### **Picloram**

#### Guideline

The interim maximum acceptable concentration (IMAC) for picloram in drinking water is 0.19 mg/L (190 µg/L).

## Identity, Use and Sources in the Environment

Picloram (Tordon) is a chloropicolinic acid-derived herbicide used in moderate quantities in Canada (50 000 to 100 000 kg in 1986) for the control of woody plants and broadleaf weeds on rights-of-way, rangelands, pastures and non-crop areas and, to a smaller extent, for the control of weeds in barley crops in the Prairie provinces.<sup>1</sup> It is used in one of five forms: the isooctyl ester, potassium salt, alkanolamine salt, diethanolamine salt and triisopropanolamine salt.<sup>2</sup>

Its solubility in water is 430 mg/L at 25°C, and its salts are highly soluble. Its vapour pressure is very low,  $8.3 \times 10^{-5}$  Pa at 35°C. Its log octanol–water partition coefficient is very low, and it is not bioconcentrated in animals.<sup>2</sup> Picloram is stable in acidic and basic soils. It does not hydrolyse in water. It is degraded by ultraviolet light and sunlight on soil surfaces or in shallow aqueous solutions within a few days to a few weeks.<sup>2</sup>

Microbial degradation of picloram is very slow in water and in soil. Under optimum conditions of heat and moisture, the half-life in soil may be as short as 30 days; under cooler Canadian conditions, however, decomposition is very slow, and the half-life in soil may be as long as 400 days, with significant quantities remaining after two or more years.<sup>2</sup> Picloram has a low dissociation constant (pK<sub>a</sub>) of 3.6. It has, consequently, little absorptive capacity in most soils over pH 4 and is highly mobile in soils, particularly in sandy soils low in organic content.<sup>2</sup> Picloram was considered a Priority A chemical for potential groundwater contamination by the U.S. Environmental Protection Agency<sup>3</sup> and ranked first of 52 chemicals in the Agriculture Canada priority scheme for potential groundwater contaminants.<sup>4</sup>

### **Exposure**

Despite its persistence and mobility in soils, picloram has been detected infrequently in surface water and groundwater in four provinces in Canada.<sup>5</sup> One positive sample was found in Ontario and two were found in Quebec, but no concentrations were reported.5 Picloram was not detected (detection limit 0.1 µg/L) in raw or treated water from 13 municipalities in Ontario during 1985.6 A maximum concentration of 17 µg/L was recorded in wells near a dump site in New Brunswick.<sup>5</sup> Additional monitoring is required in surface water and farm wells on the Prairies, the area of highest use. In a 1979 analysis of types of farm well contamination arising from pesticide use, picloram was the only pesticide found to contaminate wells by subterranean movement as a result of normal use of the herbicide rather than through drift, runoff, poor well construction, back siphoning or direct spills. In one shallow well, the concentration rose from 0 to 1.5 µg/L 287 days after use in a field some distance from the well. A maximum concentration of 11 µg/L was reached 333 days after use.7

In a national survey in the United States, picloram was found in 359 of 653 surface water samples and in five of 77 groundwater samples. The maximum concentration found was 4.6  $\mu$ g/L in surface water and 1.0  $\mu$ g/L in groundwater. Eighty-five percent of all values were below 0.13 and 1.0  $\mu$ g/L in surface water and groundwater, respectively.<sup>8</sup>

The theoretical maximum dietary intake of picloram is estimated to be negligible—only 0.02 µg per person per day for an adult Canadian, based on negligible residues (0.1 mg/kg) in barley. Wild fruits that had been sprayed accidentally during right-of-way and forestry clearance spraying contained residues above 0.5 mg/kg if sprayed at the time of fruiting. It was estimated that about 0.3% of the wild fruit harvest in Ontario is sprayed with various herbicides, and less than half (0.15%) is treated with picloram at the time of fruiting. No information was available on actual residues in foods in either Canada or the United States.

# Analytical Methods and Treatment Technology

Picloram may be monitored in water by methods suitable for chlorinated acid pesticides, using gas or gas–liquid chromatography and electron capture detection. Resulting 10 Detection limits reported in several monitoring studies in Ontario and Alberta were between 0.01 and 0.3  $\mu$ g/L, with 0.1  $\mu$ g/L the most commonly reported value. Self-11.12

No information was available on techniques for removal of picloram from drinking water. However, picloram is strongly adsorbed on acid organic substances such as peat moss and on activated charcoal, and it is likely that a useful method could be derived for its removal from water supplies.<sup>2</sup>

#### **Health Effects**

Absorption of picloram through the gastrointestinal tract is rapid and almost complete. In human volunteers, the absorption half-time was 20 minutes. After oral administration of 5 and 0.5 mg/kg bw radiolabelled doses, concentrations in the blood were proportional to the dose administered and were highest during the first hour. Picloram was rapidly excreted unchanged in the urine. Most of the dose (77 to 86%) was excreted within the first six hours, and 94% of the dose was recovered after 72 hours. Dermal absorption was much slower, with a half-time of 12 hours, and only 0.2% of the applied dose was absorbed. The patterns of absorption and excretion were similar in the rat. After the application of the similar in the rat.

The acute toxicity of picloram is relatively low, with oral  $\rm LD_{50}$  values in the range 2000 to 8000 mg/kg bw for the rabbit, mouse, guinea pig and rat.<sup>2</sup> The potassium salt of picloram appeared to be somewhat more toxic, with oral  $\rm LD_{50}$  values in the range 600 to 1000 mg/kg bw for the rat.<sup>16</sup> No reports on picloram poisoning in humans were found.

