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COMMENT

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FDA REGULATION OF 3D-PRINTED ORGANS AND  
ASSOCIATED ETHICAL CHALLENGES

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## INTRODUCTION

“The liveliest—literally—field of 3D printing may sound like something from a sci-fi movie, but (spoilers) it’s real and happening now.”<sup>1</sup> Indeed, this new field is “nothing less than the start of a new industrial revolution,”<sup>2</sup> and 3D printing promises to be a “disruptive” force in the market.<sup>3</sup> This spring, Boeing passed Federal Aviation Administration safety tests for the first printed structural components for a plane.<sup>4</sup> The plane manufacturer will start using 3D-printed parts in its engines, which will yield faster manufacturing processes and billions of dollars in savings.<sup>5</sup>

The potential applications of this new technology are endless. Industry leaders and world leaders alike recognize and are excited by this opportunity. As then-President Obama said, “3D printing has the potential to revolutionize the way we make almost everything.”<sup>6</sup>

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<sup>1</sup> Arif Sirinterlikci & Lauren Walk, *Bioprinting: Science or Fiction?*, MANUFACTURING ENGINEERING 51 (2014).

<sup>2</sup> *How 3D Printing Will Reshape the World*, CNN, <http://edition.cnn.com/TECH/specials/make-create-innovate/3d-printing/> [<https://perma.cc/BR8L-M6N3>].

<sup>3</sup> See, e.g., Rebecca Neu, *3D Printing: A Revolutionary Advance for the Field of Urology?*, TECH. INNOVATION MGMT. REV., Mar. 2014, 19, 19 (foreshadowing 3D printing as “one of the top ten most disruptive technologies of the coming decade”); Andrew Tsai & Chinh H. Pham, *Fast Forward: Even Companies That Don’t Embrace 3D Printing Will Need to Weigh Risks* 24 CORPORATE COUNSEL 25 (2017) (“3D printing technology has become truly disruptive to a wide range of industries and businesses.”).

<sup>4</sup> Mariella Moon, *Boeing Uses First FAA-Approved 3D-Printed Parts for the 787*, ENGADGET (Apr. 11, 2017), <https://www.engadget.com/2017/04/11/boeing-faa-approved-3d-printed-metals-787/> [<http://perma.cc/9V5Y-L8XT>].

<sup>5</sup> *Id.*

<sup>6</sup> President Barack Obama, 2013 State of the Union Address (Feb. 12, 2013).

One of the applications that holds incredible promise is 3D printing in the medical context, which includes the possibility of 3D-printed organs for humans.<sup>7</sup> There will come a time in the not-so-distant future when our children or grandchildren will balk at the notion that, just a generation ago, people died because their doctors could not locate an organ—or only one with high risks of rejection—to complete the transplant. According to health care technology expert Tom Todorow, the introduction of 3D-printed organs into the medical landscape is a relative certainty; not a question of if, but when.<sup>8</sup> Root Analysis, a medical technology consulting company, anticipates that it should be possible to print kidneys in six years, with livers to follow soon after.<sup>9</sup> The prospect of printed organs necessitates the following question: is the market ready for 3D-printed organs? The answer, with some reservations about the ethical challenges ahead, is yes: the regulatory regime as it currently stands can handle 3D-printed organs.

Before delving into the questions surrounding 3D printing in the medical field specifically, the U.S. organ shortage crisis warrants attention. On average, twenty-two people die every day while awaiting an organ transplant.<sup>10</sup> The waitlist for organs is over 116,000 people long and, every 10 minutes, someone new is added.<sup>11</sup> Over the last 5 years, the number of organ transplants has increased by 20 percent, hitting a new record of over 33,500 transplants in 2016.<sup>12</sup> The organ supply will not catch up with the current demand without some assistance from another source—such as printers that can manufacture organs.

The implications of pervasive implementation of 3D printing with biological material, also known as “bioprinting,” are vast. They present never-before-seen hurdles, which are particularly complicated due to the vulnerability of the patients, who often need new organs to survive, involved. In this Comment, I limit the scope of this inquiry to the most immediate challenges of embracing 3D-printed organs in our health care market: potential statutory roadblocks, regulatory concerns over manufactured organs, and ethical challenges of which we must remain aware. I submit one path by which 3D-printed organs can fit in our current legal and regulatory framework. I

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<sup>7</sup> See Neu, *supra* note 3, at 21-22 (“Considering the social and financial costs of current therapy options, the technology of 3D [organ] printing holds promise for not only providing a superior quality of life for suffering patients but also reducing the long-term costs of care.”).

<sup>8</sup> Interview with Tom Todorow, Chief Fin. Officer, Children’s Hosp. of Phila. (Mar. 30, 2017).

<sup>9</sup> *A Tissue of Truths—Printed Human Body Parts Could Soon be Available for Transplant*, ECONOMIST (Jan. 28, 2017), <http://www.economist.com/news/science-and-technology/21715638-how-build-organs-scratch> [<https://perma.cc/BWG8-PZW9>] [hereinafter *A Tissue of Truths*].

<sup>10</sup> *Organ Procurement and Transplantation Network*, U.S. DEP’T HEALTH & HUM. SERVS., <https://optn.transplant.hrsa.gov> [<https://perma.cc/724N-J86S>].

<sup>11</sup> *Id.*

<sup>12</sup> *Id.*

also define who should be charged with regulating them and propose how future regulators should do so. Finally, I raise additional concerns of 3D-printed organs that will require deeper analysis as more information becomes available, including the myriad ethical challenges presented by this new technology.

The U.S. Food and Drug Administration (FDA) is the appropriate body to regulate 3D-printed organs because a manufactured organ must be treated differently than a human organ, which can be transplanted as “simply” part of the practice of medicine. It remains to be seen how the FDA will gather sufficient data to satisfy premarket approval requirements, determine who gets access and when, and how to govern the marketing of 3D-printed organs because the output is individualized. But the process by which the organs are created can be scaled dramatically. In so doing, those in charge must also confront unique, multifaceted ethical challenges.

## I. WHAT IS 3D PRINTING AND WHO CARES?

### A. *The History and Mechanics of 3D Printing*

The concept of 3D printing has existed for decades, but industries, scientists, and engineers only recently started to appreciate its full potential. Chuck Hull, an American inventor with a background in engineering and physics, created the concept of 3D printing back in the 1980s, yet he was only just formally recognized for this accomplishment.<sup>13</sup>

Three-dimensional outputs from a 3D printer are created, in some ways, by similar means as a conventional two-dimensional printer. Instead of the two-dimensional layer of ink traditionally seen on a printed page, the 3D printer puts billions of layers of whatever material composes the “ink” on top of one another to create the object.<sup>14</sup> Together, they form the output that the printer was instructed to create.

3D printing is also sometimes called “additive manufacturing,” in reference to the “additive” process by which the printer creates its three-dimensional output. Rather than moving across a piece of paper to place a single layer of ink dots, the 3D printer goes back and forth many more times, “laying down successive layers of materials” from computer-aided design (CAD) files that

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<sup>13</sup> See Sam Davies, *3D Printing Inventor Chuck Hull Accepts Nomination as Winner of 2017 Washington Award*, TCT MAG. (Feb. 21, 2017), <http://www.tctmagazine.com/3d-printing-news/3d-printing-inventor-chuck-hull-winner-washington-award/> [<https://perma.cc/ABY2-NGQJ>] (receiving the Western Society of Engineers’ Washington Award, presented to an engineer “whose innovation and accomplishments have had a positive impact on humankind”).

<sup>14</sup> See Tsai & Pham, *supra* note 3 (defining 3D printing as “the laying down of successive layers of materials”).

the physicians and engineers worked together to create.<sup>15</sup> These printers do not use conventional printer ink, but rely on a variety of materials, “includ[ing] plastics, polymers, glass, metal, wax, edible goods and even human tissue.”<sup>16</sup>

In the early 2000s, scientists “discovered that living cells could be sprayed through the nozzles of inkjet printers without damaging them.”<sup>17</sup> Hull himself was surprised at how quickly it became apparent that this technology could, and was going to, revolutionize the medical field.<sup>18</sup>

When bioprinting an organ, a patient’s own cells are used, rather than using synthetic materials. A commonly used method begins with a biopsy to remove some of a patient’s cells. The biopsied cells are subsequently subjected to a “growth medium to proliferate cell growth and multiplication and to form aggregate cells that are the base of ‘bioink.’”<sup>19</sup> The “bioink” is then layered in the same way as described above. Sometimes an additive must be used to ensure that the bioink is printed in the right shape. This additive can be removed once the printing process is complete, at which point the “as-formed bioprinted tissue is left to grow”<sup>20</sup> or it can be made of biocompatible material<sup>21</sup> or can be biodegradable.<sup>22</sup> Currently, researchers are working to determine how to print complicated and intricate bodies of blood vessels that will produce the necessary supply of blood and oxygen through a printed

<sup>15</sup> *Id.*

<sup>16</sup> *Id.*

<sup>17</sup> *A Tissue of Truths*, *supra* note 9; cf. Sam Fifer & Dimitry Kapmar, *A Look at the Patentability Of 3-D Printed Human Organs*, LAW360 (May 28, 2013, 12:58 PM), <https://www.law360.com/articles/439549/a-look-at-the-patentability-of-3-d-printed-human-organs> [<https://perma.cc/5YS4-YCPJ>] (drawing a parallel between bioprinting and the famous replicator from the Star Trek series).

<sup>18</sup> See Matthew Ponsford & Nick Glass, “*The Night I Invented 3D Printing*,” CNN (Feb. 14, 2014), <http://www.cnn.com/2014/02/13/tech/innovation/the-night-i-invented-3d-printing-chuck-hall/> [<https://perma.cc/2RVN-TN8A>] (discussing in an interview about the success of 3D printing that he was surprised about “[s]ome of the medical applications,” and that “it became pretty clear that this was going to work”).

<sup>19</sup> Gabriela I. Coman, *3-D Bioprinting: 5 Things Medical Device Cos. Should Know*, LAW360 (Feb. 18, 2016, 10:53 AM), <https://www.law360.com/articles/760558/3-d-bioprinting-5-things-medical-device-cos-should-know> [<https://perma.cc/C7RG-TS6C>].

<sup>20</sup> *Id.*

<sup>21</sup> See Jenny Morber, *Custom Organs, Printed to Order*, PBS (Mar. 18, 2015), <http://www.pbs.org/wgbh/nova/next/body/3d-printed-organs> [<https://perma.cc/A84Z-2MZK>] (discussing biomedical researcher Roger Narayan’s substitution of vitamin B12 as a biocompatible material for the toxic polymers typically used in 3D printing).

