

3D Printed Pharmaceuticals and Devices Article Series: Assessing, Managing, and Insuring Against Risk in the Next Era of Drugs and Medical Devices – Part 1

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3D printing, by even cautious projections, has sweeping implications for the future of drugs and medical devices. Pharmaceuticals can now be printed into custom layers and shapes to speed up or control absorption rates, and highly customized surgical implants promise shortened surgery times, reduced invasiveness, and speedier recoveries. Doctors at the University of Michigan have already made, using 3D printers, tracheal splints that replicate the tracheas of young children, enabling life-saving surgeries on those with collapsed windpipes.¹ The implanted devices can be used until outgrown and then absorbed by the patients' bodies.²

The 3D printing and product market is growing rapidly. In 2013 the global market for 3D printing hit \$2.5 billion, and is projected to grow to \$16.2 billion by 2018.³ But with the immense promise for innovation comes an uncertain landscape for risk and liability. The U.S. Food and Drug Administration's treatment of these products is in its incipient stages. UL and the International Organization for Standardization (ISO) are beginning their processes for developing standards.⁴ And courts are only beginning to attempt to apply existing product liability law to this new form of manufacturing and distribution. Protecting against liability under such conditions, through a combination of risk mitigation and insurance coverage, requires a hybrid approach that considers the potential for new types of liability and anticipates problems that 3D printing may pose for existing insurance coverage.

Though the potential risks posed by 3D printing span many areas, from intellectual property, to environmental regulation, to workplace hazards, this series of articles focuses on product liability law and related regulatory issues. How the standards that courts and regulatory agencies apply to traditional drugs and devices might evolve with respect to 3D printed drugs and devices as the technology moves forward are still largely unknown. But those who are moving into this rapidly expanding industry or using this technology should consider those risks that have been identified, and work with insurers and risk managers to limit their exposure through a combination of insurance and best practices. The following is a three-part overview of how the U.S. Food and Drug Administration (FDA) is beginning to address this new technology, how courts and claimants may address several aspects of the emerging technology, and some attendant considerations regarding risk mitigation and insurance.

The 3D Printing Process

3D printing, or additive manufacturing, is not entirely new. The beginnings of the technology—termed stereolithography by its inventor—were patented over 30 years ago. But recent decreases in the cost to manufacture 3D printers and the promise of high efficiency and high customization

¹ MARY F. MASON, *3D printed splint saves the life of a baby*, BIOMEDICAL ENGINEERING, <http://bme.umich.edu/3d-printed-splint-saves-the-life-of-a-baby/> (last visited June 24, 2016).

² *Id.*

³ Andrea Chang, *3-D printing market projected to grow to \$16.2 billion in 2018*, (Mar. 31, 2014), available at <http://articles.latimes.com/2014/mar/31/business/la-fi-tn-3d-printing-20140331>.

⁴ See, e.g., *Testing and Certification*, UL, <http://industries.ul.com/additive-manufacturing/3d-printing-testing-certification> (last visited June 24, 2016).

have driven the boom seen today. The process of 3D printing is conceptually straightforward. 3D printing builds an object from an electronic data file, such as a 3D scan or CAD file. The digital image is sliced into thin layers and some form of additive manufacturing is used to build the object, layer-by-layer.

In addition to stereolithography, which builds a product by adding droplets of material, objects can be created in other ways. They can be “printed” out of blown powder that is melted with a laser beam until it forms a bond. They can also be created with thermal extrusion where thermoplastic filaments are heated through a nozzle. Or they can be made using technologies such as Selective Laser Melting, Selective Laser Sintering, Electron Beam Melting, an Ink-Jetting Photopolymer process, and even bioprinting—where a 3D printer and imaging technologies combine to print biological human tissue such as human organs or human tissue in three dimensions.⁵ Each of these processes poses distinct advantages for certain product types, as well as unique risks for failures of the processes, for substandard or contaminated raw materials, or even for occupational or environmental hazards stemming from the production process.

3D Printed Drugs and Medical Devices – Current Products and Future Trends

The FDA ventured into a new era in pharmaceuticals in August 2015 when it approved Spritam, Apria Pharmaceuticals Co.’s 3D printed seizure drug.⁶ Spritam is made through a proprietary technology that uses 3D printing to produce a porous formulation of a pill that rapidly disintegrates with a sip of liquid. Via the 510(k) process, the FDA has already cleared more than 85 3D printed devices, including hearing aids, dental crowns, bone tether plates, skull plates, hip cups, spinal cages, knee trays, facial implants, screws, surgical instruments, and Invisalign® braces.

More and increasingly sophisticated devices are projected. Companies are already endeavoring to build living human tissue that will function like native tissue and be capable of being grafted directly onto burned or wounded skin.⁷ And they hope to create more sophisticated organs, such as livers and kidneys.

An Uncertain Landscape for Risk

It starts with regulation – how the FDA treats 3D printed drugs and devices

The FDA currently divides medical devices into three classes. Class I devices are subject to “general controls,” or, the least stringent regulatory control. Class II devices are subject to a higher level of control, referred to as “special controls.” Class III devices are considered devices for which there is insufficient information to assure safety and effectiveness solely through general or special controls. For these devices, the FDA requires special control and premarket approval.⁸ Many 3D

⁵ See *Types of 3D printers or 3D printing technologies overview*, 3D PRINTING FROM SCRATCH, <http://3dprintingfromscratch.com/common/types-of-3d-printers-or-3d-printing-technologies-overview/> (last visited June 24, 2016) and *Bioprinting process*, ORGANOVO, <http://organovo.com/science-technology/bioprinting-process/> (last visited June 24, 2016).

