U.S. FOOD & DRUG ADMINISTRATION

Discussion Paper:
3D Printing Medical Devices at the Point of Care

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Disclaimer: This paper is for discussion purposes only and is not draft or final guidance. It is meant to facilitate early input from groups and individuals outside the Agency. The Agency intends to use such input in developing future guidance. As such, this document is not intended to convey any current policy regarding 3D printing at the point of care.

1. Introduction

The Center for Devices and Radiological Health (CDRH) is committed to assuring that patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products. As part of providing this assurance, CDRH recognizes that innovations in manufacturing and product delivery are as important as innovations in device design and functions. CDRH has been encouraging advanced manufacturing for many years, including the use of new and emerging production and distribution methods incorporating automation, computation, software, sensing, and networking. One of the most promising and well-known advanced manufacturing technologies is 3D printing.

3D printing[1] at the point of care (PoC) may serve an important public health purpose, and may provide for rapid and agile production of devices, including but not limited to patient-matched devices[2] and anatomical models for surgical planning. This technology has the potential to help a healthcare facility (HCF) quickly respond to patient needs, bring personalized care to patients in a timely manner, and lead to new innovations in patient care and treatment. 3D printing at the PoC can take different forms depending upon a number of factors, including the capabilities of the HCF engaging in the 3D printing activities and the complexity of the product or its printing. Most PoC 3D printing situations will have unique considerations, and an HCF's capabilities, expertise, and experience factor into determining which devices are appropriately 3D printed at the PoC.

FDA recognizes that HCFs may not have the same level of experience or familiarity with FDA's regulatory framework for medical devices as traditional manufacturers. An HCF should, however, ensure that any medical devices 3D printed at the PoC will be high-quality, perform as intended, and will not expose patients to unreasonable risk of illness or injury. There are different ways in which an HCF could engage

[1] A brief background on the 3D printing process and how it is used in healthcare is presented in Appendix – Additional 3D printing Background.

[2] Consistent with FDA's guidance, "Technical Considerations for Additive Manufactured Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/technical-considerations-additive-manufactured-medical-devices, "patient-matched" means anatomically-matched devices and surgical instrumentation created by using a patient's own medical 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). For further information on custom device exemptions, refer to the FDA guidance document "Custom Device Exemption," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/custom-device-exemption.

in 3D printing at the PoC, with important questions and considerations associated with each potential situation.

The use of 3D printing during the Coronavirus Disease 2019 (COVID-19) pandemic highlights both the flexibility and challenges of 3D printing at the PoC. Traditional manufacturing is built on a model of batch production dependent on functioning supply chains to provide sufficient raw materials and other components. Many United States companies have experienced supply chain disruption during the COVID-19 pandemic.[3] In response to medical device shortages during the COVID-19 pandemic, individuals and facilities collaborated with manufacturers of 3D printers and collectively used 3D printing technologies to produce face shields, face mask holders, nasopharyngeal swabs, and ventilator parts from locally-available materials.[4]

Through multiple interactions with external stakeholders,[5, 6, 7, 8] FDA has developed an initial outline for a regulatory approach for devices manufactured using 3D printing at the PoC. This discussion paper provides FDA's initial thoughts for early public input on potential PoC manufacturing scenarios and paths prior to proposing draft guidance for 3D printing of medical devices at the PoC.[9] FDA received many inquiries about the regulatory responsibilities of entities performing 3D printing at the PoC. These inquiries underscore the importance of a rational, understandable approach for the 3D printing of medical devices. There are challenges presented by 3D printed medical devices at the PoC, observed before and during the COVID-19 pandemic, which include:

- **Assuring devices 3D printed at the PoC are safe and effective:** FDA regulation is designed to provide a reasonable assurance that devices are safe and effective; this assurance applies regardless of where and how a product is manufactured.
- **Assuring appropriate control of devices 3D printed at the PoC:** Appropriate controls during product design and manufacturing help assure that product specifications are met; these approaches are well-defined for traditional manufacturing but are less defined for 3D printing at the PoC.
- **Clarifying the responsible entity:** Under the Federal Food, Drug, and Cosmetic (FD&C) Act, specific requirements apply depending on the activities an entity conducts across a device's life

[3] https://www.dnb.com/content/dam/english/economic-and-industry-insight/DNB_Business_Impact_of_the_Coronavirus_US.pdf.
[4] Manero A, et al. 2020. Int J Environ Res Public Health 17(13):4634.
[5] FDA 3D Printing Workshop (2014) - http://wayback.archive-it.org/7993/20170111083117/http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm397324.htm.
[6] FDA participation at RAPID MMI (2015) - https://web.archive.org/web/20150315222434/https://www.rapid3devent.com/wp-content/uploads/2015/01/glance.pdf.
[7] FDA/RSNA SIG Joint Meeting (2017) - https://wayback.archive-it.org/7993/20201220003539/https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/fdacdrh-rsna-sig-joint-meeting-3d-printed-patient-specific-anatomic-models-august-31-2017.
[8] ASME 3D Printing at the Point of Care (2019 – 2020) - https://resources.asme.org/poc3dp-events.
[9] During the COVID-19 pandemic, FDA entered into a Memorandum of Understanding with the Department of Veterans Affairs and National Institutes of Health to provide engineering support and scientific expertise in evaluating, developing, and testing designs for 3D printed devices, among other activities. https://www.fda.gov/about-fda/domestic-mous/mou-225-20-008.

cycle. There may be uncertainty regarding responsibilities for activities related to 3D printing at the PoC, including device design, testing, FDA premarket submissions, manufacturing, quality control, complaint handling, adverse event reporting, and corrective actions. The entities responsible for 3D printing at the PoC should understand the requirements related to these activities.