<sup>22</sup> Cf. Clare Scott, *Wake Forest Researchers Successfully Implant Living, Functional 3D Printed Human Tissue into Animals*, 3DPRINT.COM (Feb. 16, 2016), <https://3dprint.com/119885/wake-forest-3d-printed-tissue/> [<https://perma.cc/8JJ3-BYFM>] (describing the Integrated Tissue and Organ Printing System’s process, which is unique in its ability to print the cells and “scaffold” simultaneously).

organ and to the rest of a patient's body.<sup>23</sup> This is a significant barrier to market entry, but technological advances continue to provide hope.<sup>24</sup>

While the application of bioprinting remains in its relatively nascent stages,<sup>25</sup> the medical field currently utilizes other, less biologically-based applications in hospitals and for training purposes.

Challenges of advancing 3D printing with biomaterials need not detract from the remarkable success 3D printing has already achieved in health care. Some 3D-printed products currently in use in the medical field include dental implants, tailored orthopedics and tools used in maxillofacial surgery.<sup>26</sup> To be clear, the arguments I submit herein refer to the novel *use* of 3D printers to create biologically-based, synthetic organs. The manufacturing process itself is regulated separately and it is not covered in this Comment. By printing an exact replica of a specific human's organ with synthetic materials, doctors can practice before performing operations on their patients.<sup>27</sup> This opportunity benefits new medical students and the most experienced surgeons alike.

Furthermore, some companies have successfully printed organic tissues,<sup>28</sup> which can be used for drug and cosmetic testing.<sup>29</sup> The FDA has also

<sup>23</sup> See Coman, *supra* note 19 (“[B]ioprinting companies are still a few years away from a fully-functioning printable organ such as the heart.”).

<sup>24</sup> See Jordan S. Miller, *Department of Bioengineering Faculty Profile*, RICE U., [http://bioengineering.rice.edu/faculty/Jordan\\_Miller.aspx](http://bioengineering.rice.edu/faculty/Jordan_Miller.aspx) [https://perma.cc/QPS2-M87J] (noting that the potential for creating 3D-printed organs “is fundamentally limited by the lack of comprehensive vascularization strategy for engineered 3D tissues”); see also Katherine Harmon, *A Sweet Solution for Replacing Organs*, SCI. AM., Apr. 2013, at 55 (describing Miller's method of using sugar molds of blood vessels, around which the 3D-printed organs can form and remodel).

<sup>25</sup> See *A Tissue of Truths*, *supra* note 8 (“As yet . . . ‘bioprinting’ remains largely experimental. But bioprinted tissue is already being sold for drug testing, and the first transplantable tissues are expected to be ready for use in a few years’ time.”). *But see id.* (describing work by researchers, who have successfully printed and implanted “ears, bones and muscles into animals, and watched these integrate properly with their hosts” and a Northwestern University group who “even printed working prosthetic ovaries for mice” through which “recipients were able to conceive”).

<sup>26</sup> *A Vision for 3D Printing in Pharma Manufacturing*, PHARMACEUTICAL TECH. (Sept. 29, 2016), <http://www.pharmtech.com/vision-3d-printing-pharma-manufacturing> [https://perma.cc/72U3-UGJS].

<sup>27</sup> See, e.g., *3-D Printed Organs Help Houston Doctors Train for Complicated Surgeries*, KTRK-TV (Dec. 14, 2016), <http://abc13.com/health/3-d-printed-organs-give-surgeons-practice-runs/1657014/> [https://perma.cc/LHZ5-47D3] (reporting on a Houston doctor who was able to complete a complex kidney surgery in less than half an hour after practicing on a 3D-printed replica beforehand).

<sup>28</sup> See, e.g., BIOBOTS <https://www.biobots.io> [https://perma.cc/G9U8-PH22] (providing quotes from industry leaders praising their company's desktop bioprinter for expanding accessibility of printing living tissue).

<sup>29</sup> See *About Organovo*, ORGANOVO, <http://organovo.com/about/about-organovo/> [https://perma.cc/XKM4-54G8] (outlining company's mission to provide printed tissues that may replicate human tissue for the purposes of drug testing); *A Tissue of Truths*, *supra* note 8 (“L'Oréal already grows about five square met[er]s of skin a year using older and slower technology. Bioprinting will permit it to grow much more, and also allow different skin types and textures to be printed.”); JOHN BERGIN,

approved drugs<sup>30</sup> and devices<sup>31</sup> created with the help of 3D printing. While most drugs are not yet patient or sub-population specific on a large scale, the technology has allowed for the creation of “devices unique to . . . specific patient[s].”<sup>32</sup> A recent example of this is FDA approval of Kymriah, a groundbreaking drug that “uses patients’ genetically altered immune cells to fight” leukemia in children and young adults.<sup>33</sup>

Among those who understand the promise of 3D printing, it is rare to find someone capable of defining the limits of its potential. Hull himself points out that 3D printing’s “traditional limits,” which include “material properties, speed, [and] making millions of things” will likely be less limiting in the very near future.<sup>34</sup> Likewise, industry expert Emil Ciurczak said “[t]he limits of 3D printing are merely the needs and imagination of the researchers modelling the products of 3D [printing].”<sup>35</sup>

### B. The Market for 3D-Printed Organs

Both the bioprinting community specifically and the pharmaceutical industry at large have taken great interest in the promise of 3D-printed organs. Startup companies committed to this area have emerged and survived, and American pharmaceutical giants such as Johnson & Johnson have taken notice.<sup>36</sup> This comes as no surprise considering that experts estimate the value of the 3D bioprinting market alone to be in the hundreds of millions of dollars

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BIOPRINTING: TECHNOLOGIES AND GLOBAL MARKETS 39 (2016) (citing Proctor & Gamble and BASF as other cosmetics companies who have partnered with the bioprinting industry for testing).

<sup>30</sup> See, e.g., Hope King, *First 3D-Printed Drug Approved by FDA*, CNN (Aug. 4, 2015), <http://money.cnn.com/2015/08/04/technology/fda-3d-printed-drug-epilepsy/> [https://perma.cc/L7NQ-6YXZ] (discussing the approval of Spritam, a 3D-printed drug, for treatment of epilepsy patients).

<sup>31</sup> See *Medical Applications of 3D Printing*, U.S. FOOD & DRUG ADMIN. (Dec. 21, 2016), <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/3DPrintingofMedicalDevices/ucm500539.htm> [https://perma.cc/4FZX-B5VC] (providing a list of commercially available 3D-printed medical devices, including guides to assist with proper surgical placements, implants and external prostheses).

<sup>32</sup> *Id.*

<sup>33</sup> Laurie McGinley & Carolyn Johnson, *FDA Clears First Gene-Altering Therapy—A Living Drug—For Childhood Leukemia*, WASH. POST (Aug. 30, 2017), [https://www.washingtonpost.com/news/to-your-health/wp/2017/08/30/fda-approves-first-of-its-kind-living-drug-for-childhood-leukemia/?utm\\_term=.a4db592cc7b6](https://www.washingtonpost.com/news/to-your-health/wp/2017/08/30/fda-approves-first-of-its-kind-living-drug-for-childhood-leukemia/?utm_term=.a4db592cc7b6) [https://perma.cc/V8US-9TTT].

<sup>34</sup> Ponsford & Glass, *supra* note 18; see also Tsai & Pham, *supra* note 3 (describing the future of 3D printing as “[e]verything and anything. Imagine waking up and printing yourself a breakfast with a customized nutritional profile based on your activity needs for the day.”).

<sup>35</sup> See *supra* note 26.

<sup>36</sup> See *A Tissue of Truths*, *supra* note 8 (“Johnson & Johnson . . . is so convinced that bioprinting will transform parts of medical practice that it has formed several alliances with interested academics and biotechnology firms.”).

already.<sup>37</sup> Furthermore, the market is growing at an annual rate of approximately forty-four percent, which puts market value estimates in the billions within five years.<sup>38</sup>

More broadly, twenty-six percent of manufacturing companies have already invested in 3D printing globally and that number is projected to climb to just under sixty percent by 2022.<sup>39</sup> The health care sector could benefit from following the manufacturing sector's example because productivity in the manufacturing sector has increased seventy-eight percent in the last fifteen years, while the health care sector has essentially remained stagnant at just six percent during that time.<sup>40</sup> While the ramp up of public investment in 3D printing was slow at the onset—with just \$300 million between 1987 and 2010—the pace and volume have increased significantly since then, with \$4 billion in public investment in the last five years and a projected \$10 billion more by 2025.<sup>41</sup> As a result, the value of the global 3D printing market is estimated to reach \$22.8 billion by 2022, which is “much faster than expected.”<sup>42</sup>

Industry reports note a list of important factors that currently act as “growth driving force[s]” for bioprinting, including the aging population, desire to move away from animal testing, clinical needs for wound care, and the continued improvement of the bioprinting field, among others.<sup>43</sup> On a larger scale, 3D printing also promises to be a substantial money saver for many players.<sup>44</sup>

With future economic projections in the billions, and industry giants from various sectors onboard, 3D printing is here to stay. The introduction of the viable and transplantable 3D-printed organ will come in our lifetime, backed by the world's brightest minds and the global economy's most formidable members. In the meantime, policymakers must construct a legal framework capable of supporting and regulating them upon their arrival. However, a preliminary hurdle remains between the economic and intellectual promise of 3D-printed organs and the construction of mechanisms to support their

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37 See BERGIN, *supra* note 29, at 7 (“The global bioprinting market is valued at an estimated \$295 million in 2016.”).

38 See *id.* (noting the “forecast value of \$1.8 billion by 2021” for bioprinting globally).

39 3D PRINTING MARKET OUTLOOK AND FORECASTS 2017–2022 22 (2016).

40 Stephanie Carlton, Member of the Governing Board for the Health Care Cost Institute, Remarks at The Future of American Health Care Panel Hosted by Wharton Public Policy Initiative (May 1, 2017).

41 See *supra* note 39, at 23.

42 *Id.* at 26, 33.

43 BERGIN, *supra* note 29, at 13.

44 See *supra* note 39, at 25 (“GE wants to bring more than 1000 3D printing machines online in the next 10 years and gain cost savings of \$3-\$5 billion.”).



introduction: the National Organ Transplant Act of 1984 (NOTA),<sup>45</sup> which, on its face, seems to proscribe paying for them as a federal crime.

