On February 2, 2024, FDA published the final rule to amend the Quality System (QS) regulation in 21 CFR part 820 (89 FR 7496, effective February 2, 2026). The revised 21 CFR part 820 is now titled the Quality Management System Regulation (QMSR). The QMSR harmonizes quality management system requirements by incorporating by reference the international standard specific for medical device quality management systems set by the International Organization for Standardization (ISO), ISO 13485:2016. The FDA has determined that the requirements in ISO 13485 are, when taken in totality, substantially similar to the requirements of the QS regulation, providing a similar level of assurance in a firm's quality management system and ability to consistently manufacture devices that are safe and effective and otherwise in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act).

This guidance document was issued prior to the effective date of the final rule. FDA encourages manufacturers to review the current QMSR to ensure compliance with the relevant regulatory requirements.

Technical Considerations for Additive Manufactured Medical Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 5, 2017.

The draft of this document was issued on May 10, 2016.

For questions about this document regarding CDRH-regulated devices, contact the Division of Applied Mechanics at (301) 796-2501, the Division of Orthopedic Devices at (301) 796-5650, or Matthew Di Prima, Ph.D. at (301) 796-2507 or by email matthew.diprima@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration

Center for Devices and Radiological Health

Center for Biologics Evaluation and Research

GRZAN

Preface

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to http://www.regulations.gov . Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2016-D-1210. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

CDRH

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please use the document number 1400002 to identify the guidance you are requesting.

CBER

Additional copies are available from the Center for Biologics Evaluation and Research (CBER)), Office of Communication, Outreach, and Development (OCOD), 10903 New Hampshire Ave., WO71, Room 3128, Silver Spring, MD 2090320903, or by calling 1-800-835-4709 or 240-402-8010, by email, ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

GRZAN

Table of Contents

I. Introduction and Scope 1
II. Background 3
III. Overview 4
IV. Definitions 5
V. Design and Manufacturing Process Considerations 6
A. Overall Device Design 8
B. Patient-Matched Device Design 8
C. Software Workflow 11
(1) File Format Conversions 11
(2) Digital Device Design to Physical Device 12
(3) Validating and Automating Software Processes 15
D. Material Controls 15
(1) Starting Material 15
(2) Material Reuse 16
E. Post-Processing 17
F. Process Validation and Acceptance Activities 17
(1) Process Validation 18
(2) Revalidation 19
(3) Acceptance Activities 20
(4) Test Coupons 20
G. Quality Data 21
VI. Device Testing Considerations 21
A. Device Description 22
B. Mechanical Testing 22
C. Dimensional Measurements 23
D. Material Characterization 24
(1) Material Chemistry 24
(2) Material Physical Properties 25
E. Removing Manufacturing Material Residues and Sterilization 25
F. Biocompatibility 27
VII. Labeling 27

GRZAN

Technical Considerations for Additive Manufactured Medical Devices

Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction and Scope

FDA has developed this guidance to provide the Agency's initial thinking on technical considerations specific to devices using additive manufacturing, the broad category of manufacturing encompassing 3-dimensional (3D) printing. Additive manufacturing (AM) is a process that builds an object by sequentially building 2-dimensional (2D) layers and joining each to the layer below, allowing device manufacturers to rapidly produce alternative designs without the need for retooling and to create complex devices built as a single piece. Rapid technological advancements and increased availability of AM fabrication equipment are encouraging increased investment in the technology and its increased use by the medical device industry. The purpose of this guidance is to outline technical considerations associated with AM processes, and recommendations for testing and characterization for devices that include at least one additively manufactured component or additively fabricated step.

This guidance is broadly organized into two topic areas: Design and Manufacturing Considerations (Section V) and Device Testing Considerations (Section VI). The Design and Manufacturing Considerations section provides technical considerations that should be addressed as part of fulfilling Quality System (QS) requirements for your device, as determined by the regulatory classification of your device and/or regulation to which your device is subject, if applicable. While this guidance includes manufacturing considerations, it is not intended to comprehensively address all considerations or regulatory requirements to establish a quality system for the manufacturing of your device. The Device Testing Consideration section describes the type of information that should be provided in premarket

notification submissions (510(k)), premarket approval (PMA) applications, humanitarian device exemption (HDE) applications, De Novo requests and investigational device exemption (IDE) applications for an AM device. The type of premarket submission that is required for your AM device is determined by the regulatory classification of your device. Questions regarding the regulatory status or requirements for specific devices, products, or entities should be addressed to the appropriate review branches through the Division for Industry and Consumer Education (DICE@fda.hhs.gov).

For devices manufactured using AM, the recommendations in this guidance supplement any device-specific recommendations outlined in existing guidance documents or applicable FDA-recognized consensus standards. Point-of-care device manufacturing may raise additional technical considerations that are not addressed in this document. In addition, this guidance does not address the use or incorporation of biological, cellular, or tissue-based products in AM. Biological, cellular or tissue-based products manufactured using AM technology may necessitate additional regulatory and manufacturing process considerations and/or different regulatory pathways. Therefore, AM questions pertaining to biologics, cells or tissue products should be directed to the Center for Biologics Evaluation and Research (CBER). Specific questions regarding jurisdiction over a combination product should be directed to the Office of Combination Products (OCP) at 301-427-1934 or combination@fda.gov.

This guidance is a leapfrog guidance, a type of guidance that serves as a mechanism by which the Agency can share initial thoughts regarding emerging technologies that are likely to be of public health importance early in product development. This leapfrog guidance represents the Agency's initial thinking and our recommendations may change as more information becomes available. The Agency encourages manufacturers to engage with the Center for Devices and Radiological Health (CDRH) or CBER through the Pre-Submission process to obtain more detailed feedback for Additively Manufactured medical devices. For more information on Pre-Submissions, please see "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff - Guidance for Industry and Food and Drug Administration Staff."[1]

For the current edition of the FDA-recognized standards referenced in this document, see the FDA-Recognized Consensus Standards Database Website.[2]

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

---

[1] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

[2] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

II. Background

AM is a rapidly growing technology that is frequently used for product research and development in many industries, and for commercial production in some industries (e.g., aerospace, medical devices). While many AM technologies exist, at the time of publication of this guidance, the most commonly used technologies in medical devices are powder bed fusion, stereolithography, fused filament fabrication, and liquid-based extrusion. Powder bed fusion systems rely on an energy source (laser or electron beam) to selectively melt or sinter a layer of powder, either a metal or polymer, which is then refreshed to create the next layer. Stereolithography systems use a vat of liquid material that is selectively cured using light, either through a laser or projection system, and create new layers by moving the build surface. Fused filament fabrication systems melt a solid filament at the point of deposition, after which the material solidifies in place, and new layers are created by moving the build surface away from the heat source. Liquid-based extrusion systems eject a liquid, which then solidifies (method of solidification could include light exposure, solvent evaporation, or other chemical process), and new layers are created by moving the build platform away from the deposition tip.

