



Designation: F1877 – 24

Standard Practice for Characterization of Particles¹

This standard is issued under the fixed designation F1877; 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 a series of recommendations, generally applicable to all medical devices, for characterization of the morphology, shape, size, and size distribution of particles. The methods utilized include sieves, optical, scanning electron microscopy (SEM), transmission electron microscopy (TEM), and electrooptical.

1.2 While characterizing the quantity or number of particles shed from medical devices is important, this is not covered within the scope of the current document. AAMI TIR 42 and USP <788> provide guidelines for determination of particle quantities in various size ranges.

1.3 These methods are appropriate for particles produced by a number of different methods. These methods can include simulated use approaches such as *in vitro* wear test machines (Test Method F732), total joint simulation systems (Guides F1714 and F1715), abrasion testing, and vascular durability testing (Guide F2942). Other methods for producing particles such as shatter boxes or pulverizers, as well as commercially available particles, and particles harvested from tissues in animal or clinical studies can be used.

1.4 Except for chemical composition, this standard does not address sample preparation procedures and/or test systems that can be affected by chemical properties (for example, solubility, miscibility). While this standard does not provide detailed recommendations regarding assessment of chemical properties of particles, these should be considered.

1.5 The particles may be metallic, polymeric, or ceramic and are released from medical device materials either acutely or chronically (for example, due to wear).

1.6 The digestion procedures to be used and issues of sterilization of retrieved particles are not the subject of this practice.

1.7 A classification scheme for description of particle morphology is included in [Appendix X3](#).

1.8 When nanoparticles (that is, having at least one dimension less than 100 nm) are known to be present or are expected, other characterization methods may be needed. For information regarding nanoparticle characterization, refer to standards that address nanoparticles (for example, ISO 21363, ISO/TR 10993-22, ISO/TR 16196).

1.9 This standard does not address ions released from medical devices.

1.10 The values stated in SI units, including units officially accepted for use with SI, are to be regarded as standard. No other systems of measurement are included in this standard.

1.11 As a precautionary safety measure for handling test samples during particle characterization analyses, removed particles from implant tissues should be sterilized or minimally disinfected by an appropriate means that does not adversely affect these particles.

1.12 *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.*

1.13 *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

[C678 Test Method for Determination of Particle Size Distribution of Alumina or Quartz Using Centrifugal Sedimentation](#) (Withdrawn 1995)³

[E11 Specification for Woven Wire Test Sieve Cloth and Test Sieves](#)

[E161 Specification for Electroformed Material and Test Sieves](#)

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 www.astm.org/contact. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

³ The last approved version of this historical standard is referenced on www.astm.org.

- E766** Practice for Calibrating the Magnification of a Scanning Electron Microscope
- E1617** Practice for Reporting Particle Size Characterization Data
- F561** Practice for Retrieval and Analysis of Medical Devices, and Associated Tissues and Fluids
- F660** Practice for Comparing Particle Size in the Use of Alternative Types of Particle Counters
- F661** Practice for Particle Count and Size Distribution Measurement in Batch Samples for Filter Evaluation Using an Optical Particle Counter (Withdrawn 2000)³
- F662** Test Method for Measurement of Particle Count and Size Distribution in Batch Samples for Filter Evaluation Using an Electrical Resistance Particle Counter (Withdrawn 2002)³
- F732** Test Method for Wear Testing of Polymeric Materials Used in Total Joint Prostheses
- F1714** Guide for Gravimetric Wear Assessment of Prosthetic Hip Designs in Simulator Devices
- F1715** Guide for Wear Assessment of Prosthetic Knee Designs in Simulator Devices (Withdrawn 2006)³
- F2942** Guide for *in vitro* Axial, Bending, and Torsional Durability Testing of Vascular Stents
- 2.2 ISO Standards:**⁴
- ISO 21363** Nanotechnologies—Measurements of particle size and shape distributions by Transmission Electron Microscopy
- ISO 13322-1** Particle size analysis—Image analysis methods—Part 1: Static image analysis methods
- ISO/TR 10993-22** Biological evaluation of medical devices—Part 22: Guidance on nanomaterials
- ISO/TR 16196** Nanotechnologies—Compilation and description of sample preparation and dosing methods for engineered and manufactured nanomaterials
- 2.3 AAMI Document:**⁵
- AAMI TIR 42:2021** Evaluation of Particulate Associated with Vascular Medical Devices
- 2.4 U.S. Pharmacopeia:**⁶
- USP <788>** Particulate Matter in Injections⁷