## II. PAYING FOR 3D-PRINTED ORGANS IS “NOTA” FEDERAL CRIME

NOTA prohibits “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.”<sup>46</sup> First, let us dispose of the reference to interstate commerce. It is without debate that the mere promise of 3D-printed organs has already proven to not only affect interstate commerce, but to also be a “disruptive” force in the U.S. economy.<sup>47</sup> Therefore, I stipulate that 3D-printed organs, insofar as their effect on interstate commerce, fall within the law’s scope. Instead, “human organ” and “valuable consideration” are the terms that distinguish 3D-printed organs from NOTA’s intended arena.

### A. 3D-Printed Organs are Not “Human Organs”

NOTA defines “human organ” as “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.”<sup>48</sup> According to the Dictionary Act, which defines important terms used in the United States Code, “human” (therein referred to as “human being”) makes reference to members of the homo sapiens species who are “born alive at any stage of development.”<sup>49</sup> The corresponding regulations to NOTA also refer to organ donors as “human being[s],” consistent with the Dictionary Act.<sup>50</sup> Therefore, human, as used in NOTA, must be the adjective meaning *from a human being*.

If the Ninth Circuit serves as any indication, we can expect the courts will find no reason to construe the definition of organs differently, as it has confined the meaning to just the statutory text.<sup>51</sup> If this narrow construction

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<sup>45</sup> National Organ Transplant Act of 1984, 42 U.S.C. § 274e (2012).

<sup>46</sup> *Id.*

<sup>47</sup> See Tsai & Pham, *supra* note 3.

<sup>48</sup> 42 U.S.C. § 274e(c)(1) (emphasis added).

<sup>49</sup> Dictionary Act, 1 U.S.C. § 8 (2012).

<sup>50</sup> Definitions, 42 C.F.R. § 121.2 (2013).

<sup>51</sup> See *Flynn v. Holder*, 684 F.3d 852, 864-65 (9th Cir. 2012) (“The statute does not prohibit compensation for donations of blood [or] . . . peripheral blood stem cells. The [HHS] Secretary has not exercised regulatory authority to define blood or peripheral blood stem cells as organs. We therefore need not decide whether prohibiting compensation for such donations would be unconstitutional.”).

persists, it seems likely that the courts would uphold compensation for other transplantations that fall outside the scope of the text itself.

One of the most recent additions to the regulations' defined organs, the vascularized composite allograft,<sup>52</sup> comes closest to describing 3D-printed organs and tissues because they are "vascularized and require[] blood flow by surgical connection of blood vessels to function after transplantation; [and] contain[] multiple tissue types,"<sup>53</sup> just as 3D-printed organs do. However, a vascularized composite allograft must specifically come "from a human donor as an anatomical/structural unit" *and* be "minimally manipulated (i.e., processing that does not alter the original relevant characteristics of the organ . . . )."<sup>54</sup> 3D-printed organs are made solely from manipulated cells. As such, they clearly fail to conform with this definition.<sup>55</sup> Accordingly, organs that are printed, rather than those that are harvested from a human being, should fall outside the scope of NOTA-defined organs.

Moreover, even if 3D-printed organs do not fall outside the scope, the law itself unambiguously delegates power to Health and Human Services (HHS) to provide a regulatory definition of a human organ. As the agency that will be tasked with regulating 3D-printed organs, HHS regulators could resolve any doubt by explicitly defining 3D-printed organs for human transplantation as distinct from organs donated from other human donors.

A law is more than words in a vacuum, and the legislative history and context in which NOTA was passed are relevant. NOTA became law with bipartisan support, including support from President Reagan.<sup>56</sup> During the 1970s and 80s, "medical science improvements and the related demand for transplant organs prompted governments to search for new ways to increase the supply of organs for donation."<sup>57</sup> In the congressional hearings about

<sup>52</sup> See generally HEALTH RESOURCES & SERVICES ADMIN., VASCULARIZED COMPOSITE ALLOGRAFT (VCA) TRANSPLANTATION COMM., IMPLEMENT THE OPTN'S OVERSIGHT OF VASCULARIZED COMPOSITE ALLOGRAFTS (VCAS) 4 [https://optn.transplant.hrsa.gov/media/1118/05\\_vca\\_implementation.pdf](https://optn.transplant.hrsa.gov/media/1118/05_vca_implementation.pdf) [<http://perma.cc/ZZ29-W5VZ>] (describing Vascularized Composite Allograft Transplantation (VCA) as "transplants composed of several different kinds of tissues (i.e., skin, muscle, bone), such as those in the hand, arm, or face, transferred from donor to recipient as a single functional unit").

<sup>53</sup> §§ 121.2(1)–(2).

<sup>54</sup> §§ 121.2(3)–(5).

<sup>55</sup> See *United States v. Regenerative Scis., LLC*, 741 F.3d 1314, 1319 (D.C. Cir. 2014) (characterizing appellant's "autologous stem cell procedure," without FDA approval, as beyond the practice of medicine and subject to regulation by the Federal Food, Drug & Cosmetic Act); Frances H. Miller, *New Wine in Old Bottles, FDA's Role in Regulating New Technologies: Introduction*, in *FDA IN THE 21<sup>ST</sup> CENTURY* 434 (Holly Fernandez Lynch & I. Glenn Cohen eds., 2015) (discussing *Regenerative Sciences* in reference to the FDA's role in regulating new technologies).

<sup>56</sup> Ronald Reagan: *Statement on Signing the National Organ Transplant Act*, AM. PRESIDENCY PROJECT, <http://www.presidency.ucsb.edu/ws/?pid=39282> [<https://perma.cc/3HY3-9YLK>] (providing President Reagan's remarks that accompanied his signing NOTA, a bipartisan effort, into law).

<sup>57</sup> *Newman v. Sathyavaglswaran*, 287 F.3d 786, 794 (9th Cir. 2002).

NOTA, legislators agreed that “it is against our system of values to auction off life to the highest bidder” and the buying and selling of “parts of human beings” is unacceptable.<sup>58</sup> Then–veteran Representative Al Gore said that “Americans understand [that] . . . [t]hings are bought and sold. People are not, and parts of people shouldn’t be, either.”<sup>59</sup> Gore, a champion and lead author of NOTA, took this a step further to suggest that allowing for the purchase and sale of organs from human beings would be contrary to the ideals supporting the abolition of slavery because “[we] don’t want to invest property rights in human beings.”<sup>60</sup> Finally, Gore made an important distinction between organ donation and blood donation: “[T]he individual who donates blood suffers no harm”<sup>61</sup> and suffers only minimal invasion. Additionally, the doctor who draws the blood “isn’t violating the Hippocratic oath.”<sup>62</sup>

Applying this rationale to the context of 3D-printed organs leads to the opposite conclusion. To create a 3D-printed organ, a doctor need only inject a needle, much like that the process for drawing blood, to take a biopsy from the *same* person set to *receive* the printed organ. In that moment and thereafter, only one person must undergo an invasive procedure: the person who elected to receive his or her own printed organ. This is not a question of one person having the power to buy someone else’s life, but rather the idea that a patient may pay to use a part of his or her own body to, with the help of technology, heal. None of the ethical or human rights concerns associated with NOTA’s prohibition are present when organ transplants come from a printer.

In sum, neither the plain text of NOTA nor its legislative history suggests that this law is meant to prohibit the introduction and use of 3D-printed organs to save lives in contemporary society.

#### B. *Market Rate Reimbursement is Not “Valuable Consideration”*

Even if manufactured organs were considered human organs, since they originated as human cells, the “valuable consideration” creating concern for lawmakers was explicitly *not* the reasonable costs associated with the transplant.<sup>63</sup>

NOTA defines “valuable consideration” in the negative, as it expressly “does not include the reasonable payments associated with the removal, transportation, implantation, processing, preservation, quality control, and storage of a human organ or the expenses of travel, housing, and lost wages

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<sup>58</sup> *National Organ Transplant Act: Hearing on H.R. 4080 Before the Subcomm. on Energy and Commerce, 98th Cong. 128 (1983)* [hereinafter *Hearing on H.R. 4080*] (statement of Rep. Gore).

<sup>59</sup> *Id.* at 112.

<sup>60</sup> *Id.* at 129.

<sup>61</sup> *Id.*

<sup>62</sup> *Id.*

<sup>63</sup> See discussion *supra* Section II.A.

incurred by the donor . . . in connection with the donation of the organ.”<sup>64</sup> Applied to the 3D-printed organ process, the corollary to “reasonable payments associated” would be reimbursement for the manufactured organ and the time spent by providers to transplant it. Likewise, the “expenses of . . . the donor” could be compared with the costs associated with collecting the cells through biopsy, printing onto the relevant scaffolding, and growing them into a transplantable organ, fit for human use. Any necessary preparatory medical attention required by the patient could rationally be covered by this section as well.

While NOTA was being debated, experts in the field, such as the President of the American Society of Transplant Surgeons Dr. Oscar Salvatierra, Jr., expressed concern that individuals may “exploit people because they are in a desperate economic situation.”<sup>65</sup> It was for this reason that the exchange of valuable consideration for human organs was proscribed. It was *not* to suggest that the operations at stake should be done at a loss or without the ability of those involved to recuperate their costs. In fact, disallowing reimbursement at a fair or “reasonable” market rate would go against the other principal aim of the bill, which was to “promote organ transplantation.”<sup>66</sup>

The Ninth Circuit echoed this reasoning when it upheld the prohibition against paying for bone marrow in 2012, spending considerable time noting the “revolting” nature of commodifying physical parts of ourselves.<sup>67</sup> Plaintiffs in this case stipulated that their offer of \$3,000 in the form of housing subsidies, scholarships or charitable donations to induce registration in their bone marrow donation network would be valuable consideration under NOTA,<sup>68</sup> which has led some to believe that paying for 3D-printed organs would be similarly categorized, and therefore barred.<sup>69</sup> I disagree. Providing market rate reimbursement for this procedure, the materials used to create the organ, and the related preparatory treatment for the patient is consistent with how the health care field operates. Providing incentives to encourage donation is completely distinguishable from compensating those who are engaged with the provision of health care services in the same way that they are compensated for every other procedure and treatment they perform. Furthermore, the issue of paying *others* for parts of *their bodies* for

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<sup>64</sup> 42 U.S.C. § 274e.

<sup>65</sup> *Hearing on H.R. 4080*, *supra* note 58, at 233.

<sup>66</sup> *Supra* note 56.

<sup>67</sup> *Flynn v. Holder*, 684 F.3d 852, 861 (9th Cir. 2012).

<sup>68</sup> *See id.* at 856 (noting the company’s concession that their payment mechanisms were valuable consideration).

