KINKOS FOR YOUR KIDNEYS: A LEGAL BLUEPRINT FOR THE REGULATION OF BIOPRINTED ORGANS

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Abstract: Three-dimensional ("3D") printing has revolutionized the manufacturing process. With the press of a button, a blueprint of a product generated from custom measurements on a computer becomes a reality. Biomedical engineers have taken this method a step further to innovate modern medical practice by using biological materials as the substrates for 3D printing.[1] In only a few years, 3D printers are expected to have the capability to produce human organs including kidneys, hearts, and livers using a patient's own cells.[2] This seemingly futuristic ability to produce functional organs on demand could save the lives of the hundreds of thousands of people on the organ donor waiting lists. However, given the unprecedented nature of a manufactured organ and its promise to medicine, a major disruption in the law may be on the horizon.

There is much scholarly debate as to the future of manufactured organs under the current law. The primary question at the center of the issue is whether the National Organ Transplant Act ("NOTA"), which regulates the use of donated organs for transplantation, will prohibit the procurement or use of these organs.[3] Additionally, the significance of a functioning human organ used for transplant lends itself to federal regulation in order to ensure the safety of its usage. Currently, the Food and Drug Administration ("FDA") regulates a handful 3D printed medical devices, including some biological products.[4] Medical devices are regulated under the Medical Device Amendments of 1976 ("MDA") which places the devices into one of three classes based primarily upon the risk of injury or illness from its use and dictates the requirements of the approval process.[5] The MDA also contains an express preemption provision prohibiting a state from establishing any requirement different from or in addition to those required by the act itself.[6] Specifically, this poses an issue for persons who wish to bring state law products liability actions. The Supreme Court of the United States has considered the scope of this preemption provision in two cases, *Medtronic, Inc.*

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1. Sean V. Murphy & Anthony Atala, *3D Bioprinting of Tissues and Organs*, NATURE BIOTECHNOLOGY, 773, 774 (2014).

2. *Id.* at 776.

3. National Organ Transplant Act, 42 U.S.C. § 273-274 (1984).

4. Richard E. Kaye, Annotation, *Federal Preemption of State Common-Law Products Liability Claims Pertaining to Medical Devices, Implants, and Other Health-Related Items*, 74 A.L.R. Fed. 2d 1 (2018)

5. Medical Device Amendments of 1976, 21 U.S.C. § 301 (1976).

6. *Id.*

v. Lohr and *Riegel v. Medtronic*.[7] These cases provide that preemption hinges on whether the state law action is based on different or additional safety requirements enacted by the state.[8]

This note will argue that the procurement of a bioprinted organ for transplant use is not barred by Title III of NOTA. Second, it will argue that under present law, manufactured organs should be classified as Class III devices, and are therefore subject to the premarket approval process. Last, this note will propose modifications to the existing law tailored specifically for the manufacture of organs to ensure they are afforded the same protections as other biological products and devices.

I. INTRODUCTION

In an era of unprecedented technological growth and advanced medical practice, novel therapeutics are eradicating life-threatening diseases, curing certain forms of cancer, and greatly improving the lives of millions of people. Today's capabilities are historically unmatched. However, despite these advances, we remain helpless when it comes to organ failure. As of 2017, there are 115,000 men, women, and children awaiting lifesaving organ transplants and every ten minutes, another person is added to the list.[9] Eight-thousand people die each year in the United States because the organs they require are not donated in time.[10]

3D printing is expected to make significant inroads in reducing the number of people who die waiting for organ transplants. Researchers have estimated that organs manufactured by 3D printers will be capable of transplantation within the next ten years. Patients will be able to give a cell sample, which will then be expanded and used as the substrate, similar to ink used by a traditional printer. The outcome will be functioning human organs composed of living cells which are specific to each patient. These will be the first synthesized organs that are actually composed of the patient's own cells, eliminating the risk of organ rejection following the transplant, which not only can be fatal, but often requires complex regimens of immunosuppressive drug therapy.

These bioprinted organs may revolutionize transplantation; however, given the unique quality of bioprinted organs, they have been subject to newly sparked legal debate. Some wonder if manufacturers will be able to obtain patent protection for blueprints used in printing even though the organ's design is a "product of nature." Others have debated the property rights in one's cells and the organs created with them. Another source of debate has been how regulations may ensure safety given the dependency humans have on functional organs.

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7. Medronic Inc. v. Lohr, 518 U.S. 470 (1996); Riegel v. Medtronic, Inc., 552 U.S. 312 (2008).
8. Riegel v. Medtronic, Inc., 552 U.S. 312 (2008).
9. Donate Life America, http://www.donatelife.net (last visited August 30, 2018)
10. *Id.*

This note will discuss the federal regulation of bioprinted organs under the existing regulatory framework, the impact of these regulations, and will make suggestions for a more tailored approach for regulation. The note will first explain the mechanism of 3D printing and, more specifically, bioprinting. It will then give an overview of the current law regarding organs, blood products, and medical devices. This note will then consider how bioprinted organs should be regulated under the existing law. It will argue that bioprinted organs should be classified as "human organs" and will therefore be subject to the National Organ Transplant Act. This note will then explore the different avenues of federal regulation under the different categories of the Food and Drug Administration, ultimately arguing that bioprinted organs should be regulated as medical devices. With this designation, bioprinted organs will be subject to the most rigorous approval process and will be subject to a federal preemption provision which could impact consumers' ability to bring state law claims against the manufacturers of the organs. Finally, this note will propose modifications to the existing regulatory framework that would more directly address this new biotechnological advance and be a better fit considering congressional intent, consumer awareness, and safety.