- **PoC training and capabilities:** Many 3D printing technologies are available; each has strengths and weaknesses for different clinical applications. Under many circumstances, the PoC facility could be responsible for complex processes, such as patient-matching or post-processing activities, to generate a final finished device. Additionally, devices can vary in risk depending on their intended use and technological characteristics. Therefore, the entities responsible for 3D printing at the PoC should have the requisite knowledge and expertise to conduct these activities.

This discussion paper discusses these challenges and presents a potential approach for regulatory oversight of 3D printing devices at the PoC. This document is not intended to propose or implement a regulatory policy. This document is intended to stimulate discussion to inform further policy development for an appropriate regulatory approach for 3D printing medical devices at the PoC. FDA expects to issue draft guidance on this topic after considering public comment on this discussion paper.

We have included questions seeking public comment and feedback. FDA also welcomes general comments and suggestions regarding 3D printing devices at the PoC outside the posed questions. Please submit your feedback to the questions throughout this discussion paper and other general comments or suggestions to https://www.regulations.gov, Docket No. FDA-2021-N-1272 by February 7, 2022. If you submit feedback to the questions specified below, please identify question numbers, as applicable. Please also review the instructions for submitting comments that are included as an attachment on https://www.regulations.gov.

2. Scope

This discussion paper is limited to medical devices where CDRH is the FDA Center with primary jurisdiction for premarket review and regulation, including 510(k) exempt devices. The concepts in this discussion paper do not apply to 3D printing of drugs, biological products, human cells, tissues, or cellular or tissue-based products (HCT/Ps) that are not regulated as devices, bioprinting, the non-device constituent parts of combination products, or device constituent parts of combination products where CDRH is not the FDA Center with primary jurisdiction for premarket review and regulation. 3D printing activities occurring at non-PoC facilities are also not included in the scope of this discussion paper.

3. Background

This discussion paper is not intended to provide a comprehensive background on 3D printing or how medical devices are regulated in the United States. Rather, for purposes of the potential approach discussed herein, this discussion paper provides a brief overview of FDA device regulation below and a brief background on the 3D printing of medical devices in Appendix – Additional 3D Printing Background.

For a general background on how medical devices are regulated in the United States, stakeholders can review the materials available on FDA's website under Device Advice.[10]

Terminology

These terms apply only for the purposes of this discussion paper:

Healthcare Facility (HCF) – the facility whose primary responsibility is providing diagnostic, therapeutic (such as medical, occupational, speech, physical), surgical, and other patient services for specific and general medical conditions. The HCF also can include the PoC 3D printing facility. The HCF's personnel may include physicians, surgeons, dentists, and other clinicians and allied health professionals such as clinical engineers, engineers, and research staff.

Traditional Manufacturer – a type of manufacturer (any person who designs, manufactures, fabricates, assembles, or processes a finished device; the full definition of a "manufacturer" is in 21 CFR 820.3(o)[11]). For the purposes of this discussion paper, FDA uses this term to separate entities who have historically manufactured devices (e.g., original equipment manufacturers, contract manufacturers) from HCFs performing such activities at a PoC 3D printing facility.

Contract Manufacturer – an entity that manufactures a device to another manufacturer's specifications.[12]

Point of Care (PoC) 3D printing facility – the physical location near or at the site of a patient (e.g., hospitals,[13] ambulatory surgical facilities,[14] outpatient treatment facilities,[15] physicians' offices,[16] or certain dental laboratories[17]) that 3D prints medical devices.

3D printing medical device production system (MDPS)[18] – a collection of the raw materials, software and digital files, main production equipment and post-processing (if applicable) equipment intended to be used by a healthcare provider or healthcare facility, to produce a specific type of medical device at

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[10] https://www.fda.gov/medical-devices/classify-your-medical-device/product-medical-device.

[11] Manufacturer means any person who designs, manufactures, fabricates, assembles, or processes a finished device. Manufacturer includes but is not limited to those who perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specification development, and initial distributors of foreign entities performing these functions. 21 CFR 820.3(o).

[12] For purposes of this discussion paper, a Contract Manufacturer is a type of Traditional Manufacturer.

[13] 21 CFR 803.3(i).

[14] 21 CFR 803.3(a).

[15] 21 CFR 803.3(s).

[16] 21 CFR 803.3(u).

[17] Domestic dental laboratories are exempt from device establishment registration and listing when they meet the 21 CFR 807.65(i) exemption. Depending on their activities, dental laboratories can also be manufacturers per 21 CFR 820.3(o) and subject to the Quality System (QS) Regulation (21 CFR Part 820).

