PINDONE

CAS number:	83-26-1
Synonyms:	Pival, 2-pivalyl-1,3-indandione, 2-trimethylacetyl-1,3-indandione
Chemical formula:	$C_{14}H_{14}O_3$
Structural formula:	—

Workplace exposure standard (retained)

TWA:	**0.1 mg/m^3**
STEL:	—
Peak limitation:	—
Notations:	—
IDLH:	**100 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 0.1 mg/m^3 is recommended to protect for effects on blood clotting in exposed workers.

A priority review of the data for the chemical in the next scheduled review of the workplace exposure standards is recommended to address unresolved uncertainties.

Discussion and conclusions

Pindone is an anticoagulant rodenticide and an insecticide.

Critical effects of exposure are anticoagulant (blood clotting) effects that occur through inhibition of prothrombin formation. Pindone is pharmacologically analogous to warfarin and inhibits the synthesis of Vitamin K-dependent clotting factors.

Limited data are available, and no inhalational toxicology or bioavailability studies are reported. Toxicity data on pindone is limited but indandiones, of which pindone is a member, are reported to cause diarrhoea, pyrexia, renal tubular necrosis and dermatitis when used clinically. No further information is available. Pindone is structurally related to warfarin and is considered less toxic with a LD_{50} of 10.3 mg/kg for pindone and 2.4 mg/kg for warfarin in rats. It causes rapid death in rats due to pulmonary and visceral congestion without haemorrhage. Chronic exposure causes multiple internal haemorrhage (ACGIH, 2018). The ACGIH (2018) have derived a TWA of 0.1 mg/m^3 by analogy with warfarin. HCOTN (2004) note that 0.1 mg/m^3 (equivalent to 1 mg/d per eight-hour work shift in workers) may not be protective of blood effects. This position is based on a seven-day LD_{50} of 0.52 mg/kg in rabbits (36.4 mg/d in a 70-kilogram worker) and a half-life in dogs of approximately five days.

The TWA of 0.1 mg/m^3 by ACGIH (2018) and SWA is recommended to be retained to limit potential cumulative anticoagulant effects. This value is consistent across the two available primary sources.

Further review of the data is recommended during the next scheduled review to address unresolved uncertainties.

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***	***TWA: 0.1 mg/m^3***
ACGIH	***2001***	***TLV-TWA: 0.1 mg/m^3***
TLV-TWA recommended to minimise the potential for anticoagulant effects *via* inhibition of prothrombin (plasma protein produced by the liver) formation. Summary of data: Limited data are available; no inhalation toxicology or bioavailability studies. No specific derivation of TWA provided. Human data: • Clinical use of β-diketones reported diarrhoea, pyrexia, renal tubular necrosis, paralysis of accommodation and exfoliative dermatitis (no further information). Animal data: • Rodenticidal dosage of pindone and warfarin (structurally related) for house mice were 4.3 mg/kg and 5.5 mg/kg; considered less toxic to rats than warfarin • Warfarin TLV-TWA: 0.01 mg/m^3 • LD_{50}: 10.3 mg/kg (rats): o causes rapid death due to pulmonary and visceral congestion without haemorrhage; compared to 2.4 mg/kg warfarin in rats • Chronically (assumed from feeding studies), vitamin K antagonist, with delayed inhibition of prothrombin formation and repeated doses have a cumulative effect on blood coagulation • Chronic exposure causes multiple internal haemorrhage. Insufficient data to recommend a skin, sensitiser or carcinogenicity notation or TLV-STEL.		
DFG	***NA***	***NA***
No report.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		

Source	Year set	Standard
HCOTN	***2004***	***TWA: 0.1 mg/m³***

Administrative OEL; insufficient data in humans.

Summary of additional data:

- $t_{1/2}$ ≈5 d observed in dogs after oral exposure:
  - may accumulate in the body
- LD_{50}: 0.52 mg/kg/d (rabbits,7 d); ≡dose 36.4 mg/d in 70 kg worker
- Exposure to OEL of 0.1 mg/m³ ≡dose 1 mg/d for a worker breathing 10 m³; administrative OEL likely to high.

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	ND	• Human health tier I assessment; no further information.
APVMA	✓	2002	• No additional information.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Insufficient data
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	—
HCIS	—
NICNAS	NA
EU Annex	NA
ECHA	—
ACGIH	—
DFG	NA
SCOEL	NA
HCOTN	—
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
Insufficient data to assign a skin notation.

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	230.26
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 9.43 mg/m^3; 1 mg/m^3 = 0.11 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.

Australian Pesticides and Veterinary Medicines Authority (APVMA) (2002) Pindone - NRA Review.

Health Council of the Netherlands (HCOTN) (2004) Pindone. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/109.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Pindone: Human health tier I assessment – IMAP report.