For medical devices, AM has the advantage of facilitating the creation of anatomically-matched devices and surgical instrumentation (called patient-matched devices) by using a patient's own medical imaging. Another advantage is the ease in fabricating complex geometric structures, allowing the creation of engineered porous structures, tortuous internal channels, and internal support structures that would not be easily possible using traditional (non-additive) manufacturing approaches. However, the unique aspects of the AM process, such as the layer-wise fabrication process, and relative lack of experience and clinical history of with respect to devices manufactured using AM techniques, pose challenges in determining optimal characterization and assessment methods for the final finished device, as well as optimal process validation and acceptance methods for these devices. The FDA held a public workshop entitled "Additive Manufacturing of Medical Devices: An Interactive Discussion on the Technical Considerations of 3D Printing" on October 8-9, 2014, to discuss these challenges and obtain initial stakeholder input. [3]

The workshop provided a forum for medical device manufacturers, AM companies, and academia to discuss technical considerations for AM medical devices. It focused on five broad themes: (1) materials; (2) design, printing, and post-printing validation; (3) printing characteristics and parameters; (4) physical and mechanical assessment of final devices; and (5) biological considerations of final devices, including cleaning, sterility, and biocompatibility. A variety of different types of materials can be used in additive manufacturing. Workshop participants noted that material control is an important aspect to ensure successful fabrication, and that final device performance is tied to the material,

---

[3] http://wayback.archive-it.org/7993/20170111083117/http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm397324.htm

machine, and post-printing processes. The interaction between the material and machine was also discussed in the process validation session, and the need for a robust process validation and acceptance protocol appropriate to the risk profile of the final device was identified. AM design procedures were also discussed, and the importance of having a good understanding of the processes and limits in the design phase was identified. There was general agreement that printing and process parameters should be captured and validated, which can include individual machine validations. The discussion on the physical and mechanical assessment focused heavily on the validation of the process and the acceptance criteria for devices and components after post-processing. The discussion on the biological considerations revealed that there is a concern across the community regarding how to achieve adequate cleaning, sterility, and biocompatibility of an AM device. Specifically, the challenge of assessing and verifying these issues in porous or internally complex devices was discussed. The feedback obtained at the workshop served as the basis for this guidance.

III. Overview

The information, characterization, and testing necessary for a device made through AM may depend on a variety of factors, including, but not limited to, whether it is an implant, an instrument, single-use versus reusable, load-bearing, and/or available in pre-specified standard sizes or is patient-matched. This guidance outlines technical aspects of an AM device that should be considered through the phases of design development, production process, process validation, semi-finished and final finished device testing**. Not all considerations described will be applicable to every device, given the variety of AM technologies, materials, and devices made with additive manufacturing.** You should determine and justify which considerations are appropriate for your device based on the material and technology being used and the intended use of the device. For example, a device made via powder bed fusion from titanium would not need to address liquid material or polymer considerations.

Similarly, not all considerations are expected to be addressed in premarket submissions of AM devices. It is anticipated that AM devices will generally follow the same regulatory requirements and submission expectations as the classification and/or regulation to which a non-AM device of the same type is subject. In rare cases, AM may raise different questions of safety and/or effectiveness. In addition, this guidance only addresses manufacturing considerations related to the AM process. If it is unclear what technical information should be provided in a premarket submission for an AM device, we strongly encourage manufacturers to engage with CDRH or CBER through the Pre-Submission process to obtain more detailed feedback. For more information on Pre-Submissions, please see "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff - Guidance for Industry and Food and Drug Administration Staff."[4]

[4] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

The overall AM process and the related sections in this guidance are shown in the flow chart below (Figure 1). The first step is the design process, which can include a standard design with discrete pre-specified sizes and models, or a patient-matched device designed from a patient's own medical images. Once the device design is converted to a digital file, the software workflow phase begins, and that file is further processed to prepare it for printing. Printing parameters are optimized, and the build file is converted into a machine-ready format. Concurrently with this step, material controls are established for materials used in the printing of the device. After printing is complete, post-processing of the built device or component (e.g., cleaning, annealing, post-printing machining, sterilization, packing and labeling) takes place. After post-processing, the final finished device is ready for testing and characterization. Your quality system should be applied across all of these processes.

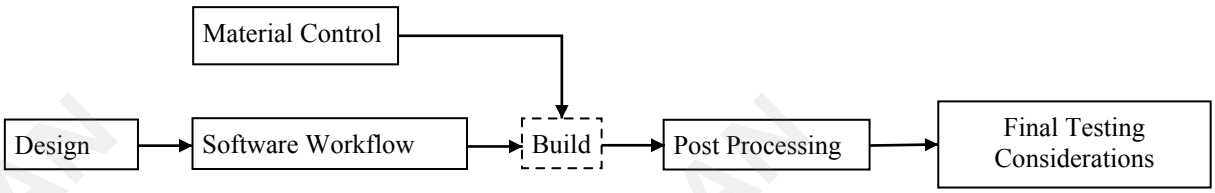


Figure 1: Flow chart of the AM process

IV. Definitions

The following definitions apply to this guidance and may not be applicable to any other documents issued by the FDA.

AM Machine (machine) – "a portion of the additive manufacturing pipeline including hardware, machine control software, required set-up software and peripheral accessories necessary to complete a build cycle for producing parts" [5]

Build Cycle – "single process cycle in which one or more components are built up in *layers* in the process chamber of the *additive manufacturing system*."[6]

Build Preparation Software – the software used to convert the digital design to a format that can be used to build a device or component through an AM process. This may include multiple software components.

Design Manipulation Software – the computer program that allows a medical device design to be modified for specific circumstances (e.g., patient-matching). This may include multiple software components.

---

[5]ISO/ASTM 52900 *Additive manufacturing — General principles — Terminology*
[6]ISO/ASTM 52900 *Additive manufacturing — General principles — Terminology*

Lot or Batch – "one or more components or finished devices that consist of a single type, model, class, size, composition, or software version that are manufactured under essentially the same conditions and that are intended to have uniform characteristics and quality within specified limits."[7]

Quality – "the totality of features and characteristics that bear on the ability of a device to satisfy fitness for use, including safety and performance."[8]

V. Design and Manufacturing Process Considerations

This section highlights technical considerations that should be addressed as part of fulfilling Quality System (QS) requirements for a regulated device made in whole or in part by AM. However, this guidance is not intended to comprehensively address all regulatory requirements for a quality system. For class II and class III devices and select class I devices, manufacturers must establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met per 21 CFR 820.30 Design Controls. Manufacturers must also establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met.[9] Where the results of a process cannot be fully verified by subsequent inspection and test, the process must be validated with a high degree of assurance and approved according to established procedures.[10] FDA interprets these regulations to require manufacturers to establish procedures including validation of the manufacturing process of AM devices to ensure that the device can perform as intended. Please note that exemption from the requirement to submit a premarket notification (510(k)) does not mean a device is exempt from compliance with QS requirements.

