TRIPHENYL PHOSPHATE

CAS number: 115-86-6

Synonyms: Celluflex TPP, disflamoll TP, phenyl phosphate, phosflex TPP, phosphoric acid, triphenyl ester, TPP

Chemical formula: $C_{18}H_{15}O_4P$

Workplace exposure standard (retained)

TWA: **3 mg/m^3**

STEL: **—**

Peak limitation: **—**

Notations: **—**

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 3 mg/m^3 is recommended to protect for liver changes in exposed workers.

Discussion and conclusions

Triphenyl phosphate (TPP) is used as a plasticiser in vehicle upholstery, fireproofing agent, component of lubricating oil and hydraulic fluids.

The critical effects of exposure are potential liver changes.

Limited human data are available. A medical evaluation of 32 male workers from a manufacturing plant found no adverse clinical effects from exposure at TWA of 3.5 mg/m^3 (ACGIH, 2018). There is equivocal evidence of sensitisation in humans (ACGIH, 2018; DFG, 1991; NICNAS, 2018). Based on animal data, TPP is of very low acute oral and dermal toxicity. A NOEL of 105 mg/kg/day is identified in rats based on increased liver weight (NICNAS, 2018).

Based on no adverse effects in workers exposed at an average concentration of 3.5 mg/m^3, a TWA of 3 mg/m^3 by ACGIH (2018) is recommended to be retained. The recommended TWA is considered adequately protective of liver changes 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 recommended based on the available evidence.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 3 mg/m^3***
ACGIH	***2001***	***TLV-TWA: 3 mg/m^3***

TLV-TWA recommended to minimise the risk of skin and eye irritation and dermatitis.

Summary of data:

TLV-TWA based on absence of effects following medical evaluation of workers exposed to TPP for up to 10 yr at average of 3.5 mg/m^3.

Human data:

- No adverse clinical effects (dermatitis, eye or respiratory tract irritation, unexplained illness or neurological disease) in 32 men in manufacturing plant exposed at TWA 3.5 mg/m^3 for 2–10 yr (average 7.4 yr):
  - slight reduction in erythrocyte ChE activity in 6 workers
  - no difference in plasma ChE activity
- *in vitro* cytotoxicity demonstrated in cultured human cells, provides some evidence of *in vitro* immunotoxicity
- Allergic or sensitisation reaction to exposure not definitive.

Animal data:

- No fatalities among groups of guinea pigs, rats or mice administered 3,000 mg/kg (in ethanol solution) orally or subcutaneously
- Oral LD_{50}: 1,320 ±280 mg/kg (mice); 3,800±260 mg/kg (rats)
- Subcutaneous administration of 500 mg/kg fatal to monkeys:
  - 1,000 mg/kg fatal to rabbits;
  - 200 mg/kg induced paralysis in cats (fatal between 300–1,000 mg/kg)
- Subcutaneous injection of 400, 700 or 1,000 mg/kg in cats; no ataxia at 400 mg/kg. Prostration occurred sometime after dosing at the higher doses
- 50% inhibition of plasma ChE activity in mice administered 200 mg/kg and in cockerels administered 1,000 mg/kg (oral or IP)
- No skin irritation following topical application in rats and mice
- No cumulative toxicity based on 3 mo study in rats dosed at 1,800 mg/kg and 380 mg/kg
- Negative results in genotoxicity tests
- No difference in incidence of pulmonary adenomas in treated or control mice (single or multiple doses)
- Not teratogenic or maternally toxic in male and female rats fed at 0, 2.5, 5, 7.5 or 10 mg/kg (91 d).

Insufficient data to recommend Skin or SEN notations or a TLV-STEL.

Not classifiable as a human carcinogen notation is assigned.

Source	Year set	Standard
DFG	***1991***	***Not assigned***
Summary of additional data: • Single dose of 1,000 mg/kg in hens produced no effects • Appears to be poorly absorbed through skin and GIT • Limited human data. No evidence reported for lethal dose of 1,000 mg/kg • Older studies in which neurotoxic changes occurred concluded to be due to impurities in the chemical: o no changes in blood, plasma or RBC ChE activity in later studies in cats • Repeated dose studies in hens confirmed absence of neurotoxic effects • Slight reduction in body weight gain and increased liver weight at the highest dose reported in dietary study in rats fed 0, 754 and 3,632 mg/kg/d (35 d) • Equivocal evidence of sensitisation • Not mutagenic in *S. typhimurium* strains TA98, TA100, TA135 and TA1537 (with or without activation): o weakly positive in micronucleus test in SHE cells • No chronic studies available • Insufficient data in humans and animals to assign MAK: o additional studies, particularly of neurotoxicity *in vivo*, is required.		
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	• LD_{50}: >10,000 mg/kg (rabbits, dermal) • No signs of toxicity caused by whole body exposure in mice at 363 mg/m^3 (6 h) or 757 mg/m^3 (2–4 h) • Very low incidence of potential skin sensitisation in humans • NOAEL of 1,500 ppm (105 mg/kg/d in males and 117 mg/kg/d in females) in rats based on increased liver weight (90 d duration) • Negative results in *in vitro* genotoxicity studies • Not considered to cause neurotoxicity • No adverse effects following repeated application to intact or abraded rabbit skin at 100 or 1,000 mg/kg/d, 5 d/wk • Single doses of 2,000, 3,000, 5,000, 8,000 or 12,500 mg/kg caused no effects in hens (observed for 2–3 wk) • Recent studies suggest may cause hormonal and/or metabolic changes.
OECD	✓	2002	• Very low acute oral and dermal toxicity • Repeated dose oral studies in rats (up to 4 mo) showed slight body weight reduction and increased liver weight; NOAEL of 161 mg/kg/d identified based on reduced body weight gain • Pure substance did not caused neuropathy in cats or hens: ○ providing support to presence of impurities causing such effects in older studies.

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	NA
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	NA
SCOEL	NA
HCOTN	NA

Source	Notations
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:	
Dermal LD_{50} ≤1000 mg/kg:	no
Dermal repeat-dose NOAEL ≤200 mg/kg:	no
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?	No

Additional information

Molecular weight:	326.28
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 13.3 mg/m^3; 1 mg/m^3 = 0.07 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) (1991) Triphenyl phosphate – MAK value documentation.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) Phosphoric acid, triphenyl ester: Human health tier II assessment – IMAP report.

Organisation for Economic Cooperation and Development (OECD) (2002) SIDS initial assessment profile – Triphenyl Phosphate.