INITIAL STATEMENT OF REASONS
TITLE 27, CALIFORNIA CODE OF REGULATIONS

PROPOSED AMENDMENT TO

SECTION 25805(b), SPECIFIC REGULATORY LEVELS: CHEMICALS CAUSING REPRODUCTIVE TOXICITY

MAXIMUM ALLOWABLE DOSE LEVEL: SULFUR DIOXIDE

SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986
PROPOSITION 65

PURPOSE AND BACKGROUND OF PROPOSED AMENDMENT

PURPOSE
This proposed regulatory amendment would adopt a Proposition 65[1] Maximum Allowable Dose Level (MADL) for sulfur dioxide (SO_2) under Title 27, California Code of Regulations, section 25805(b) [2]. The proposed MADL for SO_2 of 220 micrograms per day was derived using scientific methods outlined in Section 25803.

PROPOSITION 65 AND LISTING OF SULFUR DIOXIDE
Proposition 65 was enacted as a voters' initiative on November 4, 1986. The Office of Environmental Health Hazard Assessment (OEHHA) 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 Act[4]. The Act requires businesses to provide a warning when they cause an exposure to a chemical listed as known to cause cancer or reproductive toxicity[5]. The Act also prohibits the discharge of listed chemicals to sources of drinking water[6].

On July 29, 2011, SO_2 was added to the Proposition 65 list as known to the state to cause reproductive toxicity, based on the findings of the state's qualified experts, the Developmental and Reproductive Toxicant Identification Committee

[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] Cal. Code of Regs., Title 27, Division 4. Chapter 1. Article 1. Preamble(a).
[4] Health and Safety Code, section 25249.12(a).
[5] Health and Safety Code section 25249.6
[6] Health and Safety Code section 25249.5

(DARTIC)[7]. The DARTIC determined that SO_2 was clearly shown, through scientifically valid testing according to generally accepted principles, to cause developmental toxicity, an endpoint of reproductive toxicity[8]. The particular type of developmental toxicity noted by the DARTIC was intrauterine growth restriction. See Appendix A for discussion of the scientific derivation of the proposed MADL.

PROPOSED REGULATORY AMENDMENT

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

Chemical name	*Level (micrograms per day)*
…	
Sulfur dioxide	220
…	

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

This proposed regulatory amendment would adopt a MADL that conforms to the Proposition 65 implementing regulations and reflects the currently available scientific knowledge about sulfur dioxide. The MADL provides assurance to the regulated community that exposures or discharges at or below the MADL are considered not to pose a significant risk of developmental or reproductive harm and are, therefore, exempt from the warning and discharge requirements of Proposition 65[9].

[7] Section 25305
[8] Section 25305(b)(1)
[9] Health and Safety Code sections 25249.9(b) and 25249.10(c)

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

OEHHA reviewed relevant studies on the developmental toxicity of sulfur dioxide, which were identified through comprehensive searches of the scientific literature. For purposes of Proposition 65, the study by Murray et al. [10, 11] in mice is the most sensitive study deemed to be of sufficient quality as defined in Section 25803(a)(7) for exposure to sulfur dioxide. OEHHA relied on the values from this study as the basis for calculating the MADL for sulfur dioxide proposed for adoption into Section 25805(b). A copy of the publications on this study by Murray et al. will be included in the regulatory file for this action, and is available from OEHHA upon request. OEHHA also relied on the attached Economic Impact Assessment in developing the proposed regulation.

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

The proposed MADL provides a safe harbor value that aids businesses in determining if they are complying with the law. The alternative to the amendment to Section 25805(b) would be to not adopt a MADL for inhalation exposures to the chemical. Failure to adopt a MADL would leave the business community without a safe harbor level to assist them in determining compliance 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 MADL 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[12] so it has no effect on very small businesses.

