

# Workplace Exposure Standard (WES) review

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*ZINC OXIDE*  
(CAS NO: 1314-13-2)

March 2020

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# 1.0

## Introduction

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

It considers the potential for exposures to zinc oxide in New Zealand, the health effects and risks, and exposure standards from other jurisdictions around the world.

The review includes a recommendation to change the WorkSafe WES for zinc oxide, which is currently set at:

- **WES-TWA** of **3mg/m<sup>3</sup>** (respirable) and **WES-STEL** of 10mg/m<sup>3</sup> (size fraction not specified) for fume, and
- WES-TWA of 10mg/m<sup>3</sup> (respirable dust) as dust, 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: Zincite; Zinc white; ZnO.

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# 2.0

## Chemical and physical properties

Zinc oxide is an odourless, non-flammable, and white to yellow-white powder at room temperature (ACGIH<sup>®</sup>, 2003).

Chemical and physical properties of zinc oxide include:

<b>Molecular weight</b>	81.37g/mol
<b>Formula</b>	ZnO
<b>Specific gravity</b>	5.61
<b>Melting point</b>	1,975°C
<b>Solubility</b>	Water: practically insoluble; soluble in dilute acetic or mineral acids; insoluble in alcohol

ACGIH<sup>®</sup>, 2003

Zinc oxide does not have any health-related classifications allocated under HSNO (EPA, 2019).

**TABLE 1:**  
Physicochemical  
properties of zinc oxide

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# 3.0 Uses

Zinc oxide is used in pigments, rubber, cosmetics, ointments, and electronic devices (ACGIH<sup>®</sup>, 2003).

Zinc oxide nanoparticles are produced for a variety of end uses including paint and lacquers, cement, concrete and glass. (DECOS, 2012).

Zinc oxide can be formed when elemental zinc is heated in air to temperatures close to its boiling point (907°C) and volatilises, immediately oxidising to the white fume of the oxide (ACGIH<sup>®</sup>, 2003).

Occupational exposure to zinc oxide can occur during production, storage, transportation and end-use, and to zinc oxide fume when zinc or zinc-containing alloys are subjected to elevated temperatures (ACGIH<sup>®</sup>, 2003).

Workers can be exposed to zinc oxide via inhalation and eye or dermal contact.

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

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# 4.0

## Health effects

### **IN THIS SECTION:**

- 4.1 Non-cancer
- 4.2 Cancer
- 4.3 Absorption, distribution,  
metabolism and excretion

## 4.1 Non-cancer

### Humans

The Deutsche Forschungsgemeinschaft [DFG] review of zinc and its inorganic compounds noted that zinc oxide fumes are able to produce a form of acute intoxication called metal fume fever after inhalation. The symptoms begin four to twelve hours after exposure with a sweetish metallic taste and a sensation of irritation in the throat. These are followed by non-specific, influenza-like symptoms such as a general feeling of illness, coughing and weakness. Some patients show none of these initial symptoms and suddenly develop chills and fever, a sensation of tightness in the chest and for the most part minor respiratory symptoms (dyspnoea). As the disease develops, other organ systems may become involved. For example, in addition to a steadily increasing temperature, frontal headache, disturbed vision, pains in the stomach, muscles and joints, nausea, vomiting or dysuria may also occur (Gordon and Fine 1993 as cited in DFG, 2014). Metal fume fever can result in severe impairment of the respiratory system to the point of pulmonary oedema and respiratory insufficiency. Metal fume fever does not occur after oral, parenteral or dermal administration of zinc oxide. (DFG, 2014).

“As exposure to zinc oxide fumes produced no clear increase in zinc levels in the blood, in most investigations, it is unlikely that inhaled zinc is absorbed to such an extent that it can cause systemic effects (Fine *et al.* 1997).

“One explanation for the pathogenesis of metal fume fever after inhaling zinc could be the stimulation of oxygen radical formation in human neutrophilic granulocytes (Lindahl *et al.* 1998).

“In several case reports immunological causes for metal fume fever are postulated (Ameille *et al.* 1992; Castet and Bouillard 1992; Farell 1987).

