Workplace Exposure Standard (WES) review

IODINE
(CAS NO: 7553-56-2)

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Te Kāwanatanga o Aotearoa
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WORKSAFE
Mahi Haumaru Aotearoa

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1.0
Introduction

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

It considers the potential for exposures to iodine in New Zealand, the health effects and risks, exposure standards from other jurisdictions around the world, and the practicability of measuring exposures.

The review includes a recommendation to change the WorkSafe WES for iodine, which is currently set at a **WES-Ceiling** of 0.1**ppm** (1**mg/m³**), as published in the special guide *Workplace Exposure Standards and Biological Exposure Indices*, 12th Ed., November 2020 (WorkSafe, 2020), and to introduce a WorkSafe WES for inorganic iodide.

The WES recommended in this document are guidance values, not prescribed exposure standards. The intention is for them to be used as **risk criteria** for health risk assessment and risk management purposes and to be applied or interpreted only by people with appropriate training and experience. The values proposed in this document are considered by WorkSafe to be health-based WES. This means they are based on minimising health risk and do not take the practicability of achieving or measuring the values into consideration. This also means that in some instances the current analytical or sampling methods will not be sensitive enough to allow measurement at a level sufficiently below the WES to assess risk with a high degree of confidence. In this case there will be some uncertainty as to whether risk is suitably managed. As with any risk assessment, the uncertainties inherent in the assessment need to be considered and minimised so far as is reasonably practicable through good risk assessment and control.

We consider it critical to set health-based values as risk criteria, so that risk assessment is based on an actual understanding of health risk, rather than merely measuring a level of exposure.

Terms that are **bold** (first occurrence only) are further defined in the Glossary.
Synonyms: I_2.

2.0 Chemical and physical properties

Elemental iodine is a heavy, greyish black to purple crystalline solid with a metallic lustre and sharp characteristic odour at room temperature (**NLM** PubChem, 2020a; **ACGIH®**, 2008; **US EPA**, 2006).

Elemental iodine has an odour threshold reported at 9.0 mg/m^3, while the irritation concentration was reported at 2.0 mg/m^3 (NLM PubChem, 2020a).

Chemical and physical properties of iodine and potassium iodide include:

SUBSTANCE	IODINE	POTASSIUM IODIDE
CAS number	7553-56-2	7681-11-0
Formula	I_2	KI
Molecular weight	253.8 g/mol	166.02 g/mol
Physical form	Greyish black to purple crystalline solid with a metallic lustre	Colourless or white crystalline solid
Specific gravity	4.93 g/cm^3 at 25°C	3.12 g/cm^3
Melting point	113.6°C	680°C
Boiling point	185.45°C	1,323°C
Relative vapour density	8.8 (air = 1)	–
Vapour pressure	0.04 kPa at 25°C	–
Solubility	Water: 0.034 g/100 mL at 25°C; soluble in chloroform, alcohol, glacial acetic acid, glycerol oils, and many other organic solvents	Water: 148 g/100 mL at 25°C
Reactivity	Emits toxic vapour at room conditions	–
Partition coefficients	logK_{OW} = 2.49	logK_{OW} = 0.04
Conversion factors	1 ppm = 10.39 mg/m^3 at 760 torr, 25°C 1 mg/m^3 = 0.096 ppm at 760 torr, 25°C	–

NLM PubChem, 2020a,b; **ECHA REACH**, 2020a,b; ACGIH®, 2008

TABLE 1: Physicochemical properties of iodine and potassium iodide

Health-related hazard classifications for iodine and potassium iodide:

SUBSTANCE	CAS NUMBER	CLASSIFICATION
Iodine (solid)	7553-56-2	6.1D (All); 6.1D (O); 6.1D (D); 6.1D (I); 6.5B; 6.9B (All); 6.9B (O) 8.2C; 8.3A
Potassium iodide	7681-11-0	6.5B

TABLE 2:
HSNO health-related hazard classifications of iodine and potassium iodide (**EPA**, 2020a,b)

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

Iodine and iodides are used primarily in the manufacture of organic and inorganic chemicals, pharmaceuticals, radiopaque contrast agents, animal feed supplements, disinfectants, stabilizers, inks, colorants, and photographic chemicals (NLM PubChem, 2020a; ACGIH®, 2008).

Iodine and iodides are also used as catalysts in the alkylation and condensation of aromatic amines; in sulphations and sulphonations; for production of synthetic rubber; as microbiocides for drinking-water and swimming pools; and, as reagents in analytical chemistry (NLM PubChem, 2020a,b; ACGIH®, 2008).

Occupational exposure to iodine or iodides can occur during production, storage, transportation and end-use.

Workers can be exposed to iodine and iodide vapour and liquid via inhalation, and eye and skin contact.

The number of workers exposed or potentially exposed to iodine and iodides in New Zealand workplaces is unknown.

4.0
Health effects

IN THIS SECTION:

Iodine is an essential element for humans as it is a component of the thyroid hormones.

The daily requirement for adults is given as 150 to 200**µg** (**DFG MAK**, 2017a).

4.1 Non-cancer

Humans

The **WHO** draft on 'Iodine in Drinking-water' summarised the acute toxicity potential in exposed humans:

> "Several biological mechanisms protect against iodine toxicity and not all exposed subjects will react to excess iodine. Acute oral toxicity is primarily due to irritation of the **GI** tract, marked fluid loss and shock occurring in severe cases (**ATSDR**, 2004). Clinical features include GI disturbance (vomiting and diarrhoea), metabolic acidosis, seizure, stupor, delirium and collapse. Oral doses of 2,000–3,000 **mg** of iodine (about 30–40 **mg/kg bw**) are estimated to be lethal to humans, but survival has been reported after ingestion of 10,000 mg. Doses of 30–250 **ml** of tincture of iodine (about 16–130 mg of total iodine/kg bw) have been reported to be fatal." (Reference cited in WHO, 2019).

The WHO draft on 'Iodine in Drinking-water' summarised the irritation/corrosion potential in exposed humans:

> "Exposure to iodine vapour results in lung, eye, and skin irritation, while high concentrations rapidly lead to pulmonary oedema (ATSDR, 2004)." (Reference cited in WHO, 2019).

The ACGIH® review of iodine and iodides noted:

> "Inhalation of iodine vapor leads to excessive tearing, tightness in the chest, sore throat, and headache. In one study, an airborne concentration of 0.3 ppm iodine vapor (3.1 mg/m^3) was reported to make work impossible, while 0.1 ppm (1.1 mg/m^3) caused no irritating symptoms (Flury and Zernik, 1931)." (Reference cited in ACGIH®, 2008).

