

Office of Environmental Health Hazard Assessment



Linda S. Adams
Secretary for Environmental Protection

Joan E. Denton, Ph.D., Director

Headquarters • 1001 I Street • Sacramento, California 95814

Mailing Address: P.O. Box 4010 • Sacramento, California 95812-4010

Oakland Office • Mailing Address: 1515 Clay Street, 16th Floor • Oakland, California 94612



Arnold Schwarzenegger
Governor

MEMORANDUM

TO: Joan E. Denton, Ph.D.
Director

VIA: George V. Alexeeff, Ph.D.
Deputy Director for Scientific Affairs

VIA: Anna M. Fan, Ph.D., Chief
Pesticide and Environmental Toxicology Branch

VIA: Robert A. Howd, Ph.D., Chief
Water Toxicology Section
Pesticide and Environmental Toxicology Branch

FROM: Jolanta Bankowska, Ph.D.
Staff Toxicologist
Pesticide and Environmental Toxicology Branch

DATE: November 28, 2006

SUBJECT: UPDATE OF THE PUBLIC HEALTH GOAL FOR 1,3-DICHLOROPROPENE

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 reevaluation of the existing PHG for 1,3-dichloropropene, also known as Telone II[®] (OEHHA, 1999). Our re-evaluation supports the previous PHG derivation in 1999. We conclude that the PHG for 1,3-dichloropropene should remain at 0.2 parts per billion (ppb).

Summary of Review

We have surveyed the scientific literature for recently published research studies to determine if there are new toxicity studies that would warrant revising the PHG of 0.2 ppb or making substantive changes to the PHG support document. We also searched for new risk assessments of 1,3-dichloropropene since the publication of the PHG document in 1999, including U.S. EPA reviews, and new risk assessment methods that might be applied to evaluation of 1,3-dichloropropene.

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No new studies were found that affect the choice of the critical studies used as the basis for the existing PHG value. Risk assessment methods for consideration of the effect of early-life exposures on carcinogenic potency are under consideration, but OEHHA guidelines have not yet been developed. No new data were found that could provide any further important insight on the toxic effects of 1,3-dichloropropene, data that could change the existing approach to the PHG establishment and/or shed more light on carcinogenicity of this compound. The following sections provide brief summaries of the current status of health risk evaluations of 1,3-dichloropropene that are pertinent to the establishment of our PHG.

Chronic Toxicity

The lowest No-Observed-Adverse-Effect Level (NOAEL) of 2.5 mg/kg-day identified by OEHHA in 1999 still remains the most appropriate value for quantitative risk assessment of noncarcinogenic effects caused by 1,3-dichloropropene (OEHHA, 1999). This NOAEL was established in rats (Stott *et al.*, 1995), with support from studies in mice (Redmond *et al.*, 1995) and dogs (Stott *et al.*, 1992). The NOAEL in rats was based on a significant decrease in body weights and a dose-related increase in basal cell hyperplasia of the non-glandular stomach mucosa of both males and females at 12.5 and 25 mg/kg-day. The LOAEL identified in this study was 12.5 mg/kg-day. In mice, the LOAEL was 25 mg/kg-day based on decreased body weights and body weight gains in males and females. The LOAEL in the dog study was 15 mg/kg-day based on an increase in hematopoiesis in bone marrow and extramedullary hematopoiesis in the spleen, consistent with a regenerative response to hypochromic, microcytic anemia. The health-protective level based on noncarcinogenic effects resulting from chronic exposures to 1,3-dichloropropene is 90 ppb.

Carcinogenicity

Two-year animal bioassays demonstrate carcinogenicity of 1,3-dichloropropene. Feeding studies in rodents by Stott *et al.* (1995) showed an increase in the incidence of benign hepatocellular adenomas (with one hepatocarcinoma) in male rats at 25 mg/kg-day, the highest dose tested. No treatment-related tumors were observed in female rats or male or female mice fed up to 50 mg/kg-day (Stott *et al.*, 1995; Redmont *et al.*, 1995). However, the thrice weekly gavage study by NTP (1985) found significant incidences of bronchioalveolar, forestomach, and urinary bladder tumors in mice at 50 mg/kg and forestomach and liver tumors in rats at 25 mg/kg. With the exception of urinary bladder tumors in mice, most tumors were benign. In rats at 50 mg/kg, four carcinomas were observed in the forestomach and one was observed in the liver. In mice, eight carcinomas in the urinary bladder and three in bronchioalveolar areas were observed at 50 mg/kg, while two were found in the forestomach at 100 mg/kg. The microencapsulated 1,3-dichloropropene used in the study of Stott *et al.* (1995) did not contain

the 1% epichlorohydrin which was used as a stabilizer in the earlier NTP gavage study (U.S. EPA, 1998). Because epichlorohydrin caused hyperplasia, papillomas and carcinomas in the forestomach of rats in a drinking water study (Konishi *et al.*, 1980), it has been hypothesized that epichlorohydrin may be partially responsible for the squamous cell papillomas and carcinomas, at least in the rat forestomach. The chronic feeding study by Stott *et al.* (1995), which did not include epichlorohydrin, found forestomach hyperplasia in rats but no carcinomas or papillomas.