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[10] Murray et al. 1979.
[11] Murray et al. 1977.
[12] Health and Safety Code, section 25249.11(b)

EVIDENCE SUPPORTING FINDING OF NO SIGNIFICANT ADVERSE ECONOMIC IMPACT ON BUSINESS

Because the proposed MADL provides a safe harbor value for businesses to use when determining compliance with Proposition 65, OEHHA does not anticipate that the regulation will 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.

APPENDIX "A"
DERIVATION OF THE PROPOSED MAXIMUM ALLOWABLE DOSE LEVEL FOR SUFUR DIOXIDE

The hazard identification document, "Evidence on the Developmental and Reproductive Toxicity of Sulfur Dioxide",[13] previously prepared by OEHHA as part of the chemical's listing process, includes discussions of studies providing the basis for the DARTIC's decision to list SO_2 as causing reproductive (developmental) toxicity under Proposition 65.

STUDY SELECTION

OEHHA reviewed the studies described in the earlier document on intrauterine growth restriction for use in determining a Maximum Allowable Dose Level (MADL), as summarized in the hazard identification document.[14] These studies include epidemiologic studies and toxicological studies in mice. [15, 16, 17]

Although epidemiologic studies of intrauterine growth restriction in humans supported identification of a reproductive hazard, they do not provide an adequate quantitative basis for derivation of a MADL. Exposure levels were generally taken from ambient air monitors and averaged over distance and long periods of time, resulting in difficulty quantifying exposures of the affected segment of the population at any point in time. Thus, the uncertainty in effect levels for individuals or subpopulations was large and neither a reliable No Observable Effect Level (NOEL) nor a Lowest Observable Effect Level (LOEL) could be ascertained from the epidemiologic studies.

Two studies in laboratory animals provided controlled exposures and showed effects on fetal growth. In a study by Murray et al.,[18, 19] CF-1 mice exposed to SO_2 by inhalation for seven hours per day showed a statistically significant

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[13] Office of Environmental Health Hazard Assessment (OEHHA), Evidence on the Developmental and Reproductive Toxicity of Sulfur Dioxide, OEHHA, California Environmental Protection Agency, Sacramento, California, February 2011, Available at http://www.oehha.ca.gov/prop65/hazard_ident/pdf_zip/So2HID022511.pdf

[14] OEHHA, 2011. Evidence on the Developmental and Reproductive Toxicity of Sulfur Dioxide.

[15] Murray FJ, Schwetz BA, Crawford AA, Henck JW, Quast JF, Staples RE (1979). Embryotoxicity of inhaled sulfur dioxide and carbon monoxide in mice and rabbits. J Environ Sci Health C 13(3):233-50.

[16] Murray FJ, Schwetz BA, Crawford AA, Henck JW, Staples RE (1977). Teratogenic potential of sulfur dioxide and carbon monoxide in mice and rabbits. Doe Symp Ser 47: 469-478.

[17] Singh J (1989). Neonatal development altered by maternal sulfur dioxide exposure. Neurotoxicology 10(3): 523-7.

[18] Murray et al. 1979.

[19] Murray et al. 1977.

reduction in fetal weight. The developmental LOEL was 23.9 parts per million (ppm), based on the measured time-weighted SO_2 concentration. Another inhalation study by Singh in CD-1 mice[20] demonstrated reduced birth weight after prenatal exposure to SO_2. This effect was statistically significant for mice exposed to SO_2 at 65 ppm. At 32 ppm, a reduction in birth weight was not statistically significant, but was comparable in magnitude to the reduction in fetal weight at 23.9 ppm reported by Murray et al.[21, 22]

For purposes of Proposition 65, the study by Murray et al. is the most sensitive study deemed to be of sufficient quality[23]. Since adverse developmental effects were seen at the lowest dose used in this study, the LOEL is divided by 10 to establish a NOEL for purposes of assessment[24].