<sup>69</sup> *See* Katherine A. Smith, “Transplanting” *Organ Donors with Printers: The Legal and Ethical Implications of Manufacturing Organs*, 49 AKRON L. REV. 739, 768 (2016) (concluding that *Flynn*’s reasoning “suggest[s] that no compensation of any kind could be given in exchange for a bioprinted organ”).

transplantation into *someone else's body* is absent in the context of printed organs because the organ is grown and manufactured from cells of *the person receiving the new organ*.

Accordingly, reasonable market rate reimbursement for the time and resources expended in an organ transplantation executed with a bioprinted organ would not constitute valuable consideration in the way proscribed by federal law.

It would be preferable to preempt any potential litigation that may delay a life-saving operation by amending NOTA<sup>70</sup> or a new round of notice and comment rulemaking by HHS to clarify the scope of their regulations promulgated pursuant to NOTA; however, neither of these must necessarily predate the introduction of 3D-printed organs into the market if one adopts the understanding of NOTA that I offer here.

### III. 3D-PRINTED ORGANS FIT IN THE EXISTING FRAMEWORK OF THE FEDERAL FOOD DRUG AND COSMETICS ACT AND CAN BE REGULATED BY THE FDA

#### A. *The FDA Is the Appropriate Agency to Regulate 3D-Printed Organs*

The FDA's statutory mission is as simple as it is important: "to promote and protect the public health."<sup>71</sup> This explicitly applies to regulation of "cellular and tissue based products."<sup>72</sup> Accordingly, the FDA is the proper agency to vet, approve, and regulate these bioprinted organs once they are ready for human transplantation.

The Federal Food, Drug and Cosmetic Act (FDCA) gives the FDA the "authority to monitor and regulate the safety of food, drugs and cosmetics."<sup>73</sup> According to the available statutory definitions, 3D-printed organs could be regulated as drugs, medical devices, biologics, or any combination of the three, which could subject them to multiple sets of regulations. Manufactured organs fall within the ambit of FDCA governance, which will require greater consideration for the appropriate classification:<sup>74</sup> "Determining whether a product is a drug, device, cosmetic, or biologic, or a combination of these components can often be tricky. The classification determination depends

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<sup>70</sup> See *Flynn*, 684 F.3d at 862 (noting that "policy and philosophical choices are for Congress to make, not [the court]" in the context of finding rational basis for prohibiting compensation for the donation of human organs).

<sup>71</sup> U.S. FOOD & DRUG ADMIN., *THE FUTURE OF DRUG SAFETY-PROMOTING AND PROTECTING THE HEALTH OF THE PUBLIC* 17 (2007).

<sup>72</sup> See *infra* note 79 and accompanying text.

<sup>73</sup> 21 U.S.C. §§ 301, 321, 331–99 (2012).

<sup>74</sup> See *supra* note 55 (discussing *United States v. Regenerative Sciences*, in which the D.C. Circuit upheld a determination that autologous stem cell procedures fall within the scope of intended FDCA regulation and constitute actions beyond just medical practice).

mainly on the intended use, mode of action, and ingredients.”<sup>75</sup> I will explore this issue further later in this Section.

B. *3D-Printed Organs Will Be Regulated Differently  
Than Human Organs for Transplantation*

Pursuant to Section 361 of the Public Health Service Act (PHS Act) and its corresponding regulations, the “FDA has implemented a risk-based approach to the regulation of HCT/Ps [human cellular and tissue based products].”<sup>76</sup> The FDA has promulgated a list of requirements by which a product may qualify for an exception that subjects it only to regulation under Section 361 of the PHS Act.<sup>77</sup> I have established that manufactured organs are, by their very nature, not “minimally manipulated,”<sup>78</sup> but more importantly, the FDA has published guidance that includes a non-exhaustive list of what is not considered an HCT/P. In relevant part, it includes vascularized human organs, whole blood or blood components and extracted human products, including “cell factors.”<sup>79</sup> Of course, the regulations cannot

<sup>75</sup> Renu Lal, *Drug, Not a Drug, or More?*, FDA/CDER SBIA CHRON. 1 (Sept. 17, 2015), <https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/UCM462854.pdf> [<https://perma.cc/DY89-ACGK>].

<sup>76</sup> U.S. FOOD AND DRUG ADMIN., HOMOLOGOUS USE OF HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS: DRAFT GUIDANCE FOR INDUSTRY AND FDA STAFF 2 (2015) [hereinafter HOMOLOGOUS USE].

<sup>77</sup> Specifically:

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.

<sup>21</sup> C.F.R. § 1271.10 (2016).

<sup>78</sup> See *supra* note 54 (presenting the regulations’ definition of minimal manipulation); see also U.S. FOOD & DRUG ADMIN., MINIMAL MANIPULATION OF HUMAN CELLS, TISSUES, AND CELLULAR TISSUE-BASED PRODUCTS: DRAFT GUIDANCE FOR INDUSTRY AND FDA STAFF 2 (2014) [hereinafter MINIMAL MANIPULATION] (providing guidance and examples of minimal manipulation and illustrating that 3D-printed organs would have both structural and non-structural tissues).

<sup>79</sup> HOMOLOGOUS USE, *supra* note 76, at 2; MINIMAL MANIPULATION, *supra* note 78, at 2; see also Paul Gadlock, *HCT/P Regulation—351 vs 361 Products*, ARENT FOX LLP (Feb. 15, 2017), [http://www.pharmaconference.com/Attendee\\_Files-PDF/HCTP2\\_2017/13%20Gadiock%20](http://www.pharmaconference.com/Attendee_Files-PDF/HCTP2_2017/13%20Gadiock%20)

reflect a class of product that does not yet exist; however, it is easy to analogize to this list and conclude that 3D-printed organs would also not qualify for the exception. The guidance document states,

If an HCT/P does not meet the criteria in 21 CFR 21.1271.10(a), and the establishment that manufactures the HCT/P does not qualify for any of the exceptions in 21 CFR 21.1271.15, the HCT/P will be regulated as a drug, device, and/or biological product under the [FDCA], and/or section 351 of the PHS Act, and applicable regulations, including 21 CFR Part 21.1271.<sup>80</sup>

Therefore, 3D-printed organs will not be regulated as HCT/Ps.

### *C. 3D-Printed Organs Should be Regulated as Biological Products*

Section 351(i) of the PHS Act defines a “biological product” as “a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, *protein* (except any chemically synthesized polypeptide), or analogous product, . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings.”<sup>81</sup> Here, the key word is “protein:” the “bioink”<sup>82</sup> used to manufacture these organs necessarily will contain human proteins required to grow the human organ for transplantation.<sup>83</sup> Biologics are typically “complex mixtures that are not easily identified or characterized.”<sup>84</sup> It makes sense logically that part of our human biology would fall within the scope of biological product regulation and oversight.

The classification also makes sense by analogy to chimeric antigen receptor T cell products, more commonly known as CAR-T therapies. For example, in March 2017, Novartis announced that the FDA accepted its Biologics License Application filing and granted priority review for one of its CAR-T products, which are “manufactured for each individual patient using

<sup>80</sup> HCT/Ps vs. Biological Products.pdf [https://perma.cc/8MTT-Q4FS] (listing cultured cartilage and nerve cells, gene therapy products, and human cells used in therapy involving the transfer of genetic material as examples of products that the FDA “determined do not meet all of the criteria in 21 C.F.R. 21.1271.10(a) and are regulated as drugs and/or biological products”).

<sup>81</sup> MINIMAL MANIPULATION, *supra* note 78, at 2-3.

<sup>82</sup> Regulation of Biological Products, 42 U.S.C. § 262(i)(1) (2016) (emphasis added). See *infra* Section IV.D for intended-use analysis.

<sup>83</sup> See *supra* notes 19–22 (discussing bioink).

<sup>84</sup> See Morber, *supra* note 21 (“For 3D bioprinting, scientists fill the ink cartridges with cells and *proteins* instead of plastic.”) (emphasis added); Janice R. Hermann, *Protein and the Body*, OKLA. COOPERATIVE EXTENSION SERVICE, <http://pods.dasn.okstate.edu/docushare/dsweb/Get/Document-2473/T-3163web.pdf> [https://perma.cc/2BG3-535Q] (noting that “body organs are all made from protein”).

<sup>85</sup> *What are “Biologics” Questions and Answers*, U.S. FOOD & DRUG ADMIN. (Aug. 5, 2015), <https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cber/ucm133077.htm> [https://perma.cc/FCF3-ZDYS].

their own T cells.”<sup>85</sup> This treatment is being hailed as “‘a living drug’ that powerfully bolsters the immune system to shut down . . . disease.”<sup>86</sup> Although it may be a less conventional setup for a combination product,<sup>87</sup> these printed organs will very likely be subject to both biologic product regulations and drug regulations because “[biological] products subject to the PHS Act also meet the definition of drugs under the [FDCA].”<sup>88</sup>

#### D. 3D-Printed Organs Should Also Be Regulated as Drugs

In its relevant terms, the FDCA defines the term “drugs” as “articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and . . . articles (other than food) intended to affect the structure or any function of the body of man or other animals.”<sup>89</sup> This definition can be broken down into its two critical components: (1) intended use, and (2) effect on the structure and function of the body.

While it does feel peculiar to characterize an organ as a drug, the manufactured organ’s intended use matches that of a drug. Under HHS regulations, promulgated pursuant to the authority delegated in the FDCA, intended use is the “‘objective intent’ of the persons legally responsible for the labeling of drugs. The intent is determined by such persons’ expressions or may be shown by the circumstances surrounding the distribution of the article.”<sup>90</sup> The 3D bioprinting industry is not yet at the labeling, marketing, and distribution stages, so we cannot yet rely on these sources to inform the organs’ intended use. However, “[i]ntended use may also be established by *consumer perception* of a product’s reputation. In other words, why is the consumer buying the product and what does the consumer expect it to do?”<sup>91</sup> Even though 3D-printed organ development is in its nascent stages, we can answer this question based on decades of experience with human organ

<sup>85</sup> *Novartis Announces First CAR-T Cell Therapy BLA for Pediatric and Young Adult Patients with r/r B-cell ALL Granted FDA Priority Review*, NOVARTIS (Mar. 29, 2017), <https://www.novartis.com/news/media-releases/novartis-announces-first-car-t-cell-therapy-bla-pediatric-and-young-adult> [<https://perma.cc/UR9X-T9TL>].

<sup>86</sup> Denise Grady, *F.D.A. Panel Recommends Approval for Gene-Altering Leukemia Treatment*, N.Y. TIMES (July 12, 2017), [https://www.nytimes.com/2017/07/12/health/fda-novartis-leukemia-gene-medicine.html?mwrsm=Email&\\_r=0](https://www.nytimes.com/2017/07/12/health/fda-novartis-leukemia-gene-medicine.html?mwrsm=Email&_r=0) [<https://perma.cc/BNM2-G32X>].

