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An American National Standard

Standard Practice for Extraction of Medical Plastics[1]

This standard is issued under the fixed designation F 619; 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.

ε[1] NOTE—Keywords were added editorially in May 1998.

1. Scope

1.1 This practice covers methods for extraction of medical plastics in liquids that simulate body fluids in their action on the plastics. This practice identifies two methods of extraction: one used for obtaining" extract liquid" to be analyzed by chemical and physical tests; and the other obtaining "extract liquid" for use in determining the biological response of animals. Further testing of the "extract liquid" is specified in other ASTM standards. The plastic after extraction may also be examined.

1.2 This practice may be used for, but is not limited to the following areas: partial evaluation of raw materials, auditing materials within the manufacturing process, and testing final products. This practice may also be used as a referee method for the measurement of extractables in plastics used in medical devices.

1.3 The values stated in SI units are to be regarded as the standard.

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:*

D 543 Test Method for Resistance of Plastics to Chemical Reagents[2]

D 570 Test Method for Water Absorption of Plastics[2]

D 618 Practice for Conditioning Plastics and Electrical Insulating Materials for Testing[2]

D 1193 Specification for Reagent Water[3]

D 1239 Test Method for Resistance of Plastic Films to Extraction by Chemicals[2]

D 1898 Practice for Sampling of Plastics[4]

E 171 Specification for Standard Atmospheres for Conditioning and Testing Materials[5]

3. Terminology Definitions

3.1 *extraction vehicle*—a liquid specified for use in testing the plastic. Specific extraction vehicles are to be designated by the ASTM standard that references this practice (see Section 7 for a list of standard extraction vehicles).

3.2 *extract liquid*— that liquid which is tested for biological and chemical/physical response; the end result of this practice.

3.3 *specimen portion*— the unit or units of plastic placed into the extraction vehicle.

3.4 *blank*—the extraction vehicle not containing the specimen under test which is used for comparison with the extract liquid.

4. Summary of Practice

4.1 Standard-size specimens of the plastic, which may closely simulate the intended device depending upon the use, are immersed in definite volumes of selected liquids (extraction vehicles) for the time and temperature specified.

4.2 A choice is made, based on the end use, of the extraction vehicles (see Section 7) and one of the combinations of time and temperature for the test (see Section 12).

4.3 The resultant test liquids (extract liquids) are kept in glass containers until used for testing. Test liquids for biological testing are kept in sterile glass containers. The test liquids for biological testing should be used within 24 h.

5. Significance and Use

5.1 These extraction procedures are the initial part of several test procedures used in the biocompatibility screening of plastics used in medical devices.

5.2 The limitations of the results obtained from this practice should be recognized. The choice of extraction vehicle, duration of immersion, and temperature of the test is necessarily arbitrary. The specification of these conditions provides a basis for standardization and serves as a guide to investigators wishing to compare the relative resistance of various plastics to extraction vehicles.

5.3 Correlation of test results with the actual performance or serviceability of plastics is necessarily dependent upon the

[1] This practice is under the jurisdiction of ASTM Committee F-4 on Medical and Surgical Materials and Devicesand is the direct responsibility of Subcommittee F04.16 on Biocompatibility.

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[2] *Annual Book of ASTM Standards,* Vol 08.01.

[3] *Annual Book of ASTM Standards,* Vol 11.01.

[4] *Annual Book of ASTM Standards,* Vol 08.02.

[5] *Annual Book of ASTM Standards,* Vol 15.09.

similarity between the testing and end-use conditions (see 12.1.2 and Note 7).

5.4 Caution should be exercised in the understanding and intent of this practice as follows:

5.4.1 No allowance or distinction is made for variables such as end-use application, for example, short-term versus long-term application or implantation.

5.4.2 No allowance is made to distinguish between a nonporous versus a porous plastic. Although no definitions are given in this practice for the following terms, such items as extraction vehicle surface tension at the specified extraction condition and plastic specimen physical structure should be taken into account.

5.5 Test Methods D 543, D 570, and D 1239 may be useful in providing supplemental information.

6. Apparatus

6.1 *Autoclave*, capable of maintaining a temperature of 121 ± 2.0°C (249.8 ± 3.8°F), and equipped with a thermometer, pressure gage, vent cock, and a rack to hold the extraction containers above the water level.

