Proposition 65 Maximum Allowable Dose Level (MADL) for Reproductive Toxicity for Disodium Cyanodithioimidocarbonate (DCDIC) for Oral Exposure

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Office of Environmental Health Hazard Assessment (OEHHA)
Reproductive and Cancer Hazard Assessment Section

Summary

The maximum allowable dose level (MADL) for disodium cyanodithioimidocarbonate (DCDIC) exposure is **56 micrograms/day (µg/day)** applicable to the oral route of exposure. Risk assessments for DCDIC use as a pesticide are usually based on the 32% pesticide formulation without correction for percent DCDIC. Thus for the 32% DCDIC pesticidal formulation, the MADL is **170 µg/day**. The MADL values were derived as described below, based on a rabbit developmental toxicity study (Rodwell 1988b).

Background

This report describes the derivation of a MADL for DCDIC (CAS No. 138-93-2).

DCDIC is a microbiocide used in water treatment systems, including food processing water systems. No pesticide use was reported in California in 2001 (CDPR 2002); uses in food processing water systems are not regulated by the California Department of Pesticide Regulation.

DCDIC is listed under Proposition 65 (the Safe Drinking Water and Toxic Enforcement Act of 1986) as known to the State to cause reproductive toxicity (developmental toxicity endpoint), effective March 30, 1999. The Proposition 65 listing of DCDIC was based on a formal identification by the U.S. Environmental Protection Agency (U.S. EPA) of DCDIC as causing developmental toxicity (U.S. EPA 1994a,b). U.S. EPA is an authoritative body under Proposition 65 for identification of chemicals as causing reproductive toxicity (Title 22, California Code of Regulations, §12306(*l*)).

Procedures for the development of Proposition 65 MADLs are provided in regulation (Title 22, Cal. Code of Regs. § 12801 and 12803). Exposure at a level 1,000 times greater than the MADL is expected to have no observable effect. As defined in regulations, a MADL is derived from a No Observable Effect Level (NOEL) based on the most sensitive study deemed to be of sufficient quality (Title 22, Cal. Code of Regs. §12803(a)(4)).

Study Selection

Relevant studies on the reproductive toxicity of DCDIC have been identified through literature searches. These studies have been reviewed and considered for the establishment of the MADL.

DCDIC has been tested for developmental toxicity in rats and rabbits as a registered pesticide. The pesticide registration studies in each of these species are the only relevant data for the development of the DCDIC MADL and meet the criteria specified in Title 22, California Code of Regulations, §12803. The pesticide formulation tested was 32% DCDIC by weight. It was produced by solution phase synthesis and is stable under the resulting alkaline conditions (pH 12).

Studies conducted for pesticide regulation consist of one rat and one rabbit developmental toxicology study performed in the same laboratory (Rodwell 1988a,b). In these two studies, the DCDIC product (32% DCDIC by weight) was diluted in water for administration by gavage on gd 6-15 in rats and gd 6-18 in rabbits. The doses were 0, 0.6, 1.9 and 5.8 mg DCDIC/kg-day in the rat study and 0, 0.96, 3.2 and 9.6 mg DCDIC /kg-day in the rabbit study. The major developmental effects were malformation at the highest dose in the rat and rabbit studies, and intrauterine mortality at the two higher doses in the rabbit study. Concurrent maternal toxicity in the rats and rabbits at the highest dose included neurotoxicity (loss of limb mobility) in both rats and rabbits and 10% maternal mortality in rabbits. The developmental NOEL for the rabbit study was 0.96 mg DCDIC /kg-day, while the LOEL of 3.2 mg DCDIC /kg-day resulted in a statistically significant decrease in implantation sites, a statistically significant increase in early resorptions and a reduction in the number of live fetuses per litter at term. Concurrent maternal toxicity included one dam that developed neurotoxicity and died. There was no maternal toxicity in the remaining 19 dams. The LOEL for the rat study was 1.9 mg DCDIC /kg-day, a higher level of exposure than the NOEL in the rabbit study.

Table 1. Developmental toxicity studies with DCDIC

Study	Species	Doses mg/kg-day (by gavage)[1] **NOEL**, LOEL	Fetal Effects at the LOEL	Maternal Effects at the LOEL
Rodwell 1988a	Rat S-D	0, 0.6, **1.9**, 5.8	Skeletal variations, ↓fetal body weight	↓ body weight neurologic
Rodwell 1988b	Rabbit NZW	0, **0.96**, 3.2, 9.6	Pre-implant loss Early resorption Malformation	Mortality, neurologic

abbreviations: S-D=Sprague-Dawley, NZW=New Zealand White, gd=gestation day

[1] doses are the amount of DCDIC administered and are calculated from the doses stated in the study for the pesticide product corrected for the percent DCDIC (32%)

The NOEL is based on the most sensitive study deemed to be of sufficient quality (Title 22, Cal. Code of Regs. § 12803(a)(4)). The studies that meet the criterion of sufficient quality are those by Rodwell (1998a,b). The most sensitive study is the rabbit study. The NOEL from the rabbit study, 0.96 mg/kg-day, was used for MADL development.

MADL Calculation

The NOEL is the highest dose level that results in no observable developmental effect, expressed in milligrams of chemical per kilogram of bodyweight per day (Title 22, Cal. Code of Regs. §12803(a)(1)). The NOEL is converted to a milligram per day dose level by multiplying the assumed human body weight by the NOEL (Title 22, Cal. Code of Regs. §12803(b)). The results obtained from the most sensitive study have been used.

NOEL = 0.96 mg/kg-day

When the applicable reproductive effect is upon the female or conceptus, human body weight of 58 kilograms is assumed.

0.96 mg/kg-day × 58 kg = 55.68 mg/day

The MADL is derived by dividing the NOEL by one thousand (1,000) to arrive at the maximum allowable dose level (Title 22 , Cal. Code of Regs. §12801(b)(1)). Thus, the adjusted NOEL is divided by 1,000 to obtain the MADL:

MADL = 55.68 mg/day ÷ 1000 = 55.68 µg/day = **56 µg/day** after rounding.

[For a pesticide formulation of 32% DCDIC, the **MADL** = 55.68 µg/day × 100 ÷ 32 = 174 = **170 µg/day** after rounding.]

The MADL of 56 µg/day DCDIC is applicable to exposure via oral, inhalation or dermal routes of exposure. If exposures occur by multiple (e.g. inhalation or dermal) routes, the total exposure to the chemical from a single source or product must be considered. If the total exposure resulting from any one or multiple routes is less than or equal to 56 µg/day, the MADL has not been exceeded.

References

California Department of Pesticide Regulation (CDPR 2002) Summary of Pesticide Use Report Data 2001 by Commodity. Available at http://cdpr.ca.gov.docs/pur.

Rodwell DE (1988a) Teratology study in rats with DCDIC. Springborn Life Sciences, Inc. Study No. 3138.23. Wareham, MA.

Rodwell DE (1988b) Teratology study in rabbits with DCDIC. Springborn Life Sciences, Inc. Study No. 3138.25. Wareham, MA.

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