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 ATRAZINE, PROPAZINE, SIMAZINE, AND THEIR CHLOROMETABOLITES 2,4-DIAMINO-6-CHLORO-*S*-TRIAZINE (DACT), DES-ETHYL ATRAZINE (DEA), AND DES-ISOPROPYL ATRAZINE (DIA)

PURPOSE AND BACKGROUND OF PROPOSED AMENDMENTS

PURPOSE

These proposed regulatory amendments would adopt Maximum Allowable Dose Levels (MADLs) for oral exposure to atrazine, propazine, simazine, and their chlorometabolites; 2,4-diamino-6-chloro-*s*-triazine (DACT)[1], des-ethyl atrazine (DEA), and des-isopropyl atrazine (DIA) under Proposition 65[2] in Title 27, California Code of Regulations, section 25805(b)[3]. The proposed MADLs were derived using scientific methods outlined in Section 25803. The proposed oral MADL for each of the six chemicals (atrazine, propazine, simazine, DACT, DEA, and DIA) is 100 micrograms per day.

PROPOSITION 65 AND LISTING OF SPECIFIED COMPOUNDS

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[4]. OEHHA has the authority to adopt and amend regulations to further the purposes of the Act[5].

The Act requires businesses to provide a warning when they cause an exposure to a chemical 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.

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[1] DACT was incorrectly identified as 2,**3**-diamino-6-chloro-*s*-triazine (instead of 2,**4**-diamino-6-chloro-*s*-triazine) in the Feb. 7, 2014 notice of intent to list the chemical and in the March 24, 2015 notice of listing. That typographical error will be corrected when the chemicals are ultimately added to the list.
[2] 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".
[3] All subsequent citations are to Title 27, California Code of Regulations, unless otherwise noted.
[4] Health and Safety Code section 25249.12 and Cal. Code of Regs., Title 27, section 25102(o)
[5] Health and Safety Code, section 25249.12(a).

Warnings are not required and the discharge prohibition is not in force when exposures are sufficiently small, as specified in the Act[6].

The rulemaking has been delayed because the listing of these chemicals under Proposition 65 was challenged in a legal proceeding[7]. This regulatory action will not be finalized until atrazine, propazine, simazine, DACT, DEA, and DIA are listed under Proposition 65 as known to the state to cause reproductive toxicity (developmental and female reproductive endpoints). The listings are based on formal identification of these chemicals by the US Environmental Protection Agency (US EPA) as causing developmental and female reproductive toxicity[8]. US EPA is a body recognized as authoritative for the listing of chemicals as known to cause reproductive toxicity under Proposition 65 (Section 25306(l)).

STUDY SELECTION

To establish the scientific basis for these proposed regulations, OEHHA reviewed studies identified in a number of US EPA documents [9,10,11,12,13,14,15], which provide the basis for the proposed listings. US EPA noted that "[n]euroendocrine effects are considered the critical endpoints for assessing the health effects of the CMG [common mechanism group] Triazines"[16]. A study by Morseth[17], identifying attenuation of the

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[6] Health and Safety Code, section 25249.9 (b) and 25249.10(c)

[7] *Syngenta v OEHHA*, Sacramento County Superior Court case #34-2014-8000-1809. Judgment was entered in favor of OEHHA on April 8, 2016. Syngenta has appealed the decision and is asking the Third District Court of Appeal for a stay of the listing of these chemicals during the pendency of the appeal. OEHHA is opposing that request. No decision has been issued on that question by the Court of Appeal.

[8] OEHHA, Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65), Notice of Intent to List Atrazine, Propazine, Simazine, and Their Chlorometabolites DACT, DEA, and DIA, California Regulatory Notice Register 2014, Vol 6-Z, pp 254-258, February 7, 2014. Available at: http://www.oal.ca.gov/res/docs/pdf/notice/06z-2014.pdf

[9] US EPA, 2002a. Atrazine (PC Code: 080803). Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision Document (Second Revision). April 11, 2002.

