

**SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986
PROPOSITION 65**

**INITIAL STATEMENT OF REASONS
TITLE 27, CALIFORNIA CODE OF REGULATIONS**

**PROPOSED AMENDMENTS TO
SECTION 25805(b), SPECIFIC REGULATORY LEVELS: CHEMICALS
CAUSING REPRODUCTIVE TOXICITY**

**MAXIMUM ALLOWABLE DOSE LEVELS (ORAL EXPOSURE) FOR
HYDROGEN CYANIDE AND CYANIDE SALTS**

PURPOSE AND BACKGROUND OF PROPOSED AMENDMENTS

PURPOSE

These proposed regulatory amendments are to adopt Maximum Allowable Dose Levels (MADLs) for oral exposure to hydrogen cyanide (HCN) and cyanide salts (CN salts) under Proposition 65¹ in Title 27, California Code of Regulations, section 25805(b)². They were derived using scientific methods outlined in Section 25803. The proposed oral MADL is 9.8 micrograms per day (expressed as cyanide) for cyanide salts that readily dissociate and release cyanide ion in solution. This corresponds to oral MADLs of 10 micrograms per day for hydrogen cyanide, 19 micrograms per day for sodium cyanide and 25 micrograms per day for potassium cyanide.

PROPOSITION 65 AND LISTING OF HCN AND CN SALTS

Proposition 65 was enacted as a ballot initiative on November 4, 1986. The Office of Environmental Health Hazard Assessment (OEHHA) within the California Environmental Protection Agency is the lead state entity responsible for the implementation of Proposition 65.³ OEHHA has the authority to adopt and amend regulations to further the purposes of the Act⁴. The Act requires businesses to provide a warning when they cause an exposure to a chemical

¹ The Safe Drinking Water and Toxic Enforcement Act of 1986, codified at Health and Safety Code section 25249.5 *et. seq.*, hereafter referred to as "Proposition 65" or "The Act".

² All subsequent citations are to Title 27, California Code of Regulations, unless otherwise noted.

³ Health and Safety Code section 25249.12 and Cal. Code of Regs., Title 27, section 25102(o)

⁴ Health and Safety Code, section 25249.12(a).

listed as known to the state to cause cancer or reproductive toxicity. The Act also prohibits the discharge of listed chemicals to sources of drinking water.

HCN and CN salts have been proposed for listing under Proposition 65 as known to the State to cause reproductive toxicity (male reproductive endpoint). The proposed listing is based on formal identification of HCN and CN salts by the U.S. Environmental Protection Agency (U.S. EPA) as causing male reproductive toxicity^{5,6}. The U.S. EPA is a body recognized as authoritative for the listing of chemicals as known to cause reproductive toxicity under Proposition 65 (Section 25306(l)).

The notice of intent to list HCN and CN salts under Proposition 65 has been issued concurrent with this regulatory proposal. OEHHA will adopt into regulation a final MADL for these compounds only if they are added to the Proposition 65 list as known to the State to cause reproductive toxicity.

STUDY SELECTION

To establish the scientific basis for the proposed regulation, OEHHA reviewed the studies identified in the U.S. EPA final reports that provide the basis for the proposed listing, and conducted a search for any other relevant studies published after the report was completed. No additional relevant studies were identified.

The U.S. EPA identified the male reproductive effects observed in adult rats by the National Toxicology Program (NTP)⁷ as the critical effects of HCN and CN salts. The study by NTP (1993) evaluated the toxicity of sodium cyanide (NaCN) in adult mice and rats following administration of NaCN via drinking water for 13 weeks. Male reproductive toxicity resulting from exposure to NaCN in drinking water was observed in both species, but the lowest observed effect level was lower in rats than mice. Hence, the study in rats is identified as the most

⁵ U.S. EPA (U.S. Environmental Protection Agency) (2010). Hydrogen Cyanide and Cyanide Salts (CASRN Various). Integrated Risk Information System. Available online at: <http://www.epa.gov/iris/subst/0060.htm>.

⁶ U.S. EPA (U.S. Environmental Protection Agency) (2010). Toxicological Review of Hydrogen Cyanide and Cyanide Salts (CASRN Various); In Support of Summary Information on the Integrated Risk Information System (IRIS). EPA/635/R-08/016F. U.S. EPA, Washington DC, September. Available online at: <http://www.epa.gov/iris/toxreviews/0060tr.pdf>.