<sup>87</sup> See generally Lal *supra* note 75, at 2 (generalizing that a product may be a combination product if it is “composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product”).

<sup>88</sup> *Frequently Asked Questions About Therapeutic Biological Products*, U.S. FOOD & DRUG ADMIN. (July 7, 2015), <https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/ucm113522.htm> [<https://perma.cc/8SNQ-TB3J>]; see also 42 U.S.C. § 262(j) (2012) (discussing the applicability of the FDCA to biological products).

<sup>89</sup> 21 U.S.C. §§ 321(g)(1)(B)–(C) (2012).

<sup>90</sup> 21 C.F.R. § 201.128 (2017).

<sup>91</sup> Lal, *supra* note 75, at 2.



transplants. Any patient seeking an organ transplant would almost necessarily be suffering from a medical ailment, whether it be a disease compromising the function of the organ to be transplanted, or a failure of the organ itself, such that it needs a replacement. Therefore, it is difficult to imagine a scenario in which someone would opt for an organ transplant for any reason other than cure, mitigation, treatment, or prevention of a disease or injury.

This second point seems fairly self-evident, but it bears mentioning given the strict regulatory environment of the health care sector. Organs compose *the* core structure and function of our bodies; a replacement organ will continue to do so, whether it comes from a donor or the patient's own cells that have undergone the additive manufacturing process. People seek organ transplants when their body is malfunctioning at its most basic level. The transplantation of a new, 3D-printed organ, would be intended to correct this malfunction and allow for improved internal bodily structure, which, in turn, would allow for better bodily functioning.

#### E. 3D-Printed Organs Should Not Be Classified as Medical Devices

The FDCA definition of medical “devices” shares the two provisions contained in the FDCA definition of drugs: (i) intended use and (ii) effect on the structure of function of the body.<sup>92</sup> However, the statute specifically notes that a medical device is an “instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory,” which has the same intended use as drugs and biological products—or the same intended use as drugs and biological devices—but “does *not* achieve its primary intended purposes through chemical action within or on the body of man . . . and which is not dependent upon being metabolized for the achievement of its primary intended purposes.”<sup>93</sup> Therefore, as the body functions by means of the chemical actions and reactions that occur within the organs, and a transplanted organ's primary intended purpose would be to accomplish these actions more effectively than the organ it replaced, a 3D-printed organ falls outside the scope of this definition.<sup>94</sup>

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<sup>92</sup> See *supra* text accompanying note 89 (defining the term “drugs”).

<sup>93</sup> 21 U.S.C. § 321(h) (2012) (emphasis added).

<sup>94</sup> See JOSEPH JONES, MEDICAL AND SURGICAL MEMOIRS 136 (1876) (“[I]f the amount of blood circulating through any organ and the chemical actions are too great, how can they be regulated without some medium of communication, and some means of regulating the chemical and physical actions?”); JOHN GRAY MCKENDRICK, A TEXTBOOK OF PHYSIOLOGY: SPECIAL PHYSIOLOGY OF ORGANS 439 (1888) (“Chemical Actions.—As has been frequently pointed out, most of the operations occurring in the tissues involve chemical changes, principally those of oxidation.”). I would like to acknowledge and thank medical students Monica Gupta (Georgetown University) and

While some expect that the implanted nature of printed organs will lead the FDA to classify them as devices, the statutory language, and analogies to manufactured organs—which are currently regulated as devices—do not support this classification. In the FDA Product Classification Database for Devices, there are only fifty-six classifications of devices that qualify as implantable and life-supporting or sustaining.<sup>95</sup> As one may expect from the list of descriptors in the statute, most of these devices are made of non-bioabsorbable material (often metal).<sup>96</sup> This is a distinguishing factor from the ink made of a person's own biological material or cells in the manufactured organs. Furthermore, the *non*-metal implants may be absorbable, which is also unlike how an organ reacts to implantation.<sup>97</sup> Rather, an organ *functions* as part of the body and with material directly from the body. Finally, perhaps one of the closest analogies that can be drawn is to replacement valves derived from donated cadaver or animal tissue.<sup>98</sup> These valves are known as “more than minimally manipulated allograft[s],” which are intended for use in the “replacement of diseased, damaged, malformed, or malfunctioning native or prosthetic . . . valves.”<sup>99</sup> This sounds analogous to the manufactured organ process and intended use; however, there is one critical difference. These valves were approved under the Humanitarian Device Exemption (HDE), which was created as a pathway for products “intended for diseases or conditions that affect small (rare) populations.”<sup>100</sup> Pursuant to Section 3052

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Mike Kitchens (University of Pennsylvania) for the background they provided in this area and their confirmation that organs' chemical actions are common knowledge in the relevant communities.

<sup>95</sup> *Implanted Device Life Sustain/Support Device Search Results*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpd/classification.cfm> [https://perma.cc/KKD3-WA3L].

<sup>96</sup> See, e.g., *Device: Synergy*, NAT'L INST. HEALTH: NAT'L LIBR. MED., <https://accessgudid.nlm.nih.gov/devices/08714729840909> [https://perma.cc/R728-GDVJ] (describing the characteristics of a “sterile non-bioabsorbable metal tubular mesh structure covered with a non-bioabsorbable polymer and a drug coating that is designed to be implanted . . .” with FDA classification as a device).

<sup>97</sup> See, e.g., *Product Classification for Absorbable Coronary Drug-Eluting Stent*, FDA ACCESS DATA, <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=1049> [https://perma.cc/VC54-SJHN] (describing an “absorbable scaffold with a drug coating placed via a delivery catheter . . . [that] [p]rovides *mechanical* support to the treated artery . . . and then gradually dissolves and is absorbed by the body” with FDA classification PNY (emphasis added)).

<sup>98</sup> See generally *Heart Valve Replacement*, ST. JUDE MED. (Nov. 7, 2016), <https://www.sjm.com/en/patients/heart-valve-disease/treatment-options/heart-valve-replacement?clset=af584191-45c9-4201-8740-5409f4cf8bdd%3ab20716c1-c2a6-4e4c-844b-dodd6899eb3a> [https://perma.cc/6TYB-ERCH] (describing tissue heart valves that “are made from animal or human tissues . . . . Once the tissue is removed from the animal or human donor, it is chemically treated to preserve the tissue and prevent immunologic reactions after it is placed in a patient.”).

<sup>99</sup> *Product Classification*, U.S. FOOD & DRUG ADMIN. (Sept. 4, 2017), <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=1047> [https://perma.cc/Q5UZ-8PNT].

<sup>100</sup> *Humanitarian Device Exemption*, U.S. FOOD & DRUG ADMIN. (June 16, 2017), <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/Pre>

of the recently passed 21st Century Cures Act, a rare disease or condition is one that occurs in “not more than 8,000 individuals in the United States per year.”<sup>101</sup> As the current waitlist for a donor organ is about 118,000 people long, bioprinted organs clearly do not qualify for this statutory exception.<sup>102</sup>

In sum, even products that appear similar to products that the FDA has determined to be “devices” are distinguishable from 3D-printed organs in important ways. Additionally, as noted above in the discussion of the statutory language itself, no matter how similar these products are, they do not appear to achieve their *primary intended purpose* through *chemical action* within the body. The current statutory and regulatory language does not mandate the regulation of 3D-printed organs as medical devices.

*F. Bioprinted Organs Manufacturers Will Be Subject to Current Good Manufacturing Practices and Current Good Tissue Practices*

The FDA has taken great care to outline the minimum requirements with which drug and HCT/P manufacturers must comply. These are known as current Good Manufacturing Practices (cGMPs), which are applicable to the facilities that print the organs, and current Good Tissue Practices (cGTPs), which are applicable to the facilities that extract and handle the biopsied human cells.<sup>103</sup> Failure to comply with cGMPs or cGTPs would result in the manufactured organ being classified as “adulterated,” which is a “prohibited act” under the FDCA.<sup>104</sup> Furthermore, these regulations governing cGMPs and cGTPs are intended to complement each other to the fullest extent possible. If and only if there is a conflict between the regulations, “the regulation more specifically applicable to the [drug product or product] in question shall supersede the more general.”<sup>105</sup> It remains to be seen which regulation the FDA will determine to be most “specifically applicable.” This

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marketSubmissions/HumanitarianDeviceExemption/default.htm [https://perma.cc/WBH6-HDBB] (citing § 3052 of the 21st Century Cures Act, Pub. L. No. 114-255).

<sup>101</sup> *Id.*

<sup>102</sup> See *supra* notes 10–12 and accompanying text (discussing the organ shortage in the United States).

<sup>103</sup> See Current Good Manufacturing Practice for Finished Pharmaceuticals, 21 C.F.R. § 211 (2015) (outlining cGMPs for drugs); Biological Products: General, 21 C.F.R. § 600 (2012) (discussing cGMPs for biological products).

<sup>104</sup> See Status of Current Good Manufacturing Practices, 21 C.F.R. § 210.1(b) (2016) (“The failure to comply with any regulation set forth in this part . . . in the manufacture, processing, packing, or holding of a drug shall render such drug to be adulterated under . . . the act, and such drug . . . shall be subject to regulatory action.”); see also Adulterated Drugs and Devices, 21 U.S.C. § 351 (2016) (outlining when a drug or device shall be deemed adulterated).

<sup>105</sup> 21 C.F.R. § 211.1 (2016); see also Current Good Tissue Practice Requirements, 21 C.F.R. § 1271.150(d) (2016) (“In the event that a regulation in part 1271 of this chapter is in conflict with a requirement in parts 210, 211, or 820 of this chapter, the regulations more specifically applicable to the product in question will supersede the more general.”).

determination is likely made based on the manufactured organs' "primary mode of action."<sup>106</sup>

The first, second, and third enumerated "prohibited acts" in the FDCA refer to "adulterated" drugs, suggesting that preventing the introduction of adulterated drugs is a high priority for the FDA.<sup>107</sup> It is important for drug producers to keep in mind that the smallest penalty for violating the FDCA's prohibited acts is a misdemeanor.<sup>108</sup> "Any person who violates a provision of section 331 of this title [the prohibited acts] shall be imprisoned for not more than one year or fined not more than \$1,000, or both" for their first, non-willful violation.<sup>109</sup> The penalty increases significantly for willful violations (with the intent to defraud or mislead) or a violation subsequent to a prior conviction for committing a prohibited act.<sup>110</sup> For the latter violations, a guilty person would be subject to up to three years in prison, a maximum fine of \$10,000, or both.<sup>111</sup>

The absence of an intent requirement in the first subpart of this penalties section gives the statute serious bite because it is, at a minimum, a strict liability misdemeanor. In other words, even an accidental violation of one cGMP could technically result in a misdemeanor conviction.<sup>112</sup> In the case of intent or multiple violations, the violating party faces a felony charge. There are two important notes about these penalties. First, the penalties are not per person or per entity that violates the prohibited acts section of the FDCA. Rather, these penalties are assessed "per occurrence," so the sum of the civil monetary penalties associated with convictions adds up quickly.<sup>113</sup>

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<sup>106</sup> *Frequently Asked Questions About Combination Products*, U.S. FOOD & DRUG ADMIN. (Oct. 20, 2016), <https://www.fda.gov/combinationproducts/aboutcombinationproducts/ucm101496.htm> [<https://perma.cc/5LB9-74A5>]; *see also* 21 C.F.R. § 3.2(m) (2017) ("Primary mode of action is the single mode of action of a combination product that provides the most important therapeutic action in the combination product . . . [which is] the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.").

