Designation: E 1073 – 01

Standard Test Method for Obtaining a Pharmacological Profile with Mice[1]

This standard is issued under the fixed designation E 1073; 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 as a simple and inexpensive initial screening procedure for new compounds with unknown pharmacological properties, or for the comparative bioassay of new members of a chemical series with class reference standards. The test method, which is applicable to most pharmacologically active compounds including pesticides, will properly rank order both acute lethality and potency with a minimum expenditure of test material. It is intended as the first step in a multi-tiered development program.

1.2 *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. Summary of Test Method

2.1 Mice are injected intravenously with a dose of the test material and then observed for reaction signs, first those that can be detected by nonmanipulative tests, and then those sensed during a series of manipulative tests.

2.2 Two technicians are required to perform the experiment. One injects the mice and records the data, while the other conducts the experiment at regularly scheduled time intervals and dictates the findings.

2.3 The results obtained using this procedure indicate the approximate median lethal dose (LD50), the approximate median level of nonlethal reactions (MED50), the reaction signs elicited at each dose level tested, and the degree of severity of those signs. In contrast to the more commonly used median effective dose (ED50), the MED50 value may have been generated by one or more responses at the same dose, and thus does not imply the 50 % level for a specific reaction sign.

2.4 By judicious selection of acceptance criteria, the elimination rate for compounds tested using this procedure can be tailored to any desired level.

3. Significance and Use

3.1 This test method is designed as an initial screening procedure for the selection of compounds worthy of more detailed study.

3.2 This test method is applicable to the study of most drugs and chemicals, and will properly estimate both lethal and minimally effective dose levels. Although it is designed for the study of single components, it can be used to study the comparative toxicity of mixtures or formulations. The method may not be applicable to oily substances which cause embolism upon injection.

3.3 This test method requires only small quantities of test materials (approximately 1 g), a fact that enhances its utility as the initial biological study for newly synthesized substances.

3.4 It is equally economical in its requirements for equipment, space, personnel, and animals. Only a small laboratory, simple test equipment, and two technicians are needed to conduct the experiments. Furthermore, an average of only thirty mice are required to conduct the entire test method.

3.5 The procedure is applicable to a wide variety of materials. When results of this test were compared with those from more detailed and specific animal tests, a high degree of correlation was obtained. Further evidence of the utility of the test was demonstrated by the fact that a high correlation of rank order potencies was found for a series of anticholinergics studied in both mice and men.

4. Apparatus

4.1 All of the apparatus used for this test method is simple and inexpensive. It can be made in any well-equipped laboratory workshop or, in some cases, obtained commercially.

4.2 The major components of the apparatus are illustrated in Figs. 1-5.

4.3 *Syringes and Needles*:

4.3.1 One-quarter millilitre glass Tuberculin syringes, fitted with 0.75 in. (19 mm), 27-gage needles are recommended for injection of all solutions except undiluted polyethylene glycol (PEG) solutions. In the latter case, 24-gage needles must be used to compensate for the viscosity of the solvent, and 50-µL syringes[2,3] are required to measure accurately the small volumes that are administered.

[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 Safety to Man.

Current edition approved Oct. 10, 2001. Published November 2001. Originally published as E 1073 – 85. Last previous edition E 1073 – 91 (1996)

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