There are some devices that are specifically exempted by regulation from most QS requirements. Manufacturers should refer to applicable regulations for their specific device type to determine what QS requirements apply. In this section, the use of the terms "document," "describe," and "identify" refers to documentation requirements according to the QS regulation and premarket submission requirements for manufacturing information determined by the regulation for a specific device type or classification, regardless of the method of manufacture. Not all considerations described will be applicable to an individual device, given the variety of AM technologies available. Similarly, a premarket submission for a specific device may not need to address all considerations. It is anticipated that AM devices will generally follow the same regulatory requirements as the classification and/or regulation to which a non-AM device of the same type is subject.

---

[7] 21 CFR 820.3(m)
[8] 21 CFR 820.3(s)
[9] 21 CFR 820.75(b)
[10] 21 CFR 820.75(a)

There are several AM technologies and different combinations of processing steps that can be used with each technology to build a device. Therefore, it is important to clearly identify each step in the printing process. A production flow diagram that identifies the steps involved in the manufacturing of the device, from the initial device design to the post-processing of the final device, can help ensure the elements of product quality are addressed during production. In addition, a high-level summary of each critical manufacturing process step may be helpful in documenting the AM process used. The characterization of each process step should include, but need not be limited to, a description of the process, and identification of the process parameters and output specifications. Since processes that optimize one design parameter may influence another, information on processing steps should demonstrate your understanding of these trade-offs and how they affect design outputs that are essential to the proper functioning of the device. Additionally, the cumulative effects of prior processes on the final finished device or component should be incorporated into the development of each process step and documented. The effects of the different steps in the AM processes can be seen in final device testing; however, determining the root cause of failures from manufacturing defects can be very difficult without a clear understanding of each step. For example, in a powder bed fusion machine, the ratio of reused to virgin powder can affect melting properties, which affects the energy needed to create consistent bonding between layers, which in turn affects final mechanical properties. Similarly, risks identified for each step of the manufacturing process, as well as mitigations of these risks, should be documented. Each AM process may have different critical steps and identified risks. It is important to use all reasonably obtainable knowledge about your specific machine's capabilities to ensure the manufacturing process outputs meet defined requirements.[11] Quantitative knowledge of the machine's capabilities and limitations can be gained through test builds, worst-case builds, or process validation (See Section V.F *Process Validation and Acceptance Activities* and Section VI.B *Mechanical Testing* for more information).

As with traditional manufacturing methods, design requirements drive the processes that can be used to reliably produce the device. It is therefore important to clearly identify key design parameters for your device, including, but not limited to, size range and available design or configuration options (e.g., range of angles between the trunnion and stem of the femoral component of a hip arthroplasty device).

While this section includes manufacturing considerations, it is not intended to comprehensively address all considerations or regulatory requirements for establishing a quality system for the manufacturing of your device. Aspects of the "Global Harmonization Task Force Process Validation Guidance"[12] may be helpful in developing process validation procedures. Additional information on design controls can be found in the "Design Control

---

[11] ISO 14971 *Medical devices - Applications of risk management to medical devices*

[12] http://www.imdrf.org/docs/ghtf/final/sg3/technical-docs/ghtf-sg3-n99-10-2004-qms-process-guidance-04010.pdf

Guidance for Medical Device Manufacturers."[13] For general questions regarding the Quality System regulation, contact the Division of Industry and Consumer Education (DICE), Office of Communication and Education, at 1-800-638-2041 or 301-796-7100 or DICE@fda.hhs.gov.

A. Overall Device Design

The innovative potential of AM may introduce variability into the manufacturing process that would not be present when using other manufacturing techniques. Specifically, we recommend that you compare the desired feature sizes of your final finished device to the minimum possible feature size of your AM technique and the manufacturing tolerances of the individual machine, given the build parameters and conditions under which the final device is expected to be made. This is to ensure that devices and components of the desired dimensional specifications can be reliably built using the chosen additive technology. Dimensional specifications for the final device or component, as well as manufacturing tolerances of the machine, should be documented. Pixelation of features, where smooth surfaces become stepped, can lead to rougher surface finishes than expected. Surface finish requirements should be outlined in the product specification.

B. Patient-Matched Device Design

Patient-matched devices (PMD) can be produced in many ways, some additive and some traditional. AM is particularly suited to making PMD; consequently, this guidance attempts to address some of the considerations relevant to AM. However, it does not provide an exhaustive list of considerations for a general patient-matching process. All AM devices, including PMD, will share the considerations described in Section V.A. Some PMD are based on a standard-sized template model that is matched to a patient's anatomy. With or without a standard-sized template, PMD may be produced within a defined design or performance envelope. This performance envelope is determined before patient-matching can be initiated and describes the minimum and maximum dimensions, mechanical performance limits, and other clinically relevant factors. Patient-matching can be accomplished by techniques such as scaling of the device using one or more anatomic references, or by using the full anatomic features from patient imaging. Note that while patient-matched or patient-specific devices are sometimes colloquially referred to as "customized" devices, they are not custom devices meeting the FD&C Act custom device exemption requirements unless they comply with all of the criteria of section 520(b). Most PMD will fall within the existing regulatory pathway for that particular

[13] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070627.htm

device type. For further information on custom device exemptions, please refer to the Custom Device Exemptions Guidance.[14]

Patient-matched device designs may be modified either directly by clinical staff, the device manufacturer, or a third party in response to clinical inputs. These inputs may be acquired from individual measurements, clinical assessments, patient imaging, or a combination thereof. Alterations to the final device, and the methods used to make the alterations, may have direct consequences to the patient. Therefore, you should clearly identify clinically relevant design parameters, the pre-determined range (min/max) for these parameters, and which of these parameters can be modified for patient-matching.

Considerations for standard-sized devices should be applied to PMD as well. In addition, for patient-matched AM devices, we recommend that you address the following, if applicable:

(1) Effects of imaging

Many AM devices and components incorporate medical imaging data. Every medical device will not need the same level of anatomic matching or imaging accuracy for optimal device performance. Several factors may affect the fit of AM devices that use patient imaging to precisely control their size or shape, including, but not limited to:

- the minimum image feature quality and resolution used for matching,
- any smoothing or image processing algorithms that may alter the dimensions of the final device when compared to the reference anatomy,
- the rigidity of the anatomic structures being imaged, and
- the clarity of anatomic landmarks used to match the device to the patient's anatomy.

