

40 C.F.R. § 799.9310

TSCA 90-day oral toxicity in rodents.

(a) *Scope.* This section is intended to meet the testing requirements under section 4 of the Toxic Substances Control Act (TSCA). In the assessment and evaluation of the toxic characteristics of a chemical, the determination of subchronic oral toxicity may be carried out after initial information on toxicity has been obtained by acute testing. The subchronic oral study has been designed to permit the determination of the no-observed-effects level (NOEL) and toxic effects associated with continuous or repeated exposure to a test substance for a period of 90 days. This study is not capable of determining those effects that have a long latency period for development (e.g., carcinogenicity and life shortening). Extrapolation from the results of this study to humans is valid only to a limited degree. However, it can be useful in providing information on health hazards likely to arise from repeated exposure by the oral route over a limited period of time, such as target organs, the possibilities of accumulation, and can be of use in selecting dose levels for chronic studies and for establishing safety criteria for human exposure.

(b) *Source.* The source material used in developing this TSCA test guideline is the Office of Prevention, Pesticides, and Toxic Substances (OPPTS) harmonized test guideline 870.3100 (August 1998, final guideline). This source is available at the address in paragraph (h) of this section.

(c) *Definitions.* The following definitions apply to this section.

Cumulative toxicity is the adverse effects of repeated doses occurring as a result of prolonged action on, or increased concentration of, the administered test substance or its metabolites in susceptible tissue.

Dose in a subchronic oral study is the amount of test substance administered daily via the oral route (gavage, drinking water or diet) for a period of 90 days. Dose is expressed as weight of the test substance (grams, milligrams) per unit body weight of test animal (milligram per kilogram) or as weight of the test substance in parts per million in food or drinking water per day.

No-observed-effects level (NOEL) is the maximum dose used in a study which produces no adverse effects. The NOEL is usually expressed in terms of the weight of a test substance given daily per unit weight of test animal (milligrams per kilogram per day).

Subchronic oral toxicity is the adverse effects occurring as a result of the repeated daily exposure of experimental animals to a chemical by the oral route for a part (approximately 10%) of the test animal's life span.

Target organ is any organ of a test animal showing evidence of an effect induced by a test substance.

(d) *Limit test.* If a test at one dose level of at least 1,000 mg/kg body weight (expected human exposure may indicate the need for a higher dose level), using the procedures described for this study, produces no observable toxic effects or if toxic effects would not be expected based upon data of structurally related compounds, then a full study using three dose levels might not be necessary.

(e) *Test procedures*—(1) *Animal selection*—(i) *Species and strain*. A variety of rodent species may be used, although the rat is the preferred species. Commonly used laboratory strains must be employed.

(ii) *Age/weight*. (A) Testing should be started with young healthy animals as soon as possible after weaning and acclimatization.

(B) Dosing of rodents should generally begin no later than 8–9 weeks of age.

(C) At the commencement of the study the weight variation of animals used must be within 20% of the mean weight for each sex.

(iii) *Sex*. Equal numbers of animals of each sex must be used at each dose level, and the females shall be nulliparous and nonpregnant.

(iv) *Numbers*. (A) At least 20 rodents (10 males and 10 females) at each dose level.

(B) If interim sacrifices are planned, the number must be increased by the number of animals scheduled to be sacrificed before the completion of the study.

(C) To avoid bias, the use of adequate randomization procedures for the proper allocation of animals to test and control groups is required.

(D) Each animal must be assigned a unique identification number. Dead animals, their preserved organs and tissues, and microscopic slides must be identified by reference to the animal's unique number.

(v) *Husbandry*. (A) Animals may be group-caged by sex, but the number of animals per cage must not interfere with clear observation of each animal. The biological properties of the test substance or toxic effects (e.g., morbidity, excitability) may indicate a need for individual caging.

This document is only available to subscribers. Please log in or purchase access.

[Purchase Login](#)