6.1.1 The autoclave preferably should have a water cooling system that will allow for the cooling of the extraction containers to about, but not less than, 22°C (71.6°F) immediately following the heating cycle.

6.1.2 Autoclaves not equipped with a water cooling system may be used. However, sealed, unvented, extraction vessels should not be removed from such an autoclave until internal temperature and pressure have reached ambient conditions. Such vessels, when hot, represent an extreme explosion hazard capable of causing serious injury or even death.

6.2 *Balance*, accurate to ±0.1 mg.

6.2.1 Caution should be exercised when performing weighings in glassware. Depending upon the required accuracy, the relative humidity should be the same for weighings at different times.

6.3 *Extraction Containers*—Suitable glass containers that protect the extract liquid from biological and chemical contamination or evaporation. One suggested container is the screw-cap culture test tube of borosilicate glass, unless a larger container is required for the size and shape for the material to be extracted. Screw caps, if used, shall have a rubber liner, whose exposed surface shall be completely covered with polytetrafluorethylene film 0.05 to 0.075 mm (0.002 to 0.003 in.) in thickness.

6.4 *Heating Equipment*:

6.4.1 *Oven*, forced air-circulation type that will maintain temperatures of 50 to 70 ± 2°C (122 to 158 ± 3.6°F).

6.4.2 *Water Bath*, capable of maintaining temperatures of 50 to 70 ± 2°C (122 to 158 ± 3.6°F).

6.5 *Micrometers*, capable of measuring dimensions of test specimens to 0.025 mm (0.001 in.).

6.6 *Room*, or enclosed space capable of being maintained at the Standard Laboratory Atmosphere, as prescribed in Practice D 618 (see 11.3).

7. Reagents and Materials

7.1 *Purity of Reagents*—Reagent grade chemicals shall be used in all tests. Unless otherwise indicated, it is intended that all reagents shall conform to the specifications of the Committee on Analytical Reagents of the American Chemical Society, where such specifications are available.[6] Other grades may be used, provided it is first ascertained that the reagent is of sufficiently high purity to permit its use without lessening the accuracy of the determination.

7.2 *Purity of Water*— Unless otherwise indicated, references to water shall be understood to mean reagent water conforming to Specification D 1193, Type II.

7.3 *Extraction Vehicles*—The following list of standard extraction vehicles is intended to simulate the main constituents of human body fluids. Aqueous solutions shall be made with distilled water. The extraction vehicles shall be:

7.3.1 *Sodium Chloride Injection*, USP, containing by weight not less than 0.85 % and not more than 0.95 % sodium chloride.

7.3.2 *Vegetable Oil*:

7.3.2.1 *Sesame Oil*, USP.

7.3.2.2 *Cottonseed Oil*, USP.

NOTE 1—To preclude the use of vegetable oil of poor or deteriorated quality, the following additional negative reactivity test, beyond the respective description in the USP, may be performed.

Select three healthy, thin-skinned albino rabbits, not previously used for any test, whose fur can be clipped closely and whose skin is free of mechanical irritation or trauma. On the day of the test, clip the fur from the dorsal surface. Divide the test area into a grid of suitably identified individual injection sites. Inject 0.2 ml intracutaneously at each of ten sites on each animal. In handling the animals, avoid touching the injection sites during observation periods. Examine the injected sites 24, 48, and 72 h after the injection. No site should show an edema or erythema over an area greater than 5 mm (0.197 in.) in diameter. Qualify a vegetable oil batch and store under adequate conditions until use. Ideal storage conditions may be under a nitrogen blanket in complete darkness. The primary objective is to prevent oxidative type reactions.

7.3.3 *Water for Injection*, USP.

7.3.4 Other extraction vehicles, as required.

NOTE 2—Depending upon the medical plastic under test and the user's needs, extraction vehicles other than those in 7.3 may be used. An example is pseudoextracellular fluid (PECF).[7]

8. Sampling

8.1 The application of this practice may be in various areas. Therefore, although some well-known quality sampling methods may be used, a statistician should be consulted to ensure a statistically valid sampling plan.

8.2 Practice D 1898 may also be consulted.

9. Test Specimen

9.1 This practice is designed primarily for application to plastics in the condition in which they are used. The plastic should be exposed to all conditions and substances as during a production run, such as washing, packaging, and sterilization.