The principal target organ for the toxicity of picloram is the liver; effects on the kidney occur at higher doses. In short-term and subchronic feeding studies on rats, dose-related elevations in liver/body weight ratios and histopathological changes (slight centrilobular hypertrophy) were observed. No-observedadverse-effect levels (NOAELs) for effects on the liver were 200 and 50 mg/kg bw per day in 14- and 90-day studies, respectively. Increases in kidney weights and kidney/body weight ratios were noted at 2000 and 300 mg/kg bw per day in the 14- and 90-day studies, respectively.<sup>17</sup> NOAELs following administration of the potassium salt of picloram to rats via drinking water were 190 and 60 mg/kg bw per day in 14- and 90-day studies, respectively. 16 The only changes noted in the 14-day study were decreases in liver enzymes (SGPT and SGOT) and a dose-related trend to decreased liver weight in males. In the 90-day study, histopathological

changes, including hepatocytic hypertrophy and an increased incidence of foci of mononuclear cells, were noted in the liver, and lesions of the tubular epithelium were seen in the kidney.

In subchronic six- and 12-month studies on Fischer 344 rats, increases in absolute and relative liver weights accompanied by changes in liver enzymes occurred at 60 mg/kg bw per day and above. Increases in relative kidney weights accompanied by slight increases in pigmentation of the convoluted tubule occurred at 200 mg/kg bw per day. The NOAEL for both studies was 20 mg/kg bw per day. <sup>17</sup> In a six-month feeding study in dogs, the NOAEL was 7 mg/kg bw per day, based on increased liver weights seen at the next highest dose, 35 mg/kg bw per day. <sup>18</sup>

Chronic bioassays were conducted in Osborne-Mendel rats and B6C3F<sub>1</sub> mice by the National Cancer Institute (NCI). No treatment-related tumours were found in mice of either sex or in male rats. The results were equivocal in female rats. A statistically significant increase in hepatic benign tumours and a dose-related trend to neoplastic changes in the thyroid were observed.<sup>19</sup> In a review of this study under the National Toxicology Program, the relationship between the appearance of tumours and treatment with picloram was questioned because of the small number of matched controls, unverified pathology, impurities in the test substance<sup>19</sup> and concurrent exposure to known carcinogens in the same room, leading to the possibility of cross-contamination.8 It was concluded that the results were suggestive of the ability of picloram to induce benign liver tumours, but that the bioassay needed to be repeated. 19

A two-year bioassay on Fischer 344 rats, the continuation of the 12-month study reported by Gorzinsky, <sup>17</sup> has recently been completed. <sup>20</sup> Fifty rats per sex per dose were administered picloram in the diet at 0, 20, 60 or 200 mg/kg bw per day. Parameters monitored included survival, body and organ weights, clinical chemistry, urinalysis, haematology, gross pathology and histopathology of 43 selected tissues. Increased mortality and reduced body weights were observed in males at the high dose level. Changes in the liver and kidney were similar to those observed at six and 12 months, <sup>17</sup> and there was no progression with continued dietary exposure. No neoplastic changes in liver or thyroid were observed in this assay, in contrast to the 1978 NCI assay. 19 The NOAEL was 20 mg/kg bw per day, based on increased liver and kidney weights, slight histopathological changes in liver and kidney and some changes in clinical chemistry parameters. 21,22

Picloram has not been found to be genotoxic in a battery of short-term tests, *in vitro* and *in vivo*, with microbes and with mammalian systems. Tests included Ames-type tests, <sup>23,24</sup> a recessive lethal test in

*Drosophila*, <sup>22</sup> chromosome aberration and sister chromatid exchange tests on CHO cells, <sup>25</sup> unscheduled DNA synthesis and DNA alkylation tests <sup>26</sup> and a mouse bone marrow micronucleus test. <sup>22</sup>

A mutagenic response was found in one assay on *Streptomyces coelicolor*,<sup>23</sup> but the biological significance of this observation is not known, as the assay has not been validated.

Picloram did not affect reproduction and was not teratogenic or foetotoxic in rats at doses up to 1000 mg/kg bw per day.<sup>27</sup> In rabbits, effects on organ weights were seen in the dams at 200 and 400 mg/kg bw per day, with a NOAEL of 40 mg/kg bw per day. There were no treatment-related effects on the foetuses.<sup>28</sup>

#### **Rationale**

Based on the two-year rat feeding/oncogenicity study reported in 1986,<sup>20</sup> negligible daily intake (NDI) was established by the Food Directorate of the Department of National Health and Welfare, as follows:<sup>21</sup>

$$NDI = \frac{20 \text{ mg/kg bw per day}}{1000} = 0.02 \text{ mg/kg bw per day}$$

#### where:

- 20 mg/kg bw per day is the NOAEL observed for changes in liver and body weights and some changes in clinical chemistry parameters<sup>20,22</sup>
- 1000 is the uncertainty factor (×10 for interspecies variation; ×10 for intraspecies variation; ×10 because of deficiencies in the data base, which lacked longer-term studies on a non-rodent species [dog] and a mammalian point mutation study)<sup>21</sup> (tests for carcinogenicity were negative in an adequate bioassay on the rat and in a less-well-conducted study on the mouse, and short-term tests supported these results).

The interim maximum acceptable concentration (IMAC) is derived as follows:

IMAC = 
$$\frac{0.02 \text{ mg/kg bw per day} \times 70 \text{ kg bw} \times 0.20}{1.5 \text{ L/d}} \approx 0.19 \text{ mg/L}$$

#### where:

- 0.02 mg/kg bw per day is the NDI, as derived above
- 70 kg bw is the average body weight of an adult
- 0.20 is the proportion of daily intake of picloram arbitrarily assigned to water (although residues in Canadian food are negligible, this apportionment would allow for additional intake from food should tolerances be set in future)
- 1.5 L/d is the average daily consumption of drinking water for an adult.

This value will remain an interim value until the appropriate studies have been completed and a full ADI established.

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