“The results of animal studies and empirical results with humans suggest that the systemic effects of zinc oxide fumes are indirectly responsible for considerable inflammatory changes in the lungs, accompanied by the release of mediators and cytokines (Blanc *et al.* 1991, 1993; Fine *et al.* 1997). Opinions vary as to which mediator plays the most important role in the pathogenesis of metal fume fever. (Blanc *et al.* 1993; Kuschner *et al.* 1997) or IL 6 (interleukin 6) (Fine *et al.* 1997).

“The development of tolerance or an adaptation in those affected by metal fume fever after repeated exposure has been known for a long time. The tolerance is reversible after a number of exposure-free days; the symptoms of metal fume fever reoccur when exposure is resumed (Nemery 1990). This adaptive reaction of lung tissue following exposure to zinc oxide is attributed to an induction of metallothionein synthesis (Cosma *et al.* 1992; Beckett *et al.* 1996).” (References as cited in DFG, 2014).

“After experimental exposure to welding fumes (cumulative exposure to 5.1g zinc oxide × min/m<sup>3</sup>, corresponding to 140–270mg/m<sup>3</sup> zinc for 15–30 minutes) or pure zinc oxide fumes in concentrations of 2.5 to 41mg/m<sup>3</sup> (0–33mg/m<sup>3</sup> zinc), changes in inflammation markers and mediators were found in the bronchoalveolar lavage (BAL) liquid or in the blood plasma. No **NOAEC** was obtained (Blanc *et al.* 1991, 1993; Fine *et al.* 1997; Kuschner *et al.* 1995, 1997).

“At a concentration of 0.5mg/m<sup>3</sup> (0.4mg/m<sup>3</sup> zinc) each, ultrafine (median particle diameter 0.04µm) and fine zinc oxide particles (median particle diameter 0.29µm) produced no noticeable effects in twelve healthy adult volunteers at rest after inhalation through a mouthpiece for two hours. The effects comprised twelve known metal fume fever symptoms (no further details) and included body temperature, haematological parameters, inflammation markers, surface markers on blood cells, electrocardiogram and cells in the sputum. Eighty % of the ultrafine and 35% of the fine particles (number of particles, not mass) were deposited (Beckett *et al.* 2005).” (References as cited in DFG, 2014).

The recent study by Monsé *et al.* (2018) of responses to inhaled non-sized zinc oxide in human volunteers under laboratory conditions concluded:

“...this study was able to demonstrate a concentration-response relationship of ZnO nanoparticles with clear systemic effects at and above 1mg/m<sup>3</sup> ZnO. The results are in accordance with previous experimental studies that showed no effects at 0.5mg/m<sup>3</sup> ZnO [Beckett *et al.*, 2005] and clear effects concerning **CRP** with concentrations between 1.1 and 1.5mg/m<sup>3</sup> ZnO-containing welding fumes [Brand *et al.*, 2014]. Similarly an increase of **SAA** was observed after inhalation of zinc or copper containing welding fumes [Baumann *et al.*, 2017], but the different exposure scenarios within these studies have to be considered. A No Effect Exposure Level (**NOEL**) derived from our study would be defined between 0.5 and 1mg/m<sup>3</sup>, although, in contrast to a previous study with 2h exposures at rest [Beckett *et al.*, 2005], initial effects were seen with ZnO exposures of 0.5mg/m<sup>3</sup> concerning CRP and SAA, which were the most sensitive parameters.” (References as cited in Monsé *et al.*, 2018).

The DFG review of zinc and its inorganic compounds noted that zinc oxide was not a dermal sensitiser:

“In a patch test comprising 100 selected leg-ulcer patients, 11 of 100 patients showed an allergic reaction to zinc ointment (60% zinc oxide and 40% sesame oil). However, 14 of 81 patients also showed a positive reaction to treatment with sesame oil alone. Therefore, a sensitizing potential of zinc oxide cannot be concluded (EU 2004 b). Two further studies investigated the effect of zinc oxide on the patch test reaction of patients with a contact allergy to colophony. A patch test performed as control with 10% zinc oxide (2.3mg/cm<sup>2</sup>) showed no positive reaction in a total of 21 tested persons (EU 2004 b; Gäfvert and Färm 1995).” (References as cited in DFG, 2014).

