



Designation: E 1483 – 92 (Reapproved 1996)

Standard Test Method for Assessing Developmental Toxicity in Rats and Rabbits¹

This standard is issued under the fixed designation E 1483; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This test method is designed to assess the potential of a pesticide or chemical to present a hazard to the unborn arising from exposure of the maternal animal during pregnancy.

1.2 This test method assumes that the user is knowledgeable in animal toxicology and related pertinent areas, and it relies heavily on the judgment of the evaluator.

1.3 The values stated in SI units are to be regarded as the standard. The values given in parentheses are for information only.

1.4 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.* For specific hazard statements, see Section 6.

2. Referenced Documents

2.1 ASTM Standards:

E 609 Definitions of Terms Relating to Pesticides²

E 943 Terminology Relating to Biological Effects and Environmental Fate²

2.2 Federal Standards:

Title 40, Code of Federal Regulations (CFR), Environmental Protection Agency, Subchapter E, Pesticide Programs: Part 160, Good Laboratory Practice Standards³

Title 21, Code of Federal Regulations (CFR), Food and Drug Administration, Part 58, Good Laboratory Practice for Nonclinical Studies³

Title 40, Code of Federal Regulation (CFR), Toxic Substance Control Act, Part 792, Good Laboratory Practice Standards³

3. Terminology

3.1 Definitions:

3.1.1 For definitions of terms used in this test method, see Definitions E 609 and Terminology E 943.

3.1.2 *developmental toxicity*—the property of a test substance that causes in utero death, structural or functional

abnormalities (teratogenic), or growth retardation during the period of fetal development. To assess that property, the test substance is administered to the maternal animal during the period of major organogenesis.

4. Summary of Test Method

4.1 Rats and rabbits have been used extensively as animal models to determine whether a test substance is potentially hazardous to the developing fetus. The use of two species is desirable because of differences in maternal and fetal metabolism, placental barriers, and chemical absorption.

4.2 The test substance is administered in graded doses to groups of pregnant animals from the time of embryonic implantation through the period during which major organ systems are formed. At least 20 pregnant rats and 12 pregnant rabbits are required for each of the three test groups and the control group.

4.3 A pilot study is conducted to establish the three dose levels for the full study.

4.4 On Day 20 of gestation for rats and Day 29 for rabbits, the pregnant females are sacrificed, the uteri are removed, and the contents are examined for embryonic or fetal deaths and live fetuses. Collected fetuses are weighed, measured, tagged, and sacrificed in preparation for complete examination.

4.5 If a limit test at an exposure of least 1000 mg/kg body weight produces no observable toxicity, a full study using three dose levels might not be necessary.

5. Significance and Use

5.1 In the assessment and evaluation of the toxic characteristics of a chemical, determination of the potential developmental toxicity is significant.

5.2 This test method is intended to permit the determination of a no-observed-effect level and the potential hazard to the unborn that may arise from exposure of the pregnant organism during gestation.

6. Hazards

6.1 Contact with all test substances and solutions should be minimized with appropriate protective clothing, gloves, eye protection, etc. The use of fume hoods and increased ventilation in test rooms is necessary when handling volatile substances. Information on acute mammalian toxicity and special handling procedures for all chemicals and products to be used should be known before this test method is employed.

6.2 The disposal of excess test substance, solutions, diets,

¹ This test method is under the jurisdiction of ASTM Committee E-35 on Pesticides and is the direct responsibility of Subcommittee E35.26 on Antimicrobial Agents.

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² *Annual Book of ASTM Standards*, Vol 11.05.

³ Available from U.S. Government Printing Office, Superintendent of Documents, Washington, DC 20402.