; Hydroxybenzene; Oxybenzene; Phenic acid; Phenylic acid; Phenyl hydroxide; Benzenol; Benzophenol.

# 2.0 Chemical and physical properties

# Phenol is a colourless to light-pink, crystalline solid at room temperature with a sweet and acrid characteristic, tarry odour (**NLM** PubChem, 2019; **NICNAS**, 2014; **ACGIH®**, 2001).

Pure phenol consists of white or clear acicular crystals, which on exposure to air and light, changes to a pink to red colouration that can be accelerated by alkalinity or impurities (ACGIH®, 2001). It can be present in liquids (phenol solutions), solid or vapour form in workplaces.

Phenol has an odour threshold reported to be 0.04–0.05ppm (SCOEL, 2003; ACGIH®, 2001).

Chemical and physical properties phenol include:

| | |
|---|---|
| **Molecular weight** | 94.11g/mol |
| **Formula** | $C_6H_6O$ |
| **Specific gravity/density** | 1.071g/m$^3$ at 20°C |
| **Melting point** | 43°C |
| **Boiling point** | 182°C |
| **Vapour pressure** | 0.027kPa at 20°C; 0.35 torr at 25°C |
| **Vapour density** | 3.24 [air = 1] |
| **Saturated vapour concentration** | 0.046% at 25°C |
| **Flash point** | Closed cup: 79°C; Open cup: 85°C |
| **Flammable limits** | Upper: 13.4%; Lower: 2.6% by volume in air |
| **Autoignition temperature** | 715°C |
| **Explosive limits** | Lower: 1.7%; Upper: 8.6% by volume in air |
| **Log KOW** | 1.47 at 30°C |
| **pKa** | 9.89 at 20°C |
| **Solubility** | Soluble in water [84g/L]; very soluble in chloroform, alcohol, ether, carbon disulphide, glycerol, petrolatum, volatile oils, and aqueous alkali hydroxides; soluble in benzene [1g/12mL]; almost insoluble in petroleum ethers |
| **Conversion factors** | 1mg/m$^3$ = 0.26ppm<br>1ppm = 3.84mg/m$^3$ at 25°C and 760 torr |

ECHA REACH, 2019a; ECHA REACH, 2008; SCOEL, 2003; ACGIH®, 2001.

**TABLE 1:** Physicochemical properties of phenol

Health-related hazard classifications for phenol:

| | **HSNO CLASSIFICATION** |
|---|---|
| **Substance** | Phenol |
| **CAS No.** | 108-95-2 |
| **Classification** | 6.1B (All); 6.1B (I); 6.1C (O); 6.1C (D); 6.6B; 6.8B; 6.9A (All); 6.9A (D); 6.9A (O)<br>8.2B; 8.3A |

**TABLE 2:**
**HSNO** health-related hazard classifications of phenol (**EPA**, 2019)

For a full listing of all HSNO health-related hazardous substances classification codes and their descriptions, see Appendix 2.

[All] Overall classification for that endpoint.
[O] Oral exposure route.
[D] Derman exposure route.
[I] Inhalation exposure route.

# 3.0
# Uses

Phenol is mainly used as an intermediate in organic synthesis for the production of bisphenol A, phenol resins, alkylphenols, caprolactam, salicylic acid, nitrophenols, diphenyl ethers, halogen phenols and other chemicals (**ECB RAR**, 2006).

Phenol is also used in cosmetics, pharmaceuticals, biocides, adhesives and impregnation agents (ECB RAR, 2006).

Phenol is naturally occurring in some foods, in human and animal wastes, and in decomposing organic material, and it is produced endogenously in the gut from the metabolism of aromatic amino acids (US EPA, 2002).

Occupational exposure to phenol can occur during production, storage, transportation and end-use.

Workers can be exposed to phenol via inhalation and eye or dermal contact (ECB RAR, 2006). As a vapour, liquid or solid, phenol can penetrate intact skin (ACGIH®, 2001)

The number of workers exposed or potentially exposed to phenol in New Zealand workplaces is unknown.

Statistics New Zealand 2019 data indicate that 5,190 New Zealand workers were working in the areas of:

- basic organic chemical manufacturing
- basic polymer manufacturing
- pesticide manufacturing
- pharmaceutical and medicinal product manufacturing
- cosmetic and toiletry preparation manufacturing (NZ.Stat, 2019).

# 4.0
# Health effects

**IN THIS SECTION:**

## 4.1 Non-cancer

### Humans

The ECHA REACH Dossier on phenol summarised the acute toxicity in exposed humans:

> "Liquid phenol in contact with the skin rapidly enters the bloodstream. From a variety of case reports clinical signs are known being documented [sic] for various occupationally exposed persons. These signs and symptoms can develop rapidly with serious consequences including shock, collapse, coma, convulsions, cyanosis, damage to internal organs, and death. Skin contact of humans with solutions, emulsions, or preparations containing 80–100% phenol for 5–30 minutes has been reported to result in death (**NIOSH**, 1976).
>
> "Phenol is reported to cause poisoning by skin absorption, vapour inhalation and ingestion (Kania, 1981). Primary route of entry is the skin. Vapours readily penetrate the skin surface with absorption efficiency equal to that of inhalation. Absorption from spilling phenolic solutions on the skin may be very rapid, and death results from collapse within 30 minutes to several hours. Death has resulted from absorption of phenol through a skin area of 64in$^2$. Where death is delayed, damage of the kidneys, liver, pancreas and spleen, and oedema of the lungs may result. The symptoms develop rapidly, frequently within 15–20 minutes following spilling of phenol on the skin. Initial skin contact produces a white wrinkled discoloration with no experience of pain due to the local anaesthetic properties of phenol, with the affected area turning brown and subsequently becoming gangrenous. Prolonged exposure may result in deposition of dark pigment (ochronosis). Phenol vapours are also well absorbed by the lungs. Inhalation causes dyspnea, cough, cyanosis, and pulmonary oedema. Ingestion of even small amounts of phenol causes severe burns of the mouth, esophagus, and abdominal pain. Patches, first white then brown with areas of necrosis, may be noted about the face and oral cavity (Kania, 1981)." (References cited in ECHA REACH, 2019 b).

The New Zealand EPA classifies phenol as a 6.1B, 6.1C and 6.9A substance – a substance that is acutely toxic and that is toxic to human target organs or systems, respectively (EPA, 2019).

The ECB RAR review of phenol summarised the irritation/ corrosion potential in exposed humans:

> "Ten percent solutions regularly produce corrosion, and occasionally skin necrosis is seen with solutions as dilute as 1%. Concentrated solutions are severely irritating to the eyes and cause conjunctival swelling with the cornea becoming white and hyperaesthetic; loss of vision has occurred in some cases. Concentration is more critical than volume with respect to local response (Kania, 1981)." (Reference cited in ECB RAR, 2006).

The New Zealand EPA classifies phenol as an 8.2B and 8.3A substance – a substance that is corrosive to dermal and ocular tissue, respectively (EPA, 2019).

