

California Environmental Protection Agency  
Office of Environmental Health Hazard Assessment

NOTICE TO INTERESTED PARTIES

September 29, 2010

OPPORTUNITY FOR PUBLIC COMMENT

**PROPOSITION 65  
REGULATORY UPDATE PROJECT**

**PRE-REGULATORY DRAFT OF POSSIBLE CHANGES TO  
TITLE 27, CALIFORNIA CODE OF REGULATIONS,  
SECTIONS 25801 AND 25803  
NO OBSERVABLE EFFECT LEVELS FOR LISTED CHEMICALS**

Proposition 65<sup>1</sup> requires that businesses provide warnings prior to exposing people to chemicals listed as reproductive toxins<sup>2</sup> and also prohibits discharges of these chemicals to sources of drinking water. The Act provides exceptions to these requirements in certain circumstances. For chemicals known to cause reproductive toxicity (i.e. birth defects or other reproductive harm), the Act provides an exemption to the warning and discharge provisions if an exposure one thousand (1,000) times higher than the level in question would not cause any observable effect.

The Office of Environmental Health Hazard Assessment (OEHHA) is the lead agency for implementation of Proposition 65. As part of its responsibilities OEHHA maintains the regulations implementing the Act. These regulations can be found in Title 27 of the California Code of Regulations, sections 25000-27000 inclusive.

OEHHA is proposing amendments to Sections 25801 and 25803 of the California Code of Regulations, Title 27. These regulations set out the procedures and criteria for determining an exposure level where there would be no observable effect.

OEHHA developed a draft regulatory amendment to Title 27, Cal. Code of Regulations, section 25801 and 25803 that would clarify these procedures and criteria. OEHHA previously solicited comments on an earlier draft of the regulations via a public workshop and written comment period ([http://www.oehha.ca.gov/prop65/public\\_meetings/04022010meet.html](http://www.oehha.ca.gov/prop65/public_meetings/04022010meet.html)). OEHHA

---

<sup>1</sup> The Safe Drinking Water and Toxic Enforcement Act of 1986, Health and Safety Code section 25249.5, et. seq., hereafter referred to as Proposition 65 or the Act.

<sup>2</sup> See [http://www.oehha.ca.gov/prop65/prop65\\_list/Newlist.html](http://www.oehha.ca.gov/prop65/prop65_list/Newlist.html).

reviewed the comments received on the earlier draft and has developed the current draft of the possible regulatory amendments and draft Initial Statement of Reasons, which are set out below. Proposed changes to the current regulation are indicated in underline/strikeout format.

**Please note: This is a pre-regulatory proposal that could change substantially before it is proposed in a formal regulatory process.** Interested parties are encouraged to provide written comments concerning this pre-regulatory concept.

In order for comments to be considered at this point in the process they must be received by 5:00 p.m. on Monday, November 1, 2010. All comments should be directed to:

Fran Kammerer  
Staff Counsel  
Office of Environmental Health Hazard Assessment  
1001 I Street  
Sacramento, CA 95814  
Or via e-mail to [fkammerer@oehha.ca.gov](mailto:fkammerer@oehha.ca.gov)

## PRE-REGULATORY DRAFT

### Title 22, California Code of Regulations

#### ARTICLE 8. No Observable Effect Levels

##### § 25801. General.

(a) The determination of whether a level of exposure to a chemical known to the state to cause reproductive toxicity has no observable effect for purposes of Section 25249.10(c) of the Act shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for the listing of a chemical as known to the state to cause reproductive toxicity. Nothing in this article shall preclude a person from using evidence, standards, assessment methodologies, principles, assumptions or levels not described in this article to establish that a level of exposure has no observable effect at one thousand (1,000) times the level in question.

(b) A level of exposure to a listed chemical shall be deemed to have no observable effect, assuming exposure at one thousand times that level, provided that the level is determined:

(1) By means of an assessment that meets the standards described in Section 12803 to determine the maximum dose level having no observable effect, and dividing that level by one thousand (1,000) to arrive at the maximum allowable dose level, or

(2) By application of a specific regulatory level for the chemical in question as provided in Section 12805.