The ECHA REACH dossier on iodine noted:

> "According to Lee *et al*. (2005) iodine is a well-known local irritant which can cause burns. In 25 subjects exposed by patch application, the irritation threshold was seen in 1% iodine in petrolatum. 5% and 10% iodine in petrolatum resulted in clear irritation (vesicles). Note that vesicles are an indication of irritation, not corrosion, as they represent disturbances at the epidermal-dermal interface (**OECD**, 1999).

> "Iodine and concentrated solutions, including **U.S.P.** tincture, are classed as poisons because of their irritating effects to the gastrointestinal tract (Lyday, P. 2005).
>
> "Although data is consistent on potential effects of the substance on skin, documentation available is not adequate to make a clear difference on whether iodine is corrosive or irritant to the skin. No reference to primary sources on animal studies or observational human experience are made in order to evaluate exposure and if severity and persistence of the effects were objectively described." (References cited in ECHA REACH, 2020a).

The WHO draft on 'Iodine in Drinking-water' summarised the sensitisation potential in humans:

> "In rare instances, a hypersensitisation reaction may occur immediately after or within several hours of oral or dermal exposure to iodide. The most striking symptoms are angio-oedema (acute, transitory swelling of the face, hands, feet, or viscera) and swelling of the larynx, which may cause suffocation (ATSDR, 2004). Iodide has been used in the past as an expectorant in the treatment of asthma and related conditions at a typical dose of 3.3 mg/kg bw (ATSDR, 2004)." (Reference cited in WHO, 2019).

The ECHA REACH dossier on iodine summarised the repeat dose toxicity potential in exposed humans:

> "Iodine is an essential micronutrient for the synthesis of thyroid hormones which are required for the normal development, growth, and function of numerous metabolic pathways. The synthesis of thyroid hormones requires a normally functioning thyroid gland, as well as an adequate intake of iodine.
>
> "An extensive set of literature is available on the effects of iodine on human physiology and on toxic effects after insufficient or excessive iodine intake (ATSDR, 2004; WHO, 2009). The principal direct effects of excessive iodine ingestion are on the thyroid gland and can be classified into three types: hypothyroidism, hyperthyroidism and thyroiditis. Iodine deficiency can result in goiter, hypothyroidism, mental retardation, reproductive impairment, cretinism, decreased child survival and varying degrees of other growth and developmental abnormalities.
>
> "The association between iodine intake and the risk of disease is U-shaped. The curve is nonsymmetrical with the most serious problems associated with iodine deficiency (Laurber *et al*., 2009).
>
> "Inorganic iodine is rapidly converted to iodide in the digestive and/or respiratory tracts (WHO, 2009). Therefore, all internal exposure is essentially related to iodide and this form [sic] the basis for the consideration of iodine and iodide salts as equivalent in toxicological terms. Although Sherer *et al*. (1991) reported that iodine and iodide may affect thyroid hormones status in different ways in rats, both treatments tend to a decrease in **T3** levels (in line with the so-called 'Wolff-Chaikoff effect') which was higher in iodine treated group. Robison *et al*. (1998) failed to confirm the differential effect of iodine and iodide on thyroid hormone imbalance in humans.
>
> "Sherer *et al*. 1991 and de Raaf – Beekhuijzen (2010) reaffirmed the fact that the effects observed after repeated oral doses of iodine are referable to modifications on thyroid function almost exclusively, authenticating the basis for reading across data from iodine and iodide salts data. Based on that, the

threshold chosen for safety assessment is based on the thyroid as main target organ. Because of differences in iodine metabolism between animals and humans, data from animals is of limited use, especially when human data are available (Hetzel and Maberly, 1986) as the case of iodine and iodide salts. For that reason, key studies for establishing No-observed- adverse-effect-levels (**NOAEL**s) and subsequent Derived-no-effects-levels (**DNEL**s) were selected from the vast epidemiological literature available which was reviewed by the United States Agency for Toxic Substances and Disease Registary (ATSDR) in 2004. A NOAEL of 0.01**mg/kg/day** has been derived for chronic oral exposure to iodine. The NOAEL is based on subclinical hypothyroidism in healthy human children (Boyages *et al*., 1989; Li *et al*., 1987). Supporting studies indicate that the NOAEL would be applicable to elderly adults who may represent another sensitive subpopulation (Chow *et al*., 1991; Szabolcs *et al*., 1997) – this means that both sensitive subpopulations have been considered." (References cited in ECHA REACH, 2020a).

The DFG MAK review of iodine and inorganic iodides noted:

"In a metal processing unit, a 2% potassium iodide solution was sprayed onto moulds. The workers were thus exposed to potassium iodide aerosols, which could be inhaled and absorbed through the skin. The potassium iodide concentration in the air was 0.534 mg/m³ (0.18 to 0.98mg potassium iodide/m³ depending on the distance from the spraying cabin). A total of 85 workers aged 19 to 59 years were employed at this workplace between 1996 and 2001. The average time spent at the workplace was 25.4 months. Before beginning employment, the blood iodine value, the base value of TSH and the peripheral thyroid gland hormone concentrations were recorded by the factory physician. In addition, urinary iodine, thyroid gland autoantibodies and thyroglobulin were later recorded in risk cases.

"Eleven workers reported pre-existing goitre. Increased iodine levels in blood (34 to 2,710**µg/l**) and increased urinary iodine values (52 to 48,696**µg/g** creatinine) were found in 59 (69.4%) and 66 workers (77.6%), respectively; 13 workers (15.3%) reported the typical complaints of iodism. Hypothyroidism (7 latent and 2 manifest cases) was chemically diagnosed by a laboratory in 9 workers (10.6%) and hyperthyroidism (3 latent and 7 manifest cases) in 10 workers (11.7%). Five of those with hyperthyroidism reported typical symptoms of thyroid hyperfunction. In 3 workers of this department (3.5%), a significantly increased thyroid autoantibody titre, suggesting autoimmune thyroiditis, was found; 2 of them developed hyperthyroidism (no other details; Otto *et al*. 2002)." (Reference cited in DFG MAK, 2017a).

The WHO draft on 'Iodine in Drinking-water' summarised the reproductive and developmental toxicity potential in exposed humans:

"Chronic exposure to excess iodine has been shown to disrupt reproductive function, secondary to thyroid gland dysfunction. Changes in the menstrual cycle, including menorrhagia (excessive uterine bleeding) and anovulation (no ovulation), spontaneous abortions, stillbirths, and premature births have been associated with hypothyroidism (Longcope, 2000a; Krassas *et al*., 2010).

"Reproductive impairments associated with hyperthyroidism include amenorrhea, alterations in gonadotropin release and sex hormone-binding globulin (**SHBG**), and changes in the levels and metabolism of steroid hormones in both females and males (Longcope, 2000b; Krassas *et al*., 2010).