[10] US EPA, 2002b. Office of Pesticide Programs. Special Docket for Pesticide Reregistration Risk Assessments. Memorandum on ATRAZINE/DACT - Fourth Report of the Hazard Identification Assessment Review Committee. TXR NO. 0050592

[11] US EPA, 2005. Propazine: Revised HED Risk Assessment for the Tolerance Reassessment Eligibility Decision (TRED) which Includes a New Use on Grain Sorghum. PC Code: 080808, DP Barcode: D323271 Memorandum from J. Morales et al. Office of Pesticide Programs and Toxic Substances (OPPTS) Health Effects Division to D. Sherman OPPTS, December 13, 2005.

[12] US EPA, 2006a. Decision Documents for Atrazine. Office of Prevention, Pesticides and Toxic Substances. Available at http://www.epa.gov/pesticides/reregistration/REDs/atrazine_combined_docs.pdf

[13] US EPA, 2006b. Triazine Cumulative Risk Assessment (March 28, 2006). Available at http://www.epa.gov/pesticides/cumulative/common_mech_groups.htm#triazine

[14] US EPA, 2006c. Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Propazine. Office of Prevention, Pesticides and Toxic Substances , EPA 738-R-06-009 Available at http://www.epa.gov/opp00001/reregistration/status_page_p.htm

[15] US EPA, 2006d. Reregistration Eligibility Decision Document for Simazine. Office of Prevention, Pesticides and Toxic Substances. EPA 738-R-06-008. Available at http://www.epa.gov/opp00001/reregistration/status_page_s.htm

[16] US EPA, 2006b. Triazine Cumulative Risk Assessment (March 28, 2006) Page 22.. Available at

pre-ovulatory luteinizing hormone (LH) surge as a biomarker indicative of hypothalamic disruption of function, observed in female Sprague-Dawley rats, was identified by US EPA as demonstrating the critical effects of atrazine. US EPA also noted that the hypothalamic-pituitary axis is involved in the development of the reproductive system, and its maintenance and functioning in adulthood.

Major findings from the study in rats, as summarized by US EPA[18], are briefly presented below.

"In a study to evaluate the effect of long-term atrazine exposure on the proestrus afternoon luteinizing hormone (LH) surge (MRID 44152102 [Morseth, 1996]) atrazine, 97.1% a.i., was administered to 360 female Sprague Dawley rats in the diet. Dose levels were 0 (negative control), 25, 50, and 400 ppm (0, 1.80, 3.65, 29.44 mg/kg-day) for 26 weeks (approximately six months).

"Body weight, body weight gain and food consumption were significantly ($p<0.05$) decreased in highest dose tested compared to controls (body weight decreased 8.5% at the end of the study and food consumption decreased 3.75% for the entire study). The percentage of days in estrus was significantly increased ($p\leq0.01$) during the 21-22 and 25-26 week time periods at the high-dose level. Percent days in estrus were also increased during the 21-22 and 25-26 week time periods at the mid dose, but the increase was only significant ($p\leq0.05$) for the 21-22 week time period. The proestrus afternoon LH surge was severely attenuated at the high dose (LH levels at most sampling time points were actually decreased compared to baseline) and less so at the mid dose (maximum increase over baseline was 157% compared to maximum increase over baseline in controls of 273%). Pituitary weights were increased at the high dose (absolute weight increased 22% and weight relative to body weight was increased 28%). Pituitary weights at the other two doses were not affected. At the high dose, there was a slight increase in animals displaying enlarged pituitaries (0% in controls compared to 3.4% at 29.44 mg/kg/day) and thickened mammary glands (0% in controls compared to 6.7% at 29.44 mg/kg/day). There were no other gross necropsy findings in the high dose that could be attributed to compound exposure and there were no compound-related gross pathology findings at the mid dose or low-dose. Selected tissues were saved for histopathology, but those results have yet to be reported.

"There were no compound related effects in mortality or clinical signs. The proestrus afternoon prolactin surge was not affected by compound exposure at any dose. The low dose had no effects on the estrous cycle, LH or prolactin surges.

