



Standard Test Method for Chronic Oral Toxicity Study in Rats¹

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1. Scope

1.1 This test method covers a long-term study to determine the effects of a substance in a mammalian species such as the rat following prolonged and repeated oral exposure. Under the conditions of the chronic toxicity test, effects that require a long latency period or that are cumulative should become manifest.

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

1.3 The values stated in SI units are to be regarded as the standard. The inch-pound units 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, CFR, Toxic Substance Control Act, Part 792, Good Laboratory Practice Standards³

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

Exposure, Chronic Toxicity³

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 a one-year period.

3.2.2 *concentration*—the weight of test substance per unit weight of the diet (expressed as milligrams per kilogram of diet). The weight of test substance per volume of H₂O (expressed as milligrams per millilitre of water), or at a constant rate in the diet (expressed as parts per million).

3.2.3 *feed efficiency*—this value is a measure of the efficiency with which the animals convert food to body weight. The calculation is the total body weight gain per total food consumed.

3.2.4 *gavage*—forced feeding, as by tube that is passed down the throat to the stomach.

3.2.5 *test substance*—pesticide or other material (element, chemical compound, formulation, known mixture) administered orally for the purpose of determining chronic toxicity.

4. Summary of Test Method⁴

4.1 One mammalian species, a rodent, is required; the rat is the preferred rodent. Forty rats (twenty females and twenty males) are used at each of the four dose levels (control-, low-, medium- and high-dosage groups). If it is determined that an interim sacrifice is necessary, the number should be increased by the number of animals scheduled to be sacrificed during the course of the study (see CFR, Title 40, Part 798).

4.2 The high-dose level in rats should elicit some signs of toxicity without causing excessive lethality. The lowest dosage level should be one that does not induce any evidence of toxicity. This level should be higher (if possible) than that expected for human exposure. The intermediate-dosage level should produce a minimal observable effect. Where appropriate, a vehicle control (the volume of which corresponds to the volume of vehicle at the highest exposure level) should be

¹ This test method is under the jurisdiction of ASTM Committee E35 on Pesticides and Alternative Control Agents and is the direct responsibility of Subcommittee E35.26 on Safety to Man.

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

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

⁴ Benitz, K. F., "Measurement of Chronic Toxicity," *Methods of Toxicology*, ed. G. E. Paget, Blackwell Scientific Publications, Oxford, England, 1970, pp. 32–131.