"Exposure to iodine may give rise to developmental defects, secondary to thyroid gland dysfunction (Boyages, 2000a.b). Hypothyroidism may be associated with impairment in neurological development of the foetus or growth retardation (Boyages, 2000a.b; Snyder, 2000a; Krassas *et al*., 2010)." (References cited in WHO, 2019).

The DFG MAK review of iodine and inorganic iodides noted that there were no studies available on the genotoxicity potential in humans following exposure (DFG MAK, 2017a).

Animals

The DFG MAK review of iodine summarised the acute inhalation toxicity in experimental animals:

"An **LC_{Lo}** value of 137**ml/m³** was given for rats after exposure for one hour. Observed effects were lacrimation, sleepiness and a decrease in body temperature (no other details; **NIOSH** 2004). In another investigation, also after exposure for one hour, an LCLo value of 80 ml/m³ was determined for the same species (no other details; NAS 1995).

"Groups of 8 to 10 guinea pigs (male and female animals) were exposed to gaseous iodine in concentrations of 0.5, 0.86, 3.1, 4.4 or 7.3 ml/m³ (about 5.5, 9.5, 34.1, 48.4 or 80.3 mg/m³) for one hour. During exposure and for one hour afterwards, the airway resistance, pulmonary compliance, time constant (mathematical product between airway resistance and pulmonary compliance), respiration rate, tidal volume and respiratory minute volume were determined every 5 minutes. The values determined before the exposure of each animal were taken as control values. After exposure for one hour, a concentration-dependent statistically significant increase in airway resistance and a decrease in the minute volume compared with the control values occurred at concentrations of 0.86 ml/m³ and above. The decrease in the respiration rate was dose-dependent and statistically significant after exposure for one hour at 3.1 ml/m³ and above. The increase in the time constant and tidal volume was dose-dependent and statistically significant at 4.4 ml/m³ and above. The decrease in pulmonary compliance was statistically significant at 7.3 ml/m³. At concentrations of 0.5 ml/m³, no statistically significant changes were observed after exposure for one hour. The author concluded that gaseous iodine has a strongly irritating effect on the upper respiratory tract at the low concentrations (0.86 ml/m³ and above), but affects also the lower respiratory tract at the high concentration of 7.3 ml/m³ (Amdur 1978).

"In the dog, 14 mg iodine/kg body weight applied intratracheally as fume led to acute pulmonary oedema within 4 hours (Luckhardt *et al*. 1920)." (References cited in DFG MAK, 2017b).

The ECHA REACH dossier on iodine summarised the acute dermal toxicity in experimental animals:

"To determine the potential for toxicity of iodine when applied dermally, the substance was tested following set forth in US EPA Health Effects Testing Guidelines, **OPPTS** 870.1200, final guideline, August 1998.

"Five healthy male and healthy female New Zealand White rabbits were dosed dermally with iodine at 2000 mg/kg bw. Since compound related mortality occurred at this level, five additional males were dosed at 1000 mg/kg bw and

five males were dosed at 500 mg/kg bw. The test article was kept in contact with the skin for 24 h. Animals were observed for toxicity and mortality at 1,2 and 4 hours postdose and daily for 14 days. Body weights and gross pathology were examined in all animals.

"The dermal **LD50** and 95% confidence limits of iodine in male rabbits is 1,425 (996–2,038) mg/kg bw. It appeared that females are not markedly more sensitive to the substance and the LD50 in females is greater than 2,000 mg/kg bw." (ECHA REACH, 2020a).

The ECHA REACH dossier on iodine summarised the irritation/corrosion potential in experimental animals:

"Based on the equivocal information from published data, two independent *in vitro* skin corrosion studies were assessed. Both studies demonstrated non-corrosive effects of the substance under the experimental conditions. Following the testing strategy from OECD guideline 404, an *in vitro* skin irritation study (following **EC** guideline B.46) was conducted. Results from this *in vitro* skin irritation study concluded that iodine was irritant under testing conditions and is thus classified as skin irritant category 2. This validated method is accepted by the European Union as a stand-alone replacement test for the rabbit *in vivo* test for classifying GHS category 2 irritant substances. Then, no further tests are deemed necessary.

EYE IRRITATION/CORROSION

"Two peer-reviewed references give indications on the irritating properties of iodine to eyes (Grant, 1986 and Lewis, 1996). This data is in line with point 3.3.2.3. of **CLP** Annex I which indicates that skin irritant substances (category 2) may be considered as leading to eye irritation (category 2)." (Reference cited in ECHA REACH, 2020a).

The ECHA REACH dossier on iodine summarised the sensitisation potential in experimental animals:

"To determine the sensitising potential of topically applied iodine, a Local Lymph Node Assay was performed in female mice. The study followed guideline EPA OPPTS 870.2600 (2003) and OECD guideline for the Testing of Chemicals No. 429 (2002)."

"Iodine was negative for excessive local irritation (< 25% increase in ear thickness) suggesting to be non irritant at the concentrations tested. The stimulation index of the substance was 1.0 at 0.25%, 1.8 at 0.5% and 2.2 at 1%. Based on these results, iodine is not a considered a dermal sensitizer agent under testing conditions. The **EC 3** concentration could no [sic] be calculated." (References cited in ECHA REACH, 2020a).

The DFG MAK review of iodine noted:

"Two experimental studies with guinea pigs are described in which iodine was found to be a weak contact allergen. No studies of respiratory sensitization have been carried out (supplement "Iod" 1999, available in German only)." (Reference cited in DFG MAK, 2017b).

The DFG MAK review of iodine summarised the repeat inhalation dose toxicity in experimental animals:

> "In a study not described in greater detail, **TC_{Lo}** values ("toxicity concentration, low", that is the lowest concentration at which effects are observed) of 1.38 or 3.1mg/m³ (0.13 or 0.28ml/m³) were given for the exposure of rats for 13 weeks (24 hours/day). At concentrations of 3.1mg/m³ (0.28ml/m³) and above, changes in the parameters of functional liver and kidney tests and endocrine changes not described in greater detail occurred. At concentrations of 1.38mg/m³ (0.13ml/m³) and above, changes in motor activity and aggressive behaviour were observed (no other details; NIOSH 2004)." (References cited in DFG MAK, 2017b).