## Animals

The DFG review of zinc and its inorganic compounds noted that:

“In animal studies, no potential for prenatal developmental toxicity was found after ingestion of zinc sulfate up to the highest zinc doses administered of 200mg/kg body weight and day in rats, and 6.8mg/kg body weight and day in mice. The substance is therefore classified in **Pregnancy Risk Group C.**” (DFG, 2014).

## 4.2 Cancer

The International Agency for Research on Cancer [IARC] does not appear to have conducted an evaluation of zinc oxide (IARC, 2019).

The US National Toxicology Program [NTP] does not appear to have conducted an evaluation of zinc oxide (NTP, 2019).

The DFG review of zinc and its inorganic compounds noted that: “no valid long-term studies of the carcinogenicity of zinc and its inorganic compounds have been performed.” (DFG, 2014).

The New Zealand EPA have not classified zinc oxide as a 6.7A or 6.7B substance – substances that are known or presumed, or suspected human carcinogens, respectively.

## 4.3 Absorption, distribution, metabolism and excretion

The DFG review of zinc and its inorganic compounds noted that:

“No quantitative data exist on the systemic availability of zinc after inhalation either in humans or in animals.

“After exposure to zinc oxide fumes, no increase in zinc levels in serum or urine were measured compared with control groups or normal values (Blanc *et al.* 1991; Knecht *et al.* 1983). In most case reports involving patients with zinc fume fever, no increased zinc concentrations in the serum were found (Noel and Ruthmann 1988). In one case study concerning a worker with metal fume fever symptoms, unusually high zinc concentrations in the urine were measured (Fuortes and Schenck 2000).

“The deposit of particles was determined during the exposure of volunteers at rest for two hours to ultrafine (median diameter 0.04µm) or fine zinc oxide particles (median of the particle diameter 0.29µm) at a concentration of 0.5mg/m<sup>3</sup> (zinc: 0.4mg/m<sup>3</sup>). For this purpose, the number of particles in the inhaled and exhaled air was measured continuously during exposure. The deposition fraction was constant throughout the entire exposure. Eighty percent of the ultrafine and 35% of the fine particles (number of particles, not mass) were deposited (Beckett *et al.* 2005).

“After inhalation exposure of rats to a zinc oxide aerosol at 4.3, of rabbits to 6.0 and of guinea pigs to 11.3mg/m<sup>3</sup> (ultrafine particles: median diameter 0.06µm, mass median diameter 0.17µm) for three hours (rats and guinea pigs) or six hours (rabbits), the proportions of the inhaled dose retained in the lung were 11.5%, 4.7% and 19.8% (Gordon *et al.* 1992).

“In rats, after 24-hour inhalation of zinc oxide fumes (zinc equivalent about 7.5mg/m<sup>3</sup>; mass median aerodynamic diameter 0.71-0.94µm), significant increases in zinc concentrations were only found in the lungs and plasma (but not in the liver, kidneys, spleen or muscles) and only up to four hours after the end of exposure, but not after 24 or 48 hours (Hollinger *et al.* 1979).” (References as cited in DFG, 2014).

“There are no indications for an increased systemic availability of zinc from *in vitro* investigations with zinc oxide after application on the intact skin of humans (EU 2004 b).” (References as cited in DFG, 2014).

“In one study, the half-life of zinc oxide in the lungs of rats after instillation was calculated to be 14 hours (EU 2004 b).

“A half-life of 6.3 hours for the zinc content in the lung was found in a study on the clearance rate of male Wistar rats 0, 2, 4, 8 and 24 hours after exposure to zinc oxide aerosol (mean aerodynamic diameter of  $1\mu\text{m}$ ) at a concentration of  $12.8\text{mg}/\text{m}^3$  for 17 hours (EU 2004 b).

“After 24-hour inhalation of zinc oxide fumes (about  $7.5\text{mg}/\text{m}^3$  zinc; mass median aerodynamic diameter  $0.71\text{--}0.94\mu\text{m}$ ) the half-life calculated for lung clearance in rats was 4.8 hours (Hollinger *et al.* 1979).” (References as cited in DFG, 2014).