The NIOSH Skin Notation Profile of phenol noted:

> "The available information indicates that phenol may be either irritating or corrosive to the skin, depending on the concentration of the phenol solution. For example, dermal exposure to liquid phenol or concentrated phenol vapor causes corrosive effects, including tissue death (necrosis), in humans [Schmidt and Maibach 1981; Foxhall *et al* . 1989; Horch *et al* . 1994],

rats [Conning and Hayes 1970], mice [Patrick *et al* . 1985], and pigs [Pullin *et al* . 1978; Hunter *et al* . 1992]. Other effects, such as erythema, inflammation, discoloration, eczema, redness, and severe edema have been reported to occur after skin contact with solid or liquid phenol [Brown *et al* . 1975; Conning and Hayes 1970]. The effects of phenol on the skin have been attributed to its ability to impair the barrier function of the stratum corneum and produce coagulation necrosis by denaturing and precipitating proteins.

"Hayashi *et al* . [1999] theorized that the skin irritation induced by phenol is caused by reactions of the substance with macromolecules found within the epidermal and dermal levels of the skin."

"Several studies involving humans and animals have shown that phenol is corrosive to the skin or is a skin irritant, depending on its concentration. Reports of necrosis and chemical burns in humans [Schmidt and Maibach 1981; Foxhall *et al* . 1989; Horch *et al* . 1994] and animals [Conning and Hayes 1970; Pullin *et al* . 1978; Patrick *et al* . 1985; Hunter *et al* . 1992] following direct contact with undiluted phenol or concentrated solutions are sufficient to demonstrate the corrosivity of phenol. More-diluted solutions are more likely to be irritating to the skin. On the basis of the data for this assessment, phenol is assigned the SK: DIR (COR) notation." (References cited in NIOSH, 2011).

The ECHA REACH Dossier on phenol summarised the sensitisation potential in exposed humans:

"Wantke *et al* . (1996, cited in **EU**-RAR 2006) investigated the sensitizing potency by measuring the specific IgE against phenol in 45 students before and after a 4-week anatomy dissection course (no details given about exposure to phenol). There was no evidence of allergic contact dermatitis caused by phenol.

"In the maximization test phenol did not act as a sensitizer in 24 volunteers after induction with 2% phenol in solution and challenge with 1% solution (Kligman, 1966; additional information in **IUCLID** Section 7.4.1)." (References cited in ECHA REACH, 2019d).

The **ATSDR** review of phenol summarised the repeated dose toxicity in exposed humans:

"In an epidemiological study of workers from the rubber industry exposed to multiple chemicals (phenol among them), phenol showed the strongest association with mortality due to ischemic heart disease. Electrocardiographic alterations have been reported following acute oral and dermal exposure to phenol, as well as vomiting and lethargy. Studies of populations whose drinking water was contaminated with phenol found increased incidences of nausea and diarrhea, but exposure to chlorophenols may have also occurred. Also, liver effects, as judged by increased serum activities of alanine aminotransferase (**ALT**) and aspartate amino transferase (**AST**), were reported in a case of prolonged inhalation exposure to phenol and in workers in an oil-refining plant, but exposure to other solvents could not be ruled out in the latter case. An increased incidence of headaches was reported among people who used drinking water contaminated with phenol and probably chlorophenols also." (ATSDR, 2008).

The NICNAS review of phenol noted:

> "Repeated oral, inhalation, and dermal exposure of humans has been reported to result in mucosal irritation, diarrhoea, dark urine, weakness, muscle pain, loss of appetite and body weight, and liver toxicity (ECB, 2006; ASTDR, 2008). There is also limited evidence of effects on the cardiovascular, haematopoetic and immunological systems, although exposure of workers to other chemicals was a possible confounding factor." (References cited in NICNAS, 2014).

The ATSDR review of phenol summarised the reproductive/developmental toxicity in exposed humans:

> "There is no evidence that phenol is a reproductive or developmental toxicant in humans. The Development and Reproductive Toxicant Identification Committee of the California EPA's Office of Environmental Health Hazard Assessment examined the weight of evidence on the reproductive toxicity of phenol and concluded that phenol had not been clearly shown to cause reproductive toxicity." (ATSDR, 2008).

## Animals

The ECB RAR review of phenol summarised the acute toxicity potential in experimental animals:

> "For animals, dermal and oral **$LD_{50}$** values are given in the literature: An oral $LD_{50}$ of 340mg/kg bw for rats (Deichmann and Witherup, 1944), of approximately 300mg/kg bw for mice (von Oettingen and Sharpless, 1946) and of less than 620mg/kg bw for rabbits (Deichmann and Witherup, 1944) are reported. A dermal $LD_{50}$ value of 660-707mg/kg bw was determined for female rats (Corning and Hayes, 1970). Although **$LC_{50}$** values are not available in the literature, rats are reported to tolerate phenol concentrations as high as 236ppm (900mg/$m^3$) for 8 hours, resulting in ocular and nasal irritation, loss of coordination, tremors, and prostration." (References cited ECB RAR, 2006).

The NIOSH Skin Notation Profile of phenol noted:

> "In animals, the dermal $LD_{50}$ values (the doses resulting in 50% mortality in the exposed population) range from 0.5 milliliter per kilogram body weight (mL/kg) to 0.68mL/kg (corresponding to 669–1500 milligrams per kilogram body weight [mg/kg]) [Conning and Hayes 1970; Brown *et al* . 1975] in rats under both occlusive and nonocclusive conditions and 1400mg/kg in rabbits [Vernot *et al* . 1977]. Corning and Hayes [1970] reported severe muscular tremors, twitching, generalized convulsions with loss of consciousness, and prostration within 10 minutes, and severe hemoglobinuria occurred at between 45 and 90 minutes after dermal exposure to phenol in water. Brown *et al* . [1975] reported hematuria and convulsions as clinical signs of phenol toxicity. Because the reported acute dermal $LD_{50}$ values for the rat and rabbit are both lower than the critical dermal $LD_{50}$ value of 2000mg/kg body weight that identifies substances with the potential for acute dermal toxicity [NIOSH 2009], phenol is considered systemically toxic by the acute dermal route." (References cited in NIOSH, 2011).

The ECHA REACH Dossier on phenol summarised the irritation/ corrosion potential in experimental animals:

**Skin irritation/corrosion**

"Further testing is scientifically unjustified as existing animal and human data show that the criteria for classification as corrosive to the skin are met.

"Mild to severe chemical burns were observed even after a 1-minute uncovered application of undiluted (molten) phenol in five male and five female rats (Brown *et al* ., 1975; see robust study summary in IUCLID Section 7.3.1). The contact of 0.5g of phenol moistened with physiological saline with the intact and abraded areas of the skin of the bellies of rabbits for a maximum period of 24 hours produced necrosis of the intact skin (limited documentation; Flickinger, 1976, see robust study summary in IUCLID Section 7.3.1). The *in vitro* study according to **OECD** Guideline 431 (Slovnaft 2009, see Section 7.3.1) revealed skin corrosive properties.

"Phenol has corrosive properties which have been also documented in IUCLID Section 7.2.3 and in the summary of Section 7.2.

