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Standard Guide for Assessing the Removal of Additive Manufacturing Residues in Medical Devices Fabricated by Powder Bed Fusion[1]

This standard is issued under the fixed designation F3335; 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 standard provides guidance for assessing the manufacturing material residues in medical devices fabricated using additive manufacturing (AM) techniques, specifically, from powder bed fusion AM technologies.

1.1.1 Some of the techniques discussed in this guide may be applicable to devices fabricated by other types of AM equipment (e.g., stereolithography). Given each AM technique's characteristics and post-processing challenges, there could be additional risks or considerations associated with some AM techniques or materials that are not addressed by this guide.

1.2 This guide covers several qualitative and quantitative assessments of the presence and amount of residue remaining in or obtained by extraction in aqueous or organic solvents from powder bed fusion AM medical components.

1.2.1 This guide identifies techniques to qualitatively determine the presence of residue and a technique to quantitatively assess it. It does not set acceptance criteria or acceptable limits for residues remaining in built parts. These methods are not the only methods to determine the presence or quantity of residual material in additive manufactured medical components.

1.3 This guide pertains to devices in their finished state (after post-processing and subsequent manufacturing processes), as applicable. This guide may also be used to evaluate the effectiveness of cleaning processes between critical steps in the manufacturing process, to ensure minimal AM residue remains for cleaning processes downstream.

1.4 This guide is not intended to evaluate the residue level in medical components that have been cleaned for reuse.

1.5 Different cleaning methods, including high energy processes, can potentially damage small structures in AM parts. This guide does not address measurement or mitigation of this risk.

1.6 This guide does not address the manufacturing occupational health issues of working with small particles (e.g., breathing hazards).

1.7 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.8 *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.*

1.9 *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]

F311 Practice for Processing Aerospace Liquid Samples for Particulate Contamination Analysis Using Membrane Filters

F1877 Practice for Characterization of Particles

F1903 Practice for Testing for Cellular Responses to Particles ***in vitro***

F1904 Practice for Testing the Biological Responses to Particles ***in vivo***

F2459 Test Method for Extracting Residue from Metallic Medical Components and Quantifying via Gravimetric Analysis

F2847 Practice for Reporting and Assessment of Residues on Single-Use Implants and Single-Use Sterile Instruments

F3127 Guide for Validating Cleaning Processes Used During the Manufacture of Medical Devices

G131 Practice for Cleaning of Materials and Components by Ultrasonic Techniques

[1] This test method is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.15 on Material 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.

2.2 *ISO Standard:*[3]

ISO 19227:2018 Implants for surgery – Cleanliness of orthopedic implants – General requirements

2.3 *Other Reference:*[4]

United States Pharmacopeia General Chapter 788: Particulate Matter in Injections

3. Terminology

3.1 *Definitions:*

3.1.1 *additive manufacturing, n*—process of joining materials to make parts from 3D model data, usually layer upon layer, as opposed to subtractive manufacturing and formative manufacturing methodologies.

3.1.2 *powder bed, n*—part bed build area in an additive manufacturing system in which feedstock is deposited and selectively fused by means of a heat source or bonded by means of an adhesive to build up parts.

3.1.3 *powder-bed fusion, n—in additive manufacturing*, process by which thermal energy selectively fuses regions of a powder bed (commonly between 10 and 200 µm of thickness).

3.1.4 *non-soluble manufacturing residue, n*—particulates remaining in the manufactured components after manufacturing and post-processing, including starting material, blast media, and other debris.

4. Summary of Guide

4.1 This guide provides an approach for assessing the presence and quantity of residual powder bed fusion material remaining in fabricated parts to help ensure that post-processing protocols yield consistent and verifiable levels of particulate residue in medical devices.

5. Significance and Use

5.1 Materials used in medical devices are selected in part for their biocompatibility, meaning that they have been demonstrated to have an acceptable biological response for the intended application. During manufacturing, most devices are exposed to a variety of processing steps and materials that have the potential to adversely affect the inherent biocompatibility of the device if they are not adequately removed prior to use.