(c) For purposes of this article, “NOEL” shall mean that no observable effect level, which is the maximum ~~dose~~ level of exposure at which a chemical has no observable reproductive effect.

(d) The chemicals specifically contained in this article do not include all chemicals listed as causing reproductive toxicity for which there is a level of exposure which has no observable effect assuming exposure at one thousand times the level in question. The fact that a chemical does not specifically appear in this article does not mean that it has an observable effect at any level.

(e) This article establishes exposure levels solely for purposes of Section 25249.10(c) of the Act. Nothing in this article shall be construed to establish exposure levels for other regulatory purposes.

NOTE: Authority cited: Section 25249.12, Health and Safety Code Section. Reference: Sections 25249.5, 25249.6, 25249.9, 25249.10 and 25249.11, Health and Safety Code.

...

### § 25803. Assessment.

(a) A quantitative assessment which conforms to this section shall be deemed to determine the level of exposure to a listed chemical which will have no observable effect, assuming the exposure at one thousand times the level in question. The assessment shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause reproductive toxicity. In the absence of principles or assumptions scientifically more appropriate based upon the available data, the following default principles and assumptions shall apply in any such assessment:

(1) Only studies producing the reproductive effect which provides the basis for the determination that a chemical is known to the state to cause reproductive toxicity shall be utilized for the determination of the NOEL.

(2) Where multiple reproductive effects provide the basis for the determination that a chemical is known to the state to cause reproductive toxicity, the reproductive effect for which studies produce the lowest NOEL shall be utilized for the determination of the NOEL. The NOEL shall be the highest dose exposure level which results in no observable reproductive effect expressed in milligrams of chemical per kilogram of bodyweight per day. This may be the no observed effect level in a scientific study or, alternatively, may be calculated by means of a generally accepted scientific methodology such as the benchmark dose methodology. Where a study (e.g., epidemiological publication) reports a range of exposure levels associated with no observed effect, the NOEL may be selected from within the range or calculated by benchmark dose or other accepted scientific methodology.

(3) The quality and suitability of available epidemiologic data shall be appraised according to generally accepted scientific principles to determine whether the study is appropriate as the basis for of an assessment, considering such Factors as for consideration in this appraisal include but are not limited to: the identification and selection of the study subjects (e.g. cases, controls, exposed and reference groups, unexposed), the reliable validity and reliability of the ascertainment of exposure, and completeness of follow-up, assessment of outcomes, and appropriateness of the statistical analysis and power of the study to detect an effect. Biases and confounding factors shall be identified and, quantified, or otherwise considered, as appropriate.

(4) Animal bioassay studies for assessment shall meet generally accepted scientific principles, including the thoroughness of experimental protocol, the degree to which dosing resembles the expected manner of human exposure, the temporal exposure pattern, the duration of study, the purity of test material, the number and size of exposed groups, and the route of exposure and the extent of occurrence of effects.

(45) The NOEL shall be based on the most sensitive study deemed to be of sufficient quality.

(56) The results obtained for the most sensitive study deemed to be of sufficient quality shall be applicable to all routes of exposure for which the results are relevant.

(67) When available data are of such quality that anatomic, physiologic, pharmacokinetic and metabolic considerations can be taken into account with confidence, they may be used in the assessment.

(78) When data do not allow the determination of a NOEL, the lowest ~~observable~~ observed effect level (~~LOEL~~) in a study shall be divided by 10 to establish a NOEL for purposes of assessment.

(b) In the absence of principles or assumptions scientifically more appropriate based upon the available data, the following default principles or assumptions shall apply in any such assessment. The NOEL shall be converted to a milligram per day dose level by multiplying it by the assumed human body weight ~~by the NOEL~~. When the applicable reproductive effect is upon the adult male, human body weight of 70 kilograms shall be assumed. When the applicable reproductive effect is upon the adult female or conceptus, human body weight of 58 kilograms shall be assumed. When data indicate that exposure of the neonate, infant, child or adolescent results in the applicable reproductive effect, the bodyweights specified below shall be assumed:

<u>Adolescent (age 11 - 18 years)</u>	<u>40 kg</u>
<u>Child (age 2 - 10 years)</u>	<u>20 kg</u>
<u>Infant (age 29 days - 1 year)</u>	<u>10 kg</u>
<u>Neonate (age 0 - 28 days)</u>	<u>3.5 kg</u>

NOTE: Authority cited: Section 25249.12, Health and Safety Code Section. Reference: Sections 25249.5, 25249.6, 25249.9, 25249.10 and 25249.11, Health and Safety Code.