[18] FDA uses the term "medical device production system" consistent with that established by the International Medical Device Regulators Forum (IMDRF): http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-200318-pmd-rp-n58.pdf. As described in the IMDRF document, "the MDPS is in keeping with the concept of a kit or system, that is, a group of products that together achieve a stated intended use —and as such, can be considered a medical device in its own right. Consequently, all applicable elements of the medical devices framework then apply to it."

the point of care, for treating or diagnosing their patients, or preventing or mitigating disease, or to affect a structure or function of the body. An MDPS includes the medical device it is intended to produce.

What is a medical device?

Section 201(h)(1) of the FD&C Act defines "device" as:

> [A]n instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is:
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> A. recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
> B. intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
> C. intended to affect the structure or any function of the body of man or other animals, and
>
> which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o).

What FDA requirements are relevant for device manufacturers?

Devices in the United States are subject to the regulatory controls in the FD&C Act and its implementing regulations in Title 21 of the Code of Federal Regulations (CFR). Generally, establishments that are engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of devices intended for human use, including entities that 3D print devices, are required, among other obligations, to register with FDA and list the devices they manufacture, prepare, propagate, compound, assemble, or process.[19, 20]

Manufacturers of finished devices, including entities who 3D print devices, are also responsible for compliance with the Quality System (QS) Regulation under 21 CFR Part 820 unless expressly exempted.[21] The QS Regulation governs the methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished devices intended for human use. In some cases, manufacturers must obtain marketing authorization through an FDA submission prior to legally marketing their device in the United States. Manufacturers and other entities have postmarket obligations, including those under the Medical Device Reporting (MDR) regulation, 21 CFR Part 803, and the regulation governing reports of corrections and removals, 21 CFR Part 806.

The activities in which an entity engages determine its regulatory responsibilities under the FD&C Act. Although HCFs generally do not engage in activities that are considered device "manufacturing" under

[19] 21 CFR 807.3(c)-(d).
[20] 21 CFR 807.20.
[21] See e.g., 21 CFR 890.3420 (external limb prosthetic component) and 21 CFR 890.3025 (prosthetic and orthotic accessory). Additionally, as provided in section 520(f)(2) of the FD&C Act and 21 CFR 820.1(e), manufacturers may request an exemption from any requirement in 21 CFR Part 820.

the FD&C Act, 3D printing activities, including post-processing, may be considered manufacturing. HCFs that engage in these activities may be subject to applicable FDA regulations for devices, including but not limited to: registration and listing under 21 CFR Part 807, the QS Regulation under 21 CFR Part 820, MDR requirements for manufacturers under 21 CFR Part 803, and reports of corrections and removals under 21 CFR Part 806 (these and other applicable device requirements under the FD&C Act and FDA regulations are hereafter collectively referred to as "FDA regulatory requirements"). There may be other situations, however, where an HCF engages in 3D printing, but the activities the HCF performs might not be considered manufacturing of devices, or situations where FDA could consider enforcement policies applicable to the HCF's 3D printing activities.

How are devices regulated in the United States?

The FD&C Act includes a comprehensive, risk-based framework for how FDA regulates devices in the United States. Devices are categorized into three different classes: class I (general controls), class II (special controls), and class III (premarket approval).

Class I devices are generally those devices for which the general controls (e.g., registration and listing, current good manufacturing practices, premarket notification) of the FD&C Act are sufficient to provide reasonable assurance of safety and effectiveness.[22] Class II devices are those devices for which general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, and for which there is sufficient information to establish special controls to provide such assurance, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines, recommendations, and other appropriate actions the Agency deems necessary to provide such assurance.[23] Class III devices are those devices for which insufficient information exists to determine that general controls and special controls would provide a reasonable assurance of safety and effectiveness, and which are purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or which present a potential unreasonable risk of illness or injury.[24]

How does CDRH regulate 3D printing?

FDA does not regulate all 3D printing activities, but generally does regulate such activities when they produce devices, i.e., products that are intended for medical purposes,[25] including software interfaces and image segmentation systems.

3D printers may be commercially distributed to the general public for general, non-medical purposes, such as for use in education, construction, art and jewelry, among other non-medical applications. When intended for these general, non-medical purposes, FDA device marketing authorization is not required,

[22] Section 513(a)(1)(A) of the FD&C Act and 21 CFR 860.3(c)(1).
[23] Section 513(a)(1)(B) of the FD&C Act and 21 CFR 860.3(c)(2).
[24] Section 513(a)(1)(C) of the FD&C Act and 21 CFR 860.3(c)(3).
[25] For the purposes of this discussion paper, "intended for a medical purpose" means intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease; or intended to affect the structure or any function of the body of man or other animals, as described in the definition of "device" set forth in section 201(h) of the FD&C Act.

and all the other device requirements of the FD&C Act do not apply to the manufacturers of these products because they do not meet the definition of a device.

Manufacturers are not generally required to list with FDA or obtain marketing authorization for general purpose manufacturing equipment, which could include general purpose 3D printers, mills, or lathes. FDA generally regulates the methods used in, and the facilities and controls used for manufacturing devices, when such devices are subject to the QS Regulation.

3D printing systems could be commercially distributed with the specific intended use to produce specific type(s) of medical devices at the PoC, referred to as MDPS in this discussion paper.[26] In this case, the MDPS is considered a system of products that together achieve an intended medical purpose, and as such, is a device under the FD&C Act. The regulatory requirements for the devices 3D printed using the MDPS would generally govern the responsibilities of the entities manufacturing and commercially distributing the 3D printing MDPS for use at the PoC.