If the device relies on anatomic features that are not accurately imaged or are not consistent over time, then the final device may not fit the patient. However, small changes in size or geometry may be difficult to identify during visual inspection of the device or through evaluation of patient imaging, and the mismatch may only be identified during device use. Process validation (see Section V.FI.A(1)) is especially important to prevent these situations. In addition, for devices intended to be fitted to or matched to soft tissues and non-rigid structures, it is important to note the range of changes that may be experienced by the soft tissue at the target location, such as deformation, when compared to the reference image. You should employ a risk-based approach, taking into consideration

[14] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM415799.pdf

intended use of the device and design methodologies, to assess the scenarios that may yield a worst-case match.

Many implantable devices and their patient-matched accessories depend on the patient's anatomy to be clinically accurate representations of the recorded images in order for the device to function as intended. Specifically, when the device is intended to match a patient's anatomy, and that anatomy can change over time (e.g., with disease progression), the time that can elapse between when the patient is imaged and when the final device is used may need to be reflected in the expiration date of the device (see Section VII Labeling). You should consider such potential time constraints associated with producing an AM device based on the intended use of your device.

(2) Interacting with design models

Patient-matched devices are often made by altering the features of a standard-sized device for each patient within a pre-determined range of device designs and size limits. This is typically accomplished through the use of anatomical matching or design manipulation software that may be developed specifically for the AM device, or through other third party software. Patient-matching may also be accomplished by manual methods using specific measurements on radiographs or key anatomic landmark measurements. Any software or procedure used to make modifications to the device design based on clinical input should include internal checks that prevent the operator from exceeding the pre-established device specifications documented in the device master record. We recommend that the design manipulation software or procedure used to make modifications to the device design identify the iteration of the design being changed by the operator. You should also identify all medical devices and accessories that the design manipulation software is validated to work with.

(3) Complex design files

Patient-matched devices that follow the patient anatomy precisely are especially vulnerable to errors in file conversion because anatomic curves are typically geometrically or mathematically complex, which can create difficulties when calculating conversions. Additionally, for patient-matched devices, all of the file conversion steps are typically performed every time a device is built, whereas for a standard-sized device, most of the file conversion steps would be performed once during the design phase. We recommend following the considerations in Section V.C.I.A(1) on maintaining data integrity throughout file conversions.

(4) Cybersecurity and Personally Identifiable Information

Proper management and care of personally identifiable information (PII) and protected health information (PHI) is essential in any clinical application. For more information on protecting PII and PHI, please refer to the HHS Guidance on

Significant Aspects of the Privacy Rule.[15] We also recommend that device designers who include interactive steps in their patient matching workflow be familiar with implementing the FDA's Guidance on the "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices"[16] It is beyond the scope of this document to provide a full discussion of how these aspects are integrated into patient matching.

C. Software Workflow

The following sections highlight considerations that are especially important in the AM process.

(1) File Format Conversions

AM typically involves interaction between several software packages, often from different manufacturers, which requires files to be compatible across the different software applications used. Patient images, design manipulation software for patient-matching, digital point clouds and meshes, and machine-readable files each have their own standards, coordinate systems, and default parameters. Additionally, each software package has different ways of interpreting those file specifications. Errors in file conversion can negatively impact final finished device and component properties, such as dimensions and geometry. Therefore, we recommend that you verify the critical attributes and performance criteria of your final products as part of the software workflow validation to ensure expected performance, especially for patient-matched devices. Factors that may cause unexpected conversion failures, such as changes to the software used, may trigger the need for revalidation (see Section V.F.I.A(2) Revalidation).

When possible, final device files for printing should be maintained and archived or referenced in robust, standardized formats that are able to store AM-specific information so that the information can be retrieved when needed. For instance, one option is the Additive Manufacturing File format (AMF) described in the ISO/ASTM 52915 *Standard specification for additive manufacturing file format (AMF)*. This, or a comparable file format or document control system, should include material information and the location of objects in a build volume and have high geometric fidelity (e.g., curved patches).

---

[15] https://www.hhs.gov/hipaa/for-professionals/privacy/guidance/significant-aspects/index.html
[16] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM356190.pdf

(2) Digital Device Design to Physical Device

When a digital device design is finalized, additional preparatory processes are needed before the device can be additively manufactured. This is commonly accomplished using build preparation software. These processes can be generally divided into four steps: 1) build volume placement, 2) addition of support material, 3) slicing, and 4) creating build paths.

i. Build Volume Placement

Placement, orientation, and packing density of devices or components within the build volume may be integral to individual device or component quality. The distance between each device or component, and whether they are identical or different designs, can affect the material properties, surface finish, and ease of post-processing. Build orientation of each device or component can also impact its functional performance by affecting the anisotropic properties of the device or component. Similarly, many machines have areas of the build volume where they function optimally and areas where they do not. For example, printing may be sub-optimal in the regions near the outer edge of the build volume and optimal at the center. The affected region may be different for every machine, even between machines of the same model.

Operation Qualification (OQ) of the printing process should include, but not be limited to, challenging the build volume placement to establish control limits which result in product that meets all predetermined requirements. These control limits may include acceptable placement regions, part proximity, and other parametric considerations. Software tools are available to trace how devices are placed and oriented. Process validation based on the risk profile of the device is preferable to a one-size-fits-all approach.

ii. Addition of Support Material

Some types of AM require temporary support structures for certain design features during printing due to the layer-by-layer printing process. The location, type, and number of supports can affect the geometric accuracy and mechanical properties of the final finished device or component. Each AM technology has different needs for support material use to ensure the successful printing of a device. For example, the critical overhang angle may be different for a stereolithography machine, an extrusion-based machine, and a metal powder bed fusion machine. Automated algorithms are often used to choose the location and number of supports. However, geometric complexities or printing limits often necessitate further manual intervention. Therefore, if your AM process requires support material, we recommend that you analyze the geometry and other requirements that could be affected by adding supports. Some common structures that may need support are:

- overhangs,
- high aspect ratio features that protrude from the main body of the device or component,
- internal features (e.g., voids, channels), and
- thin features prone to warping.

Support material can be removed physically or by chemical means. Removal of support material may cause surface marks or leave residues on or in the device. Manufacturing material removal processes (cleaning) should ensure that residues are removed to the level where they do not impact the safety or effectiveness of the product (see Section VI.E Removing Manufacturing Material Residues and Sterilization). The complete description of the support material geometry and the removal process method should be included in the Device Master Record (DMR).

iii. Slicing

Most AM techniques use a layer-by-layer printing process to fabricate components. This necessitates slicing the models into layers. Nominal layer thickness is determined by the machine specification and software capabilities, and an evaluation of the raw material. However, technical characteristics of the machine and physical properties of the material may influence the achievable layer thickness. The surface texture of a device or component, bonding between and curing of each layer, and sensitivity to power fluctuations can all be affected by the choice of layer thickness. For example, the depth of material cured in a stereolithography system is primarily controlled by the energy density and additives in the liquid polymer. If the energy density is changed to reduce layer thickness and the additives are not adjusted properly, the layers may not cure or bond together completely. For systems where layers are created by melting the material, the layer thickness can similarly influence the energy needed to create a uniform melt pool to enable bonding to the layer below.

