



IODINE

CAS number: 7553-56-2

Synonyms: —

Chemical formula: I₂

Workplace exposure standard (amended)

TWA: 0.01 ppm (0.1 mg/m³)

STEL: —

Peak limitation: 0.1 ppm (1 mg/m³)

Notations: —

IDLH: 2 ppm

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.01 ppm (0.1 mg/m³) is recommended to protect for thyroid toxicity in exposed workers.

A peak limitation of 0.1 ppm (1 mg/m³) is recommended to protect for severe irritation from acute exposure.

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

Discussion and conclusions

Iodine and iodide salts are essential nutrients and used as feedstock supplements, catalysts, inks, and disinfectants.

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 thyroid effects than healthy (euthyroid) populations.

Inhalational absorption contributes to total iodine intake (ACGIH, 2018). In euthyroid populations, the maximally tolerated daily intake is approximately 1 mg (ACGIH, 2018; DFG, 2014), but varies depending on the population's history of iodine deficiency. Below this maximum, a daily intake of 0.15 to 0.2 mg is recommended to maintain normal thyroid function. This is based in part on an epidemiologically determined NOAEL of 0.01 mg/kg/day for hypothyroidism in a euthyroid population (DFG, 2014; ECHA, 2019). The difference of the maximally tolerated and recommended intakes is used to estimate acceptable systemic exposure from occupational iodine sources by the ACGIH (2018) and DFG (2014). From this difference, the ACGIH (2018) estimates an air concentration that would not increase the total iodine burden in exposed workers above a maximally tolerated intake of 1.1 mg/day, corresponds to a TLV-TWA of 0.01 ppm.



The maximum iodine tolerance of exposed Australian populations of workers is unclear from the available source material, but the lack of a TWA is considered insufficiently protective of systemic thyroid effects. Therefore, a TWA of 0.01 ppm as published by ACGIH (2018) is recommended to protect for these systemic effects and the extrapolation of the oral NOAEL to a inhalational DNEL of $\approx 0.07 \text{ mg/m}^3$ or 0.01 ppm published by ECHA (2019). Examination of the maximally tolerated intake of iodine in Australian populations is recommended during subsequent reviews to assess the suitability of the interim TWA.

The peak limitation of 0.1 ppm is recommended to protect for severe irritation reported in acutely exposed workers above 0.3 ppm (ACGIH, 2018).

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

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

There are insufficient data to recommend a skin notation.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	Peak limitation: 0.1 ppm (1 mg/m³)
ACGIH	2008	TLV-TWA: 0.01 ppm (0.1 mg/m³); TLV-STEL: 0.1 ppm (1 mg/m³)
<p>Assessment grouped with common iodide salts, e.g. sodium and potassium iodide (NaI and KI). TLV-TWA intended to minimise potential for hypothyroidism from excess iodine intake. TLV-STEL intended to protect for acute irritation.</p> <p>Summary of data:</p> <p>Inhaled iodine is rapidly reduced to iodide. Recommended dietary intake and MTD without adverse thyroid function effects published by US Institute of Medicine are 150 µg/d and 1.1 mg/d, respectively, and used for TLV-TWA derivation. Assuming a respiratory volume of 10 m³, and complete systemic absorption of inhaled or ingested iodine, a TLV-TWA of 0.01 ppm (0.1 mg/m³) is expected to maintain total iodine burden within the 1 mg/d margin of safety inferred from the difference between the recommended and maximally tolerated daily doses.</p> <p>TLV-STEL derived from NOAEL of 0.1 ppm for acute irritation in worker study.</p> <p>Human data:</p> <ul style="list-style-type: none"> Intolerable working conditions reported at 0.3 ppm vapour due to dyspnoea, sore throat and headache <ul style="list-style-type: none"> no irritating symptoms at 0.1 ppm in exposed workers No respiratory tract irritation at 1 mg/m³ vapour in volunteers (n=6, 8 min); Epidemiological studies suggest increased risk of thyroid cancer associated with excess exposure in populations with dietary deficiency Severe transient neonatal goitre and hypothyroidism in infants with mothers exposed to KI at 13–11 mg/kg/d during pregnancy (no further details provided). <p>Animal data:</p> <ul style="list-style-type: none"> Respiratory irritation at 0.5 ppm in acute inhalation study (guinea pigs, 1 h); increased resistance and decreased minute volume at 3–4 ppm, decreased lung compliance suggestive of adverse pulmonary effects at 7 ppm, <ul style="list-style-type: none"> when exposed in combination with sodium chloride aerosol, pulmonary effects observed at 0.4 ppm Increased thyroid weights at 260 mg/L iodide in drinking water in repeat feeding study (rats, young and mature, 6 wk); <ul style="list-style-type: none"> increased pituitary weight and thyroid-stimulating hormone levels in young rats cited study indicates that effects at this concentration do not provide evidence for hypothyroidism in adult rats Decreased survival rates in males at 100 and 1,000 ppm potassium iodide in drinking water in chronic carcinogenicity study (rats, 2 yr) <ul style="list-style-type: none"> salivary gland tumours reported in 1,000 ppm group; ≈2,500 times higher than the maximum tolerable daily human intake Thyroid tumour promotion activity of KI demonstrated in rats with co-administration of known tumour initiators Iodine, NaI, and KI non-mutagenic <i>in vitro</i>; KI caused DNA fragmentation and was cytotoxic in thyroid lymphocytes via free-radical formation. 		