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# 5.0

## Exposure standards

### **IN THIS SECTION:**

- 5.1 Other exposure standards
- 5.2 DFG
- 5.3 ACGIH®

## 5.1 Other exposure standards

Table 2 below shows the zinc oxide 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
	mg/m <sup>3</sup>	mg/m <sup>3</sup>
Australia	10 <sup>1,2</sup> 5 <sup>3</sup>	10 <sup>3</sup>
Austria	5 <sup>3,4</sup>	
Belgium	10 <sup>1</sup> 2 <sup>5,6,10</sup> 5 <sup>3</sup>	10 <sup>5,6,10</sup> 10 <sup>3</sup>
Canada – Ontario	2 <sup>1,4</sup>	10 <sup>1,4</sup>
Canada – Québec	10 <sup>1</sup> 5 <sup>3</sup>	
Denmark	4 <sup>3</sup>	8 <sup>3</sup>
Finland	2 <sup>5</sup>	10 <sup>5,6</sup>
France	10 <sup>1</sup> 5 <sup>3</sup>	
Hungary	5 <sup>3</sup>	20 <sup>3</sup>
Ireland	2 <sup>3</sup>	10 <sup>3,7</sup>
Israel	2 <sup>3</sup>	
Japan – JSOH	1 <sup>1,8</sup> 4 <sup>1,9</sup>	
Latvia	0.5 <sup>5</sup>	
New Zealand	10 <sup>1,10</sup> 3 <sup>3</sup>	10 <sup>3</sup>
People's Republic of China	3 <sup>1</sup>	5 <sup>1,6</sup>
Poland	5 <sup>3</sup>	10 <sup>3</sup>
Romania	5 <sup>3</sup>	10 <sup>3,6</sup>
Singapore	10 <sup>1</sup> 5 <sup>3</sup>	
South Korea	2 <sup>3,8</sup>	

<sup>1</sup> Dust.

<sup>2</sup> Inhalable dust containing no asbestos and <1% crystalline silica.

<sup>3</sup> Fume or respirable dust.

<sup>4</sup> Respirable aerosol.

<sup>5</sup> Zinc oxide<sup>11</sup>.

<sup>6</sup> 15 minutes average value.

<sup>7</sup> 15 minutes reference period.

<sup>8</sup> Respirable dust.

<sup>9</sup> Total dust: particles with a flow speed of 50 to 80cm/sec at the entry of a particle sampler.

<sup>10</sup> Respirable fraction.

<sup>11</sup> Total dust.

<sup>12</sup> Ceiling limit value (15 min).

JURISDICTION OR ADVISORY BODY	8-HOUR LIMIT VALUE	SHORT-TERM LIMIT VALUE
Spain	10 <sup>1</sup> 2 <sup>3</sup>	10 <sup>3</sup>
Sweden	5 <sup>1</sup>	
Switzerland	3 <sup>1,10</sup> 3 <sup>3,4</sup>	3 <sup>1,6,10</sup> 3 <sup>3,4</sup>
USA - NIOSH	5 <sup>1,11</sup> 5 <sup>3</sup>	15 <sup>1,11,12</sup> 10 <sup>3,6</sup>
USA - OSHA	15 <sup>1</sup> 5 <sup>3</sup>	
UK	5 <sup>3</sup>	10 <sup>3</sup>

**TABLE 2:**  
Exposure standards  
for zinc oxide from  
around the world

It is noted that the only organisations from whom we get information as to how and why they set occupational exposures standards on zinc oxide were DFG and ACGIH®.

## 5.2 DFG

The Deutsche Forschungsgemeinschaft (German Research Foundation) review of zinc and its inorganic compounds, including zinc oxide in their conclusion noted that:

“After oral exposure, the critical toxicity of zinc compounds lies in their influence on copper metabolism. After inhalation, on the other hand, the irritant effects in nose and throat or pulmonary toxicity predominate.

“Due to the different effects depending on particle size, separate MAK values are derived for respirable and inhalable fractions. Both of these values must be observed.