Your choice of layer thickness should be documented, and reflect a balance between the above-mentioned effects, accuracy, quality, and printing speed.

iv. Build Paths

The build path, the path traced by the energy or material delivery system (e.g., laser or extruder), can impact the quality of the final finished device or component. For example, if the delivery system sweeps from left to right on the build volume, then makes the next pass from right to left, one side of the device or component has more time to cool or harden. Similarly, the space between each line of the build path and the path speed will change the amount of melting and re-melting that the boundaries of each line of material will experience. In addition, the build path may result in an orientation or

anisotropy in the device or component. We recommend that you assess whether differences in the build path significantly affect the performance of each component or device. If so, it is important to maintain consistency of the build path between identical devices and components. If more than one build path is used, each build path should be evaluated and documented.

Some machines may allow portions of a device or component to have different energy delivery or build path specifications that do not change the geometry of the component or device but may influence the final device performance. Other machines may allow the fill density of a component to be specified separately from patterns in the component's geometry. For example, if the geometry shows a solid wall, it is possible to fill that solid space with a sparse honeycomb instead. These voids are easily formed with an extrusion-based machine. The fill density and fill pattern of parts that are not fully dense (i.e., not a solid) should be documented. If a non-solid fill density is used, we recommend that you identify whether internal voids are externally accessible or if they are sealed. If the voids are sealed but may be compromised during the course of the intended clinical use, you should identify the fluid or gas that fills the voids. The risk associated with patient exposure to the materials in the voids should also be assessed.

v. Machine Parameters and Environmental Conditions

Each AM technology and machine model has a unique set of parameters and settings that can be modified by the device manufacturer and those that are configured at the time of calibration (typically by the machine manufacturer). Maintaining proper calibration and performing preventative maintenance have been identified as key factors to achieve low rejection rates of devices and components from an individual machine.

Environmental conditions within the build volume can also affect quality of the part. For machines without a self-contained, well-controlled build volume, the ambient temperature, atmospheric composition and flow patterns can impact solidification/polymerization rate, layer bonding, and the final mechanical properties of the component. Therefore, it is critical to establish and maintain procedures to adequately control environmental conditions within the build volume.

Optimal settings and parameters for a single model of a machine can vary greatly when printing different devices or components. Furthermore, optimal settings and parameters can vary between machines of the same model even when printing the same devices or components. Some parameters that can be modified by the device manufacturer and may have a significant impact on the device or component quality include, but are not limited to:

- instantaneous power of the energy delivery system (e.g., temperature gradients of deposition nozzle for fused filament systems, energy density of laser or electron beam for powder bed fusion or stereolithography),
- build speed or beam speed,
- build path,
- total energy density, and
- focal point or nozzle diameter.

Machine parameters should be documented, and the machine should be qualified for use in its installation location. Aspects of the "Global Harmonization Task Force Process Validation Guidance"[17] also address Installation Qualification.

(3) Validating and Automating Software Processes

If you use a workflow that automates one or more software steps, you should refer to FDA Guidance on "General Principles of Software Validation[18]. For more information on validating the manufacturing process, please refer to Section V.F Validation and Acceptance Activities.

D. Material Controls

(1) Starting Material

In the AM process, the starting material may undergo significant physical and/or chemical changes. As such, the starting material can have a significant effect on the success of the build cycle, as well as on the properties of the final finished device. Therefore, to ensure the consistency of the incoming raw material and the final product, the following information regarding each starting material used, as well as any processing aids, additives, and cross-linkers used, should be documented:

- the identity of the material or chemical by common name, chemical name, trade names, Chemical Abstracts Service (CAS) number, or recognized consensus material standard,
- material supplier,

[17] http://www.imdrf.org/docs/ghtf/final/sg3/technical-docs/ghtf-sg3-n99-10-2004-qms-process-guidance-04010.pdf
[18] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm085281.htm

- incoming material specifications and material certificates of analysis (COAs), with the test methods used for the COAs. Applicable materials standards and test methods (e.g. ISO or ASTM) should be referenced.

The specifications for incoming materials and test methods should be based on the AM technology used (e.g., material specifications will be different for powder based vs. stereolithography machines), the intended use of the final medical product, and the information available. The specifications of the incoming materials (e.g., powders, liquid monomer/polymer systems) may be different from the properties of the finished devices.

Examples of specifications for commonly used material types and machine technologies may include, but are not limited to:

- if the material is a solid: particle size and distribution and relevant rheological performance for powders, or filament diameter and diametric tolerances for filaments,
- if the material is a fluid: viscosity or viscoelasticity, and pot life,
- if the material is a polymer or monomer mixture: composition, purity, water content, molecular formula, chemical structure, molecular weight, molecular weight distribution, glass transition temperatures, melting and crystallization point temperatures, purity information (e.g., purity of polymer/monomer and identification and quantity of relevant impurities, both inorganic and organic, as applicable),
- if the material is metal, metal alloy, or ceramic: chemical composition and purity,
-
- if materials of animal origin are used, refer to: "Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices,"[19] and
- if the material is a composite, the mix ratio with specifications provided for each component.

In addition, when any material specification is changed, the effect on the build process and the final device should be well-understood and documented.

(2) Material Reuse

Some AM approaches (e.g., powder bed fusion, stereolithography) allow efficient use of raw material by reusing the material that is not incorporated into the device

[19] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073816.pdf

(e.g., unsintered powder or uncured resin). However, the reused material could be exposed to conditions (e.g., heat, oxygen, humidity, ultraviolet energy) that may alter it from the virgin state. Therefore, we recommend that you describe the material reuse process, which may include, but not be limited to, a description of processes such as filtering reused material, a limit on the percent of reused material, or monitoring for changes in chemistry, oxygen, or water content. We also recommend that you document evidence or provide a rationale that material reuse does not adversely affect the final device. This may include an assessment of the reuse protocol by conducting studies on the effect of material reuse on the properties of the final finished device (see Section V.F.I.A(1) Validation).

E. Post-Processing

Final device performance and material properties can be affected by post-processing steps of AM (i.e., manufacturing steps occurring after the printing process). These steps could include removing manufacturing residues from the device, heat treatments of the device to relieve residual stress, and final machining. All post-processing steps should be documented and include a discussion of the effects of post-processing on the materials used and the final device. As stated previously, manufacturers must establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met.[20] The broad utility and ability to make multiple devices at once through AM means that some post-processing may be documented for a design, a device, or a build. We recommend that you identify any potentially detrimental effects of post-processing and describe mitigations implemented. For example, one common heat treatment method for metal devices is Hot Isostatic Pressing (HIP). This process can reduce residual porosity and increase fatigue life but has also been shown to reduce the modulus and yield strength of the material. Therefore, care should be taken to ensure both the AM and HIP processes maintain device performance.

