



CAPTAN

CAS number: 133-06-2

Synonyms: Captane, N-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide

Chemical formula: $C_9H_8Cl_3NO_2S$

Structural formula: —

Workplace exposure standard (interim)

TWA: 5 mg/m³

STEL: —

Peak limitation: —

Notations: Carc. 2, DSEN

IDLH: —

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

Recommendation and basis for workplace exposure standard

An interim TWA of 5 mg/m³ is recommended to protect for irritation in exposed workers.

There are limited inhalational data available in humans and some evidence of reversible toxicity in rats in a repeat inhalational study (NICNAS, 2016). Further assessment of additional data sources is to confirm the critical effects in humans is recommended at the next scheduled review.

Discussion and conclusions

Captan is used as a fungicide in agricultural and therapeutic applications.

Skin irritation and positive dermal patch test responses are reported in various worker case studies (ACGIH, 2018), with overall evidence indicating low toxicity. Carcinogenic effects are only reported at high oral doses in animal models (ACGIH, 2018; NICNAS, 2016). It is considered a confirmed animal carcinogen with unknown relevance to humans. Accordingly, the ACGIH sets a TLV-TWA at 5 mg/m³ measured by the inhalable dust fraction (ACGIH, 2018).

There are limited toxicological data for inhalational exposures with available data primarily from oral studies. Irritation is reported in animals with a reported NOAEL of 12.5 mg/m³ for local irritant effects in a repeat dermal study in rabbits. Reversible lung effects were reported in a repeat inhalational study in rats at 15 mg/m³ (NICNAS 2016).

The recommended TWA of 5 mg/m³ is considered to protect for irritation and other effects in exposed workers. However, the data are limited, and a further review of additional sources is recommended to confirm the critical effects in humans.



Recommendation for notations

Classified as a category 2 carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Classified as a skin sensitiser and not a respiratory sensitiser according to the GHS.

Further assessment of data to inform a skin notation is recommended for priority review based on evidence of systemic toxicity in animals. There are reports of dermal sensitisation from occupational exposure and reactivity in patch testing in humans (ACGIH, 2018). These data support the recommended DSEN notation. Dermal route of exposure is reported to cause low degree of toxicity (ACGIH, 2018). However, systemic effects have been observed in repeat dermal dose studies with rabbits (NICNAS, 2016).

