# PICLORAM

**CAS number:** 1918-02-1

**Synonyms:** 4-Amino-3,5,6-trichloropicolinic acid, Amdon®, Borolin®, Tordon®

**Chemical formula:** $C_6H_3Cl_3N_2O_2$

**Structural formula:** —

### Workplace exposure standard (retained)

**TWA:** **10 mg/m³**

**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 10 mg/m³ is recommended to protect for possible effects on the liver and kidneys in exposed workers.

## Discussion and conclusions

Picloram is a herbicide used for control of woody plants and broadleaf weeds.

Critical effects of exposure are toxicity of the liver and kidneys. Low acute toxicity in rodents, dogs and cattle.

No inhalational data are available. No effects reported in volunteers ingesting 0.5 or 5 mg/kg (duration and number of doses not provided) in the limited human toxicological data available (ACGIH, 2018). In animals, picloram is considered of low acute toxicity. The primary adverse effect in rats and dogs from sub-chronic feeding studies is renal changes and increased liver weights in rats fed 225 mg/kg/day. A NOAEL of 7 mg/kg/day is derived from a six-month feeding study in male and female dogs (ACGIH, 2018). Results of carcinogenicity testing in rodents is equivocal. Increase in pituitary and adrenal neoplasia in rats is unreliable due to potential cross-contamination (ACGIH, 2018; NTP, 1978). Based on hepatocellular hypertrophy and increased liver weights, a NOAEL of 20 mg/kg/day is derived from a chronic study in rats (ACGIH, 2018).

In the absence of inhalation data, the NOAEL of 20 mg/kg/day in rats is extrapolated to an equivalent inhalational concentration of approximately 47 mg/m³. The TWA of 10 mg/m³ by ACGIH is recommended to be retained and is expected to be protective of liver and kidney effects reported in animals.

## 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: 10 mg/m$^3$*** |
| | | |
| ***ACGIH*** | ***2001*** | ***TLV-TWA: 10 mg/m$^3$*** |

TLV-TWA recommended to minimise the potential for liver and kidney effects.

No derivation of TLV-TWA presented.

Summary of data:

Human data:

- No adverse effects reported in 6 male volunteers ingesting 0.5 or 5 mg/kg:
  - 76% of dose excreted in urine unchanged within 6 h ($t_{1/2}$= 2.9 h)
- No evidence of skin sensitisation following application of 5% aqueous solution on volunteers.

Animal data:

- Low acute toxicity in rodents, dogs and cattle
- Acute NOAEL: 400 mg/kg/d (7 d) and 200 mg/kg/d (14 d) in female dogs:
  - highest dose (1,600 mg/kg/d) induced vomiting and weight loss
- Sub-chronic NOAEL: 50 mg/kg/d (male and female rats, in feed for 13 wk) and 7 mg/kg/d (male and female dogs, in feed for 6 mo) based on increased liver weight
- Chronic NOAEL: 20 mg/kg/d (rats, in feed for 2 yr) based on hepatocellular hypertrophy and increased liver weight, doses of 0, 20, 60 or 200 mg/kg/d
- Moderate changes in liver and kidneys (no further information) and slightly reduced bw gains in female rats fed 225 mg/kg/d (90 d)
- Dogs administered ≤150 mg/kg/d in diet (duration not stated) did not display treatment-related changes
- 2 yr feeding study in male and female rats and mice, doses up to 723 mg/kg/d, did not provide evidence of carcinogenicity in mice or male rats:
  - equivocal evidence in female rats (statistically significant increase in benign liver tumours)
- Findings of increase in pituitary and adrenal neoplasia in male and female rats at 7,437 and 14,875 ppm:
  - questioned by US NTP as cross-contamination may have occurred
- Increased incidence of tumours of the spleen in male mice fed 5,062 ppm (lifetime study)
- No evidence of mutagenicity in *S. typhimurium* (in presence or absence of activating system) or AP72 bacteriophage
- Picloram assays in *S. coelicolor* suggestive of a forward spot mutation
- Negative results for mutagenicity in bone marrow of male and female rats fed up to 2,000 mg/kg/d.

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

| 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 | • $LD_{50}$: >4,000 mg/kg body weight (rabbits, dermal)<br>• No abnormal chromosome numbers induced in *D. melanogaster*, and chromosomal aberrations not induced in human lymphocytes or mouse bone marrow cells *in vivo*. |
| NICNAS | × | | • Tier I for agriculture use. |
| NTP | ✓ | 1978 | • Report on carcinogenicity studies cited in ACGIH (2001); results equivocal. |
| US EPA | ✓ | 1987 | • No additional information. |
| US NIOSH | ✓ | 2007 | • No established REL<br>• PEL=15 mg/m$^3$ (TWA, total dust) and 5 mg/m$^3$ (TWA, respirable dust). |

### 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 | NA |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | NA |

| Source | Notations |
|---|---|
| ACGIH | Carcinogenicity – A4 |
| DFG | NA |
| 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: | |
| 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? No

## Additional information

| | |
|---|---|
| Molecular weight: | 241.46 |
| 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.

International Agency for Research on Cancer (IARC) (1991) Picloram. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Toxicology Program (NTP) (1978) US National Cancer Institute: Bioassay of Picloram for Possible Carcinogenicity – Technical Report Series No. 23.

US Environmental Protection Authority (US EPA) (1987) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Picloram.

US National Institute for Occupational Safety and Health (NIOSH) (2007) NIOSH Pocket Guide To Chemical Hazards – Picloram.