<sup>107</sup> Prohibited Acts, 21 U.S.C. §§ 331(a)–(c) (2012). The prohibited acts include:

(a) [t]he introduction or delivery for introduction . . . of any . . . drug . . . that is adulterated or misbranded. (b) The adulteration or misbranding of any . . . drug (c) The receipt . . . of any . . . drug . . . that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise.

*Id.*

<sup>108</sup> The penalties for violating the FDCA apply equally to the individuals and the entities through which they act. *See* Dictionary Act: Words denoting number, gender, and so forth, 1 U.S.C. § 1 (2012) (clarifying that "the words 'person' and 'whoever' include corporations, companies, associations, firms, partnerships, societies, and joint stock companies, as well as individuals").

<sup>109</sup> 21 U.S.C. § 333(a)(1) (2013).

<sup>110</sup> § 333(a)(2).

<sup>111</sup> *Id.*

<sup>112</sup> Given prosecutorial discretion as well as the lack of government resources, the likelihood that the government would bring that case seems small.

<sup>113</sup> *Amarin Pharma, Inc. v. U.S. Food & Drug Admin.*, 119 F.Supp. 3d 196, 203 (S.D.N.Y. 2015).

Second, and indisputably more important to all companies that provide any kind of health care service or product, is the threat of exclusion from government-sponsored health programs, such as Medicare and Medicaid. According to former Representative Allyson Schwartz, the government pays for approximately fifty percent of health care in this country,<sup>114</sup> so exclusion from these government-funded programs would be seriously damaging to companies involved in the health care sector. The Office of the Inspector General “has the authority to exclude individuals and entities from [f]ederally funded health care programs,” pursuant to the Social Security Act.<sup>115</sup> The statutory minimums vary depending on the nature and amount of the offenses.

In addition to the many, meticulously detailed requirements for cGMPs, creators of 3D-printed organs will also likely be subject to current Good Tissue Practices (cGTP),<sup>116</sup> because the organs are “tissue-based product[s].”<sup>117</sup> Establishments that manufacture tissue-based products “that are regulated as drugs, devices, and/or biological products” under the FDCA are required to “register and list” their tissue-based products following the procedures promulgated under 21 C.F.R. § 207, regulating the registration and listing of human drugs.<sup>118</sup>

An important subpart of cGTPs is the Donor Eligibility Requirements.<sup>119</sup> However, as the tissue used to grow the new, manufactured organ would be both biopsied from and received by the same individual, 3D-printed organs would fall in the specific “Autologous Use” exception to these regulations.<sup>120</sup> Accordingly, they will not be subject to the rigorous testing requirements meant to protect against the spread of communicable disease. This is a rational and efficient carveout by the FDA, because testing someone’s tissue before reinserting it into his or her own body would, of course, not serve the purpose of preventing the spread of disease. Thus, the only relevant requirements from this subsection regarding donor eligibility would be those

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<sup>114</sup> Allyson Schwartz, CEO of the Better Medicare Alliance; Former Member of the House of Representatives, Panelist at the Wharton Public Policy Initiative Talk about The Future of American Health Care (May 1, 2017).

<sup>115</sup> *Exclusions: Background Information*, OFF. INSPECTOR GENERAL, <https://oig.hhs.gov/exclusions/background.asp> [<https://perma.cc/UJD8-RJ8Y>] (explaining OIG exclusion authority and discretion).

<sup>116</sup> Current Good Tissue Practice, 21 C.F.R. §§ 1271.145–320 (2017) (describing the elements of current good tissue practice).

<sup>117</sup> Applicability of Current Good Manufacturing Practice Regulations, 21 C.F.R. § 210.2(a) (2017).

<sup>118</sup> Human Cells, Tissues, and Cellular and Tissue-Based Products, 21 C.F.R. § 1271 (2017).

<sup>119</sup> See generally 21 C.F.R. §§ 1271.45–90 (2017) (describing donor eligibility requirements under cGTPs).

<sup>120</sup> See Are There Other Exceptions and What Labeling Requirements Apply? 21 C.F.R. § 1271.90(a) (2016) (clarifying that there is no requirement to make a donor-eligibility determination or perform donor screening/testing when the relevant “cells and tissues” are “for autologous [involving one individual as both donor and recipient] use”).

governing labeling to ensure the person gets the organ grown from his or her own cells.<sup>121</sup>

Technically, according to the defined scope of this chapter of federal regulations, certain regulations apply to human tissue used for transplantation and to establishments or individuals involved in the “screening, testing, processing, storage, or distribution” of such.<sup>122</sup> However, tissue, herein referred to as “human tissue,” is defined as

any tissue derived from a human body and recovered before May 25, 2005, which: (1) [i]s intended for transplantation to *another* human . . .; (2) [i]s recovered, processed, stored, or distributed by methods that do not change the tissue function or characteristics; (3) [i]s not currently regulated as a human drug, biological product, or medical device; (4) [e]xcludes . . . vascularized human organ[s] . . .<sup>123</sup>

3D-printed organs do not fit this definition and therefore fall outside of its scope.

As with all FDA-regulated bodies, manufacturers of tissue-based products must allow for FDA inspection at the agency’s discretion.<sup>124</sup> In reality, it is rare for a facility to come out of an inspection without any observations that require remediation,<sup>125</sup> and consequences of an FDCA violation can vary. However, these penalties can be quite significant, and can go so far as to immediately shut down manufacturing.<sup>126</sup> This would render the 3D printing of any organs in queue incomplete until further notice, which could have major, life-altering or ending consequences for the patients who await these transplants and/or serve as the death knell for the additive manufacturing company at issue. However, holding these companies to the FDA’s rigorous

<sup>121</sup> See § 1271.90(c) (“As applicable, you must prominently label a [tissue-based product] . . . as follows: (1) FOR AUTOLOGOUS USE ONLY, if it is stored for autologous use. (2) NOT EVALUATED FOR INFECTIOUS SUBSTANCES, unless you have performed all otherwise applicable screening and testing . . .” (internal quotation marks omitted)).

<sup>122</sup> Human Tissue Intended for Transplantation, 21 C.F.R. § 1270.1(a) (2017).

<sup>123</sup> *Id.* at 792 (emphasis added).

<sup>124</sup> Inspections, 21 C.F.R. § 1271.400 (2017) (explaining that the FDA possesses total discretion in the time, manner, and frequency of inspections of manufacturer facilities, and further that the FDA’s representatives “may use other appropriate means to record evidence of observations during inspections”).

<sup>125</sup> See, e.g., Warning Letter from Marisa Heayn, Consumer Safety Officer, U.S. Food & Drug Admin. to Roger J. Hinton, Managing Dir., Porton Biopharma Ltd. (Jan. 19, 2017), <https://www.fda.gov/iceci/enforcementactions/warningletters/2017/ucm538105.htm> [<https://perma.cc/N25W-5ADN>] (listing several violations after inspecting Porton Biopharma’s drug manufacturing facility).

<sup>126</sup> See Orders of Retention, Recall, Destruction, and Cessation of Manufacturing, 21 C.F.R. § 1271.440(a)(3) (2017) (describing that the FDA’s most severe penalty for noncompliance with cGTPs is “an order to cease manufacturing until compliance with the regulations of this part has been achieved. When FDA determines there are reasonable grounds to believe there is a danger to health, such order will be effective immediately . . .”).

benchmarks is appropriate in the context of printing something as critical as an entire organ because any lower standard could present extraordinary danger or further complications for the patients who need these transplants.

#### IV. ETHICAL CONSIDERATIONS FOR TRANSPLANTING 3D-PRINTED ORGANS

Accepting my proposition that 3D-printed organs are well on their way, and that the existing legal and regulatory framework has the tools to make itself ready for their arrival, we are left to question the ethical permissibility of using these manufactured organs for transplantation into humans, while lacking significant safety and efficacy data. The consideration of ethical challenges presented by transplantation of 3D-printed organs raises more questions than answers at this point in the technology's development and is a vast area, worthy of its own Comment; however, there are a few aspects of manufactured organs to which researchers and health care providers ought to pay careful attention as these organs evolve from new, experimental products to a more commonplace set of treatment options. I raise them here for further consideration.

##### A. *There is No Applicable Constitutional Right to Access Unapproved 3D-Printed Organs*

Pursuant to the famous *Abigail Alliance* case, there is no constitutional right to access unapproved drugs.<sup>127</sup> According to the D.C. Circuit, this right was neither fundamental nor deeply rooted in the nation's history and traditions (using the *Glucksberg* standard),<sup>128</sup> but I challenge others interested in this field to consider whether organ transplantation is distinguishable, due to the longer history of organ transplantation in this country. Congress may be trying to pass legislation to provide greater access to experimental treatments for the terminally ill, as many states have,<sup>129</sup> but some are dubious that this is the proper solution to help this population.<sup>130</sup> Perhaps the FDA

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<sup>127</sup> *Abigail All. for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 711 (D.C. Cir. 2007) (en banc).

<sup>128</sup> Hyman, Phelps & McNamara, P.C., *D.C. Circuit Court Rules in Abigail Alliance Case; Affirms District Court Ruling That There is No Fundamental Right of Access to Experimental Drugs for the Terminally Ill*, FDA LAW BLOG (Aug. 7, 2007, 1:41 PM), [http://www.fdalawblog.net/fda\\_law\\_blog\\_hyman\\_phelps/2007/08/dc-circuit-cour.html](http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2007/08/dc-circuit-cour.html) [https://perma.cc/J84G-5B6T].