How do the capabilities of a PoC 3D printing facility factor into device safety and effectiveness?

PoC 3D printing facilities may have a wide range of 3D printing equipment and experience, which means that PoC 3D printing facilities may have differing abilities to manufacture devices. When devices are manufactured at the PoC, it may be possible for a PoC 3D printing facility to leverage existing processes within their HCF. For example, HCFs may follow or conform to:

- internal processes;
- accreditations (e.g., Joint Commission, Utilization Review Accreditation Commission);
- state regulations;
- voluntary consensus standards; and
- clinical practice guidelines.

Because devices vary in complexity and risk, an individual HCF PoC 3D printing facility may be capable of 3D printing some devices but not others. Other devices may not be appropriate to manufacture at the PoC based on available technology and expertise.

4. Approach for Discussion

FDA is considering the following concepts in developing a potential approach for 3D printing devices at the PoC:

- **Employ a risk-based approach** – The extent of FDA oversight should correspond with the risks associated with both the printed device itself and 3D printing the device at the PoC.
- **Device specification should not change based on location of manufacture** – The manufacturing location or site (i.e., traditional manufacturing facility vs. PoC) should not alter the manufacturer's ability and obligation to ensure that a device meets its predetermined specifications.

[26] See definition in "Terminology."

- **Capabilities available at a PoC HCF can help mitigate production risks** – The capabilities, oversight, training, and experience of the HCF in 3D printing all influence the ability to successfully make a device at the PoC.
- **Entities should understand their responsibilities** – 3D printing at the PoC can raise confusion or ambiguity about who is responsible for a device's total product life cycle. Entities should understand which requirements under the FD&C Act apply to them and their activities.
- **Leverage existing controls** – A least burdensome approach should be used to provide reasonable assurance that safe and effective devices are 3D printed at the PoC. This may include, for example, reliance on existing standards and processes.

In any 3D printing situation, risk is an important consideration, and includes both the risks involved in 3D printing the device (for example, the complexity of printing, the materials used, the post-processing needed), and the risks related to the use of the device (for example, intended use of the device, biocompatibility, including the nature and duration of body contact). The sources and types of risks should be carefully considered for all devices, whether the device is an anatomical model used for treatment planning purposes, or will be used by or implanted in a patient, though the types of risk mitigations may differ depending on the probability and severity of risks. HCFs may have differing abilities to manage these different risks, and the risk considerations may necessarily be different depending on the 3D printing scenario. As 3D printing becomes more available and accessible, HCFs are likely to engage with the technology in different ways, which may present unique regulatory questions.

With these considerations in mind, the next section discusses three potential 3D printing scenarios FDA believes may arise, describes potentially important considerations for each scenario, and poses questions about the scenarios on which FDA would like stakeholder feedback. FDA has also summarized these scenarios in **Figure 1**. This section also contains illustrative examples of each scenario. The scenarios and examples are not exhaustive, and we recognize that there may be other different situations or uses of 3D printing by HCFs at the PoC, where stakeholder feedback would be helpful. The questions are intended to help FDA better understand how HCFs might engage with 3D printing, and to help all relevant stakeholders, including FDA, think about the important regulatory considerations for 3D printing activities.

Briefly, the three scenarios are:

1. HCF using a 3D printing MDPS, where the MDPS manufacturer assumes responsibilities for FDA regulatory requirements and manufacturing of devices printed by the HCF using the MDPS.
    - In this situation, the PoC 3D printing facility within the HCF uses an MDPS to 3D print devices covered by the MDPS. Generally, in a situation like this, the responsibility for FDA compliance lies with the manufacturer of the MDPS, and the PoC 3D printing facility within the HCF is the user of the MDPS.
2. Traditional Manufacturer on or near the HCF site
    - In this situation, the HCF itself does not engage in any 3D printing activities. Rather, the HCF develops a business relationship with a Traditional Manufacturer whereby the Traditional Manufacturer is "co-located" on or near the HCF site (i.e., at the PoC), and as part of this relationship, the Traditional Manufacturer with the co-located 3D printing facility provides the HCF with 3D printed devices. As discussed in more detail below, in

this situation the Traditional Manufacturer is generally responsible for compliance with FDA's regulatory requirements.

3. HCF assuming all Traditional Manufacturer responsibilities
    - In this situation, the PoC 3D printing facility within the HCF would not use an MDPS, and would not work with a Traditional Manufacturer to 3D print devices. Rather, the HCF has chosen to engage in the activities of a Traditional Manufacturer in their PoC 3D printing facility. In this situation, the HCF would be responsible for complying with FDA regulatory requirements applicable to device manufacturers.

Potential 3D Printing Scenarios and Considerations

Scenario 1: HCF using a medical device production system (MDPS)

Traditional manufacturers, when required (typically based on device risk), must obtain premarket clearance or approval for a device that would be made using a 3D printing MDPS at the PoC by the HCF. If it is consistent with FDA's submission bundling policy,[27] one marketing submission could be used to demonstrate that multiple raw materials, scanners, and/or printers could be used as part of the MDPS to consistently produce safe, effective, and high quality devices. The manufacturer of the marketed MDPS would be responsible for complying with FDA regulatory requirements.

