Title 27, 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 25803 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 25805.

(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.

(f) Whenever the lead agency proposes to formally adopt a regulation pursuant to Sections 25801 through 25821, such as a maximum allowable dose level, the lead agency shall provide each member of the Developmental and Reproductive Toxicant Identification Committee notice of the proposed action, the proposed change to the regulation, and a copy of the initial statement of reasons supporting the proposal for their review and comment. The Committee shall be given at least 45 days to comment. Any

such comment by members of the Developmental and Reproductive Toxicant Identification Committee shall become a part of the formal rulemaking record. Nothing in this section shall be construed to require the members of the Developmental and Reproductive Toxicant Identification Committee to submit any comments. This procedure complies with the peer review requirements of section 57004 of the California Health and Safety Code.

NOTE: Authority cited: Section 25249.12, Health and Safety Code. Reference: Sections 25249.5, 25249.6, 25249.9, 25249.10, 25249.11 and 57004, 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 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 an assessment. Factors for consideration in this appraisal include but are not limited to: the identification and selection of study subjects (e.g., cases, controls, exposed and unexposed), validity and reliability of the ascertainment of exposure, 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, 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.

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

(6) 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.

(7) 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.

(8) When data do not allow the determination of a NOEL, the lowest observed effect level 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. 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:

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

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

§ 25805. Specific Regulatory Levels: Chemicals Causing Reproductive Toxicity

(a) Exposure to a chemical at a level which does not exceed the level set forth in subsection (b) for such chemical has no observable effect assuming exposure at one thousand (1,000) times that level.

(b) Chemical Name	Level (micrograms/day)
Acrylamide	140
Avermectin B1	4.4
Benzene	24 (oral) 49 (inhalation)
Butyl benzyl phthalate	1200 (oral)
Cadmium	4.1
Chromium (hexavalent compounds)	8.2 (oral)
Cyanide salts that readily dissociate in solution (expressed as cyanide)	9.8 (oral)
2,4-D butyric acid (2,4-DB, 2,4-dichlorophenoxy-butyric acid)	910
1,2-Dibromo-3-chloropropane (DBCP)	4.3 (inhalation) 3.1 (oral)
Di(*n*-butyl)phthalate (DBP)	8.7
Di(2-ethylhexyl)phthalate (DEHP), for intraveneous exposures only	4200 (adults) 600 (infant boys, age 29 days – 24 months) 210 (neonatal infant boys, age 0-28 days) [Levels for male children and adolescents can be calculated by application of the default body-weights specified in Title 27, California Code of Regulations, Section 25703(a)(8) to the procedure specified in Title 27, California Code of Regulations, Sections 25801 and 25803]
Di(2-ethylhexyl)phthalate (DEHP), for oral exposures only	410 (adults) 58 (infant boys, age 29 days-24 months) 20 (neonatal infant boys, age 0-28 days) [Levels for male children

	and adolescents can be calculated by application of the default body-weights specified in Title 27, California Code of Regulations, Section 25703(a)(8) to the procedure specified in Title 27, California Code of Regulations, Sections 25801 and 25803]
Di-*n*-hexyl phthalate (DnHP)	2200 (oral)
Di-isodecyl phthalate (DIDP)	2200
m-Dinitrobenzene	38 (oral)
Disodium cyanodithioimidocarbonate	56 (oral) [170 (oral) as 32% pesticidal formulation]
Ethyl dipropylthiocarbamate	700 (oral and inhalation) 6700 (dermal)
Ethylene glycol monoethyl ether (EGEE)	750 (oral) 960 (inhalation)
Ethylene glycol monoethyl ether acetate (EGEEA)	1100 (oral) 1400 (inhalation)
Ethylene glycol monomethyl ether	63 (oral)
Ethylene glycol monomethyl ether acetate	98 (oral)
Ethylene oxide	20
Hydramethylnon	120 (oral)
Hydrogen cyanide	10 (oral)
Lead	0.5
Linuron	460
Methanol	47000 (inhalation) 23000 (oral)
Methyl bromide as a structural fumigant	810 (inhalation)
N-Methylpyrrolidone	3200 (inhalation) 17000 (dermal)
Potassium cyanide	25 (oral)
Potassium dimethyldithiocarbamate	720
Quizalofop ethyl	590
Sodium cyanide	19 (oral)

Sodium dimethyldithiocarbamate	23 (oral) [58 (oral) as 40% pesticidal formulation]
Sulfur dioxide	10000
Thiophanate-methyl	600 (oral)
Toluene	7000

(c) Unless a specific level is otherwise provided in this section, an assessment by an agency of the state or federal government that is the substantial equivalent of the assessment described in subsection (a) of Section 25803, and establishes a maximum allowable dose level in the manner provided in paragraph (b)(1) of Section 25801, shall constitute the allowable dose level having no observable effect within the meaning of Section 25249.10(c) of the Act.

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

§ 25821. Level of Exposure to Chemicals Causing Reproductive Toxicity

(a) For purposes of the Act, "level in question" means the chemical concentration of a listed chemical for the exposure in question. The exposure in question includes the exposure for which the person in the course of doing business is responsible, and does not include exposure to a listed chemical from any other source or product.

(b) For purposes of Section 25249.10(c) of the Act, the level of exposure to a chemical listed as causing reproductive toxicity shall be determined by multiplying the level in question (stated in terms of a concentration of a chemical in a given medium) times the reasonably anticipated rate of exposure for an individual to a given medium. The reasonably anticipated rate of exposure shall be based on the pattern and duration of exposure that is relevant to the reproductive effect which provided the basis for the determination that a chemical is known to the state to cause reproductive toxicity. (For example, an exposure of short duration is appropriate for a teratogenic chemical, whereas a chronic or protracted exposure is appropriate for one that retards fetal growth.)

(c) The following assumptions shall be used to calculate the reasonably anticipated rate of exposure to a chemical listed as causing reproductive toxicity, unless more specific and scientifically appropriate data are available:

(1) The assumptions set forth in subsection (d) of Section 25721 shall be used to calculate the reasonably anticipated rate of exposure to a chemical listed as causing reproductive toxicity, unless more specific and scientifically appropriate data are available.

(2) For exposures to consumer products, the level of exposure shall be calculated using the reasonably anticipated rate of intake or exposure for average users of the consumer product, and not on a per capita basis for the general population. The rate

of intake or exposure shall be based on data for use of a general category or categories of consumer products, such as the United States Department of Agriculture Home Economic Research Report, Foods Commonly Eaten by Individuals: Amount Per Day and Per Eating Occasion, where such data are available.

(3) Where a maternal exposure to a chemical listed as causing reproductive toxicity has an effect on the conceptus (embryo or fetus), the level of exposure shall be based on the reasonably anticipated rate of exposure for the mother during the nine-month gestation period.

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