<sup>129</sup> See *Ohio Becomes 33<sup>rd</sup> State to Adopt Right to Try Law for Terminally Ill*, GOLDWATER INST. (Jan. 5, 2017), <http://www.goldwaterinstitute.org/en/work/topics/healthcare/right-to-try/ohio-becomes-33rd-state-to-adopt-right-to-try-law/> [https://perma.cc/2E9C-QM5J] (reporting that thirty-three states have passed right-to-try laws).

<sup>130</sup> See generally Alison Bateman-House, Kelly McBride Folkers, & Arthur Caplan, 'Right to Try' Won't Give Patients Access to Experimental Drugs. Here's What Will HEALTH AFF. BLOG (May 3, 2017),

will allow 3D-printed organs to enter the market through the Expanded Access for Investigational New Drug (IND) pathway<sup>131</sup> or another exception, but this would likely require updates or amendments to the current frameworks. How to do this well, let alone most effectively, is a topic for further research. What is clear is that placebo-controlled clinical trials are clearly not ethically permissible because they would involve withholding organ transplants from those who need them or subjecting perfectly healthy people to risky organ transplants that they do not need. Additionally, animal trials are already underway;<sup>132</sup> but it remains to be seen whether the FDA will accept data from these investigations. What the FDA may allow is comparative studies. For kidneys, this may mean comparing human organ transplantation with manufactured organ transplantation or even comparing dialysis treatment with manufactured organ transplantation. Additionally, such a comparative study would require the Agency to approve a trial that, by design, cannot be blinded because of the differing timing, processes, and treatments associated with each of the procedures.

Despite the uncertainty, there is historical evidence that when a population has no other option, risk tolerance in the absence of safety and effectiveness data is higher than in any other situation, and the FDA may be willing to develop new frameworks to support introduction of a lifesaving treatment. For example, during the Ebola epidemic, World Health Organization (WHO) experts concluded “that it was ethical to offer non-registered experimental interventions to Ebola patients, conditional on the collection of evidence to inform the broader community on their efficacy.”<sup>133</sup> Just because diseases affecting organ function or failure are not typically

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<http://healthaffairs.org/blog/2017/05/03/right-to-try-wont-give-patients-access-to-experimental-drugs-heres-what-will/> [<https://perma.cc/NDK7-PMUX>] (explaining why right to try laws will not increase access to experimental drugs and exploring other potential avenues through which that goal might be achieved).

<sup>131</sup> See generally Expanded Access to Investigational Drugs for Treatment Use, 74 Fed. Reg. 40,900 (Aug. 13, 2009) (clarifying the 1987 regulations that expanded access to investigational, new drugs for treatment).

<sup>132</sup> See, e.g., Serenitie Wang & Katie Hunt, *Chinese Company Implants 3-D Printed Blood Vessels into Monkeys*, CNN (Jan. 10, 2017), <http://www.cnn.com/2017/01/10/health/china-3d-printed-blood-vessels/> [<https://perma.cc/E6BP-D5SW>] (“Chinese scientists working for Sichuan Revotek have successfully 3-D printed blood vessels and implanted them in rhesus monkeys . . . It is a major step on the road to mass printing human organs for transplants.”).

<sup>133</sup> *Compassionate Use of Experimental Treatments for Ebola Virus Disease: Outcomes in 14 Patients Admitted from August to November, 2014*, WORLD HEALTH ORG., [http://www.who.int/medicines/ebola-treatment/outcomes\\_experimental\\_therapies/en/](http://www.who.int/medicines/ebola-treatment/outcomes_experimental_therapies/en/) [<https://perma.cc/CYC7-5GF6>]; see also *infra* note 135 (discussing the new frameworks developed by the WHO in order to support the introduction of a lifesaving treatment for Ebola).



infectious does not mean the situation here is any less urgent, as evidenced by the organ transplant waiting lists.<sup>134</sup>

### B. *Perhaps Money Can Buy Organs*

With every emerging technology, it is almost always those with the most financial resources and influence that learn about new developments first and have access before everyone else.<sup>135</sup> 3D-printed organs will likely be no exception. Given the high-tech nature of the process, news of its arrival is likely to start at the top for those with the greatest access to industry developments and with the highest levels of education and resources. Accordingly, the first patients in the door asking to have a manufactured replacement organ will be those who have been informed that the possibility exists. Of course, this uneven access poses ethical problems because there are fairer ways to determine who gets the first manufactured organs than by wealth, industry access, or education level.

The FDA response in its final rule regarding Expanded Access to Investigational Drugs for Treatment and Use addressed the issue of access in two important ways. First, it noted the likelihood that demand will exceed supply of these investigational drugs and that access determinations “should be as equitable as reasonably possible.”<sup>136</sup> Rather than attempt to set standards to apply to all INDs, the FDA took the pragmatic approach to allow these analyses to be done on a “case specific” basis.<sup>137</sup> As part of this process, “[the] FDA believes it is advisable” to undertake consultation with “relevant patient or disease advocacy organizations, professional societies, and other affected constituencies to devise the most appropriate mechanism for allocating a limited drug supply in a specific situation.”<sup>138</sup> In this case, the Organ Procurement and Transplantation Network, a “public–private partnership that links all professionals involved in the U.S. donation and transplantation

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<sup>134</sup> See *supra* notes 9–11 and accompanying text (discussing organ waitlists and the organ shortage).

<sup>135</sup> See Adrienne LaFrance, *Technology, the Faux Equalizer*, ATLANTIC (Mar. 31, 2016), <https://www.theatlantic.com/technology/archive/2016/03/half-full-tech/476025/> [<https://perma.cc/7VE9-SW4M>] (“New technologies are for the elite who can afford them” (quoting Judith Donath, author of *THE SOCIAL MACHINE: DESIGNS FOR LIVING ONLINE*)); see also Susan Donaldson James, *Who Gets Ebola Drugs? AIDS, Dialysis and Cancer ‘Cures’ Point the Way*, NBC NEWS (Aug. 19, 2014), <http://www.nbcnews.com/storyline/ebola-virus-outbreak/who-gets-ebola-drugs-aids-dialysis-cancer-cures-point-way-n181891> [<https://perma.cc/G8U7-HKZW>] (raising ethical questions about the distribution of Ebola drugs).

<sup>136</sup> 74 Fed. Reg. 40,904 (Aug. 13, 2009).

<sup>137</sup> *Id.*

<sup>138</sup> *Id.* at 40,905.

system,” established by NOTA, should be involved.<sup>139</sup> These members have the most experience managing organ waitlists and prioritization among very sick and vulnerable groups of people and have already developed thoughtful and robust systems to determine how best to allocate organs and in what order.<sup>140</sup> The ethical challenges associated with what factors one can permissibly include in these calculations are endless, and they should be left to those with the most expertise and the least susceptibility to bias in the process.

Second, the FDA acknowledges the reality that, with the “investigational” label, insurance companies are unlikely to pay for these transplantations, despite the agency’s hope that the companies “make well-reasoned reimbursement decisions that will not impinge on the availability of investigational drugs for treatment use.”<sup>141</sup> Unfortunately, the FDA “has no inherent authority to dictate” any requirements for insurance and other third party payers’ reimbursement policies.<sup>142</sup> The predictable consequence is that, if insurance companies decide not to reimburse for manufactured organ transplants, access would likely be foreclosed for “some patients (e.g., those who lack the financial resources to pay out-of-pocket).”<sup>143</sup>

As such, perhaps financial resources and the access they provide will be inescapable factors in determining who gets the first 3D-printed organs, and ultimately which populations will have the most lives saved by this new technology, despite the fact that experts in the field have developed fairer ways to allocate such precious resources. Eventually, the issue presented by greater demand than supply of printers to manufacture new organs will fade as the printing process gets faster and more printers are made available, but this challenge merits considerable attention and every possible safeguard in the meantime. The FDA subtly tipped its hand regarding its views on this matter in their responses to comments about the proposed rule. It explicitly took “no position on how the terms ‘reasonable,’ ‘necessary,’ or ‘medically necessary’ in health insurance contracts should be interpreted” for INDs.<sup>144</sup> In other words, the FDA seems to be challenging the insurers to come out in favor of coverage for these INDs when they are “necessary,” even though they are technically still investigational.

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<sup>139</sup> *About the Organ Procurement and Transplantation Network (OPTN)*, U.S. DEP’T OF HEALTH & HUM. SERVS., <https://optn.transplant.hrsa.gov/governance/about-the-optn/> [<https://perma.cc/U4XH-55G6>].

<sup>140</sup> *See, e.g., Organ Procurement and Transplantation Network Allocation Calculators*, U.S. DEP’T OF HEALTH & HUM. SERVS., <https://optn.transplant.hrsa.gov/resources/allocation-calculators/> [<https://perma.cc/P4TT-XKWX>] (providing access to and explanation of the formulas used to determine appropriate allocations of donated organs to those on the transplant waiting lists).

<sup>141</sup> 74 Fed. Reg. 40,907 (Aug. 13, 2009).

<sup>142</sup> *Id.*

<sup>143</sup> *Id.*

<sup>144</sup> *Id.*

C. *Will Insurers Ever Cover a Procedure to Keep Sick Beneficiaries Alive Longer?*

While insurers have long refused to cover treatments that have yet to be fully approved by the FDA,<sup>145</sup> it is unclear whether they will, without legal requirement, decide to cover 3D-printed organs even after they have achieved full approval. Those who will seek bioprinted organs will be extremely sick. From the insurers' perspective, this is their most expensive population, and, *economically speaking*, it is better for business when these people pass away because continuing to finance their treatment can be incredibly expensive.<sup>146</sup> With these two data points, it seems directly averse to insurers' financial interests to substantially extend a very sick beneficiary's life by covering a bioprinted organ. Hopefully the legislative framework will not lag too far behind the technological advances in this field, such that 3D-printed organs will rise to become the standard of care or necessary, lifesaving treatments that insurers will have no choice but to include on their formularies.

One initial exception to this financial disincentive might be kidneys for dialysis patients: "economist Mark Schnitzler and transplant surgeon Arthur Matas estimated that each kidney transplant saves society \$90,000" because "a transplant costs far less than keeping a patient on dialysis."<sup>147</sup> Therefore, financial and humane incentives align in this circumstance. Fortunately, kidneys will likely be the first bioprinted organs to market because they are slightly lower risk (we only need one to survive) and the demand created by dialysis patients is already significant.<sup>148</sup> Perhaps the precedent set by kidneys will alleviate the need to take up this fight with insurance companies and other payers.