MDPS marketing authorization could facilitate the use of pre-configured settings for the HCF to 3D print devices at the PoC. Generally, a PoC 3D printing facility using an MDPS in accordance with its labeling would not be considered a manufacturer. The operator at the PoC 3D printing facility within the HCF would be considered a user of a legally marketed device when using the system consistent with the labeling, including the indications for use. There may be exceptions; for example, certain actions taken by the PoC 3D printing facility when using the MDPS may raise additional considerations regarding the responsibility for FDA compliance. It is important for HCFs to understand the risks related to 3D printing generally, as well as the risks related to the particular 3D printed device, when using an MDPS. In addition, it is important for HCFs to consider the potential risks if they use the MDPS inconsistent with the labeling and intended use, including the risks to patients.

Some 3D printed devices may need post-processing—such as machining, precision drilling, heat treatment, or sterilization—to be ready for use on a patient. In certain cases, these post-processing activities undertaken by the HCF could have regulatory implications. Post-processing information would be important to include in FDA marketing submissions for FDA review and in labeling to enable HCFs to use the MDPS to print safe, effective, and high-quality devices at the PoC.

Examples

a. A Traditional Manufacturer received 510(k) clearance for a 3D printing MDPS that makes patient-matched anatomic skeletal models used to assist in a physician's surgical planning procedures and during the surgery itself. The 510(k)-cleared MDPS includes or specifies in the

[27] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/bundling-multiple-devices-or-multiple-indications-single-submission.

labeling a compatible scanner, design and manufacturing software, design limitations coded into the software, raw materials, compatible printer(s), and associated tooling. A HCF uses the cleared 3D printing MDPS in accordance with its labeling.

b. A Traditional Manufacturer received 510(k) clearance for a 3D printing MDPS that can be used to make dental abutment collars and posts that are patient-specific. The 510(k)-cleared MDPS includes or specifies in the labeling a compatible scanner, design and manufacturing software, design limitations (e.g., size ranges, angulation) coded into the software, raw materials, compatible printer(s), and associated tooling. The remainder of the dental abutment is provided prefabricated by the Traditional Manufacturer to the HCF. A HCF uses the cleared 3D printing MDPS in accordance with its labeling.

c. An HCF's 3D printing facility already owns a 3D printer that is part of, and uses the same raw materials as specified by, a 510(k)-cleared MDPS manufactured by a Traditional Manufacturer for 3D printing of polymer-based cranioplasty plates made at the PoC. The 510(k)-cleared device includes or specifies in the labeling the validated software, materials, printer settings, and directions for additional processing to be compatible with special locking screws.

Discussion Questions

1. What challenges would a manufacturer of an MDPS face in being generally responsible for FDA regulatory requirements for devices 3D printed by the HCF at the PoC using the MDPS? Does the need for post-processing make a difference in these challenges; if so, how?
2. PoC 3D printing facilities in an HCF may need to conduct certain activities after using an MDPS (e.g., heat treatments, drilling). Because the QS Regulation would require the manufacturer's verification and validation of the MDPS, some aspects of the QS Regulation may be satisfied. Are there aspects of the QS Regulation that may not (or should not) be covered by the MDPS manufacturer's verification and validation such that more is needed to sufficiently address post-processing activities?
3. Are there any post-processing activities that should not be undertaken by an HCF? If so, why? Should 3D printed devices that require certain levels of post-processing only be printed by a "Traditional Manufacturer" and not by an HCF? Why or why not?
4. How could the use of MDPS to 3D print devices at the PoC fit into FDA's existing adverse event reporting system under 21 CFR part 803 for user facilities and manufacturers, considering that user facilities may be conducting activities that could be considered manufacturing?

Scenario 2: Traditional Manufacturer co-located at or near the HCF site

HCFs may engage Traditional Manufacturers to 3D print devices at the PoC, including by co-locating the manufacturer on or near the HCF's site. A Traditional Manufacturer, including a contract manufacturer, may be located on the HCF's site, such as in the HCF's building, or office suite or on its campus. The Traditional Manufacturer may also be located near the HCF, such as in the same office building, or in

another building close to the HCF. The Traditional Manufacturer could use the co-located manufacturing site to 3D print certain devices the HCF requests. The Traditional Manufacturer with the co-located manufacturing site would be responsible for compliance with FDA regulatory requirements.

There may still be questions about the co-located Traditional Manufacturer's regulatory responsibilities. For example, the 3D printing that occurs at these co-located manufacturing sites may be specific to patient need. Such patient-specific changes to an already authorized device could require a new submission to FDA. In such cases, the Traditional Manufacturer could use the guidance documents "Deciding When to Submit a 510(k) for a Change to an Existing Device"[28] and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device"[29] or "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process"[30] to determine if a new marketing submission is required pursuant to 21 CFR 807.81(a)(3) or 21 CFR 814.39.

