FERBAM

CAS number:	14484-64-1
Synonyms:	Carbamate, ferbeck, ferric dimethylthiocarbamate
Chemical formula:	$C_9H_{18}FeN_3S_6$
Structural formula:	—

Workplace exposure standard (amended)

TWA:	**5 mg/m^3**
STEL:	**—**
Peak limitation:	**—**
Notations:	**—**
IDLH:	**800 mg/m^3**

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

Recommendation and basis for workplace exposure standard

A TWA of 5 mg/m^3 is recommended to protect for central nervous system effects and potential irritant effects in exposed workers.

Discussion and conclusions

Ferbam is used as a fungicide. Critical effects of exposure are central nervous system impairment, changes in bodyweight and spleen damage as reported in animal studies (ACGIH, 2018). Very limited human exposure data indicate irritation of eyes and respiratory tract may occur before potential central nervous effects are elicited (ACGIH, 2018).

Adverse neurological effects are reported in a chronic rat feeding study at 2.5 mg/kg/day (DFG, 2003). These effects are not described in summaries of the same study in reports published by the ACGIH (2018) and IARC (1976).

A NOAEL of 5 mg/kg/day for seizures in dogs is reported with a corresponding LOAEL of 25 mg/kg/day and is used as a starting point for the derivation of the recommended TLV-TWA of 5 mg/m^3 (ACGIH, 2018). A corresponding NOAEC of 35 mg/m^3 was extrapolated from the NOAEL of 25 mg/kg/day (ACGIH, 2018). ACGIH (2018) did not provide additional evidence of how the TLV-TWA was derived. Presumably, an uncertainty factor of 10 was applied to this NOAEC and the result rounded up to 5 mg/m^3. This TWA of 5 mg/m^3, as assigned by ACGIH, is consideredsufficient to protect for identified effects in exposed workers.

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.

A skin notation is not warranted based on the available evidence.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	*1991*	*TWA: 10 mg/m^3*

Source	Year set	Standard
ACGIH	***2009***	***TLV-TWA: 5 mg/m^3***

TLV-TWA intended to protect for CNS impairment, changes in body weight and spleen damage reported in animal studies.

Summary of data:

TLV-TWA based on NOAELs of repeat oral dose studies with animals; NOAEL of 5 mg/kg for central nervous effects in dogs used as starting point. Assuming 100% absorption, an air concentration of 35 mg/m^3 would deliver an effective oral dose at the NOAEL (further assumptions not specified). A UF is applied to arrive at the TLV-TWA of 5 mg/m^3 (UF derivation not discussed).

Human data:

- Irritating to eyes and respiratory tract, higher concentrations (not specified) expected to cause CNS depression
- Large oral doses (not specified) cause gastrointestinal disturbances.

Animal data:

- Oral LD_{50}: 1,130 mg/kg (rats); 3,400 mg/kg (mice); 3,000 mg/kg (rabbits)
- LD_{50}: >4,000 mg/kg (rabbits, dermal)
- LC_{50}: 400 mg/m^3 (rabbits, 4 h)
- 1/35 positive responses solution in sensitisation study as 25% aqueous (guinea pigs, n=35, challenged with 5, 10 and 25%, no further information provided)
- Two repeat feeding studies (rats, 4 wk, 13 wk or 2 yr) report LOAEL for decreased body weight and spleen changes at ≈66 mg/kg/d and mortality above ≈109 mg/kg/d:
  - NOAEL: 12.5 mg/kg/d (2 yr), 23 mg/kg/d (13 wk) and 37.5 mg/kg/d (4 wk)
  - anaemic effects at 325 mg/kg/d (4 wk)
  - brain lesions at 125 mg/kg/d (2 yr)
  - no evidence for carcinogenicity in 2 yr study
- 2 repeat feeding studies (dogs, 28 d or 1 yr) report LOAEL for reduced blood cell count (28 d) and seizures/mortality (1 yr) at 25 mg/kg/d:
  - NOAEL: 5 mg/kg/d (28 d and 1 yr)
  - seizures and deaths occurred after 5–9 wk
- Mutagenic *in vitro* but not *in vivo* except at 1,000 mg/kg/d oral doses where increased number of sperm abnormalities was reported (mice, 5 d):
  - NOAEL: 500 mg/kg for oral and ip administration
- No maternal or foetal adverse effects at 23 mg/kg, abnormal ossification but no maternal toxicity at 228 mg/kg (mice, gestational d 6–14)
- 40–70% absorbed within 24 h at 500 mg/kg (rats, route unspecified); 23% excreted in urine, 18% in expired air, 3% in bile and <1% accumulated in tissue.

A skin notation is not recommended based on low dermal toxicity observed in rabbits; slight dermal sensitisation effects reported in guinea pigs do not warrant a sensitiser notation. Insufficient data available to recommend a TLV-STEL.

Source	Year set	Standard
DFG	***1999***	***Not assigned***
Summary of additional data: Previous MAK of 15 mg/m^3 withdrawn due to the publication of additional data that prompted re-evaluation. No MAK currently established due to the lack of a NOAEL or adequate *in vivo* genotoxicity data in the available animal studies and insufficient human exposure data. Data regarding skin absorption and sensitisation potential are not discussed. Embryotoxic at maternally toxic oral doses. Animal data: • Can produce carcinogenic nitrosamines in combination with nitrite under acidic conditions, carcinogenicity has however not been affirmed in chronic animal studies • Repeat feeding study with exposure groups of 9, 37 and 96 mg/kg/d (rats, 80 wk) reported reduced body weight gain and reduced food consumption in all exposure groups: o reduced spleen, thyroid and testes weights at 37 mg/kg/d (male rats) o ataxia, hair loss and paralysis in hind limbs at 96 mg/kg/d (female rats) • No effect on fertility when treated males were mated with untreated females at 23–109 mg/kg/d (rats, 13 wk); mortality and reduced body weight gain at 109 mg/kg/d: o no effect on fertility when female rats were fed 15–51 mg/kg/d (2 wk) and mated with untreated males • Mutagenic in some strains of *Salmonella* at 1,000–5,000 µg/plate without metabolic activation; no *in vivo* data presented • Adverse neurologic effects observed after 3–4 mo in all groups of repeat feeding/carcinogenicity study with treatment range: 2.5–250 mg/kg/d (rats, 2 yr): o chronic lung and kidney inflammation in older rats o brain lesions in highest dose group (unrelated to neurological effects) o no evidence for carcinogenicity.		
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	✓	2018	• Tier I assessment: agricultural and therapeutic uses are excluded from assessment.

Source		Year	Additional information
IARC	✓	1976	• No adverse effects except brain lesions at highest dose group in 2 yr feeding study, also cited in ACGIH (2018) • Induces accumulation of acetaldehyde when ingested with ethanol in animals (species not specified) • Despite negative carcinogenicity, available data insufficient to determine carcinogenicity in animals • Ferbam reacts with nitrite under acidic conditions to form nitrosamines.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Insufficient data
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	—
HCIS	—
NICNAS	NA
EU Annex	NA
ECHA	—
ACGIH	Carcinogenicity – A4
DFG	—
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
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:	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 not warranted

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	416.5
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.

Deutsche Forschungsgemeinschaft (DFG) (2003) Ferbam – MAK value documentation.

European Chemicals Agency (ECHA) (2016) Ferbam – REACH assessment.

International Agency for Research on Cancer (IARC) (1976) Ferbam. IARC Monographs on the evaluation of the carcinogenic risk to humans, volume 12.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) Iron, tris(dimethylcarbamodithioato-S,S')-, (OC-6-11)-: Human health tier I assessment – IMAP report.

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