



Standard Test Method for Cardiac Sensitization Study on Dogs¹

This standard is issued under the fixed designation E 1674; 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 covers an inhalation procedure to investigate the cardiac sensitization of volatile chlorinated hydrocarbons and other volatile solvents.

1.2 This test method is primarily a screening tool. The procedure does permit a rank order of the sensitization potential of the compounds tested, but is not recommended for establishing significant effect levels.

1.3 This test method assumes that the user is knowledgeable in mammalian toxicology, electrocardiography with animals and other pertinent areas, and relies heavily on the judgment of the investigator.

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.*

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

3. Terminology

3.1 *Definitions*—for terms used in this test method, see Definitions E 609 and Terminology E 943.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *cardiac sensitization*—the reaction of the heart to adrenaline (epinephrine) resulting in the production of ventricular arrhythmias.

4. Summary of Test Method³

4.1 Six healthy male dogs are employed for each test material. After the initial acclimation period, the dogs are trained to maintain a standing position while supported in a

cloth sling and wearing an inhalation mask over their nose and mouth.

4.2 Since dogs can vary markedly in their cardiac response to intravenous injection of adrenaline (epinephrine), each dog is evaluated to select an appropriate dose. The selected dose is used in all subsequent work.

4.3 All six dogs are tested on the same day, one at a time. Each animal is placed in the sling, fitted with the inhalation mask and standard electrocardiogram (ECG) leads connected to an electrocardiograph.

4.4 The test proceeds as follows:

4.4.1 At zero time start the ECG recording.

4.4.2 At 2 min, administer the selected dose of adrenaline into the cephalic vein.

4.4.3 At 7 min, start the inhalation of vapor of the test material. Monitor the concentration of test material administered.

4.4.4 At 12 min, administer a challenge injection of adrenaline.

4.4.5 At 17 min, stop the vapor inhalation and the ECG recording.

4.4.6 Return the dogs to their kennels. They should be tested on a Monday, Wednesday, and Friday regimen.

4.5 The dogs are exposed to a 2.5 % concentration of the test material the first time; then exposed to 5 % on the next test day. If necessary, the dogs are exposed successively to 10 %, 15 %, and 20 % as needed. As soon as ventricular tachycardia is evidenced, the testing is stopped. If no appearance of ventricular arrhythmia occurs in the ECG recording at the highest concentration and there are no other deleterious events, then no cardiac sensitization has occurred.

5. Significance and Use

5.1 This test method is designed to provide information as to any dose level of test material that gives rise to clear signs of compound-induced cardiac sensitization.

5.2 Cardiac sensitization has occurred in humans during periods of stress while being exposed to high concentrations of some unsubstituted and halogenated hydrocarbons.³

5.3 The dog is employed for this study because the conclusions from this test method can be applied to man with much

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 October 10, 1999. Published November 1999. Originally published as E 1674 - 95. Last previous edition E 1674 - 95.

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

³ Reinhardt, C. F., Azar, A., Maxfield, M. E., Smith, P. E. Jr., and Mullin, L. S., "Cardiac Arrhythmias and Aerosol Sniffing," *Archives of Environmental Health*, Vol. 22, No. 2, February 1971, pp. 265-279.