Devices that are intended for applications where fatigue is a factor may require minimum surface finish or roughness specification to reduce the chance of failure. The desired surface roughness can often be achieved through various post-processing steps (e.g., mechanical polishing); however, hard-to-reach spaces may remain in the as-built state. These spaces should be assessed for their effects on mechanical performance (including fatigue) of the device or component. See Section VI for Device Testing Considerations.

F. Process Validation and Acceptance Activities

[20] 21 CFR 820.75(b)

(1) Process Validation

Device quality, such as feature geometry, overall dimensions, material characteristics, and mechanical properties, are impacted by AM process parameters, process steps, and raw material properties, as described in the sections above. In addition, for an identical device or component, quality may vary when built using different AM machines, even when the same machine model, parameters, process steps, and raw materials are used. Therefore, knowledge of how the variability of each input parameter and processing step affects the final finished device or component is critical to ensuring part quality. Where the results of a process cannot be fully verified by subsequent inspection and testing, the process must be validated with a high degree of assurance and approved according to established procedures.[21] In addition all documentation must conform to the existing guidelines in the Quality System regulation for device validation. Process validation must be performed to ensure and maintain quality for all devices and components built in a single build cycle, between build cycles, and between machines, where the results of a process (i.e., output specifications) cannot be fully verified by subsequent inspection and test.[22] Software also must be validated for its intended use according to an established protocol[23] (i.e., software workflow).

For validated processes, the monitoring and control methods and data must be documented.[24] This section provides some examples of methods for ensuring the consistency of quality. The list is meant to be representational of the type of factors to consider when performing process validation. It can be used as a reference point but is not exhaustive. The following examples may have the greatest applicability to powder bed fusion technologies, which comprise a large portion of AM medical devices. Methods could include:

- in-process monitoring of parameters such as:
  - temperature at the beam focus,
  - melt pool data,
  - build-space environmental conditions (e.g., temperature, pressure, humidity),
  - power of the energy delivery system (e.g., laser, electron beam, extruder), and
  - status of mechanical elements of the printing system (e.g., recoater, gantry)

  In-process monitoring may also be helpful for processes that are not validated, but is not required.

[21] 21 CFR 820.75(a)
[22] See 21 CFR 820.75(a)
[23] See21 CFR 820.70(i), and "General Principles of Software Validation; Final Guidance for Industry and Staff."
[24] See 21 CFR 820.75(b)(2)

- manual or automated visual inspection with defined acceptance criteria,
- non-destructive evaluation (see Section V.E.3 Verification), and
- test coupon evaluation (see Section V.E.4 Test Coupons).

Not every AM system will be able to perform all these measurements, either because the process does not use them or because of technological limitations. Test methods used for process monitoring and control must be validated.[25] For example, analysis should be conducted to confirm that test coupons used are representative of the final finished device or component and representative of a certain area within the build volume.

A single failed component or device in a build cycle may not necessitate the rejection of all other devices or components within that build cycle. The criteria for determining whether to reject a single device or component, or the entire build, should be established before testing.

(2) Revalidation

Changes to the device, manufacturing process, or process deviations should be identified and analyzed for the potential risks they introduce. Based on this assessment, the change or deviation may trigger the need for revalidation of the process.[26] Manufacturers should rely on existing FDA Guidance for their regulatory pathway[27,28,29,30] when considering a change to a previously cleared or approved device that uses AM. Some examples of triggers for revalidation specific to AM are:

- software changes (e.g., change or update of build preparation software),
- changes in material (e.g., supplier, incoming material specification, reused powder, new formulation) or material handling,
- change in the spacing or orientation of devices or components in the build volume,
- changes to the software workflow (see Section V.B.2 Digital Device Design to Physical Device),
- physically moving the machine to a new location, and

---

[25] See 820.72(a) and 820.250(a)
[26] See 820.70(b) and 820.75(c)
[27] Deciding When to Submit a 510(k) for a Change to an Existing Device (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080235.htm)
[28] 30-Day Notices, 135-Day Premarket Approval (PMA) Supplements and 75-Day Humanitarian Device Exemption (HDE) Supplements for Manufacturing Method or Process Changes (www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM080194.pdf)
[29] Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm089360.pdf
[30] Changes or Modifications During the Conduct of a Clinical Investigation (www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm082158.pdf)

- changes to post-processing steps or parameters.

(3) Acceptance Activities

Acceptance activities are integral to process control. Many AM technologies can produce more than one device or component simultaneously at different locations in the build volume. Each of these devices or components can be copies of a single design or different designs. This makes it more challenging to ensure repeatability and consistency within a build cycle and across lots.

Some acceptance activities for individual devices or components can be performed through non-destructive evaluation (NDE). Specifically, NDE techniques can be used for the verification of geometry, morphology, and some performance characteristics. Techniques include, but are not limited to:

- ultrasound,
- computed tomography (CT) or micro-CT,
- x-ray (in cases with simple geometry),
- dye penetration,
- confocal microscopy, and
- hyperspectral imaging.

Some techniques are not suitable for some materials, designs, or intended uses. General NDE testing protocols can be found from the ASTM and ISO Committees on Nondestructive Testing. Protocols specific to AM can be found from the ISO/ASTM Committee on Additive Manufacturing Technologies.[31] If an NDE technique is used in your process validation or acceptance activities, the choice of technique used should be discussed and documented.

(4) Test Coupons

A test coupon is a representative test sample of the device or component. The design of test coupons and placement within the build volume can be especially important for AM. Coupons can be simple shapes suitable for destructive mechanical testing, or they may contain one or more structural features (e.g., surface porosity, internal channels) representative of the component or device that can be assessed using destructive techniques. We recommend that coupons be used to help with your process validation and to identify worst-case conditions in your manufacturing process (e.g., worst-case orientation and location in build volume). Test coupons can also be used for in-process monitoring by placing them in build volume locations that are known to have the worst-case outputs. However, test coupons may not be needed if the process is validated per Quality

[31] http://www.astm.org/COMMIT/SUBCOMMIT/F42.htm

System requirements and coupon testing is not a process monitoring activity defined in your quality system. These test coupons can confirm that the build cycle has met its performance specification for that portion of the build volume if the test coupons meet the performance specifications. For example, test coupons may be placed at the edges of the build volume if edges are known to have less optimal build quality. They may also be placed randomly in between components or devices to produce a sampling of the build quality. Data to demonstrate that test coupons are representative of the components, in-process devices, or finished devices should be documented. Many factors can alter how well a test coupon represents any given part in the build space. When coupons are used, they should be validated to accurately and reproducibly represent the one or more printed parts within a specific build volume.