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[6] "Reagent Chemicals, American Chemical Society Specifications," Am. Chemical Soc., Washington, D.C. For suggestions on the testing of reagents not listed by the American Chemical Society, see "Reagent Chemicals and Standards," by Joseph Rosin, D. Van Nostrand Co., Inc., New York, N. Y., and the "United States Pharmacopeia."

[7] Homsy, C. A., "Bio-Compatibility in Selection of Materials for Implantation," *Journal of Biomedical Materials Research*, Vol. 4, 1970, pp. 341–356.

The extraction is to be done on the end-use item, specimen portions thereof, or representative molded or extruded test specimens of the formulated compound that are preconditioned by the same processing.

NOTE 3—Changes to a plastic formulation, specifically additives, such as plasticizers, stabilizers, antioxidants, pigments, and lubricants are perhaps more prone to produce differences in the extract liquid than the polymer itself.

9.2 *Specimen Size*— Use a surface-to-volume ratio that closely approximates or is greater than that of the final product. Suitable-size containers will allow a 20-mL extraction vehicle volume for each of the following specimen sizes:

9.2.1 The total surface area of a specimen (both sides) is equivalent to 120 cm^2(18.6 $in.^2$) when the specimen thickness is 0.50 mm (0.020 in.) or less, or equivalent to 60 cm^2 (9.3 $in.^2$) when the thickness is greater than 0.50 mm (0.020 in.).

9.2.2 An alternative for specimens of intricate geometry or those specimens with a thickness greater than 1.0 mm (0.039 in.) is a specimen whose weight is 4.0 g (0.14 oz).

9.2.3 Specimens shall be of such dimensions as to conveniently fit within the extraction container and their total surface area shall be completely covered by the extraction vehicle.

9.2.4 It may be necessary to subdivide the specimen, utilize inerts and noncontaminating spacers or weights or both, or initially agitate the extraction vehicle to ensure the entire specimen surface is contacted.

9.3 *Number of Specimen Portions*—In both procedures set forth in Section 12, test at least three specimen portions with each extraction vehicle to account for variability.

10. Preparation of Apparatus

10.1 Clean all reusable glassware thoroughly with a chromic acid cleansing mixture, or if necessary, with hot nitric acid, followed by prolonged rinsing with tap water and then at least two rinses with distilled water.

10.2 Clean cutting devices by an appropriate method, for example, successive cleaning with suitable solvents prior to use in subdividing the sample.

10.3 Clean all other equipment by thorough scrubbing with a suitable detergent and prolonged rinsing with tap water and then at least two rinses with distilled water.

10.4 Render containers and devices used for extraction and in transfer and administration of the extract liquids, sterile and dry by a suitable process.

NOTE 4—If ethylene oxide is used as the sterilizing agent, allow adequate conditioning for complete degassing. Ethylene oxide residuals may vary among different material formulations.

11. Specimen Portion and Conditioning

11.1 *Biological Response Extraction*—Select and cut to size, as in 9.2 and 9.3, at least three specimen portions for each extraction vehicle to be used.

11.2 *Extraction for Chemical/Physical Testing*:

11.2.1 Select and cut to size, as in 9.2 and 9.3, three specimen portions for each extraction vehicle to be used.

11.2.2 Unless otherwise indicated, there is no requirement to adhere to sterile procedure for this testing.

11.3 *Conditioning*— Although desirable, no conditioning is required. If a conditioning environment is required, the following shall be observed:

11.3.1 Unless otherwise specified, condition specimen portions in accordance with Procedure A of Practice D 618 in the Standard Laboratory Atmosphere which is 23 ± 2°C (73.4 ± 3.6°F) and 50 ± 5 % relative humidity, as described in Specification E 171. If closer tolerances are required, ±1°C (1.8°F) and ±2 % relative humidity may be specified.

11.3.1.1 *Specimen Portions 7 mm (0.28 in.) in Thickness and Under*—Condition in Standard Laboratory Atmosphere for 40 h.

11.3.1.2 *Specimen Portions Greater than 7 mm (0.28 in.) in Thickness*—Condition in the Standard Laboratory Atmosphere for 88 h.

NOTE 5—Care should be taken not to compromise sterility for biological response specimen portions.