⁷ NTP (National Toxicology Program). (1993). NTP technical report on toxicity studies of sodium cyanide (CAS No. 143-33-9) administered in drinking water to F344/N rats and B6C3F1 mice. NTP TR 37; NIH Publication 94-3386. Public Health Service, U.S. Department of Health and Human Services; NTP, Research Triangle Park, NC. Available online at http://ntp.niehs.nih.gov/ntp/htdocs/ST_rpts/tox037.pdf.

sensitive study. Major findings from the study in rats are briefly summarized below.

NTP (1993) treated seven groups of F344 rats, 10 male and 10 female animals per group, from six weeks old at the beginning of exposure, for 13 weeks with NaCN in drinking water at concentrations of 0, 3, 10, 30, 100 or 300 parts per million (ppm). NTP estimated the doses were equivalent to 0, 0.16, 0.48, 1.4, 4.5, and 12.5 milligrams per kilogram bodyweight per day (mg/kg-day) of CN⁻ in male rats and 0, 0.16, 0.53, 1.7, 4.9, and 12.5 mg/kg-day in female rats, respectively. Endpoints for male reproductive effects, including weights of the testis, epididymis, and cauda epididymis, counts of testicular spermatids, counts and motility of epididymal sperm, were evaluated only in rats exposed to 0 (control), 30, 100 or 300 ppm of NaCN in drinking water. Table 1 provides an overview of the data on the male reproductive effects of NaCN, based on the data reported by NTP and summarized by the U.S. EPA⁸.

Table 1. Male reproductive effects of NaCN in rats from the NTP 1993 study

NaCN level in H ₂ O (ppm)	0	30	100	300
Estimated CN ⁻ dose (mg/kg-day)	0	1.4	4.5	12.5
Body weights (g)	338±5	335±5	338±4	319±5*
Organ weights (g)				
Testis	1.58±0.03	1.56±0.02	1.52±0.02	1.46±0.02**
Epididymis	0.448±0.006	0.437±0.005	0.425±0.007	0.417±0.005**
Cauda epididymis	0.162±0.003	0.150±0.004*	0.148±0.004*	0.141±0.003**
Testicular spermatid counts				
10 ⁷ /gram of testicular tissue	11.35±0.38	10.88±0.53	10.92±0.37	10.57±0.33
10 ⁷ /testis	17.86±0.61	16.94±0.81	16.58±0.63	15.42±0.44*
Epididymal sperm parameters				
Concentration (10 ⁶ /gram cauda epididymal tissue)	615±42	684±40	699±33	709±45
Count (10 ⁶ /cauda epididymis)	99.4±6.8	102.9±7.5	102.8±4.9	99.4±5.8
Motility (% motile)	94.24±0.58	90.67±1.25*	92.09±0.85*	90.66±1.46*

Data reported as mean±SEM. *: statistically significant from control, p<0.05.

** : statistically significant from control, p<0.01.

As shown in Table 1, oral exposure to NaCN at estimated doses of ≥ 1.4 mg CN⁻ /kg-day for 13 weeks caused statistically significant reductions in the weight of cauda epididymis and the motility of epididymal sperm. Because

⁸ U.S. EPA (U.S. Environmental Protection Agency) (2010). Toxicological Review of Hydrogen Cyanide and Cyanide Salts (CASRN Various); In Support of Summary Information on the Integrated Risk Information System (IRIS). EPA/635/R-08/016F. U.S. EPA, Washington DC, September. Available online at: <http://www.epa.gov/iris/toxreviews/0060tr.pdf>.

male reproductive effects were not evaluated in groups exposed to lower doses of NaCN, the NTP study did not find a no observable effect level (NOEL). Among all the relevant studies available to OEHHA, the dose of 1.4 mg CN⁻/kg-day is the lowest dose of the cyanide ion that causes male reproductive effects resulting from oral exposure. This dose is thus identified by OEHHA as the lowest observable effect level (LOEL).