**PRE-REGULATORY DRAFT**  
**INITIAL STATEMENT OF REASONS**  
**TITLE 27, CALIFORNIA CODE OF REGULATIONS**  
**PROPOSED AMENDMENTS TO SECTIONS 25801 AND 25803**  
**NO OBSERVABLE EFFECT LEVELS**  
**SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986**

**PURPOSE**

The Safe Drinking Water and Toxic Enforcement Act of 1986, commonly known as Proposition 65,<sup>3</sup> 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 state entity responsible for the implementation of the Act. OEHHA has the authority to promulgate and amend regulations to further the purposes of the Act.<sup>4</sup> 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. The Act also prohibits the discharge of listed chemicals to sources of drinking water.

The Act provides exceptions to these requirements in certain circumstances. For chemicals known to cause reproductive toxicity, an exemption to the warning and discharge provisions is provided if there would be no observable effect given an exposure one thousand (1,000) times the level of exposure in question.

OEHHA is proposing amendments to Sections 25801 and 25803 of the California Code of Regulations, Title 27.<sup>5</sup> These sections, which fall within Article 8 of the Proposition 65 implementing regulations, set out the procedures and criteria for determining an exposure level where there would be no observable reproductive effect. This level divided by 1000 results in a maximum allowable dose level (MADL) for a listed chemical. The MADL is the highest level of exposure at which a warning is not required or a discharge not prohibited.

Section 25801(c) defines a no observable effect level, or “NOEL,” to mean the maximum dose level at which a chemical has no observable reproductive effect. The more specific term “dose” is currently described in two different ways in the article – first, as an amount per bodyweight (milligram of chemical per kilogram of

---

<sup>3</sup> Codified at Health and Safety Code section 25249.5 et. seq., hereafter referred to as “Proposition 65” or “The Act”

<sup>4</sup> Health and Safety Code section 25249.12(a)

<sup>5</sup> All further references are to sections of Title 27, of the California Code of Regulations, unless otherwise noted.

body weight) in section 25803(a)(1) and second, as an amount of daily exposure (milligrams of chemical per day) in section 25803(b). To remove this inconsistency, the proposed amendments will use the more general term “maximum” or “highest exposure level” for the “no observed effect level” and reserve the term “dose” for amounts such as the MADL.

Section 25803(a)(2), adopted in 1989, emphasizes a practice used at the time to establish drinking water health advisories, air reference exposure levels, clean-up levels for hazardous waste sites and other regulatory guidance levels. The practice was widely used by expert scientific organizations and regulatory agencies, including the National Academy of Sciences, U.S. Environmental Protection Agency (U.S. EPA) and the California Department of Health Services. The practice involved selecting the empirical no observed effect level – the highest exposure level in a study observed to have no effect – as the point of departure. This was the most commonly accepted procedure for establishing a regulatory standard in 1989.

The proposed amendments to the current regulation explain that the default procedures in the regulation are to be used “in the absence of principles or assumptions scientifically more appropriate based upon the available data.” Thus, the regulation takes into account the fact that other procedures may be more scientifically appropriate for certain data sets. One such procedure that has become commonly accepted is the benchmark dose methodology. This is currently the preferred method for establishing guidance levels. In California, this method is used to establish reference exposure levels for air pollutants and public health goals for drinking water. The U.S. EPA has accepted and uses this method, and established scientific advisory bodies such as its Science Advisory Board have endorsed it. The proposed amendments to existing Section 25803(a)(1) of the regulation specifically recognize the benchmark dose methodology as an acceptable means of deriving a no observed effect level. This change does not preclude use of other generally accepted scientific methodologies, if they are more appropriate to the data in question.