3. Terminology

3.1 Definitions of Terms Specific to This Standard:

3.1.1 aggregate, *n*—a jumbled mass or collection of two or more particles or aggregates, or a combination thereof, held together by relatively weak cohesive forces caused by weak chemical bonding or an electrostatic surface charge generated by handling or processing.

3.1.2 aggregate, *n*—a dense mass of particles held together by strong intermolecular or atomic cohesive forces that is stable with normal mixing techniques, including high-speed stirring and ultrasonics.

3.1.3 aspect ratio (*AR*), *n*—a ratio of the major to the minor Feret diameters of a particle (see 12.3.3).

3.1.4 elongation (*E*), *n*—ratio of the particle length to the average particle width (see 12.3.4).

3.1.5 equivalent circle diameter (*ECD*), *n*—the diameter of a circle with an area equivalent to the area of the particle (see 12.3.2 and Appendix X1).

3.1.6 Feret diameter, *n*—the mean value of the distance between pairs of parallel tangents to a projected outline of a particle.

3.1.7 form factor (*FF*), *n*—a dimensionless number relating area and perimeter of a particle, as determined in 12.3.6.

3.1.8 irregular, *adj*—referring to a particle that cannot be described as round or spherical. A set of standard nomenclature and reference figures are given in Appendix X2.

3.1.9 matrix, *n*—particle-free sample that represents the starting composition of test samples prior to preparation (for example, digestion/harvest) or analysis.

3.1.10 method qualification, *n*—the process of evaluating the accuracy, precision, and bias of sample preparation and particle characterization analyses of test particle suspensions based on comparison with defined samples of particles with similar properties. The purpose is to qualify the acceptability of the analytical outcomes.

3.1.11 morphology, *n*—referring to size, shape, structure, and texture.

3.1.12 particle, *n*—the smallest discrete unit detectable as determined in test methods.

3.1.13 particle breadth, *n*—distance between touch points of the shortest Feret pair, orthogonal to length.

3.1.14 particle length, *n*—distance between the touch points of maximum Feret pair. This value will be greater than or equal to the maximum Feret diameter.

3.1.15 reference particles, *n*—particle samples with defined properties (for example, size, shape, composition, density, population distribution, agglomeration) that are used for method qualification.

3.1.16 rectangular, *adj*—referring to a particle that approximates a square or rectangle in shape.

3.1.17 roundness (*R*), *n*—a measure of how closely an object represents a circle as determined in 12.3.5.

3.1.18 spherical, *adj*—referring to a particle that approximates a sphere in a three-dimensional space and that projects as a round (or circular) shape in a two-dimensional space. A sphere is a three-dimensional, geometrical shape that has all its surface points equidistant from a common point.

3.1.19 spiked matrix, *n*—matrix with reference particles added at known concentration(s).

⁴ Available from American National Standards Institute (ANSI), 1180 Avenue of the Americas, 10th Floor, New York, NY 10036, <http://www.ansi.org>.

⁵ Available from Association for the Advancement of Medical Instrumentation (AAMI), 4301 N. Fairfax Dr., Suite 301, Arlington, VA 22203-1633, <http://www.aami.org>.

⁶ Available from U.S. Pharmacopeial Convention (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, <http://www.usp.org>.

⁷ USP <788> is intended to provide recommendations for particulate evaluations of injections and parenteral infusions, and is generally not applicable to medical devices. While limitations of this standard exist and the method used should be validated, it provides some useful information (for example, particle quantification methods, system cleanliness recommendations).