II. A BACKGROUND OF BIOPRINTING

3D printing is simply a slight modification to the two-dimensional ("2D") printing of words and images on paper. Similarly, bioprinting is only a slight modification to 3D printing. The differences lie between the substrates used. For 2D printing, simple ink is utilized. 3D printing operates on the same principle as a traditional household 2D printer. Rather than ink, it prints with substrates such as liquid, powder, or sheet material.[11] Bioprinting, on the other hand, uses biological materials such as active cells and lipids.[12] These are only the most basic differences.

Researchers hope that bioprinting techniques may be mastered in an effort for biologically active organs to go from science fiction to reality. In order to understand how to go from digital blueprint to functioning organ, the principles behind 3D printing provide the foundation for the understanding of bioprinting.

A. Three-Dimensional Printing

The term "manufacture" comes from the Latin expression *manu factus,* which quite literally means made by hand.[13] With the use of machines and other technology in the manufacturing process, this etymology hardly holds true to the

11. C. Lee Ventola, *Medical Applications for 3D Printing: Current and Projected Uses*, 39 P&T 704, 704 (2014).

12. Murphy & Atala, supra note 1, at 773.

13. *Manu factus*, THE MERRIAM-WEBSTER DICTIONARY (11th ed. 2004).

use of the word today. One clear example of this change in production technique is 3D printing. Over the last few decades, printing capabilities have advanced from printing two-dimensional words and images on pieces of paper to printing three dimensional shapes and products.[14] The production of 3D objects via printing is accomplished through a process called "additive" manufacturing.[15] Through additive manufacturing, an object is constructed by adding layer after layer of a selected substrate.[16]

While many understand 3D printing to be a new technology, 3D printing was actually invented by Charles Hull in the early 1980's.[17] Hull called the process "stereolithography," which used an .stl file format to interpret the data in a Computer-Assisted Design ("CAD") file.[18] The CAD files are still utilized in today's 3D printing process and contain the blueprint to be communicated electronically to the 3D printer.

Despite the fact that there are dozens of mechanisms for 3D printing, the general process is the same.[19] The 3D printer follows the instructions in the CAD file to produce the foundation for the product by moving the print-head along the x-y plane of the printing space.[20] Once the foundation is developed, the print head can move through the z axis, adding layer by layer and building the product up vertically.[21]

There are a variety of different 3D printers available to consumers in today's market. The type of 3D printer utilized for a particular product typically depends on the materials that will be used, the substrate, and how the layers of the finished product will be bonded.[22] For example, the Selective Laser Sintering printers traditionally use powdered material as the substrate, Thermal Inkjet printers utilize "ink"-like materials with thermal and electromagnetic technology to deposit tiny droplets, and Fused Deposition Modeling use beads of heated plastic.[23] Today, 3D printers are used both commercially and by consumers in their own homes.[24]

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14. Murphy & Atala, supra note 1, at 773.
15. Theirry Rayna & Ludmila *Striukova, From Rapid Prototyping to Home Fabrication: How 3D Printing is Changing Business Model Innovation,* TECHNOLOGICAL FORECASTING AND SOCIAL CHANGE, 214, 215 (2016).
16. *Id.*
17. Ventola, supra note 11, at 704.
18. *Id.*
19. *Id.*
20. *Id.*
21. *Id.*
22. *Id.* at 705.
23. *Id.*
24. Rayna & Striukova, *supra* note 15, at 216.

B. Bioprinting Basics

3D bioprinting operates through a similar mechanism as conventional 3D printing. With bioprinting, the substrate is a biological material such as proteins, sugars, lipids, biochemicals, and living cells.[25] The most prominent mechanisms for bioprinting include biomimicry, autonomous self-assembly, and mini-tissue building blocks.[26] Thermal inkjet printers are widely used in bioprinting.[27] These printers function by electrically heating the print head to trigger pulses of pressure that force droplets from the nozzle.[28]

To generate a tissue or organ, an engineer begins by isolating stem cells.[29] Stem cells are widely known as cells that are not yet differentiated, or not yet a specialized cell with specialized function, allowing great flexibility in clinical settings.[30] Because they are not differentiated, they can be influenced by proteins and other cells to become a specific kind of cell, i.e. hepatocyte, or liver cell.[31] The stem cells are then treated with growth factors and allowed to proliferate in a laboratory.[32] The cells are then seeded onto scaffolding by the printer head.[33] It is important that the scaffolding material is compatible with the biological materials and the printing process.[34] Generally, the scaffolding is constructed from naturally derived polymers or synthetic molecules.[35] Once the cells are aligned in place, nature takes over. The cells begin to fuse and form more complex tissue structures.[36] The scaffolding directs further proliferation of the cells and aids in their differentiation into specialized, functioning tissues before collapsing upon itself leaving only the interconnected tissue networks behind.[37]

