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SUBJECT: Update of PHG - Bentazon

Under the Calderon-Sher California Safe Drinking Water Act of 1996, the Office of Environmental Health Hazard Assessment (OEHHA) develops public health goals (PHGs) for regulated chemicals in drinking water and reviews and updates the risk assessments every five years (Health and Safety Code Section 116365(e)(1). This memorandum represents an update of the literature review and evaluation for the existing PHG for bentazon (OEHHA, 1999). Our re-evaluation supports the previous PHG derivation in 1999, and no new data would justify a significant change to the document.

Summary of review

Bentazon is also known by its trade name Basagran. The Public Health Goal (PHG) of 200 ppb (0.2 mg/L) for bentazon was developed by OEHHA and published in February 1999. Bentazon is a post-emergence herbicide used for selective control of broadleaf weeds and sedges in food and feed crops by contact action. Main crops treated with bentazon include alfalfa, beans, corn, peanuts, peas, asparagus, cereals, peppers, peppermint, rice, and sorghum. The

PHG of bentazon is based on a No-Observed-Adverse-Effect Level (NOAEL) of 3.2 mg/kg-day derived from a chronic dog dietary exposure study. The NOAEL was based on several observed noncarcinogenic effects, signs of clinical toxicity, hematological changes suggestive of anemia, and decreased body weight gain. The U.S. Environmental Protection Agency has not established a Maximum Contaminant Level (MCL) for bentazon. The California MCL for bentazon is 18 ppb, which was established in 1989. This level was based on a 1988 Proposed Maximum Contaminant Level derived by the Hazard Evaluation Section of the Department of Health Services (currently OEHHA), based on a less complete toxicological database for bentazon than was available for our 1999 review.

Relevant findings since PHG development

Very few new toxicity studies were found in the current literature review. Garagna *et al.* (2005) studied the effect of bentazon on spermatogenesis in mice exposed to 30 µg/L (parts per billion) bentazon in drinking water. Experimental groups consisted of: 1) adult (3-months old) male mice exposed through drinking water for 100 days; 2) male mice exposed in utero, through mother's milk, and through drinking water for 100 days after birth.

Histopathological analysis of testes of treated animals in both groups showed that the frequency of defective tubules was comparable to that found in control groups. The cell associations of the 12 stages of the seminiferous epithelium were correct as well as the architecture of the epithelium. The spermatocyte/spermatid ratio was the same as in controls. However, the authors reported that the frequency of stages VII, IX, and XII of the cycle of the seminiferous epithelium of adult mice and of stages I, III, and VII of mice exposed in utero and for 100 days after birth was different compared to the control mice. Sperm number and morphology were not affected by the treatment. Bentazon showed no genotoxic effects on spermatozoa, pachytene spermatocytes, and bone marrow cells.

The possible significance of the reported epithelial changes and what type of mechanism could account for such changes, considering the very low exposure, is unclear. The approximate dose to adult male mice given bentazon at 30 µg/L in drinking water would be 0.007 mg/kg-day ((0.03 mg/L x 0.007 L/day)/0.03 kg). In an earlier chronic study, the NOAEL for testicular effects (calcification) in mice was 100 ppm of bentazon in the diet, resulting in a dose of 12 mg/kg-day (Tajima *et al.,* 1984). Therefore, the results of Garagna *et al*. appear to be either spurious or simply uninterpretable.

A genotoxicity evaluation in *Drosophila melanogaster* reported positive results for bentazon genotoxicity in the wing spot test in a sensitive strain (a high-bioactivation cross) but not in the standard fruit fly strain (Kaya *et al*., 2004). This limited result does not change the overall conclusion of no evidence of genotoxic potential in humans.

An evaluation of immunotoxicity of pesticides on sheep leukocytes *in vitro* showed positive effects for bentazon at 0.1 to 10 mM (decreased lymphocyte activation) and at 100 mM (decreased spontaneous migration of leukocytes) (Pistl *et al*., 2003). Effects at these very high concentrations *in vitro* do not indicate a concern at the present low regulatory levels.

Finally, two human poisoning reports were published. Turcant *et al.* (2003) and Wu *et al.* (2008) note two deaths apparently caused by heart failure and renal failure, respectively, after large accidental or suicidal doses of bentazon. Turcant *et al.* estimated the dose causing lethality in an adult male as 240 g, while Wu *et al.* reported the dose in their case as 1764 mg/kg. These case reports do not affect the PHG.

Conclusion

The available new data do not indicate a need for revising the PHG level or the PHG document for bentazon. Because the California MCL is considerably lower than the current PHG level, we also see no need to revise the document based on the recommended changes in risk assessment methods (use of benchmark dose modeling, higher drinking water consumption values) since publication of the original review.

References:

Garagna, S, Vasco C, Merico V, Esposito A, Zucotti M, Redi CA (2005). Effects of a low dose of bentazon on spermatogenesis of mice exposed during foetal, postnatal and adult life. Toxicology 212:165-174.

Kaya B, Marcos R, Yanikoğlu A, Creus A (2004). Evaluation of the genotoxicity of four herbicides in the wing spot test of Drosophila melanogaster using two different strains. Mutat Res 557(1):53-62.

Pistl J, Kovalkovicová N, Holovská V, Legáth J, Mikula I (2003). Determination of the immunotoxic potential of pesticides on functional activity of sheep leukocytes in vitro. Toxicology. 188(1):73-81.

Tajima M, Takehara K, Shirasu Y, Itabashi M, Maruyama Y, Kudow S (1985). Studies on the 24-month chronic toxicity of Bentazone, Reg. No. 51,929 (ZNT No. 81/273) in mice.

Turcant A, Harry P, Cailleux A, Puech M, Bruhat C, Vicq N, Le Bouil A, Allain P (2003). Fatal acute poisoning by bentazon. J Anal Toxicol 27(2):113-7.

Wu IW, Wu MS, Lin JL (2008). Acute renal failure induced by bentazone: 2 case reports and a comprehensive review. J Nephrol 21(2):256-60.