“The critical effects for fine and ultrafine zinc oxide particles are the occurrence of zinc fever and an increase in inflammation markers. Zinc oxide concentrations of 0.5mg/m<sup>3</sup> (zinc: 0.4mg/m<sup>3</sup>) caused neither preclinical zinc fever effects nor an increase in inflammation markers in test persons after 2-hour exposure (Beckett *et al.* 2005). As no **LOAEC** is available from this study, a higher **NOAEC** could possibly have been determined with a corresponding study design. From this **NOAEC**, a MAK value for zinc of 0.1mg/m<sup>3</sup> for the respirable fraction of zinc compounds is obtained by linear extrapolation applied as a simplifying assumption for an exposure lasting eight hours.

“A study with exposed workers is used for the derivation of a MAK value for the inhalable fraction. Neither lung function disorders nor asthmatic symptoms were found in 234 zinc ore smelting workers with an average 5.5 years of zinc oxide exposure (total dust 2.5 to 4.5mg/m<sup>3</sup>, zinc content 90%) (Roto 1980). From this, a MAK value for the inhalable fraction of the aerosols of zinc compounds equivalent to 2mg/m<sup>3</sup> zinc can be derived.

“When both MAK values are observed, impairment of copper metabolism, which may occur after ingestion of zinc, is not to be expected. A **NOAEL** of 30mg zinc per day for a decrease in **ESOD** activity was derived for test persons after oral doses. At the proposed MAK values, this level is not reached even assuming that most of the inhaled substance is ingested and absorbed by swallowing.

**Peak limitation**

“The respirable fraction is assigned to **Peak Limitation Category I**, with an excursion factor of 4, as no local irritant effects in test persons were reported in the study described above, also after exposure to zinc at 0.4mg/m<sup>3</sup> for two hours.

“The inhalable fraction is also assigned to Peak Limitation Category I. An excursion factor of 2 is established for this fraction. Due to the more severe irritant effects of zinc chloride, an excursion factor of 1 is established for this substance.

**Absorption through the skin**

“From the highest reported flux of 0.6µg/cm<sup>2</sup> and hour in *in vitro* studies with human skin, an absorption of 1.2mg zinc is to be expected after skin contact on both hands and lower arms (contact surface 2000cm<sup>2</sup>) for one hour. This value is approximately 4% of the NOAEL of 30mg zinc per day. Thus, designation with an “H” is not required for zinc and its inorganic compounds.

**Sensitization**

“In spite of a wide range of possible exposures to inorganic zinc compounds, for example in cosmetic and pharmaceutical preparations, contact sensitization through zinc and its salts has been reported only in a very few individual cases. Animal studies with zinc oxide and zinc sulfate revealed negative results. No data are available on respiratory sensitization. Zinc and inorganic zinc compounds are thus not designated with either “Sh” or “Sa”.

**Carcinogenicity**

“No valid long-term studies of the carcinogenicity of zinc and its inorganic compounds have been performed. *In vitro* investigations of genotoxicity show clastogenic effects at high, partly cytotoxic concentration ranges. Apart from negative results from *in vitro* micronucleus and chromosome aberration tests mainly after oral administration or intraperitoneal injection, a positive finding of chromosome aberrations after short-term and medium-term intraperitoneal injection is available. The Commission does not consider this study to be relevant for the evaluation as these effects were accompanied by (insufficiently documented) toxicity; comparable concentrations under workplace conditions will not be attained; and additionally, the intraperitoneal injection bypasses the regulation of zinc homeostasis after oral and inhalation exposure.

“For these reasons, zinc and its inorganic compounds are not classified in one of the categories for carcinogens.

**Germ cell mutagenicity**

“No mutagenic effects on germ cells can be implied from the available data on genotoxicity. Zinc is therefore not classified in one of the categories for germ cell mutagens.

**Prenatal toxicity**

“If the MAK value is observed, zinc fume fever is not to be expected, nor is there a risk of embryotoxic effects for the offspring of exposed pregnant women. In animal studies, no potential for prenatal developmental toxicity was found after ingestion of zinc sulfate up to the highest zinc doses administered of 200mg/kg body weight and day in rats, and 6.8mg/kg body weight and day in mice. The substance is therefore classified in Pregnancy Risk Group C.