4. Summary of Practice

4.1 When evaluating particles generated from medical devices, the final device within their designated commercial packaging, including sterilization as applicable, should be used in all evaluations.

4.2 Particles produced by implant wear *in vivo* in animal or clinical studies are harvested from tissues after digestion utilizing methods such as those in Practice F561.

4.3 Particles generated *in vitro* or obtained from commercial sources are used as received, or after digestion if they were generated in protein solutions, and further separation if there are signs of aggregation. Harvesting and further processing should maintain the original range and physical and chemical characteristics of particles from *in vivo* or *in vitro* studies. For routine analysis, the particles are characterized by the terms of morphology and by size using Feret diameters and equivalent circle diameter (ECD). For more detailed studies, several methods that may be utilized for numerically characterizing their dimensions and size distribution are described.

5. Significance and Use

5.1 The biological response to materials in the form of small particles, as produced from implant wear, abrasion, or erosion, often is significantly different from that to the same materials in bulk form (that is, an implant component). Additionally, the morphology (for example, size and shape, surface characteristics), volume distribution, and species of these particles are major determinants of device-related biological responses; therefore, this practice provides standardized nomenclature for describing particles. Such a unified nomenclature will be of value in interpretation of biological tests of responses to particles, in that it will facilitate separation of biological responses per different particle characteristics such as size, shape, and volume.

5.2 Particles released due to wear from implants *in vivo* may result in an adverse biological response which will affect the long-term survival of the device. Characterization of such particles will provide valuable information regarding the safety and effectiveness of device designs or methods of processing components and the mechanisms of wear.

5.3 The morphology of particles produced in laboratory tests of wear and abrasion often is affected by the test conditions, such as the magnitude and rate of load application, device configuration, and test environment. Comparison of the morphology, size, and quantity of particles produced *in vitro* with those produced *in vivo* will provide valuable information regarding the degree to which the method simulates the *in vivo* condition being modeled.

5.4 Particles harvested from particle-release studies (for example, cell culture experiments, third body wear simulation) that are to be used for testing should be representative of the entire spectrum of possible particles produced from clinical use of the device/material under review (for example, due to wear, abrasion, or erosion). Therefore, efforts should be made to ensure that the particles for testing were produced from *in vivo* / *in vitro* studies that mimicked the clinical use conditions as

much as possible. When there is uncertainty regarding the characteristics of particles produced from *in vitro* or bench testing, particles from clinical studies (for example, retrievals) can be used to enhance the clinical representativeness of testing and its predictive power for characterizing potential biological responses.

6. Interferences

6.1 Particles may form aggregates or agglomerates during preparation and storage. These could result in an increase in measured particle size. It is essential that care be taken to resuspend particles prior to analysis and to note any effects of the dispersant used. Details regarding resuspension of particles prior to analysis are provided in AAMI TIR 42.

6.2 Particles from wear tests or harvested from tissues may contain a mixture of materials. In order to determine all potential sources of particle generation, appropriate methods should be utilized to determine the chemical composition of the entire particulate sample. Care should be taken when separating the particles and analyzing the physical characteristics and chemical composition of the isolated particles.

6.3 Many automated particle counters operate on the assumption that the particles are spherical. These methods may not be appropriate for nonspherical debris. Additional methods should be used to verify size, shape, and quantity using methods that take aspect ratio into consideration, for example, SEM or TEM image analysis.

7. Apparatus

7.1 *Scanning Electron Microscope (SEM)* (see Practice E766, ISO 19749):

7.1.1 Standard SEM equipment can be utilized for many studies. In special instances, such as with polymeric particles, a low acceleration voltage (1 to 2 kV) machine with a high brightness electron source, such as a field emission tip, may be utilized.

7.1.2 Elemental analysis may be accomplished with an energy dispersive X-ray spectrometer (EDS) with SEM.

7.1.3 Fourier transform infrared spectroscopy (FTIR) and Raman spectroscopy are robust analytical methods to identify the chemical composition (that is, chemical compounds present) of bulk or individual particles.

