CAPTAFOL

CAS number:	2425-06-1
Synonyms:	Difolatan, 1H-Isoindole-1, 3(2H)-dione, 3a, 4, 7, 7a-tetrahydro-2-[(1, 1, 2, 2-tetrachloroethyl)thio], folcid, tetrachloroethylthiotetrahydrophthalimide
Chemical formula:	$C_{10}H_9Cl_4NO_2S$
Structural formula:	

Workplace exposure standard (retained)

TWA:	**0.1 mg/m^3**
STEL:	**—**
Peak limitation:	**—**
Notations:	**Carc. 1B, Sk., DSEN**
IDLH:	**—**
Sampling and analysis:	The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.1 mg/m^3 is recommended to protect for effects on the liver and kidney and sensitisation in exposed workers.

Discussion and conclusions

Captafol is used as a broad-spectrum fungicide for fruits, vegetables, ornamental plants and turf grasses.

No human studies with reliable quantitative information are available. Captafol has been shown to be a dermal sensitiser and a potential respiratory sensitiser based on reports of dermatitis and asthma in occupationally exposed workers.

A 12 month oral study in dogs reported a LOAEL of 2 mg/kg/day for adverse changes in the liver and kidneys (ACGIH, 2018). The TWA of 0.1 mg/m^3 is derived using the oral LOAEL of 2 mg/kg/day and converting it to inhalational exposure. An uncertainty factor of 100 was applied and the value is then rounded down to account for reported dermal and respiratory sensitiser effects in exposed workers.

Recommendation for notations

Classified as a category 1B 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. A review of the GHS classification is recommended for dermal and respiratory sensitisation due to case reports of dermal and respiratory sensitiser effects.

A skin notation is recommended based on the evidence of adverse effects following dermal contact in humans.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.1 mg/m^3***
ACGIH	***2017***	***TLV-TWA: 0.007 ppm (0.1 mg/m^3)***

TLV-TWA recommended to protect for possible liver, kidney and sensitiser effects in exposed workers.

Summary of data:

TLV-TWA of 0.1 mg/m^3 is derived using the oral dose of 2 mg/kg (LOEL in dogs) and converting it to an inhalational exposure of 14 mg/m^3 (assuming 70 kg human breathing 10 m^3, 8 h shift and 100% absorption). An uncertainty factor of 100 is applied and the value is then rounded down to account for possible sensitiser effects.

Human data:

- No studies with reliable quantitative data
- Considered a dermal and respiratory sensitiser based on reports of occupational dermatitis and asthma
  - sensitisation estimated to occur in 10–40% of people occupationally exposed
- Marked vesiculation and oedema of hands and face and wheezing reported in a worker at a distributing plant
  - reported effects occurred only after brushing against large bags of captafol
- Occupational asthma reported in a worker following chronic exposure over years (no further information)
- Of 133 workers, 23% exposed workers had history of occupationally induced dermatitis
  - irritant dermatitis more common than allergic
- Case-control study found statistically significant increases in pancreatic cancer in residents living in areas with high use of pesticides
  - confounding identified by other cancer risk factors and chemical use
- Reported adverse effects following contact to skin warrants skin notation.

Animal data:

- LOEL of 100 mg/kg/d from oral study in rats and mice with kidney and liver as target organs
- 12 mo oral study in dogs reported LOEL of 2 mg/kg/d (changes in liver and kidney)
- Separate 2 yr oral study in dogs reported a NOEL of 10 mg/kg/d (changes in liver and kidney)
- In rats and mice, oral exposure caused tumours in various tissues including vascular system, GIT and liver
  - rats also developed tumours in the kidneys.

Positive for mutagenicity in bacteria and yeast and other cellular systems. Inactive in *in vivo* mutagenicity tests.

Source	Year set	Standard
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
IARC	✓	1991	• Probably carcinogenic to humans • Active in a wide range of tests for genetic effects.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Yes
Is the chemical carcinogenic with a mutagenic mechanism of action?	Insufficient data

Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	NA
HCIS	Carcinogenicity – category 1B, Skin sensitisation – category 1
NICNAS	NA
EU Annex	Carcinogenicity – category 1B, Skin sensitisation – category 1
ECHA	Carcinogenicity – category 1B, Skin sensitisation – category 1
ACGIH	Carcinogenicity – A3, Skin, DSEN, RSEN
DFG	NA
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 2A
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:	yes
Dermal LD_{50} ≤1000 mg/kg:	no
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD_{50}/Inhalation LD_{50} <10:	
In vivo dermal absorption rate >10%:	
Estimated dermal exposure at WES >10%:	
	a skin notation is warranted

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	349.1
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.

European Chemicals Agency (ECHA) (2006) Captafol (ISO); 1,2,3,6-tetrahydro-N-(1,1,2,2-tetrachloroethylthio)phthalimide – REACH assessment.

Tenth Adaptation to Technical Progress Commission Regulation (EU) 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).

International Agency for Research on Cancer (IARC) (1991) Occupational Exposures in Insecticide Application, and some Pesticides. IARC Monographs on the evaluation of the carcinogenic risk to humans, Volume 53.