Examples

a. A Traditional Manufacturer has 510(k) clearance for a spinal fusion cage. The Traditional Manufacturer works with an HCF to bring 3D printing to the PoC. The Traditional Manufacturer leases a physical space within an HCF to 3D print their 510(k)-cleared spinal fusion cages at the PoC. The Traditional Manufacturer uses their own equipment and implements their existing quality system at this device establishment.

b. A Traditional Manufacturer has 510(k) clearance for an intervertebral body fusion device. The Traditional Manufacturer works with an HCF to use a third party based at the HCF in a PoC 3D printing facility to make the 510(k) cleared intervertebral body fusion device.

Discussion Questions

5. Design changes may happen frequently (e.g., different sizes or geometries) when devices are 3D printed at co-located PoC manufacturing sites in response to clinical feedback. Beyond FDA's existing modifications policies referenced in the above section, are there other considerations for co-located manufacturers that FDA should take into account so that manufacturers in this situation understand their obligations?
6. Are there specific considerations for HCFs and/or manufacturers when a Traditional Manufacturer co-locates at or near the PoC that are different from traditional non-3D printed manufacturing processes for devices? For example, are there particular risks that manufacturers and/or HCFs should consider when manufacturing or using such devices?

Scenario 3: HCF assuming all Traditional Manufacturer responsibilities

[28] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device.
[29] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-software-change-existing-device.
[30] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process.

a. General considerations

HCFs may choose to assume all the responsibilities of a Traditional Manufacturer in engaging in 3D printing at the PoC. In this scenario, the HCF would not use an MDPS, and would not rely on a co-located Traditional Manufacturer to 3D print devices at the PoC. Instead, the HCF would assume all the responsibilities of a Traditional Manufacturer, including complying with FDA regulatory requirements.

HCFs may have existing policies, procedures, and expertise that would help them engage in manufacturing. For example, the HCF may have internal quality management systems or be in conformance with existing, defined quality standards or recognized third-party accreditation, as well as existing complaint handling and adverse event reporting processes and procedures. The HCF may also have staff that are already trained or certified to operate and maintain appropriate equipment necessary to 3D print different types of devices at the PoC, including any needed post-processing. These existing capabilities and expertise at the HCF may better enable the HCF to transition to a system where they would assume all the responsibilities of a Traditional Manufacturer and comply with FDA regulatory requirements.

Examples

a. An HCF decides to 3D print patient matched titanium cranioplasty plates within their PoC 3D printing facility.
b. An HCF decides to use their PoC 3D printing facility to 3D print a daily activity assist device (e.g., a prosthetic adaptor for grooming). The PoC 3D printing facility has an appropriate 3D printer and post-processing equipment for this application, as well as trained personnel with the background and training to operate and maintain the 3D printing system.
c. A HCF decides to use 3D printed patient-specific anatomic models to assist physicians' visualization during treatment planning. In the past, the PoC 3D printing facility within the HCF has used image analysis, segmentation software, and a 3D printer to retrospectively make physical anatomic models of old surgical cases. From this experience, the PoC 3D printing facility knows the accuracy and limits of their imaging, printing, and post-processing workflow. The HCF would now like to use these patient-specific anatomic models prospectively to plan the treatment of current patients.

Discussion Questions

7. What parts of FDA's regulatory framework as applied to 3D printing would be the easiest to implement for HCFs engaging in the activities of a Traditional Manufacturer?
8. What parts of FDA's regulatory framework as applied to 3D printing would present the greatest challenge to implement for HCFs that choose to engage in the activities of a Traditional Manufacturer? Do you have recommendations for ways in which FDA may exercise oversight or

regulate in a least burdensome manner that still provides reasonable assurance of safety and effectiveness and protects and promotes the public health?

b. Considerations for very low risk devices

Certain devices generally pose very low risk to patients, and the Agency is considering whether and how it might be appropriate to provide a level of regulatory flexibility when these very low risk devices are 3D printed at an HCF.

What constitutes a very low risk device could be informed by the device's inherent risks and benefits, intended use, and the risks introduced by 3D printing generally and at the PoC. If devices are determined to be very low risk, this may also help determine whether certain devices can be appropriately 3D printed at the PoC. FDA is considering developing a list of important characteristics that would help identify very low risk devices.

FDA is seeking stakeholder feedback on the types of considerations, device features, and intended uses that may be important to define the extent of any regulatory flexibility the Agency may choose to exercise over such devices.

Discussion Questions

Note: To help identify considerations for "very low risk" devices, stakeholders are encouraged to review a variety of sources, including publicly available information in discussion papers from professional societies[31] or FDA's product code database,[32] as well as considering the devices an HCF wishes to 3D print at the PoC. Evaluation of products that may be considered to merit inclusion in this potential approach could be used to help refine the considerations for what could be considered a "very low risk" device. Stakeholders are also encouraged to provide comments and feedback on the three examples above.

9. How should each of the following be weighed or considered to assess whether the device being 3D printed is very low risk? Are there other considerations that should also be included?

    a. Intended use, such as for personal assistive, quality of life devices, or life supporting/sustaining, whether the product would be adjunct to standard clinical methods or procedures, or redundancies will be available (such as an ergonomic scalpel handle when other handles are available);
    b. Device class;
    c. Nature and duration of body contact (e.g., intact skin for < 24 hours, mucosal membrane, permanent implant);

[31] See e.g., "Physicians as Manufacturers: The Rise of Point-of-care Manufacturing," available at https://www.sme.org/smemedia/white-papers-and-reports/3d-printing-fuels-the-rise-of-point-of-care-manufacturing/.
[32] Available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm.

d. Available information about safe use, including history of material used and other available information;
e. Whether the device is intended to be sterilized;
f. Whether the product is patient-matched or a discrete stock size (e.g., 14 French); and
g. Nature of reasonably foreseeable adverse events.