MADL CALCULATION

The following calculations were performed in accordance with Section 25803 to derive the oral MADL for HCN and CN salts that readily dissociate and release cyanide ion (CN⁻) in solution. The first step is to calculate an oral MADL for CN⁻:

- When data do not allow the determination of a NOEL, the LOEL in a study shall be divided by 10 to establish a NOEL for purposes of assessment (Section 25803(a)(8)).

$$1.4 \text{ mg CN/kg-day} \div 10 = 0.14 \text{ mg/kg-day}$$

- To calculate the NOEL dose as an intake, a 70 kg body weight for a man is assumed:

$$0.14 \text{ mg CN/kg-day} \times 70 \text{ kg} = 9.8 \text{ mg/day}$$

- The MADL is derived by dividing the NOEL by 1,000 (Section 25801(b)(1)). Thus, the adjusted NOEL was divided by 1,000 to obtain the MADL for cyanide:

$$\text{MADL}_{\text{oral}} = 9.8 \text{ mg CN/day} \div 1000 = \mathbf{9.8 \text{ micrograms CN/day}}$$

MADLs for HCN and some common cyanide salts are calculated by adjusting for the difference in molecular weights between the molecule to which exposure occurs and CN, which has a molecular weight (in atomic units) of 26.

$$\begin{aligned} \text{MADL}_{\text{oral}} \text{ for CN salt} &= 9.8 \times ([\text{molecular weight of CN salt}] / 26) \\ &= 0.38 \times \text{molecular weight of CN salt} \end{aligned}$$

Hydrogen cyanide: $\text{MADL}_{\text{oral}} = 27 \times 0.38 = \mathbf{10 \text{ micrograms/day}}$
(after rounding)

Sodium cyanide:	$MADL_{oral} = 49 \times 0.38 = 19$ micrograms/day (after rounding)
Potassium cyanide:	$MADL_{oral} = 65 \times 0.38 = 25$ micrograms/day (after rounding)

These MADLs apply to exposure by the oral route. For the purpose of Proposition 65, exposure by dermal contact or inhalation or via multiple routes that leads to an absorbed dose equivalent to that resulting from oral exposure at the MADL is the maximum allowable dose level.

PROPOSED REGULATORY AMENDMENTS

The proposed change to Section 25805(b) is provided below in underline:

<i>Chemical name</i>	<i>Level (micrograms per day)</i>
...	
<u>Cyanide Salts that readily dissociate in</u>	
<u> solution (expressed as cyanide)</u>	<u>9.8 (oral)</u>
<u>Hydrogen cyanide</u>	<u>10 (oral)</u>
<u>Sodium cyanide</u>	<u>19 (oral)</u>
<u>Potassium cyanide</u>	<u>25 (oral)</u>

PROBLEM BEING ADDRESSED BY THIS PROPOSED RULEMAKING

Proposition 65 does not provide guidance regarding how to determine whether a warning is required or a discharge is prohibited. OEHHA is the implementing agency for Proposition 65 and has the resources and expertise to examine the scientific literature and calculate a level of exposure, in this case a MADL, that does not require a warning or a discharge is not prohibited.

NECESSITY

If HCN and CN salts are added to the Proposition 65 list, these proposed regulatory amendments would adopt MADLs that conform with the Proposition 65 implementing regulations and reflect the currently available scientific knowledge about HCN and CN salts. MADLs provide assurance to the regulated community that exposures or discharges at or below them are considered not to pose a significant risk of developmental or reproductive harm. Exposures at or below

the MADLs are exempt from the warning and discharge requirements of Proposition 65⁹.

BENEFITS OF THE PROPOSED REGULATION

See “Benefits of the Proposed Regulation” under ECONOMIC IMPACT ANALYSIS below.

TECHNICAL, THEORETICAL, AND/OR EMPIRICAL STUDIES, REPORTS, OR DOCUMENTS

OEHHA reviewed the 2010 U.S. EPA Toxicological Review of Hydrogen Cyanide and Cyanide Salts and the 2010 U.S. EPA Updated Integrated Risk Information System (IRIS) entry for hydrogen cyanide and cyanide salts^{5,6}. OEHHA determined that the 13-week drinking water study by NTP, the most sensitive study identified by the U.S. EPA, was of sufficient quality as required by Section 25803(a)(5), and that there were no subsequently published studies that were more sensitive. OEHHA used the values from this study as the bases for calculating the oral MADLs for HCN and CN salts proposed for adoption into Section 25805(b). A copy of the 2010 U.S. EPA reports and the study by NTP (1993) will be included in the regulatory file for this action, and are available from OEHHA upon request. OEHHA relied on the attached Economic Impact Assessment in developing this proposed regulation.