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 0.5 mg/m³
ACGIH	2014	TLV-TWA: 5 mg/m³ (inhalable particulate matter)
TLV-TWA is based on the inhalable particulate fraction due to its low toxicity. TLV-TWA considered to protect against irritation and potential biological effects. Summary of data: Human data: • Urticaria, eczema and positive patch test results reported in treatment and worker studies (concentrations generally not specified). Animal data: • LC₅₀: >5,700 mg/m³ (rats, 2 h), 4,500 mg/m³ (male mice, 2 h), 5,000 mg/m³ (female mice) • LD₅₀: 518 mg/kg (male mice, ip), 462 mg/kg (female mice, ip) • Ovines and bovines more susceptible than rats and mice ○ lethal dose in sheep 250 mg/kg • NOAEL: 100 mg/kg/d for increased liver/kidney weight in feeding study (dogs, 48 wk following 18 wk at unspecified lower dosage) • No carcinogenic effects at or near MTD in several long-term feeding studies (rats and mice, up to 80 wk) except in one strain of mice: ○ dose-related carcinogenicity only in B6C3F1 mice at 8,000–16,000 ppm in diet • Some cited studies suggest impurities may contribute to isolated reports of carcinogenicity in animals • No carcinogenic or co-carcinogenic effects observed in topical exposure study (mice, 1 yr) • Little or no embryotoxic or teratogenic effects in multiple animal models ○ decreased fertility noted in male mice given 50–100 mg/kg/d for 5 d • Mutagenic <i>in vitro</i>, but is readily detoxified and non-mutagenic <i>in vivo</i> • Hepatorenal, cytocellular, and genotoxicity may increase if diet is protein deficient.		
DFG	NA	NA
No report.		
SCOEL	NA	NA
No report.		
OARS/AIHA	NA	NA
No report.		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓ 2016	Human data: - Death reported following oral exposure to 1,071 mg/kg (no further information provided) - Dermal sensitisation with 0.5% (amount and solvent unspecified) in exposed farmers (n=122, 9%) and unexposed workers (n=63, 8%) Animal data: - Repeat dose inhalation study (rats, nose-only, 0, 0.13, 0.60, 5.06, and 12.98 mg/m³, 6 h/d, 5 d/wk, 13 wk): - NOAEL: 0.6 mg/m³ for signs of toxicity - respiratory and adverse changes to lung, trachea, larynx and nasal passages reported in male rats after wk 1 at 15 mg/m³ 4 males died in wk 5 and 13 at 15 mg/m³ (12.98 µg/L) - effects observed in lungs and nasal passages were reversible after 4 wk - NOAEL: 110 mg/kg/d for systemic toxicity in repeat dermal study (rabbits, 6 h/d, 21 d) - NOAEL of 12.5 mg/m³ for local skin effects. Carcinogenicity: - Carcinogenic mechanism of action not fully understood - toxic metabolite, thiophosgene, implicated from chronic intestinal irritation reported in mouse dietary studies - Dose-related increase in thyroid adenomas in repeat feeding study (rats, n=50/sex/dose, 62 wk) - Mutagenic in Chinese hamster V79 lung cells and human lymphocytes.
IARC	✓ 1983	- No case reports and epidemiological studies of carcinogenicity in humans available - Experiments in mice provide limited evidence for carcinogenicity - Available data insufficient to evaluate the carcinogenicity in humans - Low embryotoxic or teratogenic potential in mice and rats at maternally tolerated doses.
US EPA	✓	Results of studies assessed to derive RfD: - NOAEL: 25 mg/kg/d (highest exposure group) for signs of toxicity, changes in general behaviour, appearance and survival (in parents and pups (rats, 102 d) - Dose-related body weight and food consumption reduction in 3-generation feeding study, treatment range: 0–500 mg/kg/d (rats) - no other measured parameters affected by treatment - NOAEL: 100 mg/kg/d for non-carcinogenic, systemic effects in oncogenic feeding study (rats, 2 yr) - NOAEL: 60 mg/kg/d in feeding study (dogs, 1 yr) - LOAEL of 300 mg/kg/d for emesis and soft stools - Maternal NOAEL: 25 mg/kg/d for teratogenic effects (rabbits) - foetal NOAEL: 60 mg/kg/d



Source	Year	Additional information
		o maternal LOAEL: 60 mg/kg/d for weight loss

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Yes

Is the chemical carcinogenic with a mutagenic mechanism of action? No

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

Notations

Source	Notations
SWA	Carc. 2, Sk:Sen
HCIS	Carcinogenicity – category 2, Skin sensitisation – category 1
NICNAS	Carcinogenicity – category 2, Skin sensitisation – category 1
EU Annex	Carcinogenicity – category 2, Skin sensitisation – category 1
ECHA	NA
ACGIH	Carcinogenicity – A3, DSEN
DFG	NA
SCOEL	NA
HCOTN	NA
IARC	—
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: yes
Dermal LD ₅₀ /Inhalation LD ₅₀ < 10:
<i>In vivo</i> dermal absorption rate > 10%:
Estimated dermal exposure at WES > 10%:
consider assigning a skin notation

IDLH

Is there a suitable IDLH value available? No

Additional information

Molecular weight:	300.6
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:	☒
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐
A biological exposure index has been recommended by these agencies:	☐ ACGIH ☐ DFG ☐ SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

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

International Agency for Research on Cancer (IARC) (1983) Miscellaneous pesticides. IARC Monographs on the evaluation of the carcinogenic risk to humans, volume 30.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) 1H-Isoindole-1,3(2H)-dione, 3a,4,7,7a-tetrahydro-2-[(trichloromethyl)thio]-: Human health tier II assessment – IMAP report.

Tenth Adaptation to Technical Progress Commission Regulation (EU Annex) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

US Environmental Protection Agency (US EPA) (1987) Captan. Integrated Risk Information System (IRIS) Chemical Assessment Summary