However, the scaffolding alone does not produce the complex vasculature required by a functioning organ. Without vasculature, bioprinted organs tend to be hollow and thin.[38] Most cells needed for transplantation such as hearts, livers, and kidneys are thick and certainly require vasculature to supply the cells with oxygen/gas exchange, nutrients, growth factors, and waste product removal—all of which are imperative for a proper functioning organ.[39] This is a wrinkle in the

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25. Murphy & Atala, *supra* note 1, at 773.
26. *Id.*
27. *Id.* at 775.
28. *Id.*
29. Christian Mandrycky & Zongjie Wong, *3D Bioprinting for Engineering Complex Tissues,* BIOTECHNOLOGY ADVANCES, 423, 428 (2015).
30. J.M.W. Slack, *Metaplasia and Transdifferentiation: From Pure Biology to the Clinic,* NATURE REVIEWS MOLECULAR CELL BIOLOGY, 369, 369 (2007).
31. *Id.*
32. Ventola, *supra* note 11, at 706.
33. *Id.* at 707.
34. Murphy & Atala, *supra* note 1, at 778.
35. *Id.*
36. Ventola, *supra* note 15, at 706.
37. *Id.*
38. *Id.* at 707.
39. *Id.*

process that engineers are working to figure out. Thermal inkjet printers are the most promising printer for this task. In fact, they have already created some vasculature with complex geometries involving branches and numerous channels.[40] This is certainly considered a stride toward a successful, functioning, manufactured organ.

III. CURRENT FEDERAL LEGISLATION

Though States typically handle health related matters, organ donations and most medical products and devices are federally regulated. While federal regulation would likely be required to ensure safe practices, the unique quality of bioprinted organs calls into question under which realm they should be regulated. They operate as human organs, though they are manufactured as a product. Organ transplants are currently regulated pursuant to the National Organ Transplant Act ("NOTA") while the FDA handles the regulation of devices, drugs, vaccines, and biologics, to name a few. Bioprinted organs would seem to fall under both, which sparks the debate as to which would be the prevailing regulatory framework, and/or how additional provisions may be needed to guide their regulation by both acts.

A. A Brief Overview of NOTA

Approved on October 19, 1984, and amended in 1988 and 1990, NOTA brought comprehensive reform to the law regarding organ donation and transplantation by, amongst other things, establishing a task force on organ procurement and transplantation and outlawing the sale of human organs.[41] NOTA is composed of four titles which, collectively, organize detailed research on the science and ethics of organ transplantation, establish organizations for the procurement of organs, institute systems for matching donor organs with recipients, and criminalize the sale of human organs.[42]

Title I of NOTA directed the Secretary of Health and Human Services to establish a Task Force on Organ Transplantation.[43] The Task Force would be tasked with the compilation of data on safety, effectiveness, and costs of various transplant treatments.[44] Additionally, the task force was directed to study immunosuppressive medications and their impact on organ rejection prevention, as well as the medical, legal, ethical, economic, and social issues presented by the

40. *Id.*
41. National Organ Transplant Act, 42 U.S.C. § 273-274 (1984).
42. *Id.*
43. National Organ Transplant Act, 42 U.S.C. § 273 (1984).
44. *Id.*

procurement and transplantation of organs.[45] The Task Force conducted its required studies, submitted its final report in April 1986, and was dissolved.[46]

Title II called for the creation of two organizations: Organ Procurement Organizations ("OPOs") and the Organ Procurement and Transplantation Network ("OPTN").[47] The OPOs were designed to identify potential donors, acquire all usable organs from the potential donors, arrange the acquisition and preservation of the donated organs, and systematically allocate donated organs among transplant centers and patients.[48] NOTA also tasked the OPTN with a number of responsibilities. The OPTN was created to establish a national list of individuals in need of organs and to create a system of matching those individuals with available organs.[49] Further, they were charged with the creation and adoption of standards of quality for acquisition and coordination of transportation of organs from OPOs to transplant centers, providing information to health professionals regarding organ donation, and collecting, analyzing, and publishing data relative to organ procurement and transplantation.[50] Currently, the United Network for Organ Sharing ("UNOS"), a private, non-profit organization, administrates the OPTN.

Perhaps the most notable segment of NOTA, Title III outlaws the sale of human organs.[51] The prohibition specifically states as follows: "It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation if the transfer affects interstate commerce."[52] Punishment for violation of this section is outlined as a fine of not more than $50,000, imprisonment for not more than five years, or both.[53]

Finally, Title IV creates a national registry for voluntary bone marrow donors.[54] The registry requires that the volunteers give informed consent to the donation of the bone marrow and that the names of the donors be kept confidential.