The WHO draft on 'Iodine in Drinking-water' summarised the reproductive and developmental toxicity in experimental animals:

> "Decreased survival of pups was reported following administration of iodine to pregnant Long-Evans rats at a concentration of 2,500**mg/kg** in the diet for 12 days in the latter part of gestation. Length of labour (parturition) was also increased (Ammerman *et al*., 1964a). Although no effects were observed on ovulation rate, implantation rate, or foetal development in female rats given doses of 0, 500, 1,000, 1,500, or 2,000mg of iodide (as potassium iodide) per kg of diet during gestation and lactation, a dose-related decrease in survival rate for pups was observed, ranging from 93% (controls) to 16% (2,000mg/kg). Milk secretion was absent or greatly diminished in females exposed to iodide and the high mortality in pups was attributed to the dams' lactational failure (Ammerman *et al*., 1964a).
>
> "Decreased survival rates were also observed in pups from pregnant rabbits fed iodine at concentrations between 250 and 1,000mg/kg feed for 2–5 days before parturition. Pregnant hamsters exposed to 2,500mg iodine/kg feed similarly showed a decreased weaning weight of pups due to reduced maternal feed intake. Litters from pregnant pigs receiving diets containing 1,500 or 2,500mg iodine/kg feed (that is, toxic dietary levels in rats and rabbits) for the 30 days prior to parturition (Arrington *et al*., 1964).
>
> "Hyperthyroidism was associated with accelerated growth linked to accelerated pituitary growth hormone turnover or a direct effect of thyroid hormone on bone maturation and growth (Snyder, 2000b). Metabolism was severely disturbed in foals born to mares receiving excess iodine (48–432mg of iodine per day) in the diet during pregnancy and lactation. The long bones of the legs of foals showed osteopetrosis (abnormally dense bones); phosphorus and alkaline phosphatase levels in the blood were elevated (EC, 2002)." (References cited in WHO, 2019).

The **IPCS CICAD** on iodine and inorganic iodides summarised the genotoxic potential in experimental animals and *in vitro* test systems:

> "A number of studies have shown that iodine does not cause mutagenic effects. Solutions of potassium iodide, molecular iodine, or povidone-iodine at concentrations of 0.1–10mg/ml did not cause mutagenic effects in L5178Y mouse lymphoma cells or transforming activity in Balb/c3T3 cells grown in culture (Merkle & Zeller, 1979; Kessler *et al*., 1980). No lethal mutations were produced in *Drosophila melanogaster* when eggs were incubated in molecular iodine at 0.38mg/ml or potassium iodide at 0.75mg/ml (Law, 1938). Molecular iodine did not cause mutagenic activity in the His+ revertant assay in *Saccharomyces cerevisiae* (Mehta & von Borstel, 1982).

> "Sodium iodate ($NaIO_3$) was found not to be mutagenic in the bacterial Ames assay, the mouse bone marrow micronucleus test, or the recessive lethal test in *Drosophila melanogaster* (Eckhardt *et al*., 1982).
>
> "Iodide is a free radical scavenger and has been shown to decrease hydrogen peroxide–induced reversion in the TA104 strain of S*almonella typhimurium* (Han, 1992)." (References cited in IPCS CICAD, 2009).

4.2 Cancer

The International Agency for Research on Cancer [**IARC**] has no evaluation on the carcinogenic potential of iodine (IARC, 2020).

The US National Toxicology Program [**NTP**] Report on Carcinogens [**RoC**], Fourteenth Edition has no evaluation on the carcinogenic potential of iodine (NTP RoC, 2016).

The New Zealand EPA has not classified iodine as a 6.7A or 6.7B substance – substances that are respectively known or presumed, or suspected human carcinogens (EPA, 2020a).

Humans

The WHO draft on 'Iodine in Drinking-water' summarised the exposure and carcinogenicity potential of iodine in humans:

> "Iodine has not been classified as a human carcinogen due to a lack of available data. Evidence from human studies is equivocal; in iodine-deficient populations, increased iodide intake has been reported as a risk factor for thyroid cancer (Harach & Williams, 1995; Bacher-Stier *et al*., 1997; Franceschi, 1998; Franceschi & Dal Maso, 1999), however more recent studies indicate contrary findings (Zimmermann & Galetti, 2015; Cao *et al*., 2017)." (References cited in WHO, 2019).

The DFG MAK review of iodine and inorganic iodides noted:

> "Goitre caused by iodine deficiency has been linked with the development of thyroid cancer as high mortality from thyroid cancer is found in the population of mountainous regions (Alps, Andes, Himalayas), which are typical iodine deficient areas. The evaluation of 12 case-control studies yielded **OR**s for thyroid cancer of 5.9 for women (**95% CI:** 4.2–8.1) and of 38.3 for men (95% CI: 5.0–291.2 with existing goitre (Franceschi *et al*. 1999).
>
> "In addition to iodine deficiency, the higher iodine intake in iodine-deficient regions after the introduction of iodine supplementation is considered to be responsible for the increase in papillary tumours in many countries (Capen *et al*. 1999). In various studies in which an increase in papillary thyroid tumours correlates with the introduction of iodine supplementation, a clear association cannot be established, as confounders such as radioactivity and improved diagnostic techniques cannot be excluded (Gomez Segovia *et al*. 2004; Harach and Ceballos 2008; Teng *et al*. 2006). In addition, it is suspected that the detection of papillary carcinomas without clinical symptoms has increased as a result of improved diagnostic standards (Capen *et al*. 1999)." (References cited in DFG MAK, 2017a).

Animals

The IPCS CICAD on iodine and inorganic iodides summarised the data on exposure and carcinogenicity in experimental animals:

> "In another study, Fischer 344 rats were given 0, 10, 100, or 1,000 mg of potassium iodide per kilogram in the drinking-water for 2 years (0, 0.55, 5.31, and 53.0 mg/kg body weight per day in males and 0, 0.66, 6.73, and 66.6 mg/kg body weight per day in females). Increased colloid in the follicular lumen and flattened epithelia, but no tumours, were detected in the thyroid gland. In the high-dose group, 7 of 80 rats (4 males, 3 females) had squamous cell carcinomas in the submandibular salivary gland. The difference was not statistically significant for the sexes separately, but was significant for both sexes combined (P = 0.014). In addition, 65 of 80 rats (31 male, 34 female) in the high-dose group exhibited lobular atrophy and ductular proliferation, and 55 of 80 rats (25 male, 30 female) exhibited squamous metaplasia in the submandibular gland (Takegawa *et al*., 1998, 2000). Survival was decreased in the high-dose group in both males and females, but no treatment-related effects were observed in tissues other than thyroid and the salivary gland.
>
> "In a two-stage carcinogenicity study, Fischer 344 rats were given potassium iodide (1,000 mg/l in drinking-water for 82 weeks) after an initiating dose of N-bis(2-hydroxypropyl)nitrosamine, or **DHPN** (2,800 mg/kg body weight). Thyroid follicular cell carcinoma was found in 18 of 25 of the treated animals, while this effect was seen in just 2 of 19 of the controls given DHPN only (Takegawa *et al*., 2000).
>
> "In another two-stage carcinogenicity study (Kanno *et al*., 1992), the thyroid tumour–promoting effects of iodine deficiency and iodine excess were investigated to estimate an optimal iodine intake range that would not promote the development of thyroid neoplasias. In this study, iodine was administered in drinking-water to groups of 20 6-week-old male F344 rats following an intramuscular initiation dose of 2,800 mg of DHPN per kilogram body weight. The dosage was supplemented with various amounts of potassium iodide up to 260mg/l in drinking-water to generate conditions ranging from severe iodine deficiency to severe iodine excess. In rats not pretreated with DHPN, iodine deficiency produced diffuse thyroid hyperplasia, together with a decrease in **T_4** and an increase in TSH. Iodine excess produced colloid goitre, normal serum T_4, and slightly decreased TSH. In DHPN-treated rats, high tumour incidences (up to 85%) were observed in animals given less than 0.80µg of iodine per day; lowest tumour rates (< 5%) were observed in animals receiving 2.6–760µg of iodine per day. In two groups receiving 2,300 and 3,000µg of iodine per day, the thyroid tumour rates were 20% and 10% (Kanno *et al*., 1992)." (References cited in IPCS CICAD, 2009).

