
40 C.F.R. § 799.9355

TSCA reproduction/developmental toxicity screening test.

(a) *Scope—(1) Applicability.* This section is intended to meet testing requirements of the Toxic Substances Control Act (TSCA) (15 U.S.C. 2601).

(2) *Source.* The source material used in developing this TSCA test guideline is the Office of Prevention, Pesticides, and Toxic Substances (OPPTS) harmonized test guideline 870.3550 (July 2000, final guidelines). This source is available at the address in paragraph (h) of this section.

(b) *Purpose.* (1) This guideline is designed to generate limited information concerning the effects of a test substance on male and female reproductive performance such as gonadal function, mating behavior, conception, development of the conceptus, and parturition. It is not an alternative to, nor does it replace, the existing comprehensive test standards in §§ 799.9370 and 799.9380.

(2) This screening test guideline can be used to provide initial information on possible effects on reproduction and/or development, either at an early stage of assessing the toxicological properties of chemicals, or on chemicals of high concern. It can also be used as part of a set of initial screening tests for existing chemicals for which little or no toxicological information is available, as a dose range finding study for more extensive reproduction/developmental studies, or when otherwise considered relevant.

(3) This test does not provide complete information on all aspects of reproduction and development. In particular, it offers only limited means of detecting postnatal manifestations of prenatal exposure, or effects that may be induced during postnatal exposure. Due (amongst other reasons) to the relatively small numbers of animals in the dose groups, the selectivity of the end points, and the short duration of the study, this method will not provide evidence for definite claims of no effects.

(c) *Definitions.* The definitions in section 3 of TSCA and in 40 CFR Part 792—Good Laboratory Practice Standards apply to this section. The following definitions also apply to this section.

Dosage is a general term comprising of dose, its frequency and the duration of dosing.

Dose is the amount of test substance administered. Dose is expressed as weight (g, mg) as weight of test substance per unit weight of test animal (e.g., mg/kg), or as constant dietary concentration parts per million (ppm).

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 kilograms per day).

(d) *Principle of the test.* (1) The test substance is administered in graduated doses to several groups of males and females. Males should be dosed for a minimum of four weeks and up to and including the day before scheduled sacrifice (this includes a minimum of two weeks prior to mating, during the mating period and,

approximately, two weeks post-mating). In view of the limited pre-mating dosing period in males, fertility may not be a particular sensitive indicator of testicular toxicity. Therefore, a detailed histological examination of the testes is essential. The combination of a pre-mating dosing period of two weeks and subsequent mating/fertility observations with an overall dosing period of at least four weeks, followed by detailed histopathology of the male gonads, is considered sufficient to enable detection of the majority of effects on male fertility and spermatogenesis.

(2) Females should be dosed throughout the study. This includes two weeks prior to mating (with the objective of covering at least two complete oestrous cycles), the variable time to conception, the duration of pregnancy and at least four days after delivery, up to and including the day before scheduled sacrifice.

(3) Duration of study, following acclimatization, is dependent on the female performance and is approximately 54 days, (at least 14 days pre-mating, (up to) 14 days mating, 22 days gestation, 4 days lactation).

(4) During the period of administration, the animals are observed closely each day for signs of toxicity. Animals which die or are sacrificed during the test period are necropsied and, at the conclusion of the test, surviving animals are sacrificed and necropsied.

(e) *Description of the method—(1) Selection of animal species.* This test standard is designed for use with the rat. If other species are used, appropriate modifications will be necessary. Strains with low fecundity or well-known high incidence of developmental defects should not be used. Healthy virgin animals, not subjected to previous experimental procedures, should be used. The test animals should be characterized as to species, strain, sex, weight and/or age. At the commencement of the study the weight variation of animals used should be minimal and not exceed 20% of the mean weight of each sex.

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