NOTE 1—For a fine powder, depending upon application, a new biological risk assessment may be required.

5.2 In additive manufacturing, components are in most cases built layer-by-layer, allowing unprecedented freedom to design complex devices. This makes it possible to build devices that are very difficult to clean, such as topological optimized parts, small internal channels, lattice structures, and especially reticulated porous structures for bone ingrowth and fixation.

5.3 Powdered fusion AM presents additional challenges. Components come out of the build volume with residual powder filling all open spaces within the device. The majority of the excess powder is typically removed by a combination of vibratory shaking, blowing with compressed gas, vacuuming, and ultrasonic cleaning in a solvent. However, the particles are typically very small and can become lodged in internal features such as pores, making removal difficult. Furthermore, particles that were immediately adjacent to the component during manufacturing can be partially sintered to the surface. Those particles can be extremely difficult to remove, are indistinguishable from loose particles when observed by most techniques, and may be at risk of detaching during the intended use of the device.

5.4 This guide provides specific evaluation techniques for measuring the effectiveness of residue removal processes, as they should be able to yield consistent results that meet the respective performance and cleanliness criteria for the intended use.

6. Cleaning Validation Approach

6.1 A typical approach to a cleaning validation should be followed. This guide only applies to the removal of residual unmelted and unsintered powder left during AM processes. Other residues from subsequent manufacturing processes are out of the scope of this guide and are covered by Guide F3127 and ISO 19227. However, these standards still detail steps to take for validation of cleaning processes used during the manufacture of medical devices that can be applied to powder bed fusion AM. Additionally, ISO 19227 presents key risk assessments to aid in cleaning process design.

6.2 One approach to validating the removal of residual powder is to use modular challenge test components that can be disassembled following the cleaning procedure(s) to allow access to locations that would otherwise be difficult to assess. Annex A1 provides an example challenge test piece.

7. Powder Bed Fusion Cleanliness Considerations

7.1 All parts fabricated with powder bed fusion AM will contain residual powder on every surface and in intentional void spaces in the design. If not removed, the powder may have the potential to come loose during implantation or other intended use conditions, thereby potentially affecting patient outcomes.

7.2 Furthermore, it is often difficult to distinguish residual powder material from particulates generated by post-processing and subsequent manufacturing operations. Raw powder material is carefully controlled, often spherical, with a narrow size distribution. However, sintering, melting, and post-processing may change the apparent shape and size of material particles. Therefore, all particulates should be treated as debris and accounted for in the risk analysis during device design and cleaning process development.

7.3 Assessment of the presence of residual powder can be performed by various quantitative or qualitative methods. The appropriate assessment tool will vary with part geometry, AM process, and post-processing steps. Assessment strategies and acceptance criteria should be determined during the cleaning process development, used for process validation, and performed as part of routine monitoring.

[3] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

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

8. Residual Powder Assessments

8.1 Many assessment techniques exist and are being continually developed for non- destructive evaluation of parts. These techniques have been selected for their particular relevance to particulate residue removal in complex geometries, but are not exhaustive. Other assessments may be more appropriate for certain geometries or specific powder bed fusion technologies. In any case, the evaluation method shall be validated and the limit of detection shall be documented.

8.2 *Visual Inspection*—Presence of residual powder within porous structures with repeating unit cells can be determined by inspection if the unit cells align to allow full thickness light penetration.

8.2.1 Align the part so that the regular open spaces of the cells are in line with a light source and imaging device. The light source may be a light table or fiberoptic lamp.

8.2.2 Use a contrasting color filter or filter paper to ensure clear visualization of the open spaces. Clogged or closed voids will be shadowed and may indicate residual material is trapped within the channels or lattice structures.

8.2.3 Visible area measurements can be made of the blocked voids to obtain a semi-quantitative result.

8.2.4 Visible area measurements cannot determine if the material is fully solidified to the structure or if it will be easily removable during normal use conditions. Other analytic techniques can be used for those assessments.