"The LOAEL is 3.65 mg/kg/day, based on estrous cycle alterations and LH surge attenuation. The NOAEL is 1.8 mg/kg/day."

OEHHA has determined that this study is the most sensitive study deemed to be of

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http://www.epa.gov/pesticides/cumulative/common_mech_groups.htm#triazine

[17] Morseth , S. L. (1996) Evaluation of the Luteinizing Hormone (LH) Surge in Atrazine-Exposed Female Sprague-Dawley Rats – (Final) 6-month Interim Report: Lab Project Number: CHV 2386-111:2386-111:6791E, prepared by Corning Hazleton Inc., as cited by US EPA (2002a), page 27.

[18] US EPA, 2002a. Atrazine (PC Code: 080803). Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision Document (Second Revision). April 11, 2002. Page 27.

sufficient quality[19]. OEHHA also conducted a search for any other relevant studies published since 2006, when the most recent of the cited US EPA reports were completed. A number of additional relevant studies were identified; however, none of those studies were deemed to be of sufficient quality for MADL development.

MADL CALCULATION

The following calculations were performed in accordance with Section 25803 to derive oral MADLs for atrazine, propazine, simazine, DACT, DEA, and DIA.

The first step is to calculate an oral MADL for atrazine:

- The NOEL in the study for purposes of assessment was demonstrated to be as follows (Section 25803(a)(8)):

  1.8 mg/kg-day

- To calculate the NOEL dose as an intake, a 58 kg body weight for a woman is assumed:

  1.8 mg atrazine/kg-day x 58 kg = 104.4 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 atrazine:

  MADLoral = 104.4 mg/day ÷ 1000 = **100 micrograms/day**
  (after rounding)

This MADL applies to atrazine exposure by the oral route. Since propazine, simazine, DACT, DEA and DIA are considered to be of equal potency to atrazine with respect to their common mechanism of reproductive toxicity[20], 100 micrograms/day is the oral MADL for each of these chemicals.

[19] Section 25803(a)(5).
[20] US EPA, 2005. Propazine: Revised HED Risk Assessment for the Tolerance Reassessment Eligibility Decision (TRED) which Includes a New Use on Grain Sorghum. PC Code: 080808, DP Barcode: D323271 Memorandum from J. Morales et al. Office of Pesticide Programs and Toxic Substances (OPPTS) Health Effects Division to D. Sherman OPPTS, December 13, 2005, Page 4.
US EPA, 2006c. Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Propazine. Office of Prevention, Pesticides and Toxic Substances , EPA 738-R-06-009, Page 4. Available at http://www.epa.gov/opp00001/reregistration/status_page_p.htm
US EPA, 2006b. Triazine Cumulative Risk Assessment (March 28, 2006), Pages 21 and 32. Available at http://www.epa.gov/pesticides/cumulative/common_mech_groups.htm#triazine

PROPOSED REGULATORY AMENDMENTS

The proposed changes to Section 25805(b) are provided below in underline:

Chemical name	*Level (micrograms per day)*
Atrazine	100 (oral)
Propazine	100 (oral)
Simazine	100 (oral)
2,4-Diamino-6-chloro-*s*-triazine (DACT)	100 (oral)
Des-ethyl atrazine (DEA)	100 (oral)
Des-isopropyl atrazine (DIA)	100 (oral)

PROBLEM BEING ADDRESSED BY THIS PROPOSED RULEMAKING

Proposition 65 does not provide explicit 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 at which discharge is not prohibited.

NECESSITY

These proposed regulatory amendments would adopt oral MADLs for each of these six chemicals that conform to the Proposition 65 implementing regulations and reflect the currently available scientific knowledge about these compounds. MADLs provide assurance to the regulated community that exposures or discharges at or below them are considered not to pose a significant risk of reproductive harm. Exposures at or below the MADL are exempt from the warning and discharge requirements of Proposition 65[21].

