

# Bendiocarb

## Guideline

*The maximum acceptable concentration (MAC) for bendiocarb in drinking water is 0.04 mg/L (40 µg/L).*

## Identity, Use and Sources in the Environment

Bendiocarb ( $C_{11}H_{13}NO_4$ ) is a carbamate insecticide used in the control of a variety of insects in residences, public health areas, food storage and handling premises and industrial facilities. It is also used in agriculture as a seed treatment and to control soil and foliar pests. Less than 5000 kg are used annually in Canada.<sup>1</sup> Bendiocarb has a vapour pressure of  $6.7 \times 10^{-4}$  Pa at 25°C; its solubility in water is 40 mg/L at 25°C.<sup>2</sup>

Bendiocarb is relatively stable in acidic aqueous systems; its half-life at pH 5 is 48 days. At pH 7, the half-life decreases to 81 hours. Under alkaline conditions, bendiocarb is readily hydrolysed, with a half-life of 45 minutes at pH 9. The extent to which bendiocarb leaches through the soil is inversely proportional to the organic matter content of the soil. The half-life in soil decreases with soil pH; half-lives of 10 and 58 days have been reported for soils of pH 2.2 and 5.2, respectively. Bendiocarb is degraded in soil to NC 7312 (2,2-dimethyl-1,3-benzodioxol-4-ol), a phenol that is much less likely to leach significantly.<sup>2</sup>

## Exposure

No data have been identified regarding levels of bendiocarb in Canadian drinking water, surface water or the foods comprising the daily diets of Canadians.

## Analytical Methods and Treatment Technology

The concentration of bendiocarb in water may be determined by adjustment of the pH to between 3 and 4, extraction with dichloromethane, derivatization, cleanup with silica gel, separation by gas-liquid chromatography and determination by electron capture detection.<sup>3</sup>

No information was identified on the effectiveness of currently available treatment technologies in removing bendiocarb from drinking water supplies.

## Health Effects

Bendiocarb is readily absorbed by the gastrointestinal tract and is rapidly metabolized. The principal route of excretion is urinary, as conjugates of NC 7312; minor amounts appear in the faeces. Over 99% of an orally administered dose of 9.8 mg bendiocarb was excreted in 22 hours in the urine of a human volunteer, with a plasma half-life and a half-life for renal elimination of 3.5 and 3.3 hours, respectively.<sup>4</sup> Between 85 and 90% of doses of radioactively labelled bendiocarb administered to experimental animals were eliminated in 24 hours in mice,<sup>5,6</sup> rats,<sup>7</sup> hamsters<sup>8</sup> and rabbits.<sup>9</sup>

No adverse effects were reported in three human volunteers administered a single oral dose of 0.004 mg/kg bw of bendiocarb as 80% wettable powder. Seventy-two hours later, the same volunteers were given an oral dose of 0.12 mg/kg bw of bendiocarb. There was a transient 21% depression in whole blood cholinesterase in one of the three subjects. A 60-year-old man was administered serial doses of 0.004, 0.012, 0.037, 0.125, 0.187 and 0.25 mg/kg bw (as wettable powder) with a minimum of 48 hours between doses. At 0.25 mg/kg bw, mild vertigo, nausea and vomiting were reported, along with a significant inhibition (30 to 40%) of whole blood cholinesterase, which returned to normal after four hours. No adverse symptoms or cholinesterase inhibition were noted at 0.125 mg/kg bw or when the same subject was administered repeated doses of 0.125 mg/kg bw with an interval of four hours between doses. The no-observed-adverse-effect level (NOAEL) was considered to be 0.125 mg/kg bw.<sup>10</sup>

Groups of CFY rats (60 male and 120 female controls, 30 males and 60 females in treated groups) were fed diets containing 0, 2 (increased to 10 after two weeks), 20 or 200 ppm bendiocarb for two years. In animals in the highest dose group, there were significant changes in several haematological and biochemical parameters, including total white blood cells, neutrophil and lymphocyte counts, levels of serum cholesterol and total protein. There was a significant dose-dependent increase in the incidence of opacities in the lenses of

males in both the 20 and 200 ppm dose groups. No significant effects on cholinesterase activity were observed at 20 ppm, whereas cholinesterase levels in the brain were significantly depressed (>20%) at 200 ppm. The lowest dose level, 2 to 10 ppm (considered to be equivalent to 0.38 mg/kg bw per day), was reported as the “marginal NOAEL.”<sup>11</sup>

There was no significant difference in the incidence of tumours between the control and treated groups in a carcinogenicity bioassay in which groups of Swiss CD-1 mice (50 per sex per group) were fed diets containing 50, 250 or 1250 ppm of technical-grade bendiocarb. The authors concluded that bendiocarb was not carcinogenic in mice.<sup>12</sup> In the two-year study in CFY rats, an increase in total lymphoreticular tumours was reported in the highest dose group (200 ppm), although the frequency of any single type of tumour was not significantly increased in any treated group. Because of what the reviewers considered to be a high incidence of spontaneous tumours in the control group and a low survival rate, the results of this study were deemed to be inconclusive with respect to carcinogenicity.<sup>11</sup> A more recent review of historical control data and statistical analysis of incidence of lymphoreticular tumours indicated that the differences between control and treated groups provided insufficient evidence of a treatment-related effect on tumorigenicity.<sup>13</sup>

Bendiocarb was not mutagenic in several bacterial test systems. Negative results for mutagenicity were also found in mammalian tests *in vivo* and *in vitro*.<sup>2</sup>

In a three-generation reproductive study in Charles River CD rats, the no-effect levels of bendiocarb administered in the diet were considered to be 10 and 50 ppm (equivalent to doses of 0.6 and 3 mg/kg bw per day, respectively) for reproductive effects (irregular oestrous cycle) and teratogenic effects (generalized subcutaneous oedema, uni/bilateral hydronephrosis and bilateral ureter, incomplete cranial ossification and subcutaneous scapular haemorrhage), respectively.<sup>14</sup> Other reported NOAELs for reproductive effects in rats are 400 ppm<sup>15</sup> and 200 ppm.<sup>16</sup> Observed toxic effects included decreased maternal body weight gain, lower pup weight at birth and depressed survival and weight gain of pups. No teratogenic effects were observed in the fetuses of Sprague-Dawley rats administered doses of bendiocarb of 0, 0.25, 1.0 or 4.0 mg/kg bw by gastric intubation.<sup>17</sup> In a teratological study in New Zealand white rabbits, there was a dose-related increase in the incidence of eye anomalies and missing pubic bones at maternal doses of 2.5 mg/kg bw per day and above.<sup>18</sup>

## Rationale

The acceptable daily intake (ADI) of bendiocarb has been derived by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO)<sup>13</sup> as follows:

$$ADI = \frac{0.38 \text{ mg/kg bw per day}}{100} \approx 0.004 \text{ mg/kg bw per day}$$

where:

- 38 mg/kg bw per day is considered to be the NOAEL in a two-year study in CFY rats<sup>11</sup>
- 100 is the uncertainty factor.

Based on the above ADI, the maximum acceptable concentration (MAC) for bendiocarb in drinking water is derived as follows:

$$MAC = \frac{0.004 \text{ mg/kg bw per day} \times 70 \text{ kg bw} \times 0.20}{1.5 \text{ L/d}} \approx 0.04 \text{ mg/L}$$

where:

- 0.004 mg/kg bw per day is the ADI derived by the FAO/WHO
- 70 kg bw is the average body weight of an adult
- 0.20 is the proportion of daily intake of bendiocarb allocated to drinking water
- 1.5 L/d is the average daily consumption of drinking water by an adult.

## References

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