**Eye irritation**

"According to OECD Guideline 405 no testing is required for corrosive substances. However, the available data in elderly studies confirmed the corrosive properties of phenol (Flickinger, 1976; see robust study summary in IUCLID Section 7.3.2). Rabbits received instillations of 100mg phenol into the conjuntival sac. Effects were recorded up to 14 days after application. Upon the application the conjunctivae became inflamed, the corneas opaque, and the rabbits gave evidence of marked discomfort. Examination of the exposed eyes 24 hours following exposure showed severe conjunctivitis, iritis, corneal opacities occluding most of the iris, and corneal ulcerations extending over the entire corneal surface. There was almost no perceptible improvement in the condition of the eyes during the observation period, and by the 14th day all of the exposed eyes exhibited keratoconus and pannus formation.

"In an eye irritation test 6 rabbits per group were exposed to 0.1ml of 5% aqueous solution of phenol. In the first group the eyes were washed for 2 minutes with 300ml of tap water 30 seconds after application and in the second group the eyes remained unwashed. All of the animals produced corneal opacity but washing enhanced the recovery of eyes damaged by phenol and in some cases decreases the severity and duration of corneal opacities. Generally, the effects of the 5% aqueous solution were irreversible after an observation period of 7 days (Murphy *et al* ., 1982; IUCLID Section 7.3.2)." (References cited in ECHA REACH, 2019c).

The NICNAS review of phenol noted that signs of respiratory irritation have been observed in a number of animal studies following acute and repeat inhalation exposure to the chemical (NICNAS, 2014).

The ECB RAR review of phenol summarised the sensitisation potential in experimental animals:

"In a modified Buehler Test ten female Hartley albino guinea pigs were treated with phenol (purity: 99.9%) as follows: For induction a 10% phenol concentration in white petrolatum was applied to the skin for 48 hours. This procedure was repeated three times a week for two weeks. Two weeks after the end of the induction procedure 1% and 0.1% phenol concentration in white petrolatum was used for challenge treatment. Exposure time was 48 hours. None of the animals showed a positive response. Control animals were not included in the study (Itoh, 1982).

> "In a Mouse Ear Swelling Assay (**MESA**) 15 female Balb/c mice received a topical application of a 5% phenol concentration on both sides of the right ear on days 0 and 2, and a scapular subcutaneous injection of 0.05ml Complete Freund´s Adjuvans on day 2. On day 9, left ear thickness was measured immediately before topical application of a 5% phenol concentration on both sides of the ear, and again 24 hours later (day 10). Ear thickness was not affected by phenol treatment demonstrating that phenol has no skin sensitising potency. The purity of phenol and the vehicle were not mentioned (Descotes, 1988)." (References cited in ECB RAR, 2006).

The ATSDR review of phenol summarised the repeated dose toxicity in experimental animals:

> "There is only one modern study of inhalation exposure of animals to phenol. The rest of the inhalation database for phenol is outdated and not useful for risk assessment, although it serves to identify some targets for phenol toxicity. However, no single especially sensitive target emerged from these studies. Short-term (5 minutes) exposure of mice to phenol caused respiratory irritation, as judged by the animals' reflex reduction in respiratory rate; a lowest-observed-effect level (**LOEL**) was not defined; but the exposure concentration that reduced the respiratory rate by 50% was 166ppm. In rats exposed nose-only intermittently to concentrations up to 25ppm for 2 weeks, phenol caused no gross or microscopic alterations in major tissues and organs, including the nasal cavity, but some rats showed an increased incidence in a red nasal discharge possibly due to the irritating properties of phenol. Phenol caused pneumonia, necrosis of the myocardium, centrilobular degeneration, and necrosis of the liver and renal lesions in rabbits and guinea pigs, but not in rats, exposed whole-body intermittently to 26ppm phenol for intermediate durations. In yet another study in rats, continuous whole-body exposure to 26ppm phenol for 15 days caused signs of neurological impairment including muscle tremors, twitching, and gait disturbances during the first 3–5 days of exposure. At termination, serum transaminases were elevated suggesting liver damage, but no histological examination was conducted. Neurological effects, including loss of coordination and tremors, were also observed in rats exposed to 234ppm phenol for 8 hours. In summary, inhaled phenol can affect several organs and tissues and produce neurological effects, but few generalizations can be made from the available studies due to the different exposure protocols used (that is, nose-only vs. whole-body; intermittent vs. continuous) and incomplete reporting. Toxicokinetics information indicates that phenol is readily absorbed through the skin of humans and animals, so that whole-body exposure may result in considerably more absorbed phenol than in nose-only exposures.
>
> "Application of phenol to the skin of animals has caused edema, erythema, necrosis, and death; the cause of death was not provided in the studies available. The effects of phenol on the skin are due to its property to impair the stratum corneum and produce coagulation necrosis by denaturing and precipitating proteins. Lethality is influenced by the surface area exposed as well as the concentration of the applied solution. Systemic effects also have been described in animals following dermal exposure to phenol. Rabbits that received a dose of phenol of 24**mg/cm²/kg** suffered cardiac arrhythmia. Tremors leading to convulsions were reported in rats following application of 107mg/kg of phenol to an unspecified surface area." (References cited in ATSDR, 2008).

The ECB RAR review of phenol summarised the reproductive/developmental toxicity in experimental animals:

> "Phenol was investigated for impairment of reproductive performance and fertility in a two-generation (drinking water) reproductive toxicity study in rats. At the highest tested concentration level, according to a mean daily uptake of 300 to 320mg phenol/kg body weight, which led to reduced water intake and consequently decreased body weight and body weight gain including organ weight impairment in the animals, no adverse effects on reproductive capability and fertility were revealed for either sex across the two generations. Furthermore, sperm parameters and estrous cyclicity had not been affected by phenol treatment. Any effects as revealed during this study were confined to the observation of impaired offspring viability and body weight gain during the pre-weaning period for the 5,000ppm treated groups for both generations. No such effects had been revealed for the lower tested dosage levels. From the evaluation of this study no adverse effects on reproductive capability and fertility could be revealed up to and including the highest dosages tested (5,000ppm in drinking water according approximately 301 (males) respectively 320 (females) mg phenol/kg bw/day. Thus it can be concluded for fertility that this endpoint has been adequately examined.
>
> "Phenol was evaluated for developmental toxicity in studies with mice and rats. From these studies there are no indications for an embryotoxic or teratogenic potential of phenol. When pregnant rats or mice had been exposed to phenol during gestation (and lactation) indications of prenatal growth retardation and impaired peri-postnatal viability and postnatal growth had been revealed. These effects had been induced at exposure levels that obviously induced systemic toxic effects in the dams and therefore are considered to be secondary and not an indication for a specific fetotoxic potential of phenol. From the overall evaluation of the available studies, for risk characterisation of reproductive toxicity with respect to development a **NOAEL**/developmental toxicity for phenol of 93mg/kg body weight is recommended. This NOAEL/developmental toxicity is based on the observations upon offspring performance and development from the 2-generation study." (References cited in ECB RAR, 2006).

The New Zealand EPA classifies phenol as a 6.6B substance – a substance that is a suspected human mutagen (EPA, 2019).

