



Standard Guide for Acute Animal Toxicity Testing of Water-Miscible Metalworking Fluids¹

This standard is issued under the fixed designation E 1302; 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 guide defines acute animal toxicity tests and sets forth the references for procedures to assess the acute toxicity of water-miscible metalworking fluids as manufactured.

1.2 Although water-miscible metalworking fluids are typically used at high dilution, dilution rates vary widely. Additionally, there is potential for exposure to the metalworking fluid as manufactured.

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:

E 758 Test Method for Mammalian Acute Percutaneous Toxicity²

E 981 Test Method for Estimating Sensory Irritancy of Airborne Chemicals²

E 993 Test Method for Evaluation of Delayed Contact Hypersensitivity²

E 1103 Test Method for Determining Subchronic Dermal Toxicity²

2.2 CPSC Standards:³

16 CFR Part 1500

16 CFR Part 1500.3

16 CFR Part 1500.40

16 CFR Part 1500.41

16 CFR Part 1500.42

2.3 DOT Standards:³

49 CFR Part 173, Appendix A

49 CFR Part 173.343a1

49 CFR Part 173.343a2

49 CFR Part 173.343a3

2.4 EPA-TSCA Standards:³

40 CFR 792

40 CFR 870.1100

40 CFR 870.1200

40 CFR 870.1300

40 CFR 870.2400

40 CFR 870.2500

40 CFR 870.2600

2.5 OSHA Standards:³

29 CFR 1910.1200

29 CFR 1910.1200 Appendix A, 3(a) and 6(a)

29 CFR 1910.1200 Appendix A, 3(b) and 6(b)

29 CFR 1910.1200 Appendix A, 3(c) and 6(c)

29 CFR 1910.1200 Appendix A, 4

3. Significance and Use

3.1 Application of this guide will provide information on the acute toxicity of water-miscible metalworking fluids and will assist the user in evaluating the potential health hazards of the fluid and developing appropriate work practices. A water-miscible metalworking fluid is a concentrate designed to be diluted in water for use.

3.2 Water-miscible metalworking fluids are complex chemical mixtures. The United States Occupational Safety and Health Administration (OSHA) Hazard Communication Standard (see A1.8) outlines procedures for the hazard determination of mixtures and states that if a mixture has not been tested as a whole, then the mixture shall be assumed to present the same hazards as do the components that comprise 1 % (by weight or volume) or greater of the mixture, except that the mixture shall be assumed to present a carcinogenic hazard if it contains a component in concentrations of 0.1 % or greater, which is considered to be a carcinogen (as defined in OSHA Standard 29 CFR 1910.1200). The determination of when to test a mixture as a whole and which toxicity tests are appropriate for the product must be made by a health professional, qualified in evaluating toxicological data.

3.3 Acute toxicology testing of water-miscible metalworking fluids consists of several individual tests including acute oral, dermal, or inhalation toxicity, eye irritation, skin irritation or corrosion, or both, skin sensitization, and sensory irritation. Certain protocols for acute oral, dermal, and inhalation toxicity

¹ This test method is under the jurisdiction of ASTM Committee E-34 on Occupational Health and Safety and is the direct responsibility of Subcommittee E34.50 on Health and Safety Standards for Metal Working Fluids.

Current edition approved March 10, 2000. Published April 2000. Originally Published as E 1302 - 89. Last previous edition E 1302 - 89 (1994)^{ε1}.

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

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

tests are limit tests; further multi-dose testing (for example, Test Method E 1103) should take place if mortality is noted on any of these tests. The referenced protocols specify the species and number of animals required. Selection of tests conducted should be designed to minimize the number of animals used.

3.3.1 Acute Oral Toxicity—Acute oral toxicity tests (see A1.1) provide information on health hazards likely to arise from short-term exposure by the oral route. Results of this type of test are used to develop warning statements on labels as may be required by OSHA Hazard Communication Standard 29 CFR 1910.1200 (see A1.8) or Federal Hazardous Substances Act (see A1.10). These are also used to establish a dosage regimen for subchronic and other testing. Endpoint: mortality.

3.3.2 Acute Dermal Toxicity—Acute dermal toxicity tests (see A1.2) provide information on health hazards likely to arise from short-term exposure by the dermal route and may provide initial information on dermal absorption and the mode of toxic action of a substance. In addition, some measure of irritation caused by the fluid may be obtained by observing local tissue damage at the sight of application. Endpoint: mortality.

3.3.3 Acute Inhalation Toxicity—Acute inhalation toxicity tests give an indication of relative toxicity (see A1.3). The results provide an indication of the potential of the fluid to cause death and other adverse health effects when inhaled for a specified time period. Endpoint: mortality.

3.3.4 Eye Irritation—Eye irritation tests provide an indication of the potential of the fluid to cause eye irritation or damage upon direct contact (see A1.4). An irritant is defined as a chemical that is not corrosive, but causes a reversible inflammatory effect on living tissue by chemical action at the site of contact. Endpoint: degree of irritation.