NOTA brought sweeping changes to an area of law that was previously quite unsettled. Currently, NOTA applies to donated organs exclusively. Nevertheless, the possibility remains that artificial organs may be determined to be within the scope of this law and subject to its practices.

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45. *Id.*
46. *Id.*
47. *Id.*
48. *Id.*
49. 42 U.S.C. §274 (1984).
50. *Id.*
51. *See Id.* §274e.
52. *Id.*
53. *Id.*
54. 42 U.S.C. §273 (1984).

B. A Look into Federal Regulation by the Food and Drug Administration

The FDA was established in 1906 due to an outpouring of consumer concern with the safety of products on the market.[55] Today, the FDA regulates a myriad of products under designations such as food, drugs, medical devices, radiation-emitting products, vaccines, blood and biologics, animal and veterinary, cosmetics, and tobacco products.[56] Aside from pharmaceutical products, the vast majority of medical products are regulated as vaccines, blood & biologics, human cell and tissue products, or medical devices.[57] Relevant to human organs, are products regulated as human cell and tissue products or medical devices.

1. FDA Regulation of Human Cell and Tissue Products

Basic biological definitions state that collections of cells form tissues and that collections of tissues form organs. With regard to federal regulation under the FDA, human tissues fall under the broad biologic product category of Human Cells and Tissue Products ("HCT/Ps").[58] The FDA regulates these products utilizing the "Tissue Rules" which were established on May 25, 2005 and are under Section 361 of the Public Health and Safety Act.[59] This section provides the authority of the FDA to establish regulatory requirements for marketing HCT/Ps.[60]

The FDA's Center for Biologics Evaluation and Research regulates HCT/Ps under 21 CFR §1270 and §1271.[61] These sections require tissue establishments to screen and test donors, to maintain appropriate procedures for the prevention of the spread of communicable diseases, and to keep sufficient records.[62] Section 1271 in particular sets out guidelines in order to determine the appropriate group by which a product should be regulated.[63] 21 CFR §1271.10(a) presents four criteria used to determine whether a product will be regulated solely under Section 361 of the Public Health and Safety Act.[64] Those products that satisfy the criteria do not require Pre-Market Approval, as they are deemed to be low risk products.[65] Products that otherwise do not satisfy the four criteria are regulated as a drug, device, and/or biological product.[66]

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55. Freddie Ann Hoffman & Peter H Pheinstein, *The Laws and Regulations Enforced by the U.S. Food and Drug Administration,* Legal Medicine (2007).
56. U.S. Food & Drug Administration, http://www.fda.gov (last visited Aug 1, 2018).
57. *Id.*
58. Mark H. Lee, *Considerations for Tissue-Engineered and Regenerative Medicine Product Development Prior to Clinical Trials in the United States*, 16 TISSUE ENGINEERING: PART B, 41-42, (2010).
59. *Id.*
60. Public Health Service Act, 42 U.S.C. §264 (2018).
61. 21 CFR §1270-1271 (2018).
62. *Id.*
63. 21 CFR §1271 (2018).
64. See *Id.* §1271.10 (2018).
65. *Id.*
66. *See Id.* §1271.20 (2018).

2. FDA Regulation of Medical Devices

The FDA's Federal Food, Drug, and Cosmetic Act was amended on May 26, 1976 to include the Medical Device Amendments of 1976 ("MDA").[67] These amendments prescribe the guidelines under which medical devices are regulated. The MDA accomplishes this by outlining the distinctive classifications of devices, performance standards, and the pre-market approval process.[68] In addition to listing the processes and procedures required to place devices on the market, the MDA also includes a federal preemption provision which can bring significant impact on persons wishing to bring products liability actions in state court.[69]

The MDA organizes medical devices into three distinct categories based, in large part, on the risk associated with the device or its utility. Class I devices encompass those that present no unreasonable risk of illness and/or injury.[70] Because of the low risk, they are only subject to "general controls" which apply to all devices and include the registration of manufacturers, record-keeping requirements, and labeling requirements.[71] Generally, Class II devices present an increased degree of risk.[72] Consequentially, additional safeguards are needed because general controls are insufficient to ensure safety. While they are still subject to the general controls, they also have "special controls" including performance standards, post market surveillance, patient registries, guidelines, and recommendations.[73] Class III devices either "present a potential unreasonable risk of illness or injury," or 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."[74] These devices must undergo an extensive premarket approval process to provide reasonable assurance of its safety and effectiveness.[75]

Manufacturers seeking premarket approval for a Class III device must submit an application.[76] The application requires a full report of all information known about the device, including details regarding any investigations or studies conducted on the device.[77] The application must also include a detailed explanation of the mechanism of operation of the device, and a full statement of all components, ingredients, and properties.[78] Manufacturers seeking approval must also provide a description of the manufacturing methods and facilities,

67. Medical Device Amendments of 1976, 21 U.S.C. § 301 (1976).
68. *Id.*
69. *Id.*
70. 21 U.S.C. §360c (1976).
71. Hoffman & Pheinstein, *supra* note 55, at 7,
72. *Id.*
73. *Id.*
74. 21 U.S.C.A. §360c (1976).
75. *Id.*
76. See *Id.* §360e(c)(1) (1976).
77. *Id.*
78. *Id.*

applicable performance standards, and samples of the device.[79] Once the application is submitted, the FDA has 180 days to issue an order approving or denying the application.[80]