“This evaluation applies to zinc and its inorganic compounds as well as to all organic zinc compounds, insofar as their toxicity is based on the release of zinc ions.” (DFG, 2014).

### 5.3 ACGIH®

The ACGIH® review of zinc oxide concluded that:

“Zinc oxide fume exposures can cause a syndrome of metal fume fever with symptoms that include chills, muscular pain, nausea, and vomiting. Recovery is usually complete in 24 to 48 hours. In early work, Drinker and associates (Drinker *et al.*, 1927b) concluded that metal fume fever would not result from occupational exposures to concentrations of zinc oxide fume below 15mg/m<sup>3</sup>.

“Moreover, work from Fine and co-workers (Fine *et al.*, 1997) has demonstrated that metal fume fever can occur after a 2-hour exposure at 2.5mg/m<sup>3</sup> for freshly formed zinc oxide. These investigators also reported that although symptoms abate in all subjects after 3 daily exposures at 5mg/m<sup>3</sup>, pulmonary inflammation and cytokine production remained elevated in some human volunteers (Fine *et al.*, 2000). Studies in rats and mice have similarly demonstrated that exposure at 1 or 2.5mg/m<sup>3</sup> zinc oxide for 3 hours can produce biochemical, cellular, and molecular changes in the mammalian lung. In particular, studies in mice have demonstrated that the pulmonary response to zinc oxide fumes is strain dependent, suggesting a genetic component in the interindividual variability in response (Wesselkamper *et al.*, 2001).

“Accordingly, a **TLV-TWA** of 2mg/m<sup>3</sup> is recommended for zinc oxide. If concentrations are kept below this level, it is believed that the incidence of metal fume fever will be low and the cases that may occur will be mild. Based upon the work by Kuschner and colleagues (Kuschner *et al.*, 1995), retaining the **TLV-STEL** at 10mg/m<sup>3</sup> is recommended. When zinc oxide fume particles are produced in welding operations, thermal cutting of galvanized steel, or brass foundry work, they are in the fine and ultrafine size fractions. Thus, the recommended TLVs for zinc oxide are for respirable particles. The larger zinc oxide particles (dust) used in manufacturing are considered by ACGIH to be particulate matter that has little adverse effect on the lung and does not produce significant disease when exposures are kept under reasonable control.” (ACGIH®, 2003).

The ACGIH® review of zinc oxide noted that data were inadequate or not available that provide the basis for recommending **Skin**, sensitizer (**SEN**), or carcinogenicity notations (ACGIH®, 2003).

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## 6.0

# Analytical methods for the assessment of airborne zinc oxide

A common method to measure zinc oxide exposure is using a modification of NIOSH Method 7303, Issue 1 (NIOSH, 2003).

Using this method, an air sample is collected onto a cellulose ester filter membrane using a sampling train set at a flow rate of 2 litres of air per minute. The sample is analysed by inductively coupled plasma – atomic emission spectroscopy (ICP-AES). The limit of quantitation of this modified method has been quoted as 2.05µg (or 0.00205mg) of zinc oxide per sample.

Collecting an air sample for 8 hours at a flow rate of 2L/min would allow a minimum concentration of less than 0.003mg of zinc oxide per cubic metre of air to be measured based on the quoted limit of quantitation.

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# 7.0 Discussion

## WorkSafe's WES for zinc oxide has been unchanged since adoption in 2016.

The toxicological database reviewed above indicates that inhaled zinc oxide is locally and systemically toxic to humans, causing zinc or metal fume fever, and increases in systemic inflammation parameters, such as C-reactive protein [CRP], interleukin-6 [IL-6] and serum amyloid A [SAA].