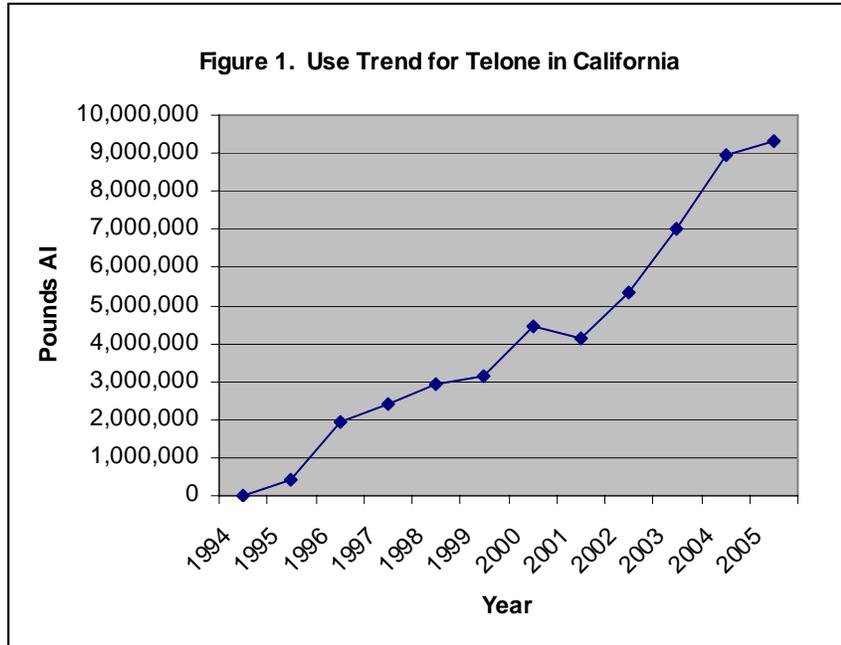
Mutagenic and Genetic Toxicology

The mutagenicity and genotoxicity of 1,3-dichloropropene have been studied in both *in vitro* and *in vivo* assays (U.S. EPA, 2000). Early bacterial studies found mutagenic activity for 1,3-dichloropropene in a variety of test systems in the absence of metabolic activation. Even though later studies showed that these findings were due to mutagenic impurities in the 1,3-dichloropropene formulations, purified 1,3-dichloropropene produced mutations in the presence of S9.

1,3-dichloropropene was found to be a relatively potent inducer of unscheduled DNA synthesis (UDS) in comparison to other tested allylic compounds (cis- >trans-1,3-dichloropropene) (Schiffmann *et al.*, 1983). 1,3-DCP exposure resulted in the induction of sister chromatid exchange *in vitro* in human lymphocytes with and without addition of a metabolic activation system (Kevekordes *et al.*, 1996).

Usage of Telone in California

The trend of increasing use (see figure 1) for 1,3-dichloropropene in California (Fan and Walters, 2005) as methyl bromide is phased out is likely to result in increasing exposures to this chemical in air. The possibility for groundwater contamination as use increases also should be considered, although in the most recent agricultural well sampling results, no 1,3-dichloropropene was detected (DPR, 2005a). The statewide total amount of 1,3-dichloropropene use doubled between the years 2000 and 2004, from 4.4 million lbs/year to over 8.9 million lbs/year. The use of 1,3-dichloropropene in California is controlled by a management plan (DPR, 2002) to limit the health risk from exposure, especially by the inhalation route. Air monitoring for this chemical was conducted in Ventura County in 2005, and may be continued in 2006 (DPR, 2005b).



Review of the Existing PHG Value

As stated in the 1999 PHG document for 1,3-dichloropropene, the critical concern is carcinogenicity, and the most important issue for the risk assessment is deriving the carcinogenic potency factor. At this time, no studies exist which would either change the carcinogenic determination or provide a basis for a revised potency factor. U.S. EPA does not currently regulate 1,3-dichloropropene in drinking water, but has established a Health Advisory level of 0.2 ppb, based on a 10^{-6} cancer risk (U.S. EPA, 1998). Establishment of the OEHHA PHG was also based on carcinogenicity, in the two oral studies (NTP 1985, Stott *et al.*, 1995). Our present review confirms this earlier determination.

After finalization of the new cancer guidelines (U.S. EPA, 2005a) and the supplemental guidance for early-life exposures (U.S. EPA, 2005b) by U.S. EPA, OEHHA is currently reviewing its procedures for assessing cancer potency, especially to ensure adequate protection of sensitive subpopulations. The U.S. EPA has proposed increasing cancer potency values that are based on animal studies which did not incorporate early-life exposures by specific amounts to allow for infant and child exposures to the chemicals (U.S. EPA, 2005b). This requires some judgment concerning how to apply the principles to specific types of chemicals in drinking water. Discussion of these factors is presently underway at OEHHA, and in the meantime, the traditional approach is being used. From the perspective of noncancer risk determinations, no new studies exist which would be more appropriate to replace the one selected for the noncancer assessment in the existing PHG document. For all these reasons,

OEHHA concludes that the PHG of 0.2 ppb is adequate to protect sensitive subpopulations, including pregnant women and their fetuses, infants, and the elderly.

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