The MDA provides an exception to the premarket approval process in order to permit the investigational use by experts to investigate the safety and effectiveness of the device.[81] Additionally, those devices that are "substantially equivalent" to those which were introduced into interstate commerce for commercial distribution before the enactment of the MDA can be approved through the premarket notification process rather than the premarket approval process.[82] The premarket notification, also known as 510(k), is a premarket submission made to the FDA to demonstrate that the device to be marketed is at least as safe and effective as a legally marketed device that is not subject to premarket approval.[83]

The MDA also includes a preemption provision.[84] It prohibits states from establishing any "requirement" which is different from, or in addition to, any requirement applicable to medical devices under the Federal Food, Drug, and Cosmetic Act.[85] There is an exemption for states that seek to assert requirements which are more stringent than those provided in the Federal Food, Drug and Cosmetic Act.[86]

The Supreme Court of the United States considered this provision in two landmark cases: *Medtronic, Inc. v. Lohr* and *Riegel v. Medtronic, Inc.*[87] In *Lohr*, the plaintiff's wife's pacemaker failed and he brought state law claims against the manufacturer.[88] Ultimately, the Supreme Court held that the MDA did not preempt a state action for strict liability and negligence against the manufacturer of the pacemaker.[89] The Court cited 21 CFR 808.1, noting that state requirements are only preempted when the FDA has established "specific counterpart regulations" or requirements applicable to a particular device.[90]

In *Riegel*, the plaintiff brought suit against the manufacturer after a catheter ruptured in his coronary artery during surgery.[91] The catheter was a Class III device which had received premarket approval from the FDA.[92] The Supreme Court expressed that while the 510(k) approval places its focus on a device's

79. *Id.*
80. See *Id.* §360e(d)(1) (1976).
81. See *Id.* §360j(g)(1) (1976).
82. See *Id.* §360c(f)(3) (1976).
83. 21 CFR 807.92(a)(3)
84. 21 U.S.C.A §360k(a) (1976).
85. *Id.*
86. *Id.*
87. Medtronic, Inc., v. Lohr, 518 U.S. 470 (1996); Riegel v. Medtronic, Inc., 552 U.S. 312 (2008).
88. Medtronic, Inc., v. Lohr, 518 U.S. 470, 481 (1996).
89. *Id.* at 484.
90. *Id.* at 483.
91. Riegel v. Medtronic, Inc., 552 U.S. 312, 320 (2008).
92. *Id.*

equivalence to an available device, the premarket approval process is hyper focused on the safety of the device.[93] Once a device is granted premarket approval, any changes made to the device must be submitted to the FDA for approval in order to ensure the safety of the device.[94] By nature, the premarket approval process imposes device-specific requirements as discussed in *Lohr*.[95] Because the catheter was granted premarket approval, the FDA had imposed specific regulations on the device. Therefore, the Supreme Court held that the MDA preempted the state claims.[96] However, the Court went on to provide an exception for circumstances when the state duties are "parallel" rather than additional to the regulation requirement.[97] When the requirements are parallel, a state may provide a remedy for claims that are premised on violations of the FDA regulations.[98]

IV. ANALYSIS

Given the unprecedented nature of the development of bioprinted organs, there are no laws or regulations that one can apply with absolute certainty. In all likelihood, Congress or Congressionally created agencies such as the FDA will consider new legislation to accommodate this product. Certainly, there will be a significant public policy interest to consider given the current demand for organs, such as kidneys and hearts, that people need to survive. This interest should be taken into account, and legislation passed specifically for this product.

However, because lives will depend bioprinted organs transplanted into real persons, they must be perfected before they can reach consumers. Additionally, legislation tailored to the product cannot be constructed until they are complete and prepared to reach the market. Therefore, one cannot expect Congress or federal agencies to prematurely legislate for a presently experimental product. If subjected to the current laws and regulations, bioprinted organs will likely be subject to NOTA and regulated by the FDA as a medical device. However, modifications to these regulations would provide Congress and federal agencies the ability to construct more suitable regulations for bioprinted organs.

A. Bioprinted Organs and NOTA

Currently, NOTA sets up the regulatory framework regarding human organs and their transplantations. While it is likely that bioprinted organs will not be subject to NOTA's donation and logistic regulations, as they will not be donated,

93. *Id.* at 323.
94. *Id.* at 319.
95. Lohr *supra* note 87, at 311
96. Riegel *supra* note 93, at 330.
97. *Id.*
98. *Id.*

the biologic characteristic of bioprinted organs may subject them to Title III. NOTA's Title III provision provides as follows:

> (a) It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation if the transfer affects interstate commerce.
>
> (b) Any person who violates subsection (a) shall be fined not more than $50,000 or imprisoned not more than 5 years, or both.[99]