MADL CALCULATION

The following calculations were performed in accordance with Section 25803 to derive the MADL for SO_2 using data and exposure parameters from Murray et al.:

- Division of the LOEL of 23.9 ppm by 10, which resulted in a NOEL of 2.39 ppm, per Section 25803(a)(7)

- Conversion of air concentration in ppm to mg/m^3 using a conversion factor of 2.64 mg/m^3 per ppm [25]

  $$(2.39 \text{ ppm} \times 2.64 \text{ [mg/m}^3 \text{ per ppm]}) = 6.31 \text{ mg/m}^3$$

- Conversion of air concentration for 7 hour (h) exposure to a 24 h day

  $$6.31 \text{ mg/m}^3 \times (7 \text{ h} \div 24 \text{ h}) = 1.84 \text{ mg/m}^3$$

- Calculation of the NOEL dose for a 30 g mouse with an inhalation rate of 0.063 m^3/day[26, 27]

  $$(1.84 \text{ mg/m}^3 \times 0.063 \text{ m}^3\text{/day}) \div (0.030 \text{ kg}) = 3.864 \text{ mg/kg/day}$$

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[20] Singh, 1989.
[21] Murray et al. 1979.
[22] Murray et al. 1977.
[23] Section 25803(a)(4)
[24] Section 25803(a)(7)
[25] OEHHA, 2011.
[26] Bond JA, Dahl AR, Henderson RF, Dutcher JS, Mauderly JL, Birnbaum LS (1986). Species differences in the disposition of inhaled butadiene. *Toxicol Appl Pharmacol* **84**: 617-627.
[27] Depledge MH (1985). Respiration and lung function in the mouse, *Mus musculus* (with a note on mass exponents and respiratory variables). *Respir Physiol* **60**: 83-94.

- Calculation of the NOEL dose for a 58 kg woman

  3.864 mg/kg/ day × 58 kg = 224.1mg/day,

  or 220 mg/day after rounding

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

  MADL = 220 mg/day ÷ 1000 = **220 micrograms/day**

APPLICABILITY OF THE MADL

This MADL is based on inhalation data. All of the studies that formed the basis for listing SO_2 were of exposure to SO_2 as a gas. There are currently no available studies on exposure solely to SO_2 by the oral route. However, based on review of relevant information[28], OEHHA has concluded that exposure to SO_2 by the oral route is expected to pose no more risk, and may pose less risk, than exposure to the equivalent amount by the inhalation route.

This MADL applies only to the specific compound SO_2, and does not apply to sulfites, bisulfites or metabisulfites. These chemicals are not currently listed under Proposition 65 and exposure to them, at any level, is not subject to the warning and discharge requirements of Proposition 65.

[28] Office of Environmental Health Hazard Assessment. Evidence on the Developmental and Reproductive Toxicity of Sulfur Dioxide, 2011. Available at http://www.oehha.ca.gov/prop65/hazard_ident/pdf_zip/So2HID022511.pdf.

ECONOMIC IMPACT ANALYSIS
Gov. Code section 11346.3(b)

It is not possible to quantify any monetary values for this proposed amendment to the regulation given that 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 developmental or reproductive harm. The law also prohibits the discharge of listed chemicals into sources of drinking water. Sulfur dioxide is listed under Proposition 65; therefore businesses that cause exposures to sulfur dioxide in the state must provide a warning if the exposure exceeds the MADL.

Benefits of the Proposed Regulation: The MADL provides a “safe harbor” value that aids businesses in determining if they are complying with the law. Some businesses may not be able to afford the expense of establishing 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 providing a safe harbor value, this regulatory proposal does not require, but may encourage, businesses to lower the amount of the listed chemical in their product 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 a specific MADL for a listed chemical 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 the exposures or discharges they cause are below the established level.

Reasonable alternatives to the proposed regulation: OEHHA determined that the only alternative to the proposed regulation would be to not adopt an inhalation MADL for this chemical. This alternative was rejected because it would fail to provide businesses with the certainty that the MADL can provide.