The ECHA REACH Dossier on phenol summarised the genotoxic potential in experimental animals and *in vitro* test systems:

> ***In vitro* test systems**
>
> "Phenol has no mutagenic properties in bacterial gene mutation tests. There is evidence for gene and chromosome mutagenic effects in mammalian cells, mainly in the presence of **MA**. However, concerning gene mutation assays most studies resulted only in weak positive results at cytotoxic dose levels. Also in chromosome mutation assays positive results were obtained mainly at cytotoxic concentrations. A test for induction of aneuploidy was negative. Evidence for sister chromatid exchange was given in mammalian cells at cytotoxic dose levels. Further indicator tests suggested genotoxic effects of phenol.
>
> *Tests with negative outcome*: bacterial gene mutation, induction of aneuploidy in mammalian cells,
>
> *Tests with positive outcome*: chromosome aberration and gene mutation in mammalian cells, **DNA** damage in mammalian cells.

> ***In vivo* test systems**
>
> "In studies investigating the systemic chromosome mutagenic activity of phenol after oral or parenteral administration weak positive or negative results were reported. Furthermore in indicator test for systemic genotoxicity no DNA strand breaks were detected in rats and no DNA adduct formation was found in rats and mice. The **SLRL** assay in Drosophila revealed also negative results.
>
> The weak positive results in micronucleus tests were found at dose levels inducing severe signs of intoxication. In the EU-RAR (2006) it was suggested that these weak clastogenic effects "may be based on an indirect mode-of-action"; possible mechanisms for the induction of micronuclei at high doses are given by hypothermia and metabolic overload. In a recently published study (Spencer *et al* ., 2007) a significant increase in micronuclei was found only in the high dose groups with prolonged hypothermia. No clastogenic effects were reported at lower dose levels. These results suggested a possible threshold mechanism above 100mg/kg bw/d for the induction of micronuclei by phenol treatment in mice via prolonged hypothermia." (References cited in ECHA REACH, 2019e).

The New Zealand EPA classifies phenol as a 6.8B substance – a substance that is a suspected human reproductive or developmental toxicant (EPA, 2019).

## 4.2 Cancer

The International Agency for Research on Cancer [**IARC**] evaluation of phenol concluded that:

> There is *inadequate evidence* in humans for the carcinogenicity of phenol.
>
> There is *inadequate evidence* in experimental animals for the carcinogenicity of phenol.

With an overall evaluation that:

> Phenol is *not classifiable as to its carcinogenicity to humans (Group 3)* (IARC, 1999).

The US National Toxicology Program [**NTP**] Report on Carcinogens [**RoC**], Fourteenth Edition has no evaluation on the carcinogenic potential of phenol (NTP RoC, 2019).

The New Zealand EPA does not classify phenol as 6.7A/B for carcinogenic potential (EPA, 2019).

### Humans

The ATSDR review of phenol summarised the carcinogenic potential in exposed workers:

> "In a nested case-control study of cancers associated with chemical exposures in the wood industry, Kauppinen *et al* . (1986) found a significantly increased risk of respiratory system cancer associated with exposure to phenol and phenol in wood dust. As is often the case in occupational settings, these exposures were confounded by smoking and exposures to other materials like pesticides; in addition, information on direct phenol measurements was not provided. The increased risk observed for exposure to phenol was almost

5-fold (odds ratio of 4.94), but showed no dose-related increase. This risk dropped to 4-fold with adjustments for smoking history, and <3-fold (and non-significant) when workers exposed to both phenols and pesticides were excluded from the analysis.

"Similar to the findings of Kauppinen *et al* . (1986), a large (14,861) cohort mortality study of workers in the phenol-formaldehyde resin manufacturing industry found nondose-related increases in the risk of several respiratory system cancers in workers exposed to phenol (Dosemeci *et al* . 1991). The authors develop a semiquantitative exposure assessment by assigning exposure levels (none, low, medium, and high) to each job category. The increased risks were small; for instance, for cancer of the larynx or lung, standard mortality ratios (**SMR**s) of 1.1 were less than those found for non-exposed workers. For a number of other cancers, including those of the esophagus, rectum, bladder, kidney, and Hodgkin's disease, the SMRs found for phenol-exposed workers were slightly elevated, but none of the increases were statistically significant when compared with those in the general population. Furthermore, none of these increases had dose-response relationships with cumulative exposure to phenol." (Reference cited in ATSDR, 2006).

## Animals

The ECHA RAR review of phenol summarised the carcinogenicity data in experimental animals:

"In 103-weeks cancer studies on F344 rats and B6C3F1 mice with oral administration of 2,500 and 5,000ppm phenol in the drinking water (≈200 and 450mg/kg bw/day for rats and 281 and 375mg/kg bw/day for mice), phenol was not carcinogenic for both sexes. The purity of the test substance was reported to be >98% for one of three batches used. The final body weight gain was reduced in high dose rats and both dose groups in mice. Water consume [sic] was reduced in both dose groups in rats (-10 and -20%) and in both dose groups in mice (-25 and -40-50%). There was no effect on food consumption and mortality. No treatment-related effects of the incidences of inflammatory, degenerative and hyperplastic lesions were seen in treated rats and mice. The incidence of leukaemia or lymphomas, pheochromocytomas, and c-cell carcinomas was significantly increased in male rats that received 2,500ppm phenol (see below). Increases in tumour incidence were only seen in the low dose group, no such effect could be observed in the high dose group. Thus, an association with administration of phenol was not established for this rat strain. In mice, no tumour induction can be associated with the administration of phenol (NIH, 1980)."

"Oral long term studies on rats and mice revealed no effect of phenol on tumour induction. A medium-term study on a transgenic mouse model did not give any indication on treatment-related proliferative responses. Phenol was shown to act as a promoter in skin cancer bioassays in mice. A weak carcinogenic effect was observed after long-term skin application of a 10% solution of phenol in benzene (without initiation), but was considered less relevant. The test solution was strongly irritative, and contained the carcinogen benzene. However, there is some concern on the basis of weakly positive *in vivo* mutagenicity data and from the phenol metabolite hydroquinone classified as a suspected carcinogen (**Category 3**). This concern is considered to be of minor significance, as long term studies revealed no relevant indication for carcinogenicity. However, in conclusion, phenol is considered not to be a carcinogen in animals." (References cited in ECB RAR, 2006).

## 4.3 Absorption, distribution, metabolism and excretion

The ECHA RAR review of phenol summarised the **ADME**:

> "Phenol is well absorbed via gastrointestinal and respiratory tract and the dermal route. Concerning the oral route a high absorption was measured in rats, sheep and pigs with 90, 85, and 84% of the orally administered phenol dose of 25mg/kg bw after 8 hours. Volunteers exposed to phenol concentrations of 6–20mg/m$^3$ via inhalation absorbed 60 to 88% of the substance. After dermal application of phenol to rats, 40% of the applied dose was excreted in the urine by 4 hours, 70% by 12 hours and the excretion was essentially complete (with 75%) by 24 hours. In body tissues phenol is rapidly distributed. It is metabolised to sulfate and glucuronide conjugates. The ratio of sulfate/glucuronide conjugates excreted in urine is species and dose-dependent with a capacity-limited sulfatation at high dosages in rats and mice. Cats showed a poor glucuronidation of phenol, only conjugation with sulfate occurred. Small amounts of conjugated hydroquinone were only detected in the metabolic profiles for humans and rats. Metabolism predominantly occurs in liver, gut and kidneys. Excretion via urine is the main elimination pathway of phenol metabolites in humans and animals for the different exposure routes." (ECHA RAR, 2006).