4.3 Absorption, distribution, metabolism and excretion

The ECHA REACH dossier on iodine summarised the absorption, distribution, metabolism and excretion (**ADME**):

> **ABSORPTION**
>
> "Iodine (**I_2**) is considered to be readily absorbed through the lungs and the gastrointestinal tract, based on available reports. Radioiodine (as I_2 vapour) was inhaled in a human volunteer study, where virtually all of the inhaled iodine was removed from the respiratory tract with a half-time of approximately

10 minutes. Much of the clearance of iodine from the respiratory tract was transferred to the gastrointestinal tract which suggested that the initial deposition was primarily in the conducting airways and moved by mucociliary clearance. The rapid absorption of iodine vapour is supported by animal studies in mice, rats, dogs, and sheep.

"Iodine that is ingested orally in the form of water soluble salts (such as potassium or sodium iodide) typically results in 100% absorption from the gastro-intestinal tract. Molecular iodine is converted into iodide in the gastro-intestinal tract and thus, information on the toxicokinetics from iodine and iodide salts is considered equivalent.

"The dermal absorption of iodine was investigated in humans that received topical applications of ^{131}I as potassium iodide or molecular iodine. Results indicated that the dermal absorption of iodine is assumed to be 1%."

METABOLISM

"The metabolism of absorbed iodine is expected to be similar, irrespective of the route of exposure to inorganic iodine. Molecular iodine (and ingested sodium iodide and inhaled methyl iodide) all undergo rapid conversion to iodide. For by-products of metabolic reactions in the gastrointestinal tract it has been suggested that these may differ for iodine and iodide, and could be responsible for differences in some reported effects.

"Iodine in the thyroid gland is incorporated into the protein, thyroglobulin. Iodine forms covalent complexes with tyrosine residues. The iodination of thyroglobulin is catalysed by the enzyme thyroid peroxidise. Iodination occurs at the follicular cell-lumen interface and the processes involved are the oxidation of iodide to form a reactive intermediate, the formation of monoiodotyrosine and diiodotyrosine residues in thyroglobulin, and the coupling of the iodinated tyrosine residues to form T4 (coupling of two diiodotyrosine residues) or T3 (coupling of a monoiodotyrosine and diiodotyrosine residue) in thyroglobulin. In the thyroid, the T4/T3 ratio is approximately 15:1; however, the relative amounts of T4 and T3 produced can depend on the availability of iodide, as low levels of iodide result in a lower T4/T3 synthesis ratio. The lipophilic T3 and T4 enter the blood via diffusion through the plasma membrane to the blood. More than 99% of both T3 and T4 combine with blood transport proteins, predominantly thyroxine binding globulin. The process is regulated by the pituitary hormone, thyroid stimulating hormone (TSH). TSH is released in response to thyrotropin releasing hormone from the hypothalamus as a response to low blood thyroid hormone level or lowered metabolic rate or body temperature.

"The main metabolic pathways for iodine outside the thyroid gland involve the catabolism of T3 and T4 and include:

- deiodination reactions
- ether bond cleavage of thyronine
- oxidative deamination and decarboxylation of the side-chain of thyronine, and
- conjugation of the phenolic hydroxyl group on thyronine with glucuronic acid and sulphate.

EXCRETION

"The main route of excretion for iodine is via the urine in the iodide form. With respect to the elimination of absorbed iodine, urinary excretion accounts for > 97% and faeces accounts for another 1–2%. However, not all iodide that is filtered by the kidney remains in the urine. During steady-state

conditions of radioiodine concentration, the renal plasma clearance was about 30% of the glomerular filtration rate. This suggests tubular reabsorption of the element. In other studies investigating the renal clearance in dogs, further evidence for tubular reabsorption of iodide was demonstrated. The exact mechanism for reabsorption has not been clearly established.

"Glucuronide and sulphate conjugates of T3, T4 and their metabolites are secreted into the bile. The total biliary secretion of T4 and metabolites was approximately 10–15% of the daily metabolic clearance of T4. In rats, about 30% of T4 clearance has been attributed for by the biliary secretion of the glucuronide conjugate and 5% as the sulphate conjugate. Once the conjugates are secreted, extensive hydrolysis occurs, with the reabsorption of iodothyronine in the small intestine.

"Other routes of excretion for absorbed iodine can be through breast milk, saliva, sweat, tears and exhaled air.

"The whole body elimination half-time of absorbed iodine has been estimated to be approximately 31 days in healthy adult males. However, considerable inter-individual variability is documented." (References cited in ECHA REACH, 2020).

The DFG MAK review of iodine and inorganic iodides summarised the mode of action for the observed effects:

"As iodine is a strong oxidant, mainly oxidative damage is thought to be responsible for the local irritating effects. The effects on the thyroid can be explained by a disturbance in the thyroid hormone balance." (DFG MAK, 2017b).

5.0 Exposure standards

IN THIS SECTION:

5.1 Other exposure standards

Table 3 below shows iodine exposure standards from around the world, as published by the Institute for Occupational Safety and Health of the German Social Accident Insurance (**IFA**, 2020).