G. Quality Data

The analysis of sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems is an essential part of any quality system. For devices produced by AM, it is important to consider whether it is necessary to keep track of the location in the build volume where a device or component was built. This will depend on information obtained during process validation activities and design specifications. For example, if process validation demonstrated that quality is not affected by location in the build volume, it may not be necessary to be able to keep track of the build volume location for each device. This level of specificity is important in identifying possible causes of failure when multiple different components or devices are made in the same build volume at the same time. Therefore, you should ensure that quality data such as build volume location can be analyzed to enable proper identification of quality problems and investigation of the cause of nonconformities.

VI. Device Testing Considerations

The following section contains a description of the type of information that we recommend that you include in a premarket submission of a device made using AM. The type and amount of data to support a substantial equivalence determination or approval will vary depending on the intended use, risk profile, and classification and/or regulation for the device type. In addition, the type of information needed for a device made through AM may also depend on a variety of factors, including but not limited to, whether it is an implant, load bearing, and/or available in pre-specified standard sizes or is patient-matched. Not all considerations described will be applicable to a single device, given the variety of devices that can be made by AM and AM technologies available. In general, if the type of characterization or performance testing outlined in each of the sub-sections below is needed for a device made using non-AM techniques, the information should also be provided for an AM device of the same device type. If you have specific questions regarding the information to support a premarket submission for an AM device, please contact the relevant review

division in CDRH or contact CBER for products containing biologics, cells or tissues. Specific questions regarding jurisdiction over a combination product should be directed to the Office of Combination Products (OCP) at 301-427-1934 or combination@fda.gov.

A. Device Description

AM facilitates the creation of intermediate and customized device sizes. Patient-matched devices are a good example of this application. Since these devices may not have discrete sizes, such as small, medium, and large, we recommend that you identify the range of dimensions for your device. In addition, you should describe any design variations, for example, amount of anatomical coverage for a cranioplasty plate. Any critical dimensions or features that are intended to be altered to match a patient should also be clearly identified, and the range of allowable values for these parameters should also be identified. Since each type of AM technology has different technical considerations, you should describe the type of AM technology used to build your device. In addition, because AM use for medical devices is relatively new, we recommend that you include a flow chart describing your AM process, including post-processing, in order to help determine if additional assessments are needed.

Due to the generally complex geometry of AM devices, we recommend that critical features of the device be clearly described in the device description and identified in technical drawings. For example, the location and thickness of porous scaffolding should be described, as these features may have reduced mechanical properties in comparison to a solid material. In the technical drawings of your device we recommend that you identify components made using AM.

B. Mechanical Testing

The type of performance testing that should be conducted on a device made using AM is generally the same as if the device was manufactured using a traditional manufacturing method. Depending on the device type, these may include material property testing such as modulus, yield strength, ultimate strength, creep/viscoelasticity, fatigue, or abrasive wear. Performance testing should be conducted on final finished devices subjected to all post-processing, cleaning, and sterilization steps. As with any recommended testing, the final finished device should be used or a rationale should be provided explaining why the test coupon used was representative of the final finished device. In addition, the worst-case combinations of dimensions and features (e.g., holes, supports, porous regions) should be considered when determining the worst-case devices for performance testing. You should also provide a discussion of how the worst-case devices were selected for each performance test conducted.

Due to the nature of AM, devices will likely have an orientation (i.e., anisotropy) relative to the build direction and location within the build space. The orientation and build location can affect the final properties and should be considered when

conducting device mechanical testing. Specifically, the build orientation (including worst-case orientation) of devices or components should be identified for each performance test. If the orientation changes with device size or design, the worst-case orientation should be identified for each configuration. Since the effect of orientation can vary based on the manufacturing technology used, a baseline study of the machine/material combination used may be helpful in determining the degree to which the build orientation will affect mechanical properties. Coupons may be used for material property assessments if there is adequate justification provided for why the coupon is representative of the final device. This justification should consider critical design elements, post-printing processes, cleaning, disinfection and/or sterilization as they relate to each type of testing. This information can be used to aid in the selection of worst-case samples with respect to orientation.

In addition, for some AM machines, the location within the build space can have an effect on mechanical properties.[32] For example, for powder bed systems, the difference in distance from the energy source to different locations in the build space (e.g., center vs. corner) could lead to variability in the mechanical properties of devices built in those locations. To determine whether build location has a significant effect on device characteristics or performance (including fatigue strength), we recommend that you perform a baseline study of your machine/material combination (see Section V.E.1 Validation). The use of coupons for your baseline study is recommended. If there is a significant effect, build location should be considered in the identification of worst-case samples for mechanical testing.

Since mechanical properties of the device may be impacted by orientation and location, it is important to ensure that production processes are properly developed, conducted, controlled, and monitored in order to ensure that devices or components are not adversely affected by fabrication orientation. The process validation described in Section V.F. Process Validation and Acceptance Activities may be used to address the impact of orientation and location.

C. Dimensional Measurements

Similar to mechanical properties, device dimensions may be affected by orientation and location within the build space. Therefore, we recommend that you specify the dimensional tolerances and perform dimensional measurements for the worst case additively manufactured devices and/or components. Samples selected for the assessment of dimensional measurements should address variability due to orientation and build location if baseline studies show a dependence on these parameters. To demonstrate consistency and reproducibility between build cycles, dimensional

[32] ASTM F3122 "*Standard Guide for Evaluating Mechanical Properties of Metal Materials Made via Additive Manufacturing Processes*"

measurements should be made on samples from multiple build cycles, and a justification should be provided on the sampling scheme used. Alternatively, you may use process validation information to demonstrate that there is negligible variability between build cycles.

While we are aware of the potential effects of orientation and build location on mechanical properties and dimensional tolerances, there may be other properties that could be affected based on the intended use and technological characteristics of the device.

D. Material Characterization

(1) Material Chemistry

Since the AM process creates the final material or alters the starting material during the process, all materials involved in the manufacturing of the device should be identified. As noted in Section V.C Material Controls, this information should include the source and purity of each material used. Certificates of Analysis and/or Materials Safety Data Sheets (MSDS) can facilitate the review of each material. The Chemical Abstract Service (CAS) number, if available, of each chemical component should be provided. If material chemistry information in a device master file (MAF) will be referenced, you should include a right to reference letter from the MAF holder in your premarket submission.[33] You should also document the material composition of the final finished device.