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 relevant studies on the developmental and reproductive toxicity of atrazine, propazine, simazine, DACT, DEA, and DIA identified in numerous US EPA documents[6]. OEHHA determined that the six-month LH surge study in rats (Morseth, 1996, as described by US EPA[22]), is the most sensitive study of sufficient quality identified by the US EPA[23,24], as required by Section 25803(a)(5), and that there were

[21] Health and Safety Code sections 25249.9(b) and 25249.10(c)
[22] US EPA, 2002a. Atrazine (PC Code: 080803). Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision Document (Second Revision). April 11, 2002. Page 27.
[23] US Environmental Protection Agency (US EPA, 2006a). Decision Documents for Atrazine. US EPA

no subsequently published studies that were more sensitive. OEHHA used the values from this study as the basis for calculating the oral MADLs for atrazine, propazine, simazine, DACT, DEA, and DIA that are proposed for adoption into Section 25805(b). Copies of the five US EPA documents (US EPA, 2002a[22]; 2005[25]; 2006a[26]; 2006b[27]; 2006c[28]) will be included in the regulatory file for this action, and are available from OEHHA upon request. OEHHA also 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 chemicals. 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. Use of the proposed MADLs by businesses is voluntary and therefore does not impose any costs on small businesses. 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.

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

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Office of Prevention, Pesticides and Toxic Substances. Available at http://www.epa.gov/pesticides/reregistration/REDs/atrazine_combined_docs.pdf

[24] US EPA, 2002a. Atrazine (PC Code: 080803). Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision Document (Second Revision). April 11, 2002.

[25] US EPA, 2005. Propazine: Revised HED Risk Assessment for the Tolerance Reassessment Eligibility Decision (TRED) which Includes a New Use on Grain Sorghum. PC Code: 080808, DP Barcode: D323271 Memorandum from J. Morales et al. Office of Pesticide Programs and Toxic Substances (OPPTS) Health Effects Division to D. Sherman OPPTS, December 13, 2005.

[26] US Environmental Protection Agency (US EPA, 2006a). Decision Documents for Atrazine. US EPA Office of Prevention, Pesticides and Toxic Substances. Available at http://www.epa.gov/pesticides/reregistration/REDs/atrazine_combined_docs.pdf

[27] US EPA, 2006b. Triazine Cumulative Risk Assessment (March 28, 2006). Available at http://www.epa.gov/pesticides/cumulative/common_mech_groups.htm#triazine

[28] US EPA, 2006c. Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Propazine. Office of Prevention, Pesticides and Toxic Substances , EPA 738-R-06-009. Available at http://www.epa.gov/opp00001/reregistration/status_page_p.htm

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.

It is not possible to quantify any monetary values for this proposed amendment to the regulation given that its use is entirely voluntary and 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. The listing of these chemicals under Proposition 65 was challenged in a legal proceeding[29]. This regulatory action will not be finalized until atrazine, propazine, simazine, DACT, DEA, and DIA are listed under Proposition 65 as known to the state to cause reproductive toxicity (developmental and female reproductive endpoints). Once Atrazine, propazine, simazine, DACT, DEA, and DIA are listed under Proposition 65, businesses will have to provide a warning if their products or activities cause exposures 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. Adopting this regulation will save these businesses those expenses and may reduce litigation costs. By adopting these 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 atrazine, propazine, simazine, DACT, DEA, and DIA 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 without providing a warning if the exposures or discharges that businesses cause are below the established levels.

[29] *Syngenta v OEHHA*, Sacramento County Superior Court case #34-2014-8000-1809. Judgment was entered in favor of OEHHA on April 8, 2016. Syngenta has appealed the decision and is asking the Third District Court of Appeal for a stay of the listing of these chemicals during the pendency of the appeal. OEHHA is opposing that request. No decision has been issued on that question by the Court of Appeal.

Reasonable alternatives to the proposed regulation: OEHHA determined that the only alternative to the proposed regulation would be to not adopt a MADL 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 MADLs, this regulatory proposal would spare businesses the expense of calculating their own MADLs, 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 amounts of atrazine, propazine, simazine, DACT, DEA, and DIA, if listed, in their products to levels that do not cause a significant exposure, thereby providing a public health benefit to Californians.