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Lawyer Insights

May 17, 2016

The FDA seeks to regulate 3D-printed medical devices

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Published in InsideCounsel

As we previously reported, the use of 3D printing for the production of medical devices has become almost commonplace. Indeed, the FDA has approved at least 85 3D-printed medical devices via its 501(k) approval pathway.

The FDA, though, has long considered further regulating the use of 3D printing for medical devices, even holding a public workshop on the topic in October 2014. Its failure to issue any guidance since then left many believing that it had opted not to impose additional regulations.

The FDA recently proved that belief wrong, releasing for public comment a draft Guidance for medical device manufacturers using additive manufacturing ("AM"), also known as 3D printing. The draft Guidance acknowledges that AM offers unique advantages over traditional manufacturing because (among other things) 3D-printed devices may "include features that are too complex to be made using other techniques" and 3D printing can create "anatomically-matched devices and surgical instrumentation by using a patient's own medical imaging."

With the comment period open until August 8, 2016, the draft Guidance seeks to regulate virtually every step of the AM process: the device design process, the printing process and the post-production process. The proposed regulations would sit on top of the agency's existing regulations for device review and approval, and will require a significant amount of information for approval. The type and amount of data required "will vary depending on the intended use, risk profile, and classification and/or regulation for the device type." Devices that are implanted, load bearing or available in standard sizes or patient matched are likely to require additional quality data.

Device design process

The first step in the development of a 3D-printed medical device is designing the device itself. For devices designed to come in pre-established discrete sizes (e.g., S, M or L), the draft Guidance requires applicants to document various specifications, including "[d]imensional specifications for the final device or component, as well as manufacturing tolerances of the machine," to ensure reliable manufacturing. For patient-matched devices, additional specifications are required, including the acceptable range of modifications to clinically relevant design parameters, the minimum diagnostic image quality acceptable for matching/measuring features, and physical information about the tissues interfacing with the device.

For certain patient-matched devices, the draft Guidance requires applicants to identify the "expiration date." Specifically, parts of a patient's anatomy can change (e.g., with disease progression), and a device printed to match a patient's anatomy may expire because the anatomy will change before the device is

used. Thus, device manufacturers will need to understand and document how patients' measurements may change over time.

The Guidance further requires that manufacturers document best practices for working with designs in applicable software. Although devices with pre-established discrete sizes require processing only once, patient-matched devices will need documented software steps to convert into machine-readable files patient data (e.g., computed tomography (CT) or magnetic resonance (MR) imaging) and device design structural information. This conversion process is particularly error-prone, given that complex patient anatomy can be difficult to map to device specifications. Thus, the Guidance requires that simulated worst-case scenarios be performed to anticipate unexpected conversion failures. The Guidance also recommends eschewing proprietary file formats in favor of "robust, standardized formats…, such as the Additive Manufacturing File format (AMF)…."

Moreover, the regulations extend to the 3D printing machine itself. "Quantitative knowledge of the machine's capabilities and limitations can be gained through test builds, worst-case builds, or process validation." Among other things, manufacturers must find a machine's "sweet spot," since "printing may be sub-optimal in the regions near the outer edge of the build volume and optimal at the center." The orientation of a device in a machine during the printing process also may affect production quality. The placement and orientation of devices becomes even more important if multiple devices are created simultaneously in the same machine.

The draft Guidance also requires that records for starting materials used in AM processes include chemical names/structures, suppliers, physical properties and certificates of analysis. Although some AM methods minimize raw material usage by recycling materials not incorporated into the final device, the applicant must document the precise processes used for recycling and take steps to measure how exposure to light, oxygen and moisture, among other things, during recycling affects the properties of final finished devices.

Process Validation

The FDA Guidance includes requirements for documenting validation steps and acceptance activities. The Guidance advises that knowledge of quality variances across different machines or "how the variability of each input parameter and processing step affects the final device or component is critical to ensuring part quality." Quality consistency must be measured using in-process monitoring of manufacturing parameters (e.g., temperature at the beam focus, build-space environmental conditions, etc.) or non-destructive evaluations (ultrasound, CT, microscopy, etc.), or by subjecting test coupons mimicking specific features of the device to destructive testing. Criteria should be established for determining whether detected abnormalities require rejection of entire lots or batches of devices.

Device testing

The FDA described specific data it expects to see in submissions, starting with a flow chart for the AM process used to manufacture each particular device. Moreover, "risks identified for each step of the manufacturing process, as well as mitigations of these risks, should be documented." For example:

- Mechanical testing should measure properties including strength, fatigue and abrasion wear.
- Testing of "worst-case combinations of dimensions and features" should identify the safe limits of device manufacturing.
- Factors that can affect interlayer bonding should be identified and characterized.

- If the AM process results in voids, incomplete bonding or other microstructural issues, testing may be required to establish no ill effects on the final device.

Essentially, the applicant must "use all reasonably obtainable knowledge about [their] specific machine's capabilities to ensure the manufacturing process outputs meet defined requirements."

Post-processing steps of 3D printing, such as cleaning excess starting material or sterilization, could present special challenges for manufacturers. Complex shapes and tortuous pathways, which 3D printing excels at creating, will pose significant issues. The Guidance recommends that applicants "identify any potentially detrimental effects of post-processing and describe mitigations implemented." This means that rigorous testing will be required to ensure that devices are free from residual manufacturing materials and properly sterilized. Although end users may not need particular skill to print devices on 3D printers, specialized training may be needed for the proper cleaning and sterilization of printed devices. The Guidance implies that manufacturers who cannot establish that end users will be able to carry out the post-processing steps adequately will not receive approval unless the manufacturers undertake post-processing themselves.

Conclusion

The draft Guidance represents the FDA's first step toward integrating 3D-printed medical devices into its regulatory approval processes. Although the FDA's thoughts may change during the comment process, applicants hoping to use AM methods now have greater insight into the FDA's expectations for future device applications.

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