JURISDICTION OR ADVISORY BODY	8-HOUR LIMIT VALUE		SHORT-TERM LIMIT VALUE	
	ppm	mg/m³	ppm	mg/m³
Australia			0.1[1]	1[1]
Austria	0.1	1	0.1	1
Belgium	0.01[2]	0.1[2]	0.1[3,4]	1[3,4]
Canada – Ontario	0.01[5]	[0.01[5,8]]	0.1[6]	
Canada – Québec			0.1[1]	1.0[1]
Denmark	0.1	1	0.1[1]	1[1]
Finland			0.1[4]	1.1[4]
France			0.1	1
Hungary		1		1
Ireland	0.01[2]	0.01[2,8]	0.1[2,4]	
Japan – JSOH	0.1	1		
Latvia		1		
New Zealand			0.1[1]	1[1]
People's Republic of China				1[1]
Poland		0.5		1
Romania	0.09	0.5	0.2[4]	1[4]
Singapore			0.1	1
South Korea	0.01[8]	0.1[8]	0.1[8]	1[8]
Spain			0.1	1
Sweden			0.1[4]	1[4]
Switzerland	0.1	1	0.1	1
USA – NIOSH			0.1[1]	1[1]
USA – OSHA			0.1	1
UK			0.1	1.1

TABLE 3: Exposure standards for iodine from around the world

It is noted that the only organisations from whom we obtained information as to how and why they set occupational exposures standards on iodine were DFG, ACGIH®, and Safe Work Australia.

[1] **Ceiling limit value**.
[2] Inhalable fraction and vapour.
[3] Vapour.
[4] 15 minutes average value.
[5] Inhalable aerosol and vapour.
[6] Vapour and aerosol.
[7] 15 minutes reference period.
[8] Applies to iodides.

5.2 DFG

The Deutsche Forschungsgemeinschaft [DFG, German Research Foundation] re-evaluation of iodine and inorganic iodides did not recommend a MAK value, but maintained the "H" notation (DFG MAK, 2017a).

Rationale:

"The critical effects are disturbances in thyroid function occurring after increased iodine or iodide intake. Germany was considered to be a country with a persistent mild iodine deficiency. The most recent studies (2003–2006 and 2005) of the iodine supply in the population revealed a low normal iodine supply in children, adolescents and healthy adults.

"Iodine is irritating to the eyes and respiratory tract of humans.

MAK VALUE AND **PEAK LIMITATION**

"In Germany, a value of 500µg iodine/day is accepted as the maximum iodine intake. The recommended daily intake is 180 to 200µg iodine/day.

"The difference between the maximum (500µg) and the recommended intake (200µg) of iodine or iodide of 300µg a day would be reached with exposure to 30µg iodine/m^3, assuming a respiratory volume of 10 **m^3** and complete absorption. The intake and elimination of iodine and iodides are homeostatically regulated in the gastrointestinal tract. This cannot be extrapolated to the inhalation of iodine and iodides. Because of the long history of iodine deficiency in Germany, there is a high prevalence of subclinical and manifest thyroid gland diseases. An increase in iodine intake is suspected of producing further disturbances in damaged thyroid glands. Therefore, no MAK value has been established, and iodine remains listed in Section IIb of the List of MAK and **BAT** Values. This also applies for inorganic iodides. The establishment of a peak limitation value is therefore not applicable.

PRENATAL TOXICITY

"After excessively high iodine intake during pregnancy, goitre has been observed in newborn babies. As no MAK value has been established, classification in one of the pregnancy risk groups is not possible.

CARCINOGENICITY AND GERM CELL MUTAGENICITY

A relationship between the introduction of iodine supplementation and an increase in papillary thyroid tumours in humans cannot be confirmed. Long-term studies in humans and animals are not available. There is no evidence of genotoxic effects from the available data. Iodine and inorganic iodides are therefore not classified in one of the categories for carcinogens or germ cell mutagens.

ABSORPTION THROUGH THE SKIN

In Germany, 500µg iodine/day is considered to be the maximum iodine intake. The recommended daily intake is 180 to 200µg iodine/ day (**BfR** 2004 a; **D-A-CH** 2000). The absorbed amounts calculated for dermal exposure to a saturated aqueous iodine solution, exceed the maximum iodine intake of 500µg/day in all models. Although the volunteer study of Harrison (1963) does not allow the quantitative assessment of dermal intake, the results, however, do indicate that the dermal penetration of iodine and inorganic iodine compounds do not differ greatly. Iodine and inorganic iodine compounds are therefore designated with an 'H' (for substances which can be absorbed through the skin).

SENSITIZATION

"Contact sensitization to iodine or preparations containing iodine has been shown also in more recent literature to be relatively rare and must also be viewed in the context of its wide application as a skin disinfectant. Furthermore, mostly patients with chronic wounds are affected, so that these findings are not relevant when assessing contact sensitization under workplace conditions. As there are no new data with experimental animals available for contact sensitization nor clinical or animal studies for respiratory sensitization, iodine and inorganic iodine compounds are not designated with **'Sh'** or **'Sa'** (for substances which cause sensitization of the skin and airways)." (References cited in DFG MAK, 2017a).

5.3 ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of iodine and iodides concluded with recommendations that a **TLV-TWA** of 0.01ppm (0.1mg/m^3) for iodine and iodides as inhalable fraction and vapour, would minimise the potential for hypothyroidism in exposed workers; and, a TLV-STEL of 0.1ppm (1mg/m^3) for iodine vapour, would minimise the potential for irritation of the upper respiratory tract and mucous membranes (ACGIH®, 2008).

Rationale:

"The primary health effect associated with exposure to excess dietary iodine is hypothyroidism. The Food and Nutrition Board of the Institute of Medicine (Institute of Medicine, 2000) has set an upper limit for iodine intake of 1.1mg/day, based on decreased thyroid function above this level. The recommended daily intake of iodine is 150µg/day, leaving about 1mg/day as a margin of safety. Based on an estimated volume of 10m^3 daily inhalation volume in adults, and acknowledging that inhaled and orally administered iodine undergoes almost complete systemic absorption, a TLV-TWA of 0.01ppm (0.1mg/m^3) is recommended for iodine.

"A primary concern for exposure to iodine vapor is irritation of the upper respiratory tract and mucous membranes. Exposure to 0.1ppm iodine vapor (1mg/m^3) was reported to have no adverse effect on workers (Flury and Zernik, 1931; Morgan *et al*., 1968). Amdur (1978) reported increased respiratory resistance and decreased compliance and frequency in the guinea pigs exposed to 4.2mg/m^3 for one hour in the presence of 10mg/m^3 sodium chloride aerosol. Based on these findings, a TLV-STEL of 0.1ppm (1mg/m^3) is recommended for iodine vapor.

"Systemic absorption of iodine through the skin is less than 0.5% of the deposited dose. Therefore, there is no basis for a **Skin** notation.