10. Understanding that different HCFs may have different 3D printing capabilities and expertise, how do a facility's capabilities and expertise factor into its ability to print a "very low risk device"?
11. What best practices or oversight programs (e.g., accreditation, certifications, clinical guidelines) or internal PoC procedures that exist currently (or may in the future) could positively contribute to device safety, effectiveness, and quality when 3D printing "very low risk" devices at the PoC?
12. If FDA determines it is appropriate to provide a degree of regulatory flexibility regarding certain requirements for devices determined to be very low risk, should this approach apply to very low risk devices 3D printed at the PoC by a co-located Traditional Manufacturer, or only to those devices printed by the HCF?

Figure 1: Potential scenarios for 3D printing devices at the PoC.

	Scenario 1 (HCF using MDPS)	**Scenario 2 (Traditional Manufacturer Co-location)**	**Scenario 3 (HCF assumes all manufacturer responsibilities)**
Entity designing/developing the device	Traditional Manufacturer	Traditional Manufacturer	HCF
Entity using the 3D printing system to produce devices	HCF	Traditional Manufacturer, including any potential Contract Manufacturer	HCF

Entity responsible for complying with applicable regulatory requirements[33]	Traditional Manufacturer	Traditional Manufacturer, including any potential Contract Manufacturer	HCF[34]

5. Additional Discussion Questions

13. How can the terminology and the parties involved in 3D printing at the PoC be improved or clarified? *See Section 3. Background* in this discussion paper for more information.
14. FDA believes we should have visibility to the entities involved in 3D printing at the PoC. Do you have recommendations for how the Agency can achieve this in a least burdensome way, for example, through existing mechanisms, such as registration and listing? Are these recommendations different if it is a Traditional Manufacturer that is printing at the PoC, or if it is an HCF using an MDPS, or an HCF assuming the responsibilities of a Traditional Manufacturer?
15. FDA is open to suggestions for other approaches/models for PoC manufacturing of medical devices that would facilitate future innovation while still providing reasonable assurance of device safety and effectiveness. Please provide other options you believe FDA should consider.
16. **COVID-19 PHE-specific questions**
    a. During the response to the COVID-19 pandemic, what information did you need to 3D print a product that you had not printed before?
    b. Are there situations where 3D printing was used during the COVID-19 pandemic that are not discussed here? If so, what are those situations, and how did you address them?
    c. Do you have suggestions for FDA based on what you learned from your experience during the COVID-19 pandemic?

6. Anticipated Outcomes of Discussion Paper

Collaboration and communication among all stakeholders and research can facilitate creating an environment for technological growth and development. Several Traditional Manufacturers have already started working with HCFs to discuss new models that use 3D printing capabilities at the PoC. Standards development organizations are also working on test methods, best practices, and guides.

Medical societies can also develop clinical guidelines and criteria to help clinicians decide when and how to make or use 3D printed devices. For example, the Radiological Society of North America (RSNA) is

[33] There are additional regulatory requirements that apply to parties referenced in this discussion paper but who are not engaged in manufacturing activities, and these requirements are not discussed in detail. For example, device user facilities as defined in 21 CFR 803.3(d) are required to report certain events to FDA and/or the manufacturer. We note that this discussion paper is not intended to comprehensively describe all regulatory requirements. Rather, as stated above, this discussion paper is intended to stimulate discussion to inform further policy development for the appropriate regulatory approach for 3D printing medical devices at the PoC.

[34] As described in Section 4, for devices that pose very low risk to patients, the Agency is considering whether it should provide a degree of regulatory flexibility with respect to the applicable requirements under the FD&C Act when these very low risk devices are 3D printed at an HCF.

developing clinical appropriateness criteria around the use of 3D printed anatomic models. Clinical and engineering training programs will also be important to adoption of 3D printing of medical devices at the PoC. These programs could help bring the same confidence to 3D printing of devices at the PoC that exists with devices currently marketed by Traditional Manufacturers. Training programs, including certification and licensing programs, could eventually become recognized professional certifications with a scope of practice that could be useful when it comes to 3D printing medical devices. In addition, there may be a certification that the PoC could obtain to assess the capabilities of a facility with respect to 3D printing design, manufacturing, post-processing, and quality control. HCFs with a specific certification level may be better suited to 3D printing at the PoC. Many manufacturing facilities can be certified to conform to quality standards, such as ISO 13485: 2016 *Medical devices — Quality management systems — Requirements for regulatory purposes* and FDA could consider an approach to quality system regulation that takes conformity to this ISO standard into account. Similarly, many HCFs already obtain accreditation from hospital certifying bodies, clinical practice standards groups, and state regulators.

FDA recognizes that 3D printing technology is developing rapidly and a solution designed for today's technology may not be applicable in future years. A durable solution will be built on a foundation of strong science, sensible clinical guidelines, and an appropriate regulatory approach that balances innovation with regulatory oversight. Such a solution can be created through stakeholder engagement, discussion, and consensus-building.

