

## **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 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.

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.

(23) 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.

(34) 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.