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## 40 C.F.R. § 799.9325

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### TSCA 90-day dermal toxicity.

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(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 dermal toxicity may be carried out after initial information on toxicity has been obtained by acute testing. The subchronic dermal 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. It can, however, provide useful information on the degree of percutaneous absorption, 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 870.3250 (August 1998, final guideline). This source is available at the address in paragraph (h) of this section.

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

*Cumulative toxicity* is the adverse effect of repeated doses occurring as a result of prolonged action or increased concentration of the administered test substance or its metabolites in susceptible tissues.

*Dose* in a subchronic dermal study is the amount of test substance applied daily to the skin for 90 days. Dose is expressed as weight of the test substance (grams, milligrams), per unit body weight of test animal (milligrams per kilogram), or as weight of the test substance per unit of surface area (milligrams per square centimeter) per day.

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

*Subchronic dermal toxicity* is the adverse effects occurring as a result of the repeated daily exposure of experimental animals to a chemical by the dermal route for a part 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 section, produces no observable toxic effects or if toxic effects would not be expected based upon data on structurally related compounds, a full study using three dose levels might not be necessary.

(e) *Test procedures*—(1) *Animal selection*—(i) *Species and strain*. A mammalian species must be used for testing. The rat, rabbit, or guinea pig may be used. Commonly used laboratory strains must be employed. If other mammalian species are used, the tester must provide justification/reasoning for their selection. When a subchronic dermal study is conducted as a preliminary to a chronic dermal study, the same species and strain must be used in both studies.

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

(B) Dosing should generally begin in guinea pigs between 5–6 weeks of age, in rats between 8–9 weeks of age, and in rabbits at least 12 weeks old.

(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 with healthy skin must be used at each dose level. The females shall be nulliparous and nonpregnant except for specially designed studies.

(iv) *Numbers*. (A) At least 20 animals (10 animals per sex) must be used 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 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 should be housed in individual cages.

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