7. Conclusion

FDA recognizes that 3D printing at the PoC contributes to the development of new device designs, clinical solutions, and enhanced approaches to rare and complex cases (e.g., invasive tumor resection, congenital heart defects). As 3D printing brings more product development opportunities to the PoC, FDA intends to continue facilitating innovation in a manner that still provides a reasonable assurance of device safety and effectiveness. Industry, professional organizations, and clinical societies have already started to develop new guidelines for 3D printing at the PoC.

The response to product shortages during the COVID-19 pandemic demonstrates that HCFs are willing and able to adopt 3D printing at the PoC when the need for certain medical devices, including certain types of personal protective equipment (PPE), outpaces the supply available to healthcare organizations because of the high demand and overall interruptions to the global supply chain. A rational and understandable approach for 3D printing at the PoC can facilitate HCFs' rapid response to future supply chain disruptions in a safe and effective manner. Expansion of 3D printing capabilities at HCFs could lead to an increased use of 3D printing technology during non-emergency situations.

This discussion paper describes factors and scenarios that FDA is considering as the Agency further explores appropriate regulatory approaches for PoC 3D printing of devices, including considerations of timely patient access to 3D printed devices that have a reasonable assurance of safety and effectiveness.

FDA will use feedback submitted to the docket to inform future policy development. We expect to publish draft and final guidance on this topic in the future. Please submit your comments regarding this discussion paper to https://www.regulations.gov, Docket No. FDA-2021-N-1272 by February 7, 2022.

Appendix – Additional 3D Printing Background

3D printing is a versatile technology for advancing state of the art devices and treatments, such as porous bone wedges, patient-specific implants, and surgical templates. One famous example included using 3D printed models for surgical planning to help surgeons separate conjoined twins.[35, 36] The technology has typically been used by Traditional Manufacturers who must comply with the FD&C Act and its implementing regulations.[37]

FDA issued guidance entitled "Technical Considerations for Additive Manufactured Medical Devices."[38] This guidance outlines technical considerations associated with additive manufacturing (AM)/3D printing processes and includes recommendations for testing and characterizing devices that include at least one AM component or additively fabricated step. Like most industrial processes, 3D printing is not usually done in a single manufacturing step. 3D printing can generally be divided into five stages:

1. The **device design stage** may include a standard design with discrete pre-specified sizes and models or a patient-matched device designed from a patient's own medical images. A PoC may require specialty sizes of a device for a sub-population or a patient may have a congenital abnormality, which the clinician believes they can better visualize with a 3D printed model. In this stage, clinical decisions are key to obtaining the right size, shape, and function of the device. For example:
    a. There are important factors that influence the safety and effectiveness of a device at this stage that both the clinician and engineer should understand. These factors include the limits of the clinical imaging, design process, material, and printer.
    b. Patient-matched devices are designed separately for each patient. Typical patient-matched devices cleared by FDA include data to show that the devices will perform as intended within a specific range of patient-matched cases. The design and software workflows, as described here, often overlap.

2. Next, the **software workflow stage** turns the design into a printable file. The completed device design is further processed to prepare it for manufacturing. This may include:
    a. Smoothing or cleaning a clinical image;
    b. Optimizing the digital representation of the file to make sure there are no holes or imperfections that will cause errors in manufacturing;
    c. Adding support or connecting structures that will enable 3D printing manufacturing;
    d. Placing parts in the build volume;

[35] https://www.newswise.com/articles/thriving-at-home-one-year-after-a-marathon-surgery-to-separate-them-formerly-conjoined-twins-jadon-and-anias-mcdonald-achieve-new-milestones-every-day.

[36] Pratt, Rosalind, et al. "Computer-assisted surgical planning and intraoperative guidance in fetal surgery: a systematic review." Prenatal diagnosis 35.12 (2015): 1159-1166.

[37] Ricles, Laura M., et al. "Regulating 3D-printed medical products." Science translational medicine 10.461 (2018): eaan6521.

[38] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/technical-considerations-additive-manufactured-medical-devices-guidance-industry-and-food-and-drug.

e. Setting build parameters; and
f. Converting the build file into a machine-ready format.

3. **Material controls** occur before manufacturing. Each machine or build should have a raw material specification that each batch should meet before use. This typically includes passing prescribed size distribution or physical property tests and a biocompatibility evaluation, if the device contacts body tissue.

4. Most devices undergo **post-processing** after 3D printing is completed. This frequently includes steps to remove the device from the build platform. This may also include processes for:
    a. Cleaning of 3D printing residues (e.g., uncured or unsintered raw material);
    b. Annealing or heat treating;
    c. Post-printing machining to obtain final dimensions or features;
    d. Biocompatibility assessment; and
    e. Terminal sterilization and cleaning.

5. After post-processing, the final finished device is ready for testing during the **process validation and acceptance activities stage**. For many cleared devices, most characterization is done before production begins. Production processes are then established, maintained, and monitored so that the manufacturer verifies the design output meets their specifications. This is called a validated process. Design parameters are often checked after each build by inspection and/or testing. These tests are important to ensure that the device continues to meet its specifications.