7.2 *Transmission Electron Microscopy (TEM)*:

7.2.1 TEM equipment can be typically used for the analysis of nanoparticles, although SEM with a field emission tip has also been successfully used to characterize particles as small as 50 to 100 nm.

7.2.2 Elemental analysis may be accomplished with an energy dispersive X-ray spectrometer (EDS) coupled with TEM.

7.3 *Optical Microscope*—An optical microscope operating in the transmission mode may be utilized. Dark field illumination may enhance visualization of some particles. Polarized light will facilitate identification of semicrystalline polymeric materials.

7.4 *Automatic Particle Counters* (see Practice E766, ISO 19749):

7.4.1 *Image Analyzer*—This instrument counts particles by size as those particles lie on a microscope slide.

7.4.2 *Optical Counter*—This instrument measures the area of a shadow cast by a particle as it passes a window. From this area, the instrument reports the diameter of a circle of equal area.

7.4.3 *Electrical Resistance Counter*—This instrument measures the volume of an individual particle. From that volume, the instrument reports the diameter of a sphere of equal volume (see Test Methods C678).

8. Reagents

8.1 Test particles should be analyzed using buffers/media that are particle free and that do not affect the physical characteristics of the particles (for example, swelling, dissolution, shape changes, or encourage aggregates or agglomerate formation).

8.2 Apparatus or labware used for analyzing particles should also be prepared using solutions that are ultra-clean and particle free.

9. Method Qualification

9.1 The methods used for particle characterization should be qualified. The information included below may be considered for method qualification. Other approaches may also be considered. The approach used for method qualification should be justified.

9.1.1 Reference particles should include populations at the lower and upper limits of the ranges of all relevant properties.

9.1.2 *Sample Handling*—Include all sample preparation and manipulation that occurs after the matrix is spiked. The process for spiked matrix and for test samples should be identical.

9.1.3 Analysis involves measurement of relevant properties of a population of particles.

9.1.4 Methods are qualified based on defined combinations of reference particle populations, matrix, sample handling, and analysis approaches. New method qualification should be performed when there is a change in parameters that is outside the scope of existing method qualification.

9.1.5 A method is considered qualified when the results of analysis of a spiked matrix acceptably correspond to the known properties of the reference particle controls. A method should be qualified, at minimum, at the lower and upper limit of the range of relevant properties. Qualification parameters (for example, accuracy, precision, bias, specificity, sensitivity) should be established based on differences between known and measured properties of the entire population of reference particle controls.

10. Specimen Preparation

10.1 Specimens from explanted tissues from animal or clinical studies may need to be harvested and digested using methods such as those described in Practice F561.

10.2 Particles from *in vitro* cell culture tests also may need to be digested and harvested.

10.3 Conditions for centrifugation of particles from wear, if necessary, should be determined according to Stoke's Law, and

resuspended in water, ethanol, or methanol. Resuspended particles may be filtered in accordance with Practice F561 prior to examination by SEM or TEM, although it should be recognized that filtration can lead to a loss of agglomeration of particles.

11. Particle Imaging by Light, Scanning, or Transmission Electron Microscopy

11.1 Images may either be captured electronically or photographically (ISO 13322) for subsequent analysis.

TABLE 1 Recommended Magnifications for Particle Imaging

Magnification	Particle Size Range (μm)
25 000	0.02 to 0.2
10 000	0.2 to 1.0
1000	1 to 10
100	10 to 100

11.2 For the characterization and measurements to be accurate, it is essential that the particles be imaged at the largest magnification possible. The magnifications in Table 1 are recommended.

NOTE 1—It may be helpful to use a range of magnification for evaluation of particles of specified sizes, given that various assessments (for example, counting of particles, shape and morphology of particles, assessment of agglomerates) may be more informative at different magnifications.

11.3 For particle size distribution measurements, divide each of the size ranges specified in Table 1 into 10 bins.

12. Particle Characterization

12.1 *Particle Shape (Morphology)*—Refer to the photographs and classify the morphology of the particles using the nomenclature in Appendix X2.