Whether NOTA or, more specifically, this particular provision of NOTA, applies to bioprinted organs first hinges on whether bioprinted organs can be classified as "human organs." Fortunately, NOTA provides the following definition for the term: "The term human organ means the human (including fetal) kidney, liver, heart, lung, pancreas, bone marrow, cornea, eye, bone, and skin or any subpart thereof and any other human organ (or any subpart thereof, including that derived from a fetus) specified by the Secretary of Health and Human Services by regulation."[100] The referenced regulation adds the intestine, esophagus, and stomach to the list of human organs.[101]

Bioprinted organs should be subject to Title III of NOTA because they meet the definition of "human organs." Bioprinted organs are constructed from human cells which are both a derivative from a fetus and a biological "subpart" of an organ. Additionally, the self-collapsing scaffolding allows the end product to not only be composed entirely of the patient's tissues, but also contain the complex architecture and vasculature that is characteristic of human organs. Furthermore, because of their design, they are purported to function exactly as human organs once incorporated into the body. It can certainly be argued that the use of the term "human" has the implication that Congress is referring to those organs from another human person which developed organically from the womb until adulthood. Despite the fact that bioprinted organs are not the first manufactured biologic product to match the capabilities of human cells and tissues, Congress has yet to amend the terminology, leaving it open for interpretation of what exactly is "human." While bioprinted organs fit into the NOTA framework at this time, Congress need only to amend the definition of "human organ" to exclude bioprinted organs should they wish to exclude bioprinted organs from regulation under NOTA.

The classification of bioprinted organs as human organs will, of course, leave them subject to the prohibition provision.[102] Therefore, the issue arises as to whether the sale of the bioprinted organ would be prohibited by NOTA. Pursuant to Title III of NOTA, it will be illegal to sell bioprinted organs for valuable consideration if the transfer affects interstate commerce.[103] The legality of the

99. 42 U.S.C. § 274e (1984).
100. *Id.*
101. 42 C.F.R. §121.13 (2010).
102. 42 U.S.C. 274e (1984).
103. *Id.*

sale depends on whether the exchange of monies for the organ would be considered valuable consideration.

NOTA lists reasonable payments associated with the removal, transportation, implantation, processing, preservation, quality control, and storage of the human organ or the expenses of travel, housing, and lost wages incurred by a donor as costs not labeled as "valuable consideration."[104] This language leaves the actual exchange of money for organs illegal, while the costs surrounding the transfer are seemingly permitted. While replacement organs used in transplantation are typically donated, the exchange is lawful. However, where manufacturers must make a profit, the sale of a bioprinted organ seems to be unlawful. It is yet to be determined whether the manufacture of organs will be a service provided by hospitals or sold by private manufacturers. Should a hospital provide the organ, printed from the patient's own cells, and charge only for the transplantation and related procedures, the transfer should be legal. They may also be capable of charging for the printing service, rather than the organ itself. While legality will be more difficult should private manufacturers provide the organs, they too should be able to legally sell the printing service to hospitals requesting the organs.

Bioprinted organs meet the definition of "human organs" provided by NOTA. The prohibition of the sale of organs in Title III is arguably the only section of NOTA that could be applicable to bioprinted organs as they are not donated or transported from one body to another. Despite this applicability, their sale will be lawful under Title III because manufacturers and/or hospitals can charge consumers/patients for the printing service. While the sale will be restricted by the phrase "valuable consideration", so long as consumers are paying manufacturers for the service alone, there should be no valuable consideration for the organ itself to result in the prohibition of the sale.

B. Regulation of Bioprinted Organs by the FDA

The previous section estimates that bioprinted organs will be subject to NOTA given the provided definition of "human organ." However, NOTA regulates the donation of organs and provides methods the transportation of organs from donor to donee. Before bioprinted organs, there was no need for NOTA to provide regulations speaking to safety of the organ itself. Therefore, there are no regulations in NOTA that can guarantee the safety of the operation of bioprinted organs. To ensure safety, the manufacture of bioprinted organs should be regulated by the FDA.

The FDA contains numerous divisions by which it organizes products. Under the existing law, bioprinted organs may fit well in one of two categories: Blood and Biologics: Human Cell and Tissue Products or Medical Devices.

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104. *Id.*

1. Regulation of Human Cell and Tissue Products

Ligaments, bone, tendons, fascia, and cartilage are only a few examples of HCT/Ps that are regulated under Blood and Biologics. As bioprinted organs, like natural organs, are composed of collections of tissues, it would make sense that bioprinted organs be regulated as HCT/Ps. However, Blood and Biologics only regulate those products that satisfy all of the qualifying criteria pursuant to 21 C.F.R. §1271. Any products that satisfy these criteria are therefore regulated by section 361 of the Public Health and Safety Act. Those that do not qualify are redirected to 21 C.F.R. §1271.20 for guidance regarding the regulation of the non-qualifying product. 21 C.F.R. §1271.10 provides as follows:

> (a) An HCT/P is regulated solely under section 361 of the PHS Act and the regulations in this part if it meets all of the following criteria:
>
> (1) The HCT/P is minimally manipulated;
>
> (2) The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;
>
> (3) The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P; and
>
> (4) Either:
>
> (i) The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
>
> (ii) The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and:
>
> (a) Is for autologous use;
>
> (b) Is for allogeneic use in a first-degree or second-degree blood relative; or
>
> (c) Is for reproductive use.[105]

Bioprinted organs do not fit the framework for HCT/Ps as they do not satisfy all of the criteria. First, "minimal manipulation" is defined as follows: "for structural tissue, processing that does not alter the original relevant

105. 21 C.F.R. §1271.10

characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement; and for cells or nonstructural tissues, processing that does not alter the relevant biological characteristics of the cells or tissues."[106] Bioprinted organs would satisfy this criterion because at the very most, the cells would be treated with a human growth factor to make them differentiate and proliferate. However, the biological characteristics of the cells would not be altered.

The second criterion requires that the HCT/P be used exclusively for homologous use.[107] Simply put, this means that a patient's cells would be used as a substrate for an organ printed solely for his or her own transplantation. This too, is satisfied as each organ would be patient specific in order to prevent rejection and obviate the use of immunosuppressive drugs.

Bioprinted organs cannot satisfy the third criterion.[108] In order to construct organs with the complex vasculature necessary to be incorporated into the human body, bioprinters require scaffolding which the cells surround until it collapses. This scaffolding is generally a synthetic polymer, which violates this criterion as they are not made of any of the accepted materials.

Bioprinted organs actually can satisfy the fourth criterion as they are dependent upon the metabolic activity for their primary function and would be for autologous use.[109] However, they still cannot be included in the class of HCT/Ps because they require the addition of another material during the manufacture process. 21 C.F.R. §1271.15 provides some exceptions for HCT/Ps such as those that are used solely for nonclinical scientific or educational purposes, or if the HCT/P will be removed and implanted in the same surgical procedure. Bioprinted organs do not meet any of the prescribed exceptions and are redirected to 21 C.F.R. §1271.20, which provides the following:

> If you are an establishment that manufactures an HCT/P that does not meet the criteria set out in § 1271.10(a), and you do not qualify for any of the exceptions in § 1271.15, your HCT/P will be regulated as a drug, device, and/or biological product under the act and/or section 351 of the PHS Act, and applicable regulations in title 21, chapter I. Applicable regulations include, but are not limited to, §§ 207.9(a)(5), 210.1(c), 210.2, 211.1(b), 807.20(d), and 820.1(a) of this chapter, which require you to follow the procedures in subparts C and D of this part.[110]

Therefore, bioprinted organs do not qualify for regulation as HCT/Ps in Blood and Biologics with the FDA and may be better suited for regulation as medical devices.

106. See *Id.* §1271.3(f).
107. 21 C.F.R. §1271.10
108. *Id.*
109. *Id.*
110. See *Id.* §1271.20.

2. Regulation of Medical Devices

The Medical Device Amendments of 1976 established three classifications for medical devices: Class I, Class II, and Class III.[111] Bioprinted organs do not qualify for a Class I or a Class II designation and therefore are not entitled to the smooth 510(k) approval process. Class I medical devices present no unreasonable risk of illness and/or injury and are only subject to "general controls" which apply to all devices.[112] Class II devices present an increased degree of risk and require "special controls."[113] While there is not much guidance offered on these classifications, the Class III generalization is much more descriptive, providing that the devices either "present a potential unreasonable risk of illness or injury," or 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."[114] Bioprinted organs transplanted into the human body would be tasked with supporting and sustaining human life. This life sustaining function is the reason that bioprinted organs may be seen as presenting an unreasonable risk of illness or injury. A malfunctioning manufactured organ could have fatal consequences. Certainly, this categorizes them as Class III devices.

While some Class III devices may qualify for exceptions to the premarket approval process, it is unlikely that bioprinted organs will side-step the rigorous process. Because of the life-saving capacity of the devices, investigational use will only be a temporary process which will not provide an exception to the premarket approval process. Additionally, bioprinted organs cannot undergo the 510(k) notification process as they will be the first device of their kind. In fact, pursuant to NOTA, the bioprinted organs are equivalent to human organs. However, human organs are not a marketable product and there is no assurance of safety with bioprinted organs solely through comparison to a natural organ.

Under existing law, bioprinted organs fit the framework for Class III medical devices required to undergo the premarket approval process. While this process will certainly suspend the time before the organs are on the market, it will ensure the safety of these organs in which we will place so much trust.

C. Recommendations for Modification to the Current Law in Response to the Availability of Bioprinted Organs

While bioprinted organs certainly fit into the framework of some current laws and regulations, regulation of bioprinted organs under same may not be best in practice. Bioprinted organs are a unique technological innovation which have the potential to save lives. This particular characteristic of bioprinted organs should provide substantial weight in favor of regulations specifically tailored in an

111. 21 U.S.C. §360c (1976).
112. *Id.*
113. *Id.*
114. *Id.*

attempt to ensure the safety of those in the vulnerable position of requiring them. Upon the entry of bioprinted organs into the market, Congress should consider modifications to NOTA to exclude bioprinted organs from regulation under the Act. Additionally, while bioprinted organs may be regulated by the FDA as medical devices, the FDA may consider a new category of regulation for bioprinted organs and other products to ensure the best approval processes and safety practices.

