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## 40 C.F.R. § 799.9370

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### TSCA prenatal developmental toxicity.

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- (a) *Scope* This section is intended to meet the testing requirements under section 4 of TSCA. This guideline for developmental toxicity testing is designed to provide general information concerning the effects of exposure on the pregnant test animal and on the developing organism; this may include death, structural abnormalities, or altered growth and an assessment of maternal effects. For information on testing for functional deficiencies and other postnatal effects, the guidelines for the two-generation reproductive toxicity study and the developmental neurotoxicity study should be consulted.
- (b) *Source*. The source material used in developing this TSCA test guideline is the OPPTS harmonized test guideline 870.3700 (February 1996 Public Draft). This source is available at the address in paragraph (h) of this section.
- (c) *Good laboratory practice standards*. The study shall be conducted in compliance with 40 CFR Part 792—Good Laboratory Practice Standards.
- (d) *Principle of the test method*. The test substance is administered to pregnant animals at least from implantation to one day prior to the expected day of parturition. Shortly before the expected date of delivery, the pregnant females are terminated, the uterine contents are examined, and the fetuses are processed for visceral and skeletal evaluation.
- (e) *Test procedures*—(1) *Animal selection*—(i) *Species and strain*. It is recommended that testing be performed in the most relevant species, and that laboratory species and strains which are commonly used in prenatal developmental toxicity testing be employed. The preferred rodent species is the rat and the preferred non-rodent species is the rabbit.
- (ii) *Age*. Young adult animals shall be used.
- (iii) *Sex*. Nulliparous female animals shall be used at each dose level. Animals should be mated with males of the same species and strain, avoiding the mating of siblings, if parentage is known. Day 0 in the test is the day on which a vaginal plug and/or sperm are observed in the rodent or that insemination is performed or observed in the rabbit.
- (iv) *Number of animals*. Each test and control group shall contain a sufficient number of animals to yield approximately 20 animals with implantation sites at necropsy.
- (2) *Administration of test and control substances*—(i) *Dose levels and dose selection*. (A) At least three-dose levels and a concurrent control shall be used. Healthy animals shall be randomly assigned to the control and treatment groups, in a manner which results in comparable mean body weight values among all groups. The dose levels should be spaced to produce a gradation of toxic effects. Unless limited by the physical/chemical nature or biological properties of the test substance, the highest dose shall be chosen with the aim to induce some developmental and/or maternal toxicity but not death or severe suffering. In the case of maternal mortality, this
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should not be more than approximately 10%. The intermediate dose levels should produce minimal observable toxic effects. The lowest dose level should not produce any evidence of either maternal or developmental toxicity (i.e., the no-observed-adverse-effect level, NOAEL) or should be at or near the limit of detection for the most sensitive endpoint. Two- or four-fold intervals are frequently optimal for spacing the dose levels, and the addition of a fourth test group is often preferable to using very large intervals (e.g., more than a factor of 10) between dosages.

(B) It is desirable that additional information on metabolism and pharmacokinetics of the test substance be available to demonstrate the adequacy of the dosing regimen. This information should be available prior to testing.

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