Designation: E1163 – 10 (Reapproved 2016)

Standard Test Method for Estimating Acute Oral Toxicity in Rats[1]

This standard is issued under the fixed designation E1163; 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 determines the lethality (LD50 value, slope and 95 % confidence interval (CI)) and signs of acute toxicity from a material using a limited number of rats. The technique used in this test method is referred to as the "Stagewise, Adaptive Dose Method."[2] This test method is an alternative to the classical LD50 test and is applicable to both liquids and solids.

1.2 This test method is not recommended for test materials which typically produce deaths beyond two days postdosing.

1.3 *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.*

2. Referenced Documents

2.1 *ASTM Standards:*[3]

E609 Terminology Relating to Pesticides

IEEE/ASTM SI 10 Standard for Use of the International System of Units (SI) (the Modernized Metric System)

3. Terminology

3.1 *Definitions:*

3.1.1 *delayed death*—an animal which does not die or appear moribund within 24 h but dies later during the observation period.

3.1.2 *gavage*—forced oral dosing, as by a tube that is passed down the throat to the stomach.

3.1.3 *LD50*—the statistically derived estimate of the dose of a test substance that would be expected to cause 50 % mortality to the test population under the specified test conditions.

3.1.4 *moribund*—at the point of death or extinction.

3.1.5 *pharmacotoxic*—gross physiological signs in response to a toxic material.

3.1.6 *signs of toxicity*—objective, observable evidence of toxicity.

3.1.7 *suspension*—a mixture in which very small particles remain suspended without dissolving.

3.1.8 *toxicity*—poisonous quality.

4. Summary of Test Method

4.1 Three to five different doses of the target compound are selected such that the doses span the entire dose response curve, with separation between the doses to be equal log intervals. One to two animals are given each dose as the first stage of the study. After 24 to 48 h, the responses to each dose are observed and used in determining the doses and animal numbers in the next stage of dosing.

4.2 The second and subsequent stages have one to four doses with one to three animals at each dose. Doses for subsequent stages are selected based on the estimates of the dose response distribution parameters and the uncertainties of these estimates. The dose response curve and its parameters are updated after each stage and dosing will stop when the 95 % confidence interval for the LD50 satisfies the following stopping rule: (upper 95 % CI – lower 95 % CI)/ (2 × LD50) < = 0.40).

4.3 The slope, LD50 and its 95 % confidence interval are calculated using the methods Feder.[2] No more than the use of 30 animals is recommended and shall constitute an additional stopping rule.

5. Significance and Use

5.1 This test method is of principal value in minimizing the number of animals required to estimate the acute oral toxicity (LD50). It also incorporates measures of variance (95 % CI) and a slope from which to make relative toxicity comparisons.

5.2 This test method is inappropriate for materials typically producing death two or more days after administration of the test compound unless the observation time between dosages is increased. This test method can be successfully applied,

[1] This test method is under the jurisdiction of ASTM Committee E50 on Environmental Assessment, Risk Management and Corrective Action and is the direct responsibility of Subcommittee E50.47 on Biological Effects and Environmental Fate.

Current edition approved Feb. 1, 2016. Published March 2016. Originally approved in 1987. Last previous edition approved in 2010 as E1163 – 10. DOI: 10.1520/E1163-10R16.

[2] Feder, P.I., Statistical Design Considerations for Stagewise, stagewise, adaptive dose allocation in dose responsive studies. In: Peace, Karl E., ed. Biopharmaceutical sequential statistical applications. New York: Marcel Dekker 1992.

[3] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.