12.2 *Routine Particle Size Determination Using Feret Diameters:*

12.2.1 The use of multiple Feret diameters is especially useful for spherical and rectangular particles.

12.2.2 Determine the particle size and aspect ratio.

12.2.3 Calculate the particle size distribution based on the volume of solution used and the size of the filters.

12.3 *Detailed Particle Shape Analysis for Irregular Shaped Particles:*

12.3.1 Five particle dimensional measurements are provided using examples shown in Appendix X1. One is a measure of particle size, while the other four are shape descriptors.

12.3.2 *Equivalent Circle Diameter (ECD) as a Measure of Particle Size:*

12.3.2.1 The ECD has the units of length and is calculated as:

$$ECD = (4 \cdot A / \pi)^{\frac{1}{2}} \quad (1)$$

where:

A = area.

12.3.3 *Aspect Ratio (AR) as a Common Descriptive Step:*

12.3.3.1 The *AR* is calculated as the ratio of the major Feret diameter (d_{max}) to the minor Feret diameter (d_{min}). The major Feret diameter is the longest straight line that can be drawn between any two points on the outline. The minor Feret diameter is the longest line perpendicular to the major diameter:

$$AR = d_{max}/d_{min} \quad (2)$$

12.3.4 The elongation (*E*) is similar to the *AR* except it is more suited for the measurement of much longer particles, especially fibrillar particles, where the major axis line does not stay within the particle boundaries. Refer to particle types *A* and *C* in [Appendix X1](#).

12.3.4.1 The *E* is calculated as the ratio of the length (*FL*) to the breadth (*FW*):

$$E = FL/FW \quad (3)$$

12.3.5 The roundness (*R*) varies from zero to one in magnitude, with a perfect circle having a value of one, and is calculated as follows:

$$R = (4A)/(\pi d_{max}^2) \quad (4)$$

where:

A = area, and

d_{max} = maximum diameter.

12.3.6 The form factor (*FF*) is similar to *R* but is based on the perimeter (*p*) of the particle outline rather than the major diameter. The *FF* is more sensitive to the variations in roughness of the particle outline.

$$FF = 4\pi A/p^2 \quad (5)$$

where:

p = perimeter of the particle outline.

12.4 Other Particles Size Determination Methods:

12.4.1 Particles larger than 20 μm may be determined by sieves described in Specifications [E11](#) and [E161](#).

12.4.2 Particles in liquid suspension may be sized as directed in Practice [F661](#) or Test Method [F662](#).

13. Chemical Analysis / Identification

13.1 SEM-EDS and TEM-EDS analyses should be conducted at a magnification suggested in [11.2](#).

13.2 Elemental analysis should be conducted for at least 10 s for each particle. Since detailed compositional analysis is of questionable reliability for micron and submicron sized particles, it is recommended that composition be determined based on identification of key elemental peaks for the major elements likely to be present in the sample.

13.3 Additional chemical analyses (that is, Fourier transform infrared and/or Raman spectroscopy) is typically needed to identify polymeric material and other particulates.

14. Report

14.1 Report the following information (see Practice [E1617](#)):

14.1.1 The source of the particles and materials as determined from chemical analyses as well as the methods for particle generation.

14.1.2 Methods utilized to digest and separate the particles.

14.1.3 Morphological description of the particles.

14.1.4 Results of particle quantity, size, and shape analysis.

15. Precision and Bias

15.1 The precision and bias of this practice have not been determined.

16. Keywords

16.1 biocompatibility; morphology; particles; SEM; TEM; wear

APPENDIXES

(Nonmandatory Information)

X1. SAMPLE FIGURES FOR CALCULATION OF PARTICLE SIZE AND SHAPE

X1.1 See [Fig. X1.1](#).⁸

⁸ The examples provided were analyzed with the NIH Image Program by Landry and Agarwal. A set of macros is available from the Department of Orthopaedics, University of Texas Health Science Center at San Antonio.