⁶ *First FDA-Approved Medicine Manufactured Using 3D Printing Technology Now Available*, APRECIA PHARMACEUTICALS (Mar. 22, 2016), https://www.aprecia.com/pdf/ApreciaSPRITAMLaunchPressRelease_FINAL.PDF.

⁷ NICHOLAS DONATO, *Organovo is a Company 3D Printing Human Tissue and its CEO is Excited About Creating Livers*, BENZIGA (Mar. 17, 2016), <http://www.benziga.com/general/biotech/16/03/7729069/organovo-is-a-company-3d-printing-human-tissue-and-its-ceo-is-excited->.

⁸ See *generally Classify Your Medical Device*, U. S. FOOD AND DRUG ADMIN., <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/> (last visited June 24, 2016) and *Premarket Approval (PMA)*, U. S. FOOD AND DRUG ADMIN., <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/ucm2007514.htm> (last visited June 24, 2016).

printed products, such as simple component parts, may not fall into the classification of a medical device. Still more may be considered Class I devices, which may not need to undergo FDA approval, clearance, or exemption. But for more complex devices, companies will need to seek premarket approval, 510(k) clearance, or exemption under either the humanitarian device exemption (HDE) or a custom device exemption (CDE).

Moreover, additional entities that play a role within the overall manufacturing process may be subject to FDA regulation and oversight. In February 2015, for example, the FDA began considering regulating smartphone medical device applications.⁹ In doing so, the FDA included entities in the chain of distribution that create and control the smartphone software as “manufacturers.” Beyond software designers and programmers, manufacturers would now include companies that develop the specifications for the applications and contract with others to perform the programming. Some commentators have suggested that even the providers who link to a website may now fall under the broadening FDA definition of manufacturer.¹⁰ Extending this analysis to 3D printing would mean an entity such as the scanning provider, the entity that does the initial scan, might be liable for defects or errors in the scanning process—or even liable as part of the distribution chain.¹¹

Early guidance

In October 2014 the FDA held a public workshop regarding 3D printing. On May 10, 2016, it issued its Draft Guidance for Industry and Food and Drug Administration Staff.¹² Rather than serving as a comprehensive summary of all regulatory requirements, the guidelines highlight some technical considerations and provide recommendations regarding the design, manufacture, and testing of 3D printed medical devices (with the exception of bioprinted devices, which are expressly exempted from the Draft Guidance).

The FDA’s Draft Guidance consists of two sections: (1) design and manufacturing, and (2) device testing. Notably, the discussion of testing contains detailed recommendations about what a manufacturer should include in a premarket submission of a 3D printed device. For design and manufacturing, the FDA suggests:

- Comparing of the minimum possible feature size of the specific 3D printing technique to be used, in addition to the manufacturing tolerances of the machine, to the desired feature sizes of the final finished device.
- Addressing image quality and the role that deformation may play in patient-matched devices, as well as identifying the predicted end of the useful life of a patient-matched device by the use of an expiration date.
- Implementing internal checks in any software used for patient-matched devices to prevent the user from exceeding pre-established specifications documented in a device master record and a system for identifying any changes made by the user.
- Testing software file conversion steps for “worst case scenarios.”
- Assessing build volume placements, use of support material, layer thickness, build paths, machine parameters, and environmental considerations before a device is 3D printed.
- Addressing the chemical properties of the material being used and how the 3D printing process may affect those properties.

⁹ See *Mobile Medical Applications: Guidance for Industry and Food and Drug Administrative Staff*, (Feb. 9, 2015) available at <http://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf>.

¹⁰ Patrick J. Comerford and Erik P. Belt, *3DP, AM, 3DS & Product Liability*, 55 SANTA CLARA L. REV. 821 (2015), p. 828., available at <http://digitalcommons.law.scu.edu/lawreview/vol55/iss4/2>.

¹¹ *Id.*

¹² *Technical Considerations for Additive Manufactured Devices Draft Guidance for Industry and Food and Drug Administration Staff* (May 10, 2016) available at <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm499809.pdf>.

- Prioritizing quality consistency and process validation, including an understanding of how the variability of each input parameter and processing step affects the final finished device or component.

For testing, the FDA recommends the following be included in the premarket submission for a 3D printed device:

- The device's range of dimensions and any dimensions that may be dependent on a patient's anatomy.
- Performance testing results that include consideration of the device's build direction, the direction in which the model is built (i.e. from top to bottom or bottom to top)
- Specification of dimensional tolerances and measurements
- Identification of all materials involved in the manufacture of the device
- Testing of material polymers to ensure they will not form chemical properties through the 3D printing process that pose a health risk for patients
- Characterization of interlayer bonding materials
- A validated cleaning and sterilization process that takes into account the complex geometry of the final device
- An evaluation of the biocompatibility of the device
- Labeling considerations for patient-matched devices that include a patient identifier, identifying use, file design iteration, as well as standards to ensure that the patient is monitored for anatomical changes between the time of imaging and device implant

The FDA is accepting comments for 90 days following the issuance of the Draft Guidance, or, through August 8, 2016. Though the guidance is currently in draft form, the dearth of other regulatory guidance will likely cause it to be highly influential pending the issuance of final guidance.

The next installment in this three-part series will discuss potential product liability risks and exposures in light of early regulatory treatment of 3D printed drugs and medical devices, challenges for products made using 3D printing under existing product liability law, and how courts have treated 3D printed devices and comparable products thus far.