The ATSDR review of phenol noted:

> "Conjugates with glucuronic acid and sulfate are the major metabolites of phenol, although small amounts of the hydroxylation products catechol and hydroquinone are also produced. Sulfotransferase and glucuronyltransferases are present in most tissues, although the major sites of phenol conjugation are the gastrointestinal tract, liver, lung, and kidney. Because of the large capacity of the intestines and liver to conjugate phenol, the fact that the first-pass effect occurs following oral exposure but not following dermal exposure may contribute to the greater potential for phenol to result in adverse effects following dermal exposure." (ATSDR, 2008).

The ATSDR review of phenol summarised the mechanistic data for toxicity:

> "Limited information is available regarding the mechanism(s) of toxicity of phenol. Phenol is irritating and corrosive at high concentrations as evidenced by numerous cases of accidental dermal exposure or intentional or accidental ingestion of phenol. Phenol impairs the stratum corneum and produces coagulation necrosis by denaturing and precipitating proteins. Studies in mice suggest that dermal application of phenol increases the formation of free radicals in the skin, and that the redox cycling of these radicals reduces antioxidant capacity, leading to significant oxidative damage of protein, DNA, and lipids (Murray *et al* . 2007).
>
> "Phenol is a hydroxylated metabolite of benzene and it further undergoes oxidative metabolism to produce other compounds; however, it is still unknown with certainty whether the parent compound or a metabolite(s) is responsible for phenol's systemic toxicity. The major tissues in which metabolism appears to occur are the liver, gut, lung, and kidney (Cassidy and Houston 1984; Powell *et al* . 1974; Quebbemann and Anders 1973; Tremaine *et al* . 1984). A study by Chapman *et al* . (1994) provided some insight on a possible toxic entity. These investigators found that incubation of whole rat conceptus *in vitro* with phenol resulted in minor dysmorphogenic and embryotoxic effect. However, addition of exogenous hepatic bioactivation

system greatly increased the toxicity of phenol. The major metabolites formed were hydroquinone, catechol, and benzoquinone and these three metabolites exhibited similar potency. Chapman *et al* . (1994) also found that adding together phenol and hydroquinone resulted in more-than-additive embryotoxicity which, according to the investigators, suggested the involvement of a peroxidative mechanism for phenol bioactivation."

"Several studies in animals have reported tremors following exposure by oral gavage (Moser *et al* . 1995; NTP 1983b). The mechanism by which phenol or metabolites exert this effect is unknown."

"It has been suggested that phenol exposure results in cardiac effects because it blocks the cardiac sodium channel subtype, with little effect on sodium channels in skeletal muscle (Zamponi *et al* . 1994). A preferential block by phenol of sodium channels in inhibitory pathways would be consistent with a net result of increased activity or even tremors, but there is no experimental support for this hypothesis." (ATSDR, 2008).

# 5.0 Exposure standards

**IN THIS SECTION:**

## 5.1 Other exposure standards

Table 3 below shows phenol exposure standards from around the world, as published by the Institute for Occupational Safety and Health of the German Social Accident Insurance (**IFA**, 2019).

| JURISDICTION OR ADVISORY BODY | 8-HOUR LIMIT VALUE | | SHORT-TERM LIMIT VALUE | |
|---|---|---|---|---|
| | ppm | mg/m³ | ppm | mg/m³ |
| Australia | 1 | 4 | | |
| Austria | 2 | 8 | 4 | 16 |
| Belgium[1] | 2 | 8 | 4[2] | 16[2] |
| Canada – Ontario | 5 | | | |
| Canada – Québec | 5 | 19 | | |
| Denmark | 1 | 4 | 2 | 8 |
| European Union | 2[3] | 8[3] | 4[2,3] | 16[2,3] |
| Finland | 2 | 8 | 4[2] | 16[2] |
| France | 2[4] | 7.8[4] | 4[2,4] | 15.6[2,4] |
| Germany – **AGS** | 2[5] | 8[5] | 4[5,6] | 16[5,6] |
| Ireland | 2 | 8 | 4[6] | 16[6] |
| Israel | 5 | 19 | | |
| Italy[7] | 2 | 8 | 4 | 16 |
| Japan – **JSOH** | 5 | 19 | | |
| Latvia | 2 | 8 | 4[2] | 16[2] |
| New Zealand | 5 | | | |
| People's Republic of China | | 10 | | |
| Poland | | 7.8 | | |
| Romania | 2 | 8 | 4[2] | 16[2] |
| Singapore | 5 | 19 | | |
| South Korea | 5 | 19 | | |
| Spain[7] | 2 | 8 | | |
| Sweden | 1 | 4 | 4[2] | 16[2] |
| Switzerland | 5 | 19 | 5 | 19 |
| The Netherlands | | 8 | | |
| Turkey | 2 | 8 | 4[2] | 16[2] |
| USA – NIOSH | 5 | 19 | 15.6[8] | 60[8] |
| USA – **OSHA** | 5 | 19 | | |
| UK | 2 | | | |

**TABLE 3:** Exposure standards for phenol from around the world

[1] Additional indication "D" means that the absorption of the agent through the skin, mucous membranes or eyes is an important part of the total exposure. It can be the result of both direct contact and its presence in the air.

[2] 15 minutes average value.

[3] Indicative Occupational Exposure Limit Value (**IOELV**).

[4] Restrictive statutory limit values.

[5] Inhalable aerosol and vapour.

[6] 15 minutes reference period.

[7] skin.

[8] **Ceiling limit value**.

It is noted that the only organisations from whom we obtained information as to how and why they set occupational exposures standards on phenol were SCOEL and ACGIH®. The **DFG** has published rationale for recommending a **BLW** (DFG, 1994, 2005).

## 5.2 SCOEL

The Scientific Committee on Occupational Exposure Limits [SCOEL] assessment of phenol recommended an 8-hour TWA of 2ppm [7.8mg/m$^3$] and a STEL of 4ppm, for occupational exposures to phenol (SCOEL, 2003).