Based on the aforementioned documentation, informed by the conclusions of the DFG and ACGIH® reviews, and in particular the findings listed below, WorkSafe considers its current WES-TWA of 3mg/m<sup>3</sup> (respirable dust) as fume with a WES-STEL of 10mg/m<sup>3</sup> (size fraction unspecified) and a WES-TWA of 10mg/m<sup>3</sup> (respirable dust) as dust, to be inadequate to manage health risks from possible workplace exposure:

- Zinc oxide has been shown to have the potential to induce zinc or metal fume fever with symptoms beginning four to twelve hours after exposure.
- Exposure can result in: a sensation of irritation in the throat; non-specific, influenza-like symptoms such as a general feeling of illness (chills and fever, a sensation of tightness in the chest), coughing and weakness; and, as the disease develops, other organ systems may become involved.
- Metal fume fever which can result in severe impairment of the respiratory system to the point of pulmonary oedema and respiratory insufficiency.
- The most sensitive markers for zinc oxide inhalation exposure in workers are increased inflammation markers, such as C-reactive protein [CRP], interleukin-6 [IL-6] and serum amyloid A [SAA].
- The DFG review of zinc and its inorganic compounds noted that different adverse effects could be expected after inhalation exposure, depending on particle size, so that MAK values for both respirable and inhalable fractions should be observed.
- The DFG review of zinc and its inorganic compounds proposed a MAK value of 0.1mg zinc/m<sup>3</sup> for the respirable fraction [Peak Limitation Category 1; excursion factor, 4], based on a NOAEC of 0.4mg zinc/m<sup>3</sup> after 2 hours exposure by volunteers (Beckett *et al.*, 2005 as cited in DFG, 2014); and, a MAK value of 2mg zinc/m<sup>3</sup> for the inhalable fraction [Peak Limitation Category 1; excursion factor, 2], based on a NOAEC from a study in smelter workers (Roto, 1980 as cited in DFG, 2014).
- Monsé *et al.* (2018) reported a NOAEC of 0.5mg ZnO/m<sup>3</sup> [0.4mg zinc/m<sup>3</sup>] and a LOAEC of 1.0mg ZnO/m<sup>3</sup> [0.8mg zinc/m<sup>3</sup>], based on systemic inflammatory parameters, in volunteers after 4 hours exposure to zinc oxide nanoparticles.
- The DFG review of zinc and its inorganic compounds concluded that zinc oxide would not be expected to pose a risk of embryotoxic effects at the proposed MAK values [0.1mg zinc/m<sup>3</sup> for the respirable fraction [Peak Limitation Category 1; excursion factor, 4]; 2mg zinc/m<sup>3</sup> for the inhalable fraction [Peak Limitation Category 1; excursion factor, 2]].

- The proposed WES-TWA of 0.1mg/m<sup>3</sup> respirable fraction for zinc oxide is set to be protective against systemic inflammatory parameters, based on NOAEC from exposed individuals (Beckett *et al.*, 2005; Monsé *et al.*, 2018 as cited in DFG, 2014).
- The proposed WES-STEL of 0.5mg/m<sup>3</sup> respirable fraction for zinc oxide is set to be protective against peak concentrations triggering acute irritation responses.
- The proposed WES-TWA of 2mg/m<sup>3</sup> inhalable fraction for zinc oxide is set to be protective against compromised lung function or asthmatic symptoms, based on reports from exposed workers (Roto, 1980 as cited in DFG, 2014).
- The proposed WES-STEL of 5mg/m<sup>3</sup> inhalable fraction for zinc oxide is set to be protective against peak concentrations triggering acute asthmatic symptoms.
- A *skin notation* is not warranted for zinc oxide, based on the expected limited absorption after dermal exposure (DFG, 2014).
- An *r<sub>sen</sub>* or *d<sub>sen</sub>* notation is not warranted for zinc oxide, based on the lack of reports of contact or respiratory sensitisation potential.

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8.0

# Recommendations

WorkSafe considers its current WES-TWA of  $3\text{mg}/\text{m}^3$  (respirable dust) for zinc oxide as fume with a WES-STEEL of  $10\text{mg}/\text{m}^3$ , and a WES-TWA of  $10\text{mg}/\text{m}^3$  (respirable dust) for zinc oxide as dust, to be inadequate to protect workers exposed in the workplace, based on today's scientific understanding.