1. Suggested Modifications to Title III of NOTA in Response to Marketable Bioprinted Organs

As explained above, there are strong arguments which claim that bioprinted organs are "human organs" and therefore subject to NOTA. While bioprinted organs fit this obligation, it is not necessarily best that NOTA govern bioprinted organs NOTA was enacted in order to regulate the transplant of donated organs including their storage and transportation from donor to donee. Because bioprinted organs are not donated but manufactured specifically for a particular patient, NOTA, with the exception of Title III, provides no guidance with respect to the regulation of bioprinted organs. Therefore, just because the bioprinted organs fit the description for those regulated under NOTA, does not necessarily mean that they should be regulated by NOTA.

While Title III does seem to be applicable to bioprinted organs, it is unnecessary. Congress enacted Title III of NOTA for policy reasons regarding the sale of human organs originating from a person. Certainly, it is unlikely that Congress considered bioprinted organs when enacting this legislation in 1984 or amending it in 1988 and 1990. Because bioprinting requires only a cell sample to develop an organ, the policy arguments behind Title III of NOTA do not hold water when applied to bioprinted organs for obvious reasons. Striking Title III, NOTA does not contain any provisions that are truly valuable to the regulation of bioprinted organs. Therefore, upon release of bioprinted organs into the market, Congress should amend NOTA to specifically exclude bioprinted organs to better serve its own purposes and to allow proper regulation of bioprinted organs through other organizations such as the FDA.

In response to marketable bioprinted organs Congress can easily exclude bioprinted organs from NOTA in two ways: First, Congress could adjust the language provided in Title III of NOTA.

> Currently, Title III of NOTA provides the following:
>
> (a) It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation if the transfer affects interstate commerce.[115]

115. 42 U.S.C. 274e.

To exclude bioprinted organs from NOTA, Congress could change this provision as follows:

> (a) It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ, *naturally developed within the human body,* for valuable consideration for use in human transplantation if the transfer affects interstate commerce.

Second, in the alternative, Congress could include an additional provision which specifically provides that human organs formed by bioprinting, or other similar synthetic processes are excluded from the Act. This additional provision could be added to subsection (a) or could be included with the definitions provided in the act. Although it was previously determined above that Title III of NOTA would not actually prohibit the sale of bioprinted organs, these recommendations would provide clear guidelines of what is intended to be regulated by NOTA.

2. Recommendations for FDA Regulation of Bioprinted Organs

While bioprinted organs surely fit into the classification of medical devices regulated by the FDA, the regulation of bioprinted organs may be better suited in a category specific to bioprinted devices or other biologically active products. A group that contains sophisticated devices, such as patient-specific bioprinted organs, as well simple devices, such as menstrual cups, may be too broad a class for appropriate regulation.

In response to the arrival of marketable bioprinted organs, the FDA should consider forming a new category for bioprinted products and materials. This would allow more specific regulation, which could improve the safety and effectiveness of the products. Specifically, a category composed of all bioprinted products may have regulations specific to the digital blueprints utilized, specific printer requirements, the printing process, the shipment of the product if applicable, and even their transplant in surgery as some products may require.

VI. CONCLUSION

There is no question of the lives that could be saved by the manufacture of human organs through bioprinting. Patients in need of a transplant could obtain a healthy organ to save their life in no time, compared to the wait they face at this time. Additionally, they could have transplantations without risk of the serious side effects such as organ rejection. Because the manufactured organs would be made from the patients own cells, the body would recognize the organ as part of itself, eliminating the need for immunosuppressive drugs. However, the organs must be fine-tuned and have their safety ensured before they reach these patients.

Placing bioprinted organs into categories within the existing law before they arrive on the market is speculative to say the least. On one hand, it seems as

though they will be subject to NOTA and could be subject to regulation by the FDA as medical devices. Based on this approach, however, bioprinted organs are operating under the umbrella of statutes and regulations enacted without comprehension of the possibility of their existence. Because of this, bioprinted organs, which would be subject to NOTA, would have to be marketed pursuant to Title III, which was enacted to prevent persons from selling their own organs. This places too many limits and restrictions on bioprinted organs without good cause, as the policy reasons behind NOTA do not apply to these manufactured organs. Also, regulation as a medical device, while possible, is not ideal as this category is simply too broad to afford all the safeguards necessary for an effective, safe, and complex product.

Upon the entry of bioprinted organs into the marketplace, Congress should amend the language of NOTA. NOTA's provisions should explicitly state that the only organs subject to it are those naturally grown inside the human body from conception to adulthood, thereby excluding bioprinted organs from its authority. Further, the FDA could take a proactive approach and add a new category of regulation specifically tailored for bioprinted products, such as organs, tissues, and other biologically active parts. This would reflect a more targeted group of products and ensure that their safety through regulations designed specifically for their purposes.