ATRAZINE

CAS number:	1912-24-9
Synonyms:	2-Chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine, 2-chloro-4-ethylamino6-isopropylamino-s-triazine
Chemical formula:	$C_8H_{14}ClN_5$

Workplace exposure standard (amended)

TWA:	**1 mg/m^3**
STEL:	**—**
Peak limitation:	**—**
Notations:	**Sk., 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

A TWA of 1 mg/m^3 is recommended to protect for reproductive and developmental effects in exposed workers.

Discussion and conclusions

Atrazine is a selective herbicide used for the control of grass and broadleaf weeds. Primary adverse effects in animals are changes in oestrous cycling and body weight changes. Effects on bone marrow, spleen and mammary tissue, and decreases in hematologic parameters in rats are also reported but not conclusive. Epidemiological studies in an atrazine manufacturing plant reported no association between exposure and prostate cancer. No studies in humans were available to correlate reported adverse health effects to airborne concentrations (ACGIH, 2018; APVMA 2008; DFG, 2013).

In a six-month feeding study in rats, oestrus cycle and a decrease in luteinizing hormone peaks were reported and a NOAEL of 1.8 mg/kg/d identified (DFG, 2013). Based on DFG defined methods and factors, the oral NOAEL was converted to an inhalational exposure concentration of 1 mg/m^3 (DFG, 2013). This value is considered protective of the critical health effects in exposed workers and is the recommended TWA.

Recommendation for notations

Not classified as a 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 skin notation is recommended based on the low NOAEL following repeated dermal dosing to animals.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 5 mg/m^3***
ACGIH	***2014***	***TLV-TWA: 2 mg/m^3***

TLV-TWA recommended to protect exposed workers against adverse haematologic, reproductive and developmental effects.

Summary of data:

Human data:

- No studies available detailing effects related to measured air concentrations
- No reports of poisoning via ingestion
- Epidemiology studies of 2,045 workers at an atrazine manufacturing plant reported no association between atrazine exposure and prostate cancer; and no evidence that employment at the plant was associated with all-cause or cause-specific mortality.

Animal data:

- Reported adverse effects include myeloid hyperplasia of the bone marrow, splenic extra-medullary haematopoiesis, decreases in hematologic parameters and mammary tumours; reported in rats starting at 25 mg/kg/d
- NOAEL (non-cancer effects): 3.5 mg/kg/d; 2 yr feeding study in rats; increased incidence of mammary gland carcinoma and fibroadenoma ≥3.5 mg/kg/d; known species and strain specific response with unknown relevance to humans
- NOEL: 50 ppm (3.3 mg/kg/d; SD rats; 6 mo feeding study); oestrous cycling; bw changes
  - SD rats considered sensitive species
- LD_{50}: >2,000 mg/kg (rats, dermal); 7,550 mg/kg (rabbits, dermal)
- NOAEL: 100 mg/kg/d in a 21 d dermal study in rabbits (max dose: 1,000 mg/kg/d)
- Not irritation to eyes and skin in rabbits (no further information)
- No dermal sensitisation to guinea pigs.

Using the NOEL of 3.3 mg/kg/d in rats as the point of departure and converting to 70 kg human, breathing 10 m^3, 8 h shift, with 100% absorption = 23.1 mg/m^3. Although not reported, it is assumed an uncertainty factor of 10 has then been applied to derive the TLV-TWA of 2.0 mg/m^3 (rounded).

DFG	***2013***	***TWA: 1 mg/m^3***

MAK derived from a study in rats observing changes in the oestrus cycle and a decrease in luteinizing hormone (LH) peaks.

Summary of additional data:

- NOAEL in rats of 1.8 mg/kg/d for change in oestrus cycle and decrease in LH peak (26 wk feeding study) used as starting point
- Inhaled concentration = (oral dose (OD) x oral absorption in animal (%) x 70 kg human body weight) / (species-specific correction factor x 100% inhalation absorption in humans x 10 m^3)
  - where: OD = 1.8 mg/kg/d; oral absorption = 80%; DFG designated species specific correction factor for rats = 4
  - considers animal continuous 7 d exposure to 5 d exposure (7÷5=1.4)
  - based on the above inhaled concentration = 3.5 mg/m^3
  - 3.5 mg/m^3 is halved to account for NOAEL in animals, divided by 1.4 for duration of exposure and rounded to a TWA of 1 mg/m^3

Source	Year set	Standard
• Negative results in most genotoxicity tests and not considered genotoxic for mammals • Reported low skin absorption • Experimental and observational studies insufficient to assign sensitising notations.		
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
APVMA	✓	2008	• Stated that JMPR (2007) reported a NOAEL from a wide range of toxicity studies of 1.8 mg/kg/d (no further information) • Reported a NOEL for Australia of 0.5 mg/kg/d mammary tumour incidence (rats; 2 yr) ○ not considered to be relevant to human health.
US EPA	✓	1993	• No additional information.

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	Sen.
HCIS	Skin sensitisation – category 1
NICNAS	NA
EU Annex	—
ECHA	—
ACGIH	Carcinogenicity – A3
DFG	—
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3

Source	Notations
US NIOSH	—

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:	yes
Dermal LD_{50}/Inhalation LD_{50} <10:	
In vivo 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:	215.68
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.

Australian Pesticides & Veterinary Medicines Authority (APVMA) (2008) Atrazine Final review report and regulatory decision.

Deutsche Forschungsgemeinschaft (DFG) (2013) Atrazine – MAK value documentation in German language.

International Agency for Research on Cancer (IARC) (1999) Atrazine. IARC Monographs on the evaluation of carcinogenic risk to humans.

US Environmental Protection Agency (US EPA) (1993) Atrazine: Integrated Risk Information System (IRIS) Chemical Assessment Summary.