The rationale for their conclusions included:

> "The briefly reported inhalation study by Sandage (1961) suggests that no systemic toxicity was produced in three experimental species (rat, mouse, Rhesus monkey) continuously exposed to 5ppm phenol for 90 days. However, because of its irritant/corrosive properties, there is concern that repeated inhalation exposure to phenol could produce local effects in the upper respiratory tract and it appears that this issue was not explored in this study. Nevertheless, a recent abstract indicates that no respiratory tract pathology (or other evidence of toxicity) was seen in rats repeatedly exposed to up to 25ppm phenol for two weeks. Hence it might be predicted that 5ppm would not have produced local respiratory tract effects in the earlier study. Assuming 100% retention and absorption of the inhalation dose, continuous exposure of rats to 5ppm would equate to a body burden of approximately 15mg/kg/day.
>
> "Earlier inhalation studies have reported toxicity in rats and rabbits exposed repeatedly or continuously to 26–52ppm phenol. There is no reliable information on the effects of repeated exposure to airborne phenol in humans.
>
> "The findings of repeated oral dosing studies in animals have been conflicting, so that the overall picture is confused. Some studies have indicated no effects in rats and mice receiving hundreds of mg/kg/day; others have reported adverse effects in mice receiving as little as 2mg/kg/day. In the opinion of the SCOEL, the quality and reliability of the overall repeated oral exposure database is inadequate for use in the derivation of an **OEL** proposal.
>
> "Hence, the SCOEL concluded that repeated daily exposure to 5ppm phenol would probably produce no local or systemic toxicity in experimental animals. An uncertainty factor of 2 was applied to allow for the absence of human data. Taking into account the preferred value approach, an 8-hour TWA of 2ppm (7.8mg/m$^3$) is recommended. The genotoxic potential of phenol *in vivo* is weak and probably metabolism-dependent, so that at low concentrations no genotoxic potential is expected and a threshold mechanism can be assumed.
>
> "It was judged that a STEL is required to protect agaist [sic] upper respiratory tract irritation. There are no human data to suggest a particular value for the STEL, but on the basis of animal data a STEL of 4ppm was recommended.
>
> "Skin penetration may make a substantial contribution to the total body burden, so a skin notation is also required. No sensitisation notation is required." (Reference cited in SCOEL, 2003).

The SCOEL recommendation also noted that:

> "Biological monitoring could be useful to assess occupational exposure to phenol. An 8-hour exposure to 2ppm phenol would correspond to a urine concentration, measured at the end of the shift, of 120mg phenol/g creatinine (Piotrowski, 1971; Ohtsuji and Ikeda, 1972; Ogata *et al* ., 1986)." (Reference cited in SCOEL, 2003).

## 5.3 ACGIH®

The American Conference of Governmental Industrial Hygienists [ACGIH®] review of phenol recommended a **TLV-TWA** of 5ppm [19mg/m$^3$] for occupational exposure to phenol to minimise the potential risk of eye and respiratory tract irritation, and cardiovascular, hepatic, renal, and neurologic toxicity (ACGIH®, 2001).

The rationale for their conclusions included:

> "Phenol is an irritant of the eyes mucous membranes, and skin (NIOSH, 1976; ATSDR, 1989; Deichmann *et al* ., 1962; Hartigan, 1900; McCord and Monster, 1924; Smith, 1922; Stajduhar-Caric, 1968; Bennett *et al* ., 1950; Schwartz, 1936). Systemic absorption can occur by all routes of exposure, and it can induce convulsions with damage to the lungs and **CNS** should the individual survive (Evans, 1952; Duvemeuil and Ravier, 1962; Hinkel, 1968; Satulsky and Helpern, 1943; Telegina and Boiko, 1972; Piotrowski, 1971; Lambotte and Degroote, 1960; Watorski, 1952; Hartigan, 1900; McCord and Monster, 1924; Smith, 1922; Stajduhar-Caric, 1968; Bennett *et al* ., 1950; Caviness, 1940).
>
> "Repeated exposure of animals to phenol vapor at concentrations ranging from 26 to 52ppm has been associated with respiratory, cardiovascular, hepatic, renal, and neurologic toxicity (Angel and Rogers, 1972). Workers and volunteers exposed at or below 5.2ppm have experienced no ill effects (IARC, 1989; Miller, 1942). Accordingly, a TLV-TWA of 5ppm is recommended for phenol." (References cited in ACGIH®, 2001).
>
> "As a vapor, liquid, or solid, phenol can penetrate intact skin and cause serious systemic effects including death. The absorption efficiency through skin is approximately equal to that by inhalation. Accordingly, a Skin notation is assigned. Animal bioassays to determine the carcinogenic potential for phenol were negative or the data were considered inadequate; therefore, an A4, Not Classifiable as a Human Carcinogen, notation is assigned. Sufficient data were not available to recommend SEN notation or a **TLV-STEL**." (ACGIH®, 2001).

The ACGIH® also noted that BEIs have been recommended for phenol (ACGIH®, 2001).

## 5.4 DFG

The Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) review of phenol noted that the former **MAK** value of 5ppm had been withdrawn. No Peak limitation, Skin or Sensitisation notations are given for phenol. Phenol is given the following notations: **Carcinogenicity Category**, 3B; **Germ cell mutation Category**, 3B; and, no Pregnancy Risk classification (DFG, 2005, 2018).

# 6.0
# Analytical methods for the assessment of airborne phenol

# A common method to measure phenol exposure is using NIOSH Method 2546 Issue 1 (NIOSH, Manual, 1994).

Using this method an air sample of 1 to 24 litres is collected onto a XAD-7 tube, using a flow rate of 0.01 to 0.1 litres per minute. Following desorption of the analyte using methanol, the sample is analysed using gas chromatography/flame ionisation detection.

This method can achieve a limit of quantitation of 1-3µg per sample. With an air volume of 0.05L/min, sample time of 8 hours and detection limit of 3µg the method could measure to 0.13mg/$m^3$.

# 7.0
# Discussion

# WorkSafe's WES for phenol has been unchanged since adoption in 1994.

The toxicological database reviewed above indicates phenol is locally and systemically toxic to humans, causing skin, eye and respiratory tract irritation/corrosion, liver, kidney, cardiovascular, immunological and neurological effects; and locally and systemically toxic to laboratory species.

Based on the aforementioned documentation, informed by the conclusions of the SCOEL, ACGIH® and DFG reviews, and in particular the findings listed below, WorkSafe considers its current WES-TWA of 5ppm to be inadequate to manage health risks from possible workplace exposure:

- Phenol has the potential to induce skin, eye and respiratory tract irritation/corrosion in exposed workers and experimental animals (ECHA REACH, 2019c; NIOSH, 2011; ECB RAR, 2006).
- Phenol has the potential to induce liver, kidney, cardiovascular, immunological and neurological effects in exposed humans and/or experimental animals by inhalation and dermal exposure (ECHA REACH, 2019; ECB RAR, 2006; ACGIH®, 2001).
- The mutagenic potential of phenol *in vivo* appears to be route/dose specific with negative or equivocal results after oral administration due to the potential for first-pass detoxification in the liver (NICNAS, 2014; ECHA RAR, 2006).
- The mechanism(s) by which phenol induces toxicity has not been fully elucidated, but it has been suggested involves phenol denaturing and precipitating proteins; free radical oxidative damage of protein, DNA, and lipids; and, via the toxic metabolites hydroquinone, catechol, and benzoquinone (ATSDR, 2008; ECHA RAR, 2006).
- The SCOEL recommended an 8-hour TWA at 2ppm with a STEL of 4ppm, based on the 5ppm NOAEL from experimental animals with an uncertainty factor of 2 for the TWA to extrapolate to humans (SCOEL, 2003).
- The ACGIH® proposed a TLV-TWA for phenol at 5ppm, based on a NOAEL of 5.2ppm from exposed workers and volunteers (ACGIH®, 2001).
- The DFG withdrew their MAK Value of 5ppm for phenol due to the reported clastogenic and tumour-promoting effects, the close metabolic association with benzene and hydroquinone, and evidence of carcinogenic effects (DFG, 2005).
- The DFG recommended a BLW for phenol at 200mg total phenol/L of urine, noting that in 5% of workers exposed up to 5ppm [the MAK Value at that time] plasma creatinine levels and levels of free phenol in the urine [measured against urinary creatinine] indicated potential kidney damage. The DFG noted that these individuals may have 'slow' polymorphs of uridine diphosphate glucuronyl transferase (**UDPG**) isozymes, resulting in higher than normal susceptibility to phenol exposures (DFG, 2005).

