



Standard Test Method for Oncogenicity Study in Rats and Mice¹

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1. Scope

1.1 This test method covers a long-term study to determine the oncogenicity potential of a substance in mammalian species such as the rat and mouse. The objective is to observe the test animals for a major portion of their life span for neoplastic lesions during exposure to various doses of a test substance by oral administration.

1.2 This test may also provide some information on long-term general toxicity.

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

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

1.5 *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.* Specific hazards statements are given in 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:³

Title 21 CFR, Part 58, Good Laboratory Practice for Non-clinical Studies, Food and Drug Administration

Title 40 CFR, Part 798, Health Effects Testing Guidelines, Subpart D, Chronic Exposure, Chronic Toxicity and Oncogenicity, Environmental Protection Agency

Title 40 CFR, Subchapter E, Pesticide Program: Part 160, Good Laboratory Practice Standards, Environmental Protection Agency

Title 40 CFR, Part 792, Good Laboratory Practice Standards, Toxic Substance Control Act

3. Terminology

3.1 *Definitions*—See Definitions E 609 and Terminology E 943.

3.2 Definitions of Terms Specific to This Standard:

3.2.1 *chronic toxicity*—the adverse effects occurring as a result of the daily exposure of mammalian species to a test substance by diet, water, capsule, or gavage for an extended period of time.

3.2.2 *gavage*—administration of the test substance by placement into the stomach through an orogastric tube.

3.2.3 *neoplastic*—capable of producing abnormal tissue growth.

3.2.4 *nulliparous*—having never borne an offspring.

3.2.5 *oncogenicity*—the condition of producing tumors.

4. Summary of Test Method (Title 40 CFR, Part 798)

4.1 Two mammalian species are required. Rats and mice are the species of choice because of their relatively short life spans, the limited cost of their maintenance, their widespread use in pharmacological and toxicological studies, and the availability of inbred strains.

4.2 One hundred twenty-four rats (62 females and 62 males) and 112 mice (56 females and 56 males) are used for each of the four dose levels (control-, low-, intermediate-, and high-dosage groups).

4.3 The test substance is administered either in the diet or water or by gavage at levels based on results from prior feeding studies. The administration of test substance is for two years for rats; it is 18 months for mice.

4.4 An interim sacrifice is made at the end of one year for both rats and mice; after 18 months the interim sacrifice is for rats only.

4.5 Daily observations of all individual animals for signs of toxicity and mortality are recorded.

4.6 Hematology blood samples are collected for analysis prior to interim sacrifices and termination of the test.

4.7 Data collected from treatment and control groups are compared statistically for changes and to note the formation of tumors. Histopathological examinations are performed on selected tissues.

5. Significance and Use

5.1 This test method should generate data to determine the presence, incidence, and severity of abnormalities (including

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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.