12. Procedure

12.1 *Biological Response Extraction*:

12.1.1 Prepare a set of four 20-mL portions of each extraction vehicle. Place one specimen portion in each of three containers; the extraction vehicle in the fourth container will serve as a blank. Secure the cap on each container.

12.1.2 *Extraction Conditions*—Employ one of the following conditions in accordance with the specified requirements. Sufficient time, in addition to that specified, should be allowed for the liquid to reach the extraction temperature. Do not agitate the extraction vehicle or extraction container during the extraction.

12.1.2.1 37 ± 1°C (95 ± 1.8°F) for 120 h.
12.1.2.2 50 ± 2°C (122 ± 3.6°F) for 72 h.
12.1.2.3 70 ± 2°C (158 ± 3.6°F) for 24 h.
12.1.2.4 121 ± 2°C (250 ± 3.6°F) for 2 h.

NOTE 6—There may be the assumption that these conditions are equivalent to one another. The same combination of plastic and extraction vehicle, when subjected to different extraction conditions, is generally known to have significantly different responses when tested. The ideal evaluation of a material should employ times and temperatures that simulate the intended use of a plastic. Exaggerated conditions of extraction attempt to provide a margin of safety with a reasonable increase in temperature. The prescribed temperature and duration should be not so severe as to affect the character of the plastic, that is, no gross physical change. In general, most plastics can withstand 50°C (122°F) for 72 h with no thermal degradation.

12.1.3 Upon removal from the heat source, cool the containers to, but not below, 22°C (71.6°F). When cool, shake the containers vigorously for 30 s and decant the extract liquid into a dry sterile container.

NOTE 7—Sealed, unvented containers used at a temperature of 121 ± 2°C, should not be handled until the internal temperature and pressure have reached ambient conditions.

12.1.4 Store the extract liquids at 22 to 30°C (71.6 to 86°F). Use the extract liquids within 24 h.

12.1.5 To minimize the number of test animals required to determine a biological response, it is permissible to pool extract liquids from three specimen portions.

12.2 *Extraction for Chemical/Physical Testing*:

12.2.1 Prepare a set of four 20-mL portions of each extraction vehicle. Unless otherwise specified, the extraction vehicles are water for injection (7.3.3) or distilled water (7.2). In

addition the use of a vegetable oil (7.3.2) is optional. Place one specimen portion in each of three containers; the extraction vehicle in the fourth container serves as a blank. Secure the cap on each container.

12.2.2 *Extraction Conditions*—Use the same conditions specified in 12.1.2.

12.2.3 Proceed in accordance with 12.1.3 and 12.1.4. In general, extract liquids do not have to be analyzed within 24 h. However, some analytical tests require that the extract liquid be analyzed within 24 h. There may be some absorption of certain species onto the borosilicate glass container. Vigorously agitate the extract liquid before removing it for testing.

13. Report

13.1 The report of any test referencing this practice shall include the following:

13.1.1 Designation of the standard referencing this practice.

13.1.2 Complete identification of plastic tested, including:

13.1.2.1 Type of device or plastic part,

13.1.2.2 Dimensions, sample and specimen portion weight,

13.1.2.3 Manufacturer's code, catalog, or formulation number, batch number or date of manufacture, trade name, and

13.1.2.4 Previous history in accordance with 9.1.

13.1.3 Extraction vehicle volume to specimen portion surface ratio (for example, 20 mL/120 cm^2 or 60 cm^2, not including edges) or weight of specimen portion to extraction vehicle volume (9.2.2).

13.1.4 Conditioning procedure used, including actual range of temperature if the standard tolerances are not used (see Practice D 618).

13.1.5 Extraction conditions; time and temperature.

13.1.6 Extraction vehicle.

13.1.6.1 If an extraction vehicle is used as allowed in 7.3.4, adequate description should be provided such that its formulation can be duplicated.

13.1.7 Results from biological and chemical/physical extract liquid tests.

13.1.8 Any observations on gross physical changes of the specimen portions or extract liquid. Such observations may include, but are not restricted to, specimen portion color change, extact liquid color change, light transmittance, and potential multiphase separation.

14. Precision

14.1 Under the accepted definitions of precisions, values cannot be given because of the variable nature of the plastics and procedures to be used. Some typical results will be reported, when available.

15. Keywords

15.1 biocompatibility; extraction; liquids; plastics; specimen size