"There are no reports of iodine-induced cancers following workplace exposures. An **A4, Not Classifiable as a Human Carcinogen**, notation is recommended for iodine because of a lack of adequate human epidemiology studies in healthy populations, and because an animal chronic bioassay of iodine in drinking water did not show evidence of iodine-induced cancer." (References cited in ACGIH®, 2008).

5.4 Safe Work Australia

In their draft review, Safe Work Australia has recommended an 8-h TWA of 0.01ppm (0.1mg/m^3) for iodine to protect for thyroid toxicity in exposed workers. They have also recommended a peak limitation of 0.1ppm (1mg/m^3) to protect for severe irritation from acute exposure.

> "Critical effects of chronic over-exposure are adverse thyroid effects including hyper- and hypothyroidism and goitre. Acute exposure at higher concentrations causes severe local irritation. Workers from populations with historic dietary iodine deficiency are more susceptible to chronic effects than healthy (euthyroid) populations." (Safe Work Australia, 2019).

6.0 Analytical methods for the assessment of airborne iodine

A common method to measure iodine exposure is using NIOSH Method 6005, Issue 2 (NIOSH, 1994).

Using this method an air sample of 15 to 225 litres is collected onto a solid sorbent tube, using a flow rate of 0.5 to 1 litre per minute. Following desorption of the analyte using a solution of sodium bicarbonate, the sample is analysed using ion chromatography.

This method can achieve a limit of detection of 1µg of iodine per sample, allowing reliable quantification at airborne concentrations above 0.004 ppm (0.04 mg/m^3).

7.0
Discussion

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

The toxicological database reviewed above indicates that iodine is locally and systemically toxic to humans, causing eye, skin and respiratory tract irritation and thyroid damage (and sequelae).

Based on the aforementioned documentation, informed by the conclusions of the DFG, ACGIH®, and Safe Work Australia reviews, and in particular the findings listed below, WorkSafe considers its current WES-Ceiling of 0.1ppm (1mg/m³) for iodine, to be inadequate to manage health risks from possible workplace exposure:

- Iodine is a potential irritant and toxicant in exposed workers inducing eye, skin and respiratory tract irritation, and thyroid damage (and sequelae, including reproductive and developmental effects) (WHO, 2019; DFG MAK, 2017a; ACGIH®, 2008).
- The ACGIH® review of iodine and iodides concluded with recommendations that a TLV-TWA of 0.01ppm (0.1mg/m³) for iodine and iodides as inhalable fraction and vapour, would minimise the potential for hypothyroidism in exposed workers; and, a TLV-STEL of 0.1ppm (1mg/m³) for iodine vapour, would minimise the potential for irritation of the upper respiratory tract and mucous membranes (ACGIH®, 2008). The TLV-TWA was based on the difference between the **RDI** for iodine (150µg/day) and the upper limit for iodine intake (1.1mg/day). The TLV-STEL was based on a NOAEL for iodine vapour of 0.1ppm (1mg/m³) for irritant effects (ACGIH®, 2008).
- The Safe Work Australia draft review of iodine recommended a TWA of 0.01ppm (0.1mg/m³), to protect for thyroid toxicity in exposed workers, with a Peak limitation of 0.1ppm (1mg/m³) to protect for severe irritation from acute exposure (Safe Work Australia, 2019). The recommended TWA was based on the difference between the RDI for iodine (150–200µg/day) and the upper limit for iodine intake (1.1mg/day), noting that the maximum iodine tolerance of exposed Australian populations of workers is unclear from the available source material. The Peak limitation was based on severe irritation reported in acutely exposed workers above 0.3ppm (Safe Work Australia, 2019).
- The proposed WES-TWA of 0.01ppm (0.1mg/m³) for iodine and inorganic iodides is intended to protect exposed workers from adverse thyroid effects (and sequelae, including reproductive and developmental effects) (DFG MAK, 2017a; ACGIH®, 2008).
- Available information indicates that iodine is not a sensitiser (DFG MAK, 2017a; ACGIH®, 2008), so a ***sen*** notation is not warranted.

8.0
Recommendations

WorkSafe considers its current WES-Ceiling of 0.1ppm (1mg/m^3) for iodine alone to be inadequate to protect workers exposed in the workplace, based on current knowledge.

It is proposed that WorkSafe:

1. adopt a WES-TWA for iodine and inorganic iodides of 0.01ppm (0.1mg/m^3) (aerosol and vapour);
2. maintain a WES-Ceiling for iodine and inorganic iodides of 0.1ppm (1mg/m^3) (aerosol and vapour);

Noting that the proposed WES-TWA and WES-Ceiling for iodine and inorganic iodides may not eliminate all risk, due to the potential contribution of dermal exposures to total body burden, and the uncertainties for any exposure triggering adverse effects in individuals with pre-existing thyroid conditions, so workplace exposures should be minimised.

Appendices

IN THIS SECTION:

Appendix 1: Glossary

TERM	MEANING
95%CI or 95% CI or CI95%	95% Confidence Interval.
A4 Not Classifiable as a Human Carcinogen	Agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of lack of data. *In vitro* or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories. An ACGIH® term.
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: https://portal.acgih.org/s/store#
ADME	Absorption, Distribution, Metabolism and Excretion.
ATSDR	Agency for Toxic Substances and Disease Registry is a federal public health agency of the USD Department of Health and Human Services.
BAT	Biologische Arbeitsstoff-Toleranzwerte [Biological Tolerance Value], a DFG term.
BfR	Bundesinstitut für Risikobewertung (German Federal Institute for Risk Assessment).
Ceiling or Ceiling Limit Value	Ceiling Limit Value – absolute exposure limit that should not be exceeded at any time.
CICAD	Concise International Chemical Assessment Document.
CLP	Classification, Labelling and Packaging – EU program.
D-A-CH	Deutschland Österreich Schweiz.
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.
DHPN	Di(2-hydroxypropyl)nitrosamine.
DNEL	Derived No Effect Level.
EC	European Commission.
EC 3 or EC_3	The amount of a substance that is required to elicit a stimulation index of 3 [in a Mouse/Murine Local Lymph Node Assay].
ECHA	The European Chemicals Agency (an agency of the European Union).
EPA	The New Zealand Environmental Protection Authority.
GI	Gastrointestinal.
"H"	DFG MAK designation: *danger of percutaneous absorption*. Equivalent to the skin notation in the WorkSafe WES special guide.
HSNO	Hazardous Substances and New Organisms Act 1996, New Zealand.
^{131}I or I-131	Radioiodine, radioisotope of iodine.
I_2	Iodine.
IARC	The International Agency for Research on Cancer – an agency of the World Health Organisation.
IFA	Institut für Arbeitsschutz der Deutschen Gestzlichen Unfallversicherung [Institute for Occupational Safety and Health of the German Social Accident Insurance].
IPCS	International Programme on Chemical Safety – a World Health Organisation Programme.