Given the iterative nature of AM, the starting material can be exposed to partial re-melting and solidification processes multiple times, which may result in unexpected or undesired material chemistries for some polymer systems. Therefore, if biocompatibility is not evaluated as described in the guidance "Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing within a Risk Management Process"[34] or if biocompatibility testing identifies a concern, additional material chemistry information may be needed. For example, a description of all material chemistry changes expected during the manufacturing of your device may be needed. In addition, based on this description and the material/machine type used, it may also be necessary to provide additional information or testing for polymers to ensure that there are no unintentionally formed chemical entities that could pose a risk to patient health.

---

[33] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/ucm142714.htm

[34] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM348890.pdf

(2) Material Physical Properties

Inter-layer bonding (adhesion/cohesion) is unique to AM and determines the ultimate structural integrity of the final finished device. As such, material properties known to affect interlayer bonding should be characterized. This information should be representative of the final finished device (subjected to all post-processing, cleaning, and sterilization steps). Material properties can be determined from the final device or using coupons. If coupons are used, a description of the coupon and a justification for why coupon testing is representative of the final device should be provided.

If your device is additively manufactured using metal or ceramic, we recommend that you characterize the microstructure, which may include but is not limited to grain size, orientation, and phase composition. Existing consensus standards for materials can be used for comparison. If the AM process results in structural inhomogeneity, microstructural voids, incomplete consolidation, or other microstructural issues, additional mechanical testing may be needed to show that these issues do not affect device performance.

If your device is additively manufactured using polymers, we recommend that you ensure the AM process is consistently creating a device or component that has properties that meet your specifications. For example, *in situ* crosslinked devices may have crosslink density gradients across the build. For AM processes that use polymer crosslinking, the percent crosslinking and degree of curing should be evaluated to ensure that the AM process results in a material that is fully cured and within specifications. For systems using a crystalline or semi crystalline material, crystallinity and crystalline morphology should be characterized to ensure that the AM process is not adversely altering the polymer structure and subsequently altering the performance (e.g., creep, material transparency) of the final device. For hydrogel materials, the percent water swelling or water content of the material should be reported to ensure that that the AM process has not adversely affected the materials' ability to uptake water.

If your device is additively manufactured using an absorbable material, we recommend that you perform *in vitro* degradation testing using final finished devices or coupons. If coupons are used, they should be representative of your final finished device in terms of both processing and properties (e.g., surface-to-volume ratio, crystallinity). This will establish whether AM has an adverse effect on the degradation profile of the material.

E. Removing Manufacturing Material Residues and Sterilization

AM facilitates the creation of devices with complex geometries, such as engineered porosity, honeycomb structures, channels, and internal voids or cavities that cannot be produced by traditional manufacturing methods. Such complex geometries in

additively manufactured devices are expected to increase the difficulty in removing manufacturing material residues (cleaning) and in sterilization due to the likelihood of increased surface area, generation of extensive tortuous pathways, and creation of internal voids with limited or no access. Additionally, AM allows porous structures to be produced earlier in the manufacturing process than many traditional methods, which could result in greater soiling by the manufacturing material of those porous structures throughout the rest of the process. Therefore, validation of the reduction of the manufacturing material residue to levels that do not adversely affect the device's quality and sterilization process validation should account for the complex geometry of your device under worst-case conditions (e.g., greatest amount of residual manufacturing materials, and a combination of largest surface area, greatest porosity, and most internal voids for sterilization validation).

Manufacturing material means any material or substance used in or used to facilitate the manufacturing process, a concomitant constituent, or a byproduct constituent produced during the manufacturing process, which is present in or on the final finished device as a residue or impurity not by design or intent of the manufacturer.[35] There is also an increased risk of residual manufacturing material, such as excess starting material or support material, remaining on the final finished device. Since residual manufacturing material may negatively affect the performance of the device, you should describe the process used to ensure removal of residual manufacturing materials to a level where they do not affect the safety and effectiveness of the device. Note that for complex geometries and trapped volumes, destructive testing may be needed to properly validate the removal of the manufacturing material.

When a manufacturing material could reasonably be expected to have an adverse effect on device quality, the manufacturer must establish and maintain procedures for the use and removal of such residual manufacturing material to ensure that it is removed or limited to an amount that does not adversely affect the device's quality. [36] It is important to note that many end user facilities may not have routine access to the equipment or materials needed to implement cleaning procedures that are designed to remove residual manufacturing materials and that personnel are likely not adequately trained to perform such cleaning procedures. Therefore, only devices that are sufficiently cleaned of residual manufacturing materials should be provided to the end user. While engineered porosity and complex geometries are generally an advantage of additive manufacturing, highly porous regions are expected to be difficult to clean in comparison to devices made with other manufacturing methods, and can also greatly increase the surface area of the device. Therefore, we also recommend that you include an overview or summary of manufacturing residue removal process and information (e.g., testing procedure and data) in your premarket submission to

[35] See 21 CFR 820.3(p)
[36] See 21 CFR820.70(h)

demonstrate that your device is cleaned of manufacturing residues before being provided to the end user.

The extent to which manufacturing material residue must be reduced is determined on case-by-case basis considering characteristics such as: manufacturing processes, intended use, materials, type and duration of exposure, intended anatomical location, and type of device. In addition, we recommend using final finished devices after they have undergone all other processing for assessment of manufacturing material removal and validation of the sterilization process. For additional information on sterilization and validation, see "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile."[37]

If additively manufacturing a reusable medical device that involves reprocessing or a device intended for end-user sterilization in health care facilities, we recommend the inclusion of reprocessing instructions in your device labeling. Please refer to the guidance, "Reprocessing Medical Devices in Health Care Settings: Validation Methods and."[38]

F. Biocompatibility

We recommend that you evaluate the biocompatibility of the final finished device as described in the guidance "Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing within a Risk Management Process."[39] If chemical additives with known toxicities are used (e.g., certain additives, catalysts, binding and curing agents, uncured monomers, plasticizers), additional information, as outlined in the guidance,[40] may be necessary.

VII. Labeling

Device labeling should be developed in accordance with applicable regulations, device-specific guidance documents, and consensus standards.

Labeling Considerations for PMD

---

[37] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm109897.pdf

[38] http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf

[39] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm348890.pdf

[40] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm348890.pdf

Since clinical staff, device manufacturers, or a designated third party might modify the design of a PMD, additional labeling information is recommended for AM devices that are patient-matched. We recommend that each AM PMD be marked or have accompanying healthcare practitioner labeling included in the packaging to identify:

- patient identifier,
- use (e.g., left distal femoral surgical guide), and
- final design iteration or version used to produce the device.

The expiration date for a patient-matched device may be driven by the patient imaging date or the design finalization date rather than the standard methods of determining device shelf life (see Section V.B.(1)). In addition, it is possible that the patient may have experienced events between the time of imaging and surgery (e.g. additional trauma), which could impact performance of the device. Therefore, we recommend that you include a precaution in your labeling that the patient should be surveyed for potential anatomical changes prior to the procedure.