3.3.5 Skin Irritation or Corrosion—Skin irritation or corrosion tests indicate the potential of the fluid to produce irritation or damage to skin (see A1.5). A corrosive chemical is one that causes visible destruction of, or irreversible alterations in, living tissue by chemical action at the site of contact. Endpoint: irritation or corrosion.

3.3.6 Skin Sensitization—A chemical sensitizer is a material that causes a substantial proportion of exposed people or animals to develop an allergic reaction in normal tissue after

repeated exposure to the chemical. A number of methods are available for measuring skin sensitization, however, there are differences in opinion on the most appropriate method. These are due to variations in compound administration and degree of reaction to a sensitizing substance. Refer to the Code of Federal Regulations (CFR) for the various protocols (see A1.6). Additionally, toxicology testing contract labs may have standard procedures for conducting these assays. Endpoint: sensitization.

3.3.7 Sensory Irritation—Upon exposure to a sensory irritant, humans experience discomfort or a burning sensation of the eyes, nose, and throat, and may also cough. Test Method E 981 (see A1.2.5) provides a means to evaluate the sensory irritant potential of airborne chemicals and mixtures as well as a means to assess the comparative irritancy of compounds and formulations. However, this test method cannot be used to evaluate the relative obnoxiousness of odors. Endpoint: upper respiratory tract irritation.

3.4 A number of federal guidelines can be used to establish general procedures for testing acute toxicity of metalworking fluids. Several references are cited in Annex A1. Regardless of the method used, Good Laboratory Practices, as outlined by the United States Environmental Protection Agency (EPA 40 CFR 792) (see A1.9) must be followed. The OSHA Hazard Communication Standard (see A1.8) outlines the responsibilities of chemical manufacturers, importers, and employers in the determination of chemical hazards and communication of information on those hazards.

3.5 The methods referenced in this guide or appropriate alternate methods such as those suggested by the Organization for Economic Cooperation and Development (OECD) are acceptable for testing the acute toxicity of water-miscible metalworking fluids. For each test outlined in Annex A1.1-A1.5, a table is included that highlights the similarities and differences between the test protocols.

4. Keywords

4.1 acute toxicity testing; dermal; eye; inhalation; metalworking fluids; oral

ANNEX

(Mandatory Information)

A1. REFERENCES FOR ACUTE ANIMAL TOXICITY TESTING

A1.1 Acute Oral Toxicity—See Table A1.1.

TABLE A1.1 Acute Oral Toxicity

Protocol	Dose/Animal Toxicity Class	Number of Groups/Dose Level	Observation Time	Additional Endpoints
CPSC	LD50 <50 mg/kg Highly toxic LD50 50 mg to 5 g/kg Toxic Rat	ns ^A	14 days	ns ^A
DOT	LD50 <50 mg/kg Poison B Rat	1	48 h	ns ^A
EPA (TSCA)	5 g/kg-limit test Rat	1	14 days	External observations of toxicity
OSHA	LD50 <50 mg/kg Highly toxic LD50 50 to 500 mg/kg Toxic Rat	ns ^A	ns ^A	ns ^A

^A Not specified.

TABLE A1.2 Acute Dermal Toxicity

Protocol	Dose/Animal Toxicity Class	Number of Groups/ Dose Level	Duration of Contact	Observation Time
CPSC	LD50 <200 mg/kg Highly toxic LD50 200 to 2000 mg/kg Toxic Rabbit	ns ^A	Up to 24 h Occluded, abraded, and intact skin	14 days
DOT	LD50 <200 mg/kg Poison B Rabbit	1	24 h	48 h
EPA (TSCA)	2 g/kg-limit test Rabbit, male and female	1	24 h Occluded and abraded skin	14 days
OSHA	LD50 <200 mg/kg Highly toxic LD50 200 to 1000 mg/kg Toxic Rabbit	ns ^A	24 h	ns ^A

^A Not specified.

A1.1.1 Consumer Product Safety Commission (CPSC): 16 CFR part 1500.3.

TABLE A1.3 Acute Inhalation Toxicity

Protocol	Concentration/ Animal Toxicity Class	Number of groups/ Dose Levels	Exposure Duration	Observation Time	Additional Endpoints
CPSC	LC50 <2 mg/L or 200 ppm - Highly toxic LC50 2 to 20 mg/L or 200–20 000 ppm Toxic Rat	ns ^A	1 h	ns ^A	ns ^A
DOT	LC50 <2 mg/L Poison B Rat	1	1 h	48 h	ns ^A
EPA (TSCA)	5 mg/L limit test Rat; male and female	1	4 h whole body	14 days	External observation of toxicity
OSHA	LC50 <2 mg/L or 200 ppm Highly toxic LC50 2 to 20 mg/L or 200–2000 ppm Toxic Rat	ns ^A	1 h	ns ^A	ns ^A

^A Not specified.

A1.1.2 Department of Transportation (DOT): 49 CFR 173.343a1.