- The proposed WES-TWA of 1ppm for phenol includes a safety factor for all non-carcinogenic endpoints, based on the above point that 5% of workers exposed up to 5ppm indicated potential kidney damage (DFG, 2005) and the 5ppm NOAEL from experimental animals (SCOEL, 2003).
- The proposed **WES-STEL** of 2ppm for phenol is set to be protective against peak concentrations triggering acute upper respiratory tract irritation. A WES-STEL is justified for phenol as acute skin, eye and respiratory tract irritation is a critical endpoint, and peak as well as cumulative exposures should be limited to adequately protect exposed workers (SCOEL, 2003).
- A *skin notation* is justified for phenol, based on the potential significant dermal exposure contribution, and reported systemic toxicity after dermal administration (ATSDR, 2008; SCOEL, 2003; ACGIH®, 2001).
- Available information indicates that there is insufficient evidence about dermal and respiratory sensitisation in humans exposed to phenol, so a ***sen*** *notation* is not warranted (SCOEL, 2003; ACGIH®, 2001).

# 8.0
# Recommendations

# WorkSafe considers its current WES-TWA of 5ppm for phenol to be inadequate to protect workers exposed in the workplace, based on today's scientific understanding.

It is proposed that WorkSafe:

1. adopt a WES-TWA for phenol of 1ppm
2. adopt a WES-STEL for phenol of 2ppm, and
3. maintain the *skin notation* for phenol.

Noting that the recommended WES-TWA of 1ppm and WES-STEL of 2ppm for phenol may not eliminate all risk, due to the potentially significant contribution from dermal absorption; the lack of a threshold for sensory irritation; and, the uncertainties from the impact of genotoxicity, so exposures should be minimised, particularly for individuals with 'slow' UDPG and/or phosphoadenosinephosphosulfate (**PAPS**) sulfotransferase phenotypes.

# Appendices

## IN THIS SECTION:

## Appendix 1: Glossary

| TERM | MEANING |
|---|---|
| ACGIH® | The American Conference of Governmental Industrial Hygienists (ACGIH®) is a member-based organisation, established in 1938, that advances occupational and environmental health. Examples of this include their annual edition of the TLVs® and BEIs® book and work practice guides. Store at: www.acgih.org/store |
| ADME | Absorption, Distribution, Metabolism and Excretion. |
| AGS | Ausschuss für Gefahrstoffe [Committee for Hazardous Substances] is a consultative body of the German Federal Ministry of Labour and Social Affairs on issues of the Ordinance on Hazardous Substances. Administered by the BAuA. |
| ALT/ALAT | Alanine Aminotransferase. |
| AST/ASAT | Aspartate Aminotransferase. |
| ATSDR | Agency for Toxic Substances and Disease Registry is a federal public health agency of the US Department of Health and Human Services. |
| BEI | Biological Exposure Index. |
| BLW | "Biological guidance value" is the amount of a chemical substance or its metabolites or the deviation from the norm of biological parameters induced by the substance in exposed humans which serves as an indicator for necessary protective measures. BLWs are assigned only for hazardous materials for which the available toxicological or occupational-medical data are insufficient for the establishment of BAT values (that is, for carcinogenic substances and suspected carcinogens in the categories 1 to 3 and for non-carcinogens for which the toxicological data are inadequate). A DFG term. |
| Carc. 2 [pre-2008, Cat. 3] | Carcinogen Category 2: Suspected human carcinogen. EU term. |
| Carcinogen category 3A | DFG MAK designation: Substances that cause cancer in humans or animals or that are considered to be carcinogenic for humans for which the criteria for classification in Category 4 or 5 are in principle fulfilled. However, the database for these substances is insufficient for the establishment of a MAK or BAT value. |
| Ceiling or Ceiling Limit Value | Ceiling Limit Value – absolute exposure limit that should not be exceeded at any time. |
| CNS | Central nervous system. |
| DFG | Deutsche Forschungsgemeinschaft (German Research Foundation), the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Federal Republic of Germany. The science-based MAK values are recommended to the German Minister of Labour and Social Affairs for possible adoption under the German Hazardous Substances Ordinance. |
| DNA | Deoxyribonucleic acid. |
| ECB | European Chemicals Bureau (an agency of the European Union and predecessor of the ECHA). |
| ECHA | The European Chemicals Agency (an agency of the European Union). |
| EPA | The New Zealand Environmental Protection Authority. |
| EU | European Union. |
| Germ cell mutagen category 3B | DFG MAK designation: Substances which are suspected of being germ cell mutagens because of their genotoxic effects in mammalian somatic cells *in vivo*; in exceptional cases, substances for which there are no *in vivo* data but which are clearly mutagenic *in vitro* and structurally related to known *in vivo* mutagens. |
| HSNO | Hazardous Substances and New Organisms Act 1996, New Zealand. |
| IARC | International Agency for Research on Cancer, World Health Organization. |
| IFA | Institut für Arbeitsschutz der Deutschen Gestzlichen Unfallversicherung [Institute for Occupational Safety and Health of the German Social Accident Insurance]. |
| IOELV | Indicative Occupational Exposure Limit Value (health-based, SCOEL parameter). |
| IUCLID | International Uniform Chemical Information Database [ECHA]. |

