Designation: F619 – 20

Standard Practice for Extraction of Materials Used in Medical Devices[1]

This standard is issued under the fixed designation F619; 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 reference method for the measurement of extractables in plastics used in medical devices. In general, it is the responsibility of the user of the standard to determine if the methods described in this standard are appropriate for the materials in their device.

1.3 This practice was initially developed for extraction of medical plastics not intended to undergo degradation or absorption during normal medical device usage. When applied to the extraction of absorbable materials, additional considerations may be necessary in the selection of extraction procedures and fluids.

1.4 For assessment of compatibility of the Single-use System material with the cell culture medium or the manufacturing processes used for cell-based therapeutics, vaccines, cell-based diagnostics, or other biopharmaceutical products, the user should refer to Guide E3231.

1.5 The values stated in SI units are to be regarded as standard. The values given in parentheses are mathematical conversions to inch-pound units that are provided for information only and are not considered standard.

1.6 *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, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.7 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D543 Practices for Evaluating the Resistance of Plastics to Chemical Reagents

D570 Test Method for Water Absorption of Plastics

D1239 Test Method for Resistance of Plastic Films to Extraction by Chemicals

E3231 Guide for Cell Culture Growth Assessment of Single-Use Material

F748 Practice for Selecting Generic Biological Test Methods for Materials and Devices

2.2 *Other Documents:*

USP NF 24 or current edition[3]

3. Definitions

3.1 *extraction vehicle*—a liquid specified for use in testing the test specimen. 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 test specimen 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.

[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] 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 volume information, refer to the standard's Document Summary page on the ASTM website.

[3] Available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

4. Summary of Practice

4.1 Standard-size specimens of the final product or materials used in its construction, 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 suitable containers as described in 6.3 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 containers. Extraction should be done under aseptic conditions for use in biological testing, unless otherwise justified. 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 or other materials used in medical devices.

5.2 The limitations of the results obtained from this practice should be recognized. The choices of the extraction vehicle, duration of immersion, and temperature of the test are 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 or other materials 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 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 and duration of use. Decisions on selection of tests to be done should be made based on Practice F748.

5.4.2 This practice was originally designed for use with nonporous, solid materials. Its application for other materials, such as those that are porous, absorptive (for example, sponge-like materials that are capable of absorbing liquid), 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 specimen. Additional procedures that fully remove the extract liquid from the test specimen, 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 test specimen physical structure should be taken into account.

NOTE 1—While there are no standardized methods available at present for determining the solvent absorption capacity of an absorptive device or material, a suggested protocol is as follows:
– Determine the volume of extraction vehicle that each 0.1 g or 1.0 cm^2 of device/material absorbs;
– then, in performing the extraction, add this additional volume to each 0.1 g or 1.0 cm^2 in an extraction mixture.

5.5 Test Methods D570 and D1239 and Practices D543 may be useful in providing supplemental information.

6. Apparatus

6.1 *Autoclave (for 121°C extractions),* 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 also necessary. Loss of fluid volume should be recorded.

6.1.1 Sealed, unvented extraction vessels should not be removed until the 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 (for other temperature extractions):*

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.[4] 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.

[4] *Reagent Chemicals, American Chemical Society Specifications*, American Chemical Society, Washington, DC. For Suggestions on the testing of reagents not listed by the American Chemical Society, see *Annual Standards for Laboratory Chemicals,* BDH Ltd., Poole, Dorset, U.K., and the *United States Pharmacopeia and National Formulary,* U.S. Pharmacopeial Convention, Inc. (USPC), Rockville, MD.

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, dimethyl sulfoxide (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 2—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.

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

9.2 *Specimen Size*—Use a specimen size as described in the following sections. Suitably sized 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 If the surface area cannot be measured or calculated due to the configuration of the sample (for example, powder) or intricate geometry of the device, a mass-to-volume of extracting fluid ratio of 0.2 g/mL shall be used. For the devices with a thickness greater than 1.0 mm (0.039 in.), an extraction ratio of 3 cm^2/mL shall be used.

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.

9.2.3.1 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 chemical, physical, and surface properties, and sized to deliver the same overall surface area as the original test specimen can alternately be utilized. The representative test specimen should undergo the same manufacturing and sterilization processes, have the same chemical, physical, and surface properties, and have the same ratio of component materials as the medical device in its final finished form.

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 that 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. 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.

NOTE 5—The total extract volume needed for a biocompatibility test will depend on the specific test and the dosing requirements for the test. For example, an extract volume greater than 20 mL will be needed for material-mediated pyrogenicity testing.