It is proposed that WorkSafe adopt a:

1. WES-TWA for zinc oxide of  $0.1\text{mg zinc oxide}/\text{m}^3$  (respirable fraction);
2. WES-STEEL for zinc oxide of  $0.5\text{mg zinc oxide}/\text{m}^3$  (respirable fraction);
3. WES-TWA for zinc oxide of  $2\text{mg zinc oxide}/\text{m}^3$  (inhalable fraction);
4. WES-STEEL for zinc oxide of  $5\text{mg zinc oxide}/\text{m}^3$  (inhalable fraction).

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# Appendices

## **IN THIS SECTION:**

**Appendix 1:** Glossary

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

**Appendix 3:** References

## 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: <a href="http://www.acgih.org/store">www.acgih.org/store</a>
cm <sup>2</sup>	Centimetre squared.
cm/sec	Centimetre per second.
CRP	C-reactive protein.
DECOS	Dutch Expert Committee on Occupational Standards. A committee of the <i>Health Council of the Netherlands</i> . The latter was established in 1902 as an independent scientific advisory body with a remit: 'to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research...' (Section 22, Health Act).
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.
dсен	A substance that can 'sensitise' the skin, 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.
EPA	The New Zealand Environmental Protection Authority.
ESOD	Erythrocyte superoxide dismutase.
"H"	DFG MAK designation: <i>danger of percutaneous absorption</i> . Equivalent to the 'skin' notation in the WorkSafe WES special guide.
HSNO	Hazardous Substances and New Organisms Act 1996, New Zealand.
IARC	The International Agency for Research on Cancer – an agency of the World Health Organisation
IFA	Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung [Institute for Occupational Safety and Health of the German Social Accident Insurance].
JSOH	Japan Society for Occupational Health.
L/min	Litres per minute.
LOAEC	Lowest Observed Adverse Effect Concentration.
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.
mg/cm <sup>2</sup>	Milligrams per square centimetre.
mg/kg	Milligrams per kilogram.
mg/m <sup>3</sup>	Milligrams of substance per cubic metre of air.
µm	Micrometre or one millionth of a metre.
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.
NOAEC	No Observed Adverse Effect Concentration.
NOEL	No Observed Effect Level.
NTP	National Toxicology Program, US Department of Health and Human Services.

TERM	MEANING
OSHA	Occupational Safety and Health Administration, US Department of Labor.
Peak Limitation Category I	Substances for which local irritant effects determine the MAK value, also respiratory allergens; Excursion factor = 1 [default]; Duration 15 minutes, average value; Number per shift = 4; Interval = 1 hour. DFG term.
Pregnancy Risk Group C	Damage to the embryo or foetus is unlikely when the MAK value or the BAT value is observed. A DFG term.
r <sub>sen</sub>	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.
"Sa"	Sensitising to airways. A DFG MAK notation.
SAA	Serum amyloid A.
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.
"Sh"	DFG MAK designation: <i>danger of sensitisation of the skin</i> .
skin	Skin absorption – applicable to a substance that is capable of being significantly absorbed into the body through contact with the skin. A term New Zealand also uses.
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.
TLV®	Threshold Limit Value (see TLV-STEL and TLV-TWA below). An ACGIH® term. Please see the <a href="#">Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®</a>
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.
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 New Zealand 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.
WES-TWA	The average airborne concentration of a substance calculated over an eight-hour working day. A New Zealand 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
<b>Acutely toxic</b>	
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
<b>Skin irritant</b>	
6.3A	Substances that are irritating to the skin
6.3B	Substances that are mildly irritating to the skin
<b>Eye irritant</b>	
6.4A	Substances that are irritating to the eye
<b>Sensitisation</b>	
6.5A	Substances that are respiratory sensitisers
6.5B	Substances that are contact sensitisers
<b>Mutagens</b>	
6.6A	Substances that are known or presumed human mutagens
6.6B	Substances that are suspected human mutagens
<b>Carcinogens</b>	
6.7A	Substances that are known or presumed human carcinogens
6.7B	Substances that are suspected human carcinogens
<b>Reproductive/developmental toxicants</b>	
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
<b>Target organ toxicants</b>	
6.9A	Substances that are toxic to human target organs or systems
6.9B	Substances that are harmful to human target organs or systems
<b>Skin corrosive</b>	
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)
<b>Eye corrosive</b>	
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](http://www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes)

### Appendix 3: References

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