D. *[Un]Informed Consent*

Informed consent is one of the most important facets of any investigational study or clinical trial because those subjecting themselves to the risks involved must do so knowingly. In the context of IND expanded

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<sup>145</sup> See Rachel Sachs, *Your Weekly Reminder That Approval and Insurance Coverage Are Often Linked*, BILL OF HEALTH: HARV. L. (Nov. 30, 2016), <http://blogs.harvard.edu/billofhealth/2016/11/30/your-weekly-reminder-that-fda-approval-and-insurance-coverage-are-often-linked/> [<https://perma.cc/Q2H5-9T8M>] ("FDA approval is often linked to insurance coverage. Medicaid must cover essentially all FDA-approved drugs, and Medicare similarly has limited ability to decline to cover FDA-approved drugs.").

<sup>146</sup> See generally Sandra G. Boodman, *Costliest 1 Percent of Patients Account For 21 Percent Of U.S. Health Spending*, KAISER HEALTH NEWS (Oct. 7, 2013), <http://khn.org/news/one-percent-of-costliest-patients/> [<https://perma.cc/3MMS-7KNT>] (analyzing how a small group of the sickest people can cost the most in health care dollars).

<sup>147</sup> Annie Lowrey, *The Kidney Trade: Can Economists Make the System for Organ Transplants More Humane and Efficient?*, SLATE (Dec. 15, 2010), [http://www.slate.com/articles/business/moneybox/2010/12/the\\_kidney\\_trade.html](http://www.slate.com/articles/business/moneybox/2010/12/the_kidney_trade.html) [<https://perma.cc/M9LH-Z3ZP>].

<sup>148</sup> See *A Tissue of Truths*, *supra* note 9 (identifying one medical-technology company that predicts 3D-printed kidneys will be possible in six years).

access and manufactured organ transplantations for those facing death or serious illness, the populations in question are “particularly vulnerable.”<sup>149</sup> Accordingly, the FDA recommends “a rigorous informed consent process” and “encourages submission of informed consent documents intended to be used” for the FDA’s feedback in these situations.<sup>150</sup> The FDA rejected commenters’ requests to “add specific informed consent requirements to the expanded access regulations” because the informed consent rules under its robust Protection of Human Subjects regulations provide the necessary guidance and safeguards as they are.<sup>151</sup> Despite the FDA’s confidence in the existing regulations for informed consent, it is unclear whether we can call consent in this area truly informed. This technology is nothing short of revolutionary, and it is difficult to find an apt analogy.

Therefore, as all of the risks are not yet known, it is quite impossible for sponsors of trials or providers of the bioprinted organs to provide a complete picture of the risks and benefits of participation in these early stages. Each person will present a unique case, and no two printed organs or procedures will be exactly alike. Given the greater potential benefits than risks for populations that are facing almost certain death without intervention, I believe it is ethically permissible to allow this imperfect consent at the earliest stages if, and only if, sponsors are clear that there is uncertainty in brand new technology and the participants accept this price of their involvement. Relatedly, the importance of not creating unrealistic optimism or unfounded hope for the first round of bioprinted organ transplants cannot be overstated.<sup>152</sup>

#### E. 3D-Printed Organs Could Put Black Markets (For Organs) Out of Business

While this final ethical consideration is outside the scope of U.S. regulations, it is equally worthy of our attention. The organ shortage has led to deaths on *both* sides of the equation. The visible suffering we see from people and their families who run out of time before being matched with a suitable organ is heartbreaking, to be sure, but their tragedies are due to systemic failures to provide enough organs to meet the demand. It is difficult to point fingers at any party as blameworthy. This is not the case for the other “invisible” group of victims of the organ shortage. We cannot just blame the

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<sup>149</sup> 74 Fed. Reg. 40,920 (Aug. 13, 2009).

<sup>150</sup> *Id.*

<sup>151</sup> *Id.*; see also Informed Consent of Human Subjects, 21 C.F.R. §§ 50.20–27 (2016) (detailing the requirements and exceptions to informed consent); Institutional Review Boards, 21 C.F.R. §§ 56.101–24 (2016) (detailing the informed consent requirements for investigations involving human subjects and the Institutional Review Board (IRB) oversight thereof).

<sup>152</sup> See *supra* note 139, at 40,920 (noting the importance of “effectively communicat[ing] . . . in a way that does not raise false expectations about a positive outcome from treatment and makes clear what is unknown about the drug”).

system for their pain and suffering. Rather, the responsible parties are members of worldwide organ trafficking rings who murder people and sell their organs for enormous profits. The ethical reprehensibility of their actions is immeasurable, but, unfortunately, business is booming.

Selling organs is illegal in every country except Iran, but it still happens; the WHO estimates, for example, that one in five kidney transplants is done with an organ bought on the black market.<sup>153</sup> For instance, a South African hospital “admitted taking about \$500,000 from an organ trafficking syndicate.”<sup>154</sup> In Brazil and Romania, kidneys (including those harvested from children) can be sold for \$6,000 each.<sup>155</sup> To put that in perspective, this single transaction pays approximately ten times what the average Brazilian<sup>156</sup> or Romanian<sup>157</sup> makes in a whole month. Notwithstanding the question of whether such large amounts of money are per se coercive, one could argue that individuals should be able to part with an unneeded organ for financial reasons, but organ trafficking extends far beyond personal choice. In the more extreme, but not uncommon, circumstances, people are kidnapped and killed by organ trafficking rings, and their bodies are gutted to allow for transplantation of all of their organs into others.<sup>158</sup> Sometimes these rings are operated by shady, back alley gangs, but other times those in the high positions of government may allegedly be behind these deals.<sup>159</sup> According to a Boston-based attorney who has experience with the development of 3D printing, the large-scale availability of organs once bioprinting becomes commonplace could be a powerful tool to undermine the organ trafficking black market and shield

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<sup>153</sup> Lowrey, *supra* note 147.

<sup>154</sup> *Id.*

<sup>155</sup> *Id.*

<sup>156</sup> See *In Booming Brazil, Census Shows Income Gap Persists*, WORLD CRUNCH, (Nov. 20, 2011) <https://www.worldcrunch.com/business-finance/in-booming-brazil-census-shows-income-gap-persists> [<https://perma.cc/JD7P-FS4L>] (citing the average monthly income in Brazil as \$678.90).

<sup>157</sup> See *Comunicat Castig Salarial*, NAT'L INST. STAT. (Nov. 6, 2015), <http://www.insse.ro/cms/en/tags/comunicat-castig-salarial> [<https://perma.cc/3US6-22QD>] (noting the average gross nominal monthly income in Romania as 2,541 lei). At the time, one lei was worth about \$0.24, converting to an average monthly income of \$612. *XE Currency Table: RON—Romanian Leu*, XE (Nov. 6, 2015), <http://www.xe.com/currencytables/?from=RON&date=2015-11-06> [<https://perma.cc/HQ2UHX2E>].

<sup>158</sup> See Paul Lewis, *Kosovo PM is Head of Human Organ and Arms Ring*, *Council of Europe Reports*, GUARDIAN (Dec. 14, 2010), <https://www.theguardian.com/world/2010/dec/14/kosovo-prime-minister-like-mafia-boss> [<https://perma.cc/E5PC-YP2C>] (“As and when the transplant surgeons were confirmed to be in position and ready to operate, the captives were brought out of their ‘safe house’ individually, summarily executed by a [Kosovo Liberation Army] gunman, and their corpses transported swiftly to the operating clinic.”).

<sup>159</sup> See *id.* (discussing a report alleging that the former prime minister of Kosovo was “the head of a ‘mafia-like’ Albanian group responsible for smuggling . . . human organs through eastern Europe”).

more of the world's most common victims from these atrocities.<sup>160</sup> This would be an enormous victory for international human rights.

#### CONCLUSION

There is no question that the FDA's regulation of products that affect our daily lives is complicated. 3D printing technology breaks new ground every day, and the Agency's existing regulatory framework certainly did not contemplate such a revolutionary and "disruptive" market shift, to provide adequate regulation and oversight. On the one hand, we want those whose very survival depends on an organ transplant to have access to bioprinting technology as soon as possible; on the other hand, we must ensure that its introduction to market is coupled with adequate oversight and safeguards.<sup>161</sup>

Many predict that kidneys will be the first 3D-printed organs to market for two reasons. First, kidney transplantation poses a lower risk because people need only one functioning kidney to survive. Second, renal failure is associated with a myriad of complicated and expensive conditions. Federal lawmakers have grappled with the complexities associated with organ transplantation for decades, but the concerns addressed in the National Organ Transplant Act (NOTA) are beyond the scope of the unique challenges of manufactured organs. Therefore, when these kidneys are ready, it will not be a federal crime to manufacture, sell and transplant them under NOTA. The FDA will dually regulate them as biological products and drugs, as their intended use will be to cure, mitigate, treat, or prevent the patient's ailment through their direct effect on the structure and function of his or her body. The proteins in these kidneys will achieve their primary intended purpose of substituting for dialysis or providing healthy organ function through the chemical action with the rest of the human body. As with any biological product and drug, the manufacturing, labeling, and transportation of these kidneys must comply with all applicable current Good Manufacturing and Tissue Practices, pursuant to the FDA's regulations under the Federal Food, Drug, and Cosmetic Act and the Public Health Services Act. However, the questions that must be answered first are: Which patients *will* be at the front of the line to receive the treatment? Which *should* be?

There is very little about 3D-printed organs that is intuitive, and its regulation will be equally complex. Nevertheless, the framework to support 3D printing exists, and the FDA need not hesitate to welcome these organs into the health care market. Bioprinting promises to revolutionize the

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<sup>160</sup> Interview with Anonymous Source (May 2, 2017).

<sup>161</sup> See Miller, *supra* note 55, at 437 ("New medical technologies are constantly pushing the regulatory envelope, creating new agency challenges for effective oversight.").

practice of medicine through the eventual eradication of organ shortage and transplant rejection problems. A careful assessment of ethical challenges posed by 3D-printed organs will remain critical as the technology becomes available for human transplantation. As other countries, such as China,<sup>162</sup> move closer to human transplantation, the richest cohorts of the United States will be able to travel to receive these 3D-printed organs even if they cannot access them at home. We must develop means to ethically bring this technology to American hospitals.

President Theodore Roosevelt rightly said, “Nothing in this world is worth having or worth doing unless it means effort, pain, [and] difficulty.”<sup>163</sup> Arriving at the day when no one dies for want of an organ transplant is certainly worth doing, and the world must brace itself to invest the requisite effort and resources to face the difficult challenges ahead. The end result is too important to choose any other course.

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<sup>162</sup> See *supra* note 132.

<sup>163</sup> President Theodore Roosevelt, Address at the Iowa State Teachers’ Association (Nov. 4, 1910).

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