8.3 *Microscopy*—Light or scanning electron microscopy can be used to visualize specimens.

8.3.1 Relatively thin porous structures (thickness of two pore diameters or less) can be viewed non-destructively. Residual powder may be observed directly through medium power light microscopy or scanning electron microscopy. Confocal laser scanning microscopy can also be a useful evaluation means to analyze various depths of the porosities.

8.3.2 The interior of thicker porous structures may be embedded and sectioned using standard metallography techniques, and residual particles quantified through analysis of reflected light microscope or scanning electron microscope (SEM) images.

8.3.3 When embedding, these techniques should be validated to ensure that the sectioning procedures do not extract loose powder particles from the embedding media.

8.3.4 It may be necessary to examine serial sections to verify that apparently unattached particles are not sintered to the device substrate.

8.3.5 Depending on the particle size of the AM powder, the use of a transparent embedding media may allow a sufficient depth of field to determine that a particle is unattached without serial sectioning.

8.4 *Spectroscopy*—Elemental evaluation may be useful in evaluating non-base particulate matter that may be introduced through the cleaning processes. Fourier transform infrared spectroscopy (FTIR) for polymers and energy-dispersive x-ray spectroscopy (EDS) or x-ray fluorescence (XRF) for metals may be useful in determining the presence of other materials and residues that may be left as part of the cleaning processes.

8.5 *Micro- or Nano-Computed Tomography (micro-CT, nano-CT)*—The presence of residual powder in highly intricate devices, either polymeric or metallic in nature, can often be assessed with micro-CT or nano-CT.

8.5.1 The scan resolution should be adequately high to permit visualization of particles in the 50th percentile of the size distribution of particulates used in the manufacturing process. At least three voxels should span the length of the smallest dimension of such particles.

8.5.2 Scan protocol and consistency can greatly affect the ability to accurately replicate imaging tests between parts or lots. Scanning protocols and post-processing should be kept consistent between specimens of the same design and material. Standard reference materials should be used to verify calibration of scans regularly.

8.5.3 Thresholding of the scan data should be performed using standardized and validated procedures to maximize contrast between the component's material and surrounding media. Special attention is required during thresholding at the boundaries of the solid component, as the component's outer edge may be difficult to differentiate from loose or partially fused particulates.

8.5.4 While this assessment method can qualitatively determine residue presence, quantitative measurements of residue can be obtained. An approach to quantifying residue within a medical device using micro-CT data was presented by Lucas et al.[5]

8.6 *Releasing and Measuring Remaining Residues*—Repeated ultra-sonication processing in a liquid or solution suitable for the material, such as alcohol, water, or water plus surfactant can release some of the remaining residues in the part. This may facilitate estimating the remaining particles or estimating their potential for release during their service life. It has been suggested that ultrasonic extraction by itself is not sufficient to remove some residues that may be removed by other processing steps, such as water jet cleaning or thorough manual cleaning. Forceful impacts, such as mallet strikes during implantation, may also dislodge residual powders that were not removed by residue release procedures. Secondary methods of confirming the remaining residues may be necessary to fully validate exhaustive extraction techniques for certain part geometries.

8.6.1 Residue release by ultra-sonication is similar to extraction and should be performed per Test Method F2459, establishing extraction efficiency.

8.6.2 Particles can then be collected by filtration until a predetermined plateau in recovered particles or the particle detection limit is reached.

8.6.3 Filters used for residue release should be allowed to stabilize in a controlled temperature and humidity environment for a minimum of 24 h prior to initial weighing to minimize weighing artifacts. Filter paper pore size should be selected according to the particle size collected. The filters and some starting materials used in powder bed fusion techniques are

[5] Lucas et al., "Evaluating Device Design and Cleanability of Orthopedic Device Models Contaminated with a Clinically Relevant Bone Test Soil," *Biomed Instrum Technol*, 2015 Sep-Oct;49(5):354-6, doi: 10.2345/0899-8205-49.5.354.