A1.1.3 Environmental Protection Agency, Toxic Substances Control Act (EPA-TSCA): 40 CFR 870.1100.

A1.1.4 Occupational Safety and Health Administration (OSHA), 29 CFR 1910.1200, Appendix A, 3(a) and 6(a).

A1.2 Acute Dermal Toxicity—See Table A1.2.

A1.2.1 CPSC: 16 CFR 1500.40.

A1.2.2 DOT: 49 CFR 173.343a3.

A1.2.3 EPA-TSCA: 40 CFR 870.1200.

A1.2.4 OSHA: 29 CFR 1910.1200, Appendix A, 3(b) and 6(b).

A1.2.5 Test Method E 758.

A1.3 Acute Inhalation Toxicity—See Table A1.3.

A1.3.1 CPSC: 16 CFR part 1500.3.

A1.3.2 EPA-TSCA: 40 CFR 870.1300.

A1.3.3 DOT: 49 CFR 173.343a2.

A1.3.4 OSHA: 29 CFR 1910.1200, Appendix A, 3(c) and 6(c).

TABLE A1.4 Eye Irritation

NOTE 1—It may not be necessary to conduct an eye irritation test if the skin irritation/corrosion test is severely positive.

Protocol	Animals (number)	Dose	Exposure Time	Observation Time and Scoring
CPSC	Rabbit (6)	0.1 mL undiluted fluid	Unwashed	24, 48, 72 h Scoring-Draize
EPA ^A (TSCA)	Rabbit (9)	0.1 mL undiluted fluid	6-unwashed 3-washed for 1 min, 20–30 s after instillation	24, 48, 72 h, 4 and 7 days (every 3 days thereafter for 13 days if injury persists) Scoring-Draize
OSHA	Rabbit (6)	0.1 mL undiluted fluid	Unwashed	24, 48, 72 h Scoring-Draize

^A EPA protocol gives an indication of what happens when the eye is washed following exposure. This may be useful information.

A1.4 Eye Irritation—See Table A1.4.

- A1.4.1 CPSC: 16 CFR 1500.42.
- A1.4.2 EPA-TSCA: 40 CFR 870.2400.
- A1.4.3 OSHA: 29 CFR 1910.1200, Appendix A, 4.

A1.5 Skin Irritation or Corrosion—See Table A1.5.

- A1.5.1 CPSC: 16 CFR 1500.41 (Irritation).
- A1.5.2 DOT: 49 CFR Part 173, Appendix A (Corrosion).
- A1.5.3 EPA-TSCA: 40 CFR 870.2500.
- A1.5.4 OSHA: 29 CFR 1910.1200, Appendix A, 4.

A1.6 Skin Sensitization (40 CFR 870–2600)

- A1.6.1 Freund’s complete adjuvant test.
- A1.6.2 Guinea pig maximization test.
- A1.6.3 Split adjuvant technique.
- A1.6.4 Buehler test.
- A1.6.5 Open epicutaneous test.
- A1.6.6 Mauer optimization test.
- A1.6.7 Footpad technique in guinea pig.
- A1.6.8 Test Method E 993.

A1.7 Sensory Irritation

- A1.7.1 Test Method E 981.

TABLE A1.5 Skin Irritation or Corrosivity

Protocol	Animals (number)	Dose	Exposure Time	Observation Time and Scoring
CPSC (Irritation)	Rabbit (6)	0.5 mL undiluted fluid	24 h multiple sites; intact and abraded skin; occluded	24 and 72 h Scoring-Draize (redness, scarring, and swelling).
DOT ^A (Corrosivity)	Rabbit (6)	0.5 mL undiluted fluid	4 h intact skin; occluded	Score and wash after 4 h. Score at 48 h for irreversible tissue alteration, necrosis, and ulceration.
EPA (TSCA) (Irritation)	Rabbit (6)	0.5 mL undiluted fluid	4 h multiple sites; intact skin; occluded	After 4 h remove occlusion, wash skin. Score at 0.5 to 1, 24, and 72 h-Draize. Observe for a maximum of 14 days until irritation subsides or determine if irreversible.
OSHA (Irritation/Corrosivity)	Rabbit (6) Same as DOT for corrosivity	0.5 mL undiluted fluid	4 h multiple sites; intact and abraded skin; occluded	24 and 72 h Scoring-Draize (redness, scarring, and swelling).

^A The DOT protocol is a measure of corrosivity only. In order to conserve animals, the laboratory may want to conduct the EPA or CPSC procedures for irritation in conjunction with the DOT protocol. Using multiple sites, at end of 4 h remove some of the occlusions and measure for DOT corrosivity.

A1.8 OSHA Hazard Communication Standard

- A1.8.1 29 CFR 1910.1200.

A1.9 Good Laboratory Practices

- A1.9.1 (EPA) 40 CFR 792.

A1.10 Federal Hazardous Substances Act

- A1.10.1 (CPSC): 16 CFR 1500.

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