TERM	MEANING
JSOH	Japan Society for Occupational Health.
LC_{LO} or LCLo	Lowest published lethal concentration.
LD_{50}	Lethal Dose for 50% of the test population.
m^3	Cubic metre.
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. Values set by the DFG.
µg	Microgram or one millionth of a gram.
µg/g	Microgram or one millionth of a gram per gram.
µg/L or µg/l	Microgram or one millionth of a gram per litre.
mg	Milligram or one thousandth of a gram.
mg/kg	Milligrams per kilogram.
mg/kg b.w. or mg/kg bw	Milligram of substance per kilogram body weight.
mg/kg bw/day or mg/kg b.w./day or mg/kg/day or mg/kg bw/d	Milligram of substance per kilogram body weight per day (exposure rate).
mg/L or mg/l	Milligram of substance per litre.
mg/m^3	Milligrams of substance per cubic metre of air.
mL or ml	Millilitre or one thousandth of a litre.
mL/m^3 or ml/m^3	Millilitres of substance per cubic metre (of air).
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.
Odds Ratio; OR	An odds ratio is a measure of association between an exposure and an outcome – the odds that an outcome will occur given a particular exposure, compared to the odds of the exposure occurring in the absence of that exposure.
OECD	Organisation for Economic Co-operation and Development.
OPPTS	Office of Prevention, Pesticides and Toxic Substances administered by the US EPA, publish test guidelines.
OSHA	Occupational Safety and Health Administration, US Department of Labor.
Peak limitation	The maximum concentration which cannot be exceeded at any time, set to protect workers from rapidly acting substances. A Safe Work Australia term.
ppm	Parts of vapour or gas per million parts of air.
RDI	Recommended Daily Intake.

TERM	MEANING
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals. An EU program and regulation.
Risk criteria	The terms of reference against which the significance of risk is evaluated. It is used to support decision making on health risk management. ISO 31000 2nd edition *Risk Management – guidelines* (2018).
RoC	Report on Carcinogens.
"Sa"	Sensitising to airways. A DFG MAK notation.
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.
"Sh"	DFG MAK designation: *danger of sensitisation of the skin*.
SHBG	Sex hormone-binding globulin.
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.
T_3	Triiodothyronine.
T_4	Thyroxine.
TCLo	Lowest toxic concentration.
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.
TSH	Thyroid stimulating hormone.
US EPA	United States Environmental Protection Agency.
U.S.P. or USP	United States Pharmacopoeia.
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-Ceiling	A concentration that should not be exceeded at any time during any part of the working day. A WorkSafe term.
WES-TWA	The average airborne concentration of a substance calculated over an eight-hour working day. A WorkSafe term.
WHO	World Health Organisation, Geneva.

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

Appendix 3: References

Agency for Toxic Substances and Disease Registry (ATSDR). (2004). *Toxicological Profile for Iodine*. TP158. www.atsdr.cdc.gov/ToxProfiles/tp158.pdf

American Conference of Governmental Industrial Hygienists (ACGIH®). (2008). *Iodine and Iodides*. Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, Documentation of the Threshold Limit Values and Biological Exposure Indices, 8th Edition. Copyright 2020. Reprinted with permission.

Deutsche Forschungsgemeinschaft (DFG). (2017a). *Iodine and inorganic iodides/Molecular iodine*. The MAK-Collection for Occupational Health and Safety 2017, Vol. 2, No. 2; pp 375-415. https://onlinelibrary.wiley.com/doi/pdf/10.1002/3527600418.mb755356e5717

Deutsche Forschungsgemeinschaft (DFG). (2017b). *Iodine*. The MAK-Collection for Occupational Health and Safety 2017; pp 1-20. https://onlinelibrary.wiley.com/doi/pdf/10.1002/3527600418.mb755356e4017

Environmental Protection Authority (EPA). (2020a). Chemical Classification and Information Database (CCID): *Iodine*. www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/5DC5D4D5-A11B-42C0-8224-20E74BD4E64A

Environmental Protection Authority (EPA). (2020b). Chemical Classification and Information Database (CCID): *Potassium iodide*. www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/398B5C55-00CF-4B74-B2DC-E4BEBFCFC153

European Chemicals Agency (ECHA) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). (2020a). Dossier for *Iodine*, accessed April 2020. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15294/1

European Chemicals Agency (ECHA) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). (2020b). Dossier for *Potassium Iodide*, accessed April 2020. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/5883/1

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA). (2020). GESTIS International Limit Values. Accessed January 2020 http://limitvalue.ifa.dguv.de

International Agency for Research on Cancer (IARC), accessed April 2020. https://monographs.iarc.fr/list-of-classifications

International Programme on Chemical Safety (IPCS). (2009). *Concise International Chemical Assessment Document 72 – Iodine and Inorganic Iodides: Human Health Aspects*. WHO, Geneva. www.inchem.org/documents/cicads/cicads/cicad72.pdf

National Institute for Occupational Safety and Health (NIOSH). (1994). *Iodine*. Method 6005, Issue 2. www.cdc.gov/niosh/docs/2003-154/pdfs/6005.pdf

National Library of Medicine (NLM) PubChem database accessed April 2020a: Compound Summary – *Iodine*. https://pubchem.ncbi.nlm.nih.gov/compound/Iodine

National Library of Medicine (NLM) PubChem database accessed April 2020b: Compound Summary – *Potassium iodide*. https://pubchem.ncbi.nlm.nih.gov/compound/4875

National Toxicology Program (NTP) Report on Carcinogens (RoC). (14th Edition, 2016). Accessed April 2020. https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html

Safe Work Australia. (2019). *Iodine – draft evaluation report WES*. https://engage.swa.gov.au/52508/widgets/273797/documents/127269

United States Environmental Protection Agency (US EPA). (2006). *Reregistration Eligibility Decision For Iodine And Iodophor Complexes*. 739-R-06-010. www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/red_G-90_27-Jul-06.pdf

WorkSafe New Zealand. (2020). Special guide *Workplace Exposure Standards and Biological Exposure Indices* (12th Ed.) November 2020. worksafe.govt.nz/topic-and-industry/work-related-health/monitoring/exposure-standards-and-biological-exposure-indices

World Health Organization (WHO). (2019). *Iodine in Drinking-water – Draft Background document for development of WHO Guidelines for Drinking-water Quality*. WHO/SDE/WSH/0x.xx/xx. WHO, Geneva. www.who.int/water_sanitation_health/water-quality/guidelines/chemicals/draft-iodine-gdwq-190924.pdf

Notes

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