| TERM | MEANING |
|---|---|
| JSOH | Japan Society for Occupational Health. |
| $LC_{50}$ | Lethal Concentration 50%: Concentration resulting in 50% mortality. |
| $LD_{50}$ | Lethal Dose 50%: Dose resulting in 50% mortality. |
| LOEL | Lowest Observed Effect Level. |
| MA | Metabolic activation. |
| MAK | Maximale Arbeitsplatz-Konzentration, (maximum workplace concentration) is defined as the maximum concentration of a chemical substance (as gas, vapour or particulate matter) in the workplace air which generally does not have known adverse effects on the health of the employee nor cause unreasonable annoyance (for example, by a nauseous odour) even when the person is repeatedly exposed during long periods, usually for 8 hours daily but assuming on average a 40-hour working week. A value set by the DFG. |
| MESA | Mouse-ear swelling assay. |
| mg | Milligram or one thousandth of a gram. |
| $mg/cm^2/kg$ | Milligrams of substance per square centimetre per kilogram body weight [dose by area of skin exposed per body weight]. |
| mg/kg | Milligrams per kilogram. |
| mg/kg b.w.<br>mg/kg bw | Milligram of substance per kilogram body weight. |
| mg/kg b.w./ day<br>mg/kg bw/d | Milligram of substance per kilogram body weight per day. |
| mg/L | Milligram of substance per litre. |
| $mg/m^3$ | Milligrams of substance per cubic metre of air. |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme is the Australian government's regulatory body for industrial chemicals. |
| NIOSH | The National Institute for Occupational Safety and Health is the United States federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and illness. |
| NLM | National Library of Medicine, administered by the US National Institutes of Health. |
| NOAEL | No Observed Adverse Effect Level. |
| NTP | National Toxicology Program, US Department of Health and Human Services. |
| OECD | Organisation for Economic Co-operation and Development. |
| OEL | Occupational Exposure Limit (equivalent to a WES). |
| OSHA | Occupational Safety and Health Administration, US Department of Labor. |
| PAPS | Phosphoadenosinephosphosulfate. |
| ppm | Parts of vapour or gas per million parts of air. |
| RAR | Risk Assessment Report. |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals. An EU program and regulation. |
| RoC/ROC | Report on Carcinogens. |
| SCOEL | The Scientific Committee on Occupational Exposure Limits is a committee of the European Commission, established in 1995 to advise on occupational health limits for chemicals in the workplace within the framework of Directive 98/24/EC, the chemical agents directive, and Directive 90/394/EEC, the carcinogens at work directive. |

| TERM | MEANING |
|---|---|
| **sen** | A substance that can 'sensitise' the respiratory system, inducing a state of hypersensitivity to it, so that on subsequent exposures, an allergic reaction can occur (which would not develop in non-sensitised individuals). It is uncommon to become sensitised to a compound after just a single reaction to it. A WorkSafe term. |
| **SEN** | A notation indicating the substance is a sensitiser. DSEN and RSEN are used in place of SEN when specific evidence of sensitisation by the dermal or respiratory route, respectively, is confirmed by human or animal data. An ACGIH® term. |
| **skin** | Skin absorption – applicable to a substance that is capable of being significantly absorbed into the body through contact with the skin. A WorkSafe term. |
| **Skin** | A notation indicating the potential for significant contribution to the overall exposure, by the cutaneous route, including mucous membranes and the eyes, by contact with vapours, liquids and solids. An ACGIH® term. |
| **SLRL** | Sex-linked recessive lethal. |
| **SMR** | Standardised Mortality Ratio (SMR) is a measure of the strength or association between exposure and mortality; a form of Relative Risk (RR) in which the outcome is death.<br>The SMR is the ratio of the number of deaths (due to a given disease arising from exposure to a specific risk factor) that occurs within the study population to the number of deaths that would be expected if the study population had the same rate of mortality as the general population (the standard).<br>By convention, the figure is usually multiplied by 100 [an SMR of 200 corresponds to a RR of 2.0]. A *value greater than 100/1.0 indicates a positive association between exposure and disease*. (This may be causal, or have other explanations, such as bias, chance or confounding). (WHEC, 2017). |
| **STEL** | Short-Term Exposure Limit. The STEL is a limit value above which exposure should not occur and usually relates to a 15-minute reference period. |
| **TLV®** | Threshold Limit Value (see TLV-STEL and TLV-TWA below). An ACGIH® term. Please see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs® |
| **TLV-STEL** | TLV-Short-Term Exposure Limit; a 15 minute TWA exposure that should not be exceeded at any time during a work day, even if the 8-hour TWA is within the TLV-TWA. An ACGIH® term. |
| **TLV-TWA** | TLV – Time-Weighted Average; the TWA concentration for a conventional 8-hour workday and a 40-hour workweek, to which it is believed that nearly all workers may be repeatedly exposed to, day after day, for a working lifetime without adverse effect. An ACGIH® term. |
| **UDPG** | Uridine diphosphate glucuronyl transferase. |
| **WES** | Workplace Exposure Standard – WESs are values that refer to the airborne concentration of substances, at which it is believed that nearly all workers can be repeatedly exposed to, day after day, without coming to harm. The values are normally calculated on work schedules of five shifts of eight hours duration over a 40 hour week. A WorkSafe term. |
| **WES-STEL** | The 15-minute time-weighted average exposure standard. Applies to any 15-minute period in the working day and is designed to protect the worker against adverse effects of irritation, chronic or irreversible tissue change, or narcosis that may increase the likelihood of accidents. The WES-STEL is not an alternative to the WES-TWA; both the short-term and time-weighted average exposures apply. Exposures at concentrations between the WES-TWA and the WES-STEL should be less than 15 minutes, should occur no more than four times per day, and there should be at least 60 minutes between successive exposures in this range. A WorkSafe term. |
| **WES-TWA** | The average airborne concentration of a substance calculated over an eight-hour working day. A WorkSafe term. |

## Appendix 2: HSNO health-related hazardous substance classifications

This is the full list of all health-related hazardous substances classifications that are listed by the NZ EPA, including those that apply to this substance.

| CLASSIFICATION CODE | MEANING |
|---|---|
| **Acutely toxic** | |
| 6.1A | Substances that are acutely toxic – Fatal |
| 6.1B | Substances that are acutely toxic – Fatal |
| 6.1C | Substances that are acutely toxic – Toxic |
| 6.1D | Substances that are acutely toxic – Harmful |
| 6.1E | Substances that are acutely toxic – May be harmful, aspiration hazard |
| **Skin irritant** | |
| 6.3A | Substances that are irritating to the skin |
| 6.3B | Substances that are mildly irritating to the skin |
| **Eye irritant** | |
| 6.4A | Substances that are irritating to the eye |
| **Sensitisation** | |
| 6.5A | Substances that are respiratory sensitisers |
| 6.5B | Substances that are contact sensitisers |
| **Mutagens** | |
| 6.6A | Substances that are known or presumed human mutagens |
| 6.6B | Substances that are suspected human mutagens |
| **Carcinogens** | |
| 6.7A | Substances that are known or presumed human carcinogens |
| 6.7B | Substances that are suspected human carcinogens |
| **Reproductive/developmental toxicants** | |
| 6.8A | Substances that are known or presumed human reproductive or developmental toxicants |
| 6.8B | Substances that are suspected human reproductive or developmental toxicants |
| 6.8C | Substances that produce toxic human reproductive or developmental effects on or via lactation |
| **Target organ toxicants** | |
| 6.9A | Substances that are toxic to human target organs or systems |
| 6.9B | Substances that are harmful to human target organs or systems |
| **Skin corrosive** | |
| 8.2A | Substances that are corrosive to dermal tissue (UN PGI) |
| 8.2B | Substances that are corrosive to dermal tissue (UN PGII) |
| 8.2C | Substances that are corrosive to dermal tissue (UN PGIII) |
| **Eye corrosive** | |
| 8.3A | Substances that are corrosive to ocular tissue |

Source: www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

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Published: March 202

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WSNZ_3718_MAR 2020

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