OEHHA is also proposing to amend existing Section 25803(a)(1) to give guidance on the valuation of a NOEL in the case where the exposure may be reported as a range rather than a single value, as occurs with epidemiology studies and certain animal studies.

The proposed amendments to existing Section 25803(a)(2) and 25803(a)(7) are corrections of terminology and revisions of phrasing to more clearly express the intent of the regulation.

The proposed amendments to Section 25803(b) would provide default body weights for children and infants. The current regulations specify default bodyweights to be used in calculation of the MADL. When the MADL is based on female or male reproductive toxicity, bodyweights of 58 and 70 kg, respectively,

are identified as the defaults. These bodyweight are relevant to reproductive effects occurring in adults, where the relevant period of exposure is in adulthood. In some instances, however, female or male reproductive toxicity can result from exposures occurring after birth but prior to adulthood. In such cases, default bodyweights relevant to the developmental period during which the exposure resulting in reproductive toxicity occurred are needed in order to adequately calculate a MADL for these age groups other than adults. The proposed addition to Section 25803(b) provides age-specific default bodyweights.

OEHHA also proposes revisions to Section 25803(b) to clarify that the earlier provision in Section 25803(a) governing “principles or assumptions scientifically more appropriate based upon the available data” is also applicable to this section.

## NECESSITY

**Subsection 25803(a)(2)** – The procedures specified in Section 25803 have always explicitly been defaults that permitted the use of principles or assumptions scientifically more appropriate based upon the available data. Despite this explicit authorization for the use of alternative procedures, some have interpreted the regulation to prohibit the use of the benchmark dose methodology. Since the benchmark dose approach is now generally accepted (and scientifically preferred where data permit) as a methodology for quantitative risk assessment, this proposed amendment will clarify the original intent of the regulation and allow for the most current and appropriate methodology to be applied.

**Subsection 25803(b)** – In order to calculate appropriately protective levels at which warnings must be provided for exposures to listed chemicals that cause reproductive toxicity, the existing regulation only expressly identifies default bodyweights for adult males and females. This amendment to the regulation is necessary in order to clarify that the reproductive effects being evaluated resulted from exposures prior to adulthood. With concomitantly lower body weight at the time of exposure, the lower body weights are more appropriate for calculation of the MADL.

## TECHNICAL, THEORETICAL, AND/OR EMPIRICAL STUDY, REPORTS, OR DOCUMENTS.

OEHHA is recognizing a current scientific consensus and did not rely upon any specific technical, theoretical, or empirical studies, reports or documents in proposing the adoption of this regulation.

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

All of the proposed amendments to the regulations are either clarifications of existing terminology or explanations of specific aspects of provisions already contained in the regulations. An alternative to the proposed revisions would be to retain the existing regulations. OEHHA has rejected that alternative because clarifying these regulations is in the best interest of both the regulated and enforcement communities and will further the health protective purposes of the Act.

#### REASONABLE ALTERNATIVES TO THE PROPOSED REGULATORY ACTION THAT WOULD LESSEN ANY ADVERSE IMPACT ON SMALL BUSINESS.

The proposed regulatory action will not adversely impact small business. Proposition 65 is limited by its terms to businesses with 10 or more employees (Health and Safety Code §§ 25249.5, 25249.6, and 25249.11(b)). The proposed revisions to the regulations may assist small businesses since they would clarify existing provisions of the regulations.

#### EVIDENCE SUPPORTING FINDING OF NO SIGNIFICANT ADVERSE ECONOMIC IMPACT ON ANY BUSINESS.

The proposed regulatory action will not have a significant statewide adverse economic impact directly affecting businesses, including the ability of California businesses to compete with businesses in other states. The proposed amendments to the existing regulation merely clarify the purpose and intent of the existing regulation.

#### EFFORTS TO AVOID UNNECESSARY DUPLICATION OR CONFLICTS WITH FEDERAL REGULATIONS CONTAINED IN THE CODE OF FEDERAL REGULATIONS ADDRESSING THE SAME ISSUES.

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.