Designation: F 619 – 02~~3~~

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.

1. Scope

1.1 This practice covers methods of extraction of medical plastics and may be applicable to other materials. This practice identifies a method for obtaining "extract liquid" for use in determining the biological response in preclinical testing. Further testing of the "extract liquid" is specified in other ASTM standards. The extract may undergo chemical analysis as part of the preclinical evaluation of the biological response, and the material 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.*

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[1] This practice is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.16 on Biocompatibility Test Methods.

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2. Referenced Documents

2.1 *ASTM Standards:* [2]

D 543 Practices for Evaluating the Resistance of Plastics to Chemical Reagents

D 570 Test Method for Water Absorption of Plastics

D 1193 Specification for Reagent Water

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

D 1898 Practice for Sampling of Plastics[3]

F 748 Practice for Selecting Generic Biological Test Methods for Materials and Devices

2.2 *Other Documents:*

USP NF 24 or current edition[4]

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, after extraction of the specimen, is used in tests.

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 defined 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. The test liquids shall be stored tightly stoppered at normal room temperature. Test liquids for biological testing are kept in sterile glass containers. Consideration should be given as to whether the extraction should be done under aseptic conditions. 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 materials is necessarily dependent upon the similarity between the testing and end-use conditions (see 12.1.2 and Note 4).

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 and duration of use. Decisions on selection of tests to be done should be made based on Practice F 748.

~~5.4.2 No allowance is made to distinguish between nonporous or porous materials or~~

5.4.2 This practice was originally designed for use with nonporous, solid materials. Its application for other materials, such as those that are ~~absorptive~~ porous, or ~~resorbable.~~ absorptive, or resorptive, should be considered with caution. Consideration should be given to altering the specified material to liquid ratio to allow additional liquid to fully hydrate the material and additional liquid or other methods to fully submerge the test article. Additional procedures that fully remove the extract liquid from the test article, such as pressure or physically squeezing the material, should also be considered as appropriate. 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) for at least 1 h and equipped with a display of temperature and pressure. A slow exhaust cycle is necessary. A rack to hold the extraction containers above the water level is

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[2] 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, Vol 08.01.~~ Standards volume information, refer to the standard's Document Summary page on the ASTM website.

~~*Annual Book of ASTM Standards*, Vol 11.01.~~

[3] Withdrawn.

~~*Annual Book of ASTM Standards*, Vol 13.01.~~

[4] Available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852.

also necessary. Loss of fluid volume should be recorded.

6.1.1 Sealed, unvented extraction vessels should not be removed until internal temperature and pressure have reached ambient conditions and the door can be opened. It is recommended that the extraction vessels be left undisturbed until any risk of boil over has passed. When the extraction vessels are cool to the touch, the lids should be sealed.

6.2 *Heating Equipment*:

6.2.1 Ovens or incubators that will maintain temperatures of 37, 50, 70 ± 2°C (98, 122, 158 ± 3°F).

6.2.2 Water baths capable of maintaining temperatures described in 6.2.1. Those with the ability to agitate the extraction vessels are preferred.

6.3 *Extraction Containers*—Suitable containers that protect the extract liquid from the biological and chemical contamination. They should allow expansion of the liquid, but then be sealed to prevent 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 of the material to be extracted. Screw caps, if used, shall have polytetrafluoroethylene liners.

6.4 *Balance*, accurate to ±0.1 mg.

6.4.1 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.

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

7. Reagents and Materials

7.1 *Purity of Reagents*—Reagent grade, or better, chemicals shall be used in all tests.[5] 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 *Extraction Vehicles*—The following list of standard extraction vehicles is intended to simulate the main constituents of human body fluids. The extraction vehicles shall be:

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

7.2.1.1 Other aqueous solutions shall be made with USP WFI (water for injection).

7.2.2 *Vegetable Oil*:

7.2.2.1 *Sesame Oil*, USP.

7.2.2.2 *Cottonseed Oil*, USP.

7.3 Other extraction vehicles as required, such as polyethylene glycol, DMSO, as specified in other standards. Vehicles should be chosen based on biotolerance, the test protocols to be used, and the ability to extract contaminants from the material to be tested.

NOTE 1—Depending upon the material under test and the user's needs, extraction vehicles other than those in 7.2 and 7.3 may be used if the reasons are justified.

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 might 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 materials in the condition in which they are used. The material should be exposed to all conditions and substances as during a production run, such as washing, packaging, and sterilization. The extraction ~~is to~~ may 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 2—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~~ specimen size as described in the ~~final product.~~ following sections. 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 0.2 g/ml.

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.

[5] *Reagent Chemicals, ~~A~~American Chemical Society Specifications* , American Chemical Society, Washington, D.C. For suggestions on the testing of reagents not listed by the American Chemical Society, see *Analar Standards for Laboratory Chemicals*, BDH Ltd., Poole, Dorset, U.~~S~~K., and the *United States Pharmacopeia ~~(USP), 12601 Twinbrook Pkwy.,~~ and National Formulary*, U.S. Pharmacopeial Convention, Inc. (USPC), Rockville, ~~MD 20852.~~ MD.

9.2.3.1 To ensure full submersion of a large or bulky specimen, it may be necessary to cut the specimen to provide for full immersion of its component pieces in the extraction vehicle. Under no circumstances shall such cutting be allowed to reduce the appropriate sample extraction ratio as determined in 9.2.1 or 9.2.2. If the specimen cannot be cut, coupons known to possess the same surface characteristics and sized to deliver the same overall surface area as the original test specimen can alternately be utilized.

9.2.4 It may be necessary to subdivide the specimen, utilize inert 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 3—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. Aseptic precautions should be used if the extract liquid is to be used in a test requiring aseptic technique or if the extract is to be stored for more than a few hours before use.

12. Procedure

12.1 *Biological Response Extraction* :

12.1.1 Prepare a set of four 20-mL portions of each extraction vehicle. Place one appropriate 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. It is recommended that the extraction be done at the highest temperature the material will withstand. If the material dissolves at 37°C, then the solution should be used in the tests. Mixing during extraction is preferable. This should be done such that the extractant is mixed with the extraction vehicle, but the fluid/specimen interface is not disturbed and air bubbles should not be formed. Mixing or agitation in the autoclave should not be attempted.

12.1.2.1 37 ± 1°C (95 ± 1.8°F) for 120 h. (For some test protocols, extraction at 37°C for 24 ± 2 h or 72 ± 2 h is specified.)

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 1h.

NOTE 4—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 suitable container.

NOTE 5—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.

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.

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 7.2, adequate description should be provided such that its formulation can be duplicated. The extraction vehicle, source, and purity should be specified.

13.1.7 Results from biological 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, extract liquid color change, light transmittance, and potential multiphase separation.

14. Precision

14.1 Under the accepted definitions of precision, values cannot be given because of the variable nature of the plastics and procedures to be used.

15. Keywords

15.1 biocompatibility; extraction; liquids; plastics; specimen size