Source	Year set	Standard
<p>Not classified as a human carcinogen based on lack of evidence in epidemiological studies and slightly increased tumorigenicity at high concentrations of iodide in drinking water with chronically exposed animals.</p> <p>A skin notation is not warranted based on poor dermal absorption and bioavailability of dermally absorbed iodine. Insufficient data to recommend a sensitiser notation.</p>		
DFG	2017	Not assigned
<p>Summary of additional data:</p> <p>Due to historical iodine deficiencies in the German population, maximally tolerated dietary iodine intake is set at 500 µg/d (cf. 1.1 mg/d in USA). Based on difference between RDI (200 µg/d) and maximally tolerated daily intake (500 µg/d) in Germany, a MAK of 0.03 mg/m³ for systemic effects, such as hypothyroidism, would be recommended. However, this derivation does not take potential local irritational effects into account, a MAK is therefore not established. The agency questions the ability to extrapolate effects observed for ingested iodine intake to inhalational exposures as iodine homeostasis is regulated in the gastrointestinal tract.</p> <p>Human data:</p> <ul style="list-style-type: none">• Maximally tolerated daily intake recommended by the World Health Organization in non-iodine-deficient populations is 1 mg/d• Populations with iodine deficiencies have lower tolerance to excess iodine and are more susceptible to adverse effects of overexposure, e.g. hyper- and hypothyroidism, and goitre• Skin lesions and hypersensitivity and autoimmune reactions can result from >300 mg/d• Dermal absorption of KI and iodine doses were 0.13–0.19% (n=3) and 0.057–0.12% (n=2), respectively in volunteers• Calculated dermal fluxes of saturated aqueous solutions in 3 studies: 0.00073, 0.001, and 0.018 mg/cm²/h• 9 cases of hyperthyroidism and 10 cases of hypothyroidism in workers exposed to average air concentrations of 0.534 mg/m³ KI (0.18–0.98 mg/m³); increased blood and urinary levels were measured respectively in 59 and 66 workers relative to their baseline levels (n=85, age: 19–59 yr, average employment 25.4 mo)• NOAEL: 0.01 mg/kg/d for hypothyroidism calculated from daily intake data in study of Chinese children aged 7–15 living in areas of high (462.5 µg/L) and low (54 µg/L) in drinking water• NOAEL: 0.5 mg/d NaI for changes in thyroid hormone levels in serum of volunteers with normally functioning thyroids in repeat oral dose study with treatment groups 0.25, 0.5, and 1.5 mg/d (14 wk). <p>Animal data:</p> <ul style="list-style-type: none">• Evidence for thyroid tumour promoting effect of KI at 1,000 ppm in diet when co-administered with known tumour initiator (rats, 20 wk, also cited by ACGIH, 2018) <p>Non-mutagenic in a comet assay with Chinese hamster ovarian cells.</p> <p>Carcinogenicity notation not warranted based on absence of carcinogenic effects in long-term human and animal studies.</p> <p>A skin notation is warranted based on calculated absorption of iodine from a saturated aqueous solution that is above the maximally tolerated daily intake.</p> <p>Sensitisation notation not warranted due to lack of evidence for sensitisation in overall dataset including lack of sensitisation caused by use of iodine as a skin disinfectant.</p>		
SCOEL	NA	NA
No report.		

Source	Year set	Standard
OARS/AIHA	NA	NA
No report.		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
NICNAS	* 2018	Tier I assessment: therapeutic uses not assessed
ECHA	✓ 2019	<ul style="list-style-type: none"> NOAEL of 0.01 mg/kg/d from epidemiological study of Chinese children (also cited in DFG, 2014) used to derive long-term derived no-effect-level (DNEL) by extrapolation to inhalational exposure; supported by studies that indicate this NOAEL is applicable to elderly adults who represent a sensitive subpopulation <ul style="list-style-type: none"> Assuming 100% absorption and respiratory rate of 10 m³ for a 70 kg individual, a corresponding long-term inhalational DNEL is ≈ 0.07 mg/m³ or 0.01 ppm Short-term DNEL adopted from the ACGIH (2018) evaluation Negative mutagenicity <i>in vivo</i> in mice and Chinese hamsters; equivocal mutagenicity <i>in vitro</i> in bacterial and mammalian cell lines.
US NIOSH	✓ 1994	IDLH based on acute inhalation toxicity data in humans.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	—
HCIS	—
NICNAS	—
EU Annex	—
ECHA	—
ACGIH	Carcinogenicity – A4
DFG	H (skin)
SCOEL	NA



Source	Notations
HCOTN	NA
IARC	NA
US NIOSH	NA

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Calculation

Adverse effects in human case study:	no
Dermal LD ₅₀ ≤ 1000 mg/kg:	
Dermal repeat-dose NOAEL ≤ 200 mg/kg:	
Dermal LD ₅₀ /Inhalation LD ₅₀ < 10:	
<i>In vivo</i> dermal absorption rate > 10%:	
Estimated dermal exposure at WES > 10%:	yes

insufficient data to assign a skin notation

IDLH

Is there a suitable IDLH value available? Yes

Additional information

Molecular weight:	126.90
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m ³ ; 1 mg/m ³ = Number ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [TLVs® and BEIs® Guidelines section](#) on the ACGIH website.



Deutsche Forschungsgemeinschaft (DFG) (2014) Iodine and inorganic iodides – MAK value documentation.

European Chemicals Agency (ECHA) (2019) Iodine – REACH assessment.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) Iodine: Human health tier I assessment – IMAP report.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Iodine.

DRAFT