REASONABLE ALTERNATIVES TO THE REGULATION AND THE AGENCY’S REASONS FOR REJECTING THOSE ALTERNATIVES

The MADLs provide “safe harbor” values that aid businesses in determining whether they are complying with the law. The alternative to the amendments to Section 25805(b) would be to not adopt a MADL for the chemical. Failure to adopt a MADL would leave the business community without a safe harbor level to assist in complying with Proposition 65.

REASONABLE ALTERNATIVES TO THE PROPOSED REGULATORY ACTION THAT WOULD LESSEN ANY ADVERSE IMPACT ON SMALL BUSINESSES

OEHHA is not aware of significant cost impacts that small businesses would incur in reasonable compliance with the proposed action. In addition, Proposition 65 is limited by its terms to businesses with 10 or more employees (Health and Safety Code, section 25249.11(b)), so it has no effect on very small businesses.

⁹ Health and Safety Code sections 25249.9(b) and 25249.10(c)

EVIDENCE SUPPORTING FINDING OF NO SIGNIFICANT ADVERSE ECONOMIC IMPACT ON BUSINESS

Because the proposed MADLs provide “safe harbor” levels for businesses to use when determining compliance with Proposition 65, OEHHA does not anticipate that the regulation would have a significant statewide adverse economic impact directly affecting businesses, including the ability of California businesses to compete with businesses in other states.

DUPLICATION OR CONFLICTS WITH FEDERAL REGULATIONS CONTAINED IN THE CODE OF FEDERAL REGULATIONS

Proposition 65 is a California law that has no federal counterpart. There are no federal regulations addressing the same issues and, thus, there is no duplication or conflict with federal regulations.

ECONOMIC IMPACT ANALYSIS**Gov. Code section 11346.3(b)**

It is not possible to quantify any monetary values for this proposed regulation because its use is entirely voluntary and it only provides compliance assistance for businesses subject to the Act.

Impact on the Creation, Elimination, or Expansion of Jobs/Businesses in California: This regulatory proposal will not affect the creation or elimination of jobs within the State of California. Proposition 65 requires businesses with ten or more employees to provide warnings when they expose people to chemicals that are known to cause cancer or reproductive harm. The law also prohibits the discharge of listed chemicals into sources of drinking water. HCN and CN salts are proposed for listing under Proposition 65; therefore, if HCN and CN salts are listed, businesses would have to provide a warning if their products or activities expose the public or employees to these chemicals.

Benefits of the Proposed Regulation: The MADLs provide “safe harbor” values that aid businesses in determining whether they are complying with the law. Some businesses may not be able to afford the expense of establishing or updating a MADL and therefore may be exposed to litigation for a failure to warn or for a prohibited discharge of the listed chemical. If HCN and CN salts are added to the Proposition 65 list, adopting this regulation will save these businesses those expenses and may reduce litigation costs. By adopting the MADLs, this regulatory proposal does not require, but may encourage, businesses to lower the amount of the listed chemicals in their products to a level that does not cause a significant exposure, thereby providing a public health benefit to Californians.

Problem being addressed by this proposed rulemaking: Proposition 65 does not provide specific guidance regarding how to determine whether a warning is required or a discharge is prohibited. OEHHA is the implementing agency for Proposition 65 and has the resources and expertise to examine the scientific literature and calculate a level of exposure that does not require a warning or trigger the discharge prohibition.

How the proposed regulation addresses the problem: The proposed regulation would adopt specific regulatory levels for HCN and CN salts to provide compliance assistance for businesses that are subject to the requirements of the Act. While OEHHA is not required to adopt such levels, adopting them provides

a “safe harbor” for businesses and provides certainty that they are complying with the law if HCN and CN salts are added to the Proposition 65 list and the exposures or discharges that businesses cause are below the established levels.

Reasonable alternatives to the proposed regulation: OEHHA determined that the only alternative to the proposed regulation would be to not adopt MADLs for these chemicals. This alternative was rejected because it would fail to provide businesses with the certainty that the MADLs can provide.

Results: By providing updated MADLs, this regulatory proposal would spare businesses the expense of calculating their own MADLs if HCN and CN salts are listed, and consequently might also enable them to reduce or avoid litigation costs. In addition, the MADLs would not require, but might encourage, businesses to reduce the amount of HCN and CN salts, if listed, in their products to levels that do not cause a significant exposure, thereby providing a public health benefit to Californians.