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HALTED INNOVATION: THE EXPANSION OF FEDERAL JURISDICTION OVER MEDICINE AND THE HUMAN BODY

Myrisha S. Lewis*

Abstract

Modern medical innovations are blurring the line between medical practice and medical devices and drugs. Historically, many techniques have been developed in medicine, without any interference from the federal government, as medical practice is (and has historically been) an area of state jurisdiction. Over the past two decades, however, the U.S. Food and Drug Administration (FDA) has been exerting jurisdiction over the human body and the practice of medicine by targeting new medical techniques for oversight and subjecting the continued use of those treatments to onerous and legally questionable regulatory requirements that hinder the use of those treatments in practice.

This Article examines developing innovations in medicine and the life sciences, including gene editing (and CRISPR-Cas9, a system of gene editing that has been the subject of significant media coverage due to its wide-ranging potential uses), forms of assisted reproductive technology that could prevent the transmission of genetic diseases, stem cell therapies, and fecal microbiota transplants. The Article makes several claims. First, the Article argues that innovations in the life sciences largely fall outside of the jurisdiction of the FDA. Second, the FDA is applying a regime intended to regulate medical devices and pharmaceuticals to new innovations in the life sciences, which has a chilling effect on innovation and patient health. The Article also reveals that States—due to their historic police powers over the practice of medicine—retain a critical piece of jurisdiction over the life sciences such that the only method of accurately and adequately regulating the life sciences must include the States. Ultimately, it is critical that the regulatory apparatus surrounding

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the life sciences be improved, as the pace of innovation indicates that the regulation of the life sciences will continue to be salient in the near and distant future.

INTRODUCTION

Scientific discovery and innovation have proven to be the keys to improving patient outcomes. Over the past century, scientific discoveries have resulted in the widespread use of organ transplantation, pacemakers, increasingly effective pharmaceuticals (which treat diseases such as Human Immunodeficiency Virus (HIV) and cancer more effectively, and in some cases, can cure diseases such as Hepatitis C), stem cell treatments, new vaccines (such as the Human Papillomavirus (HPV) vaccine), and more recently, gene therapy.¹

Innovation is encouraged through various methods, including the societal celebration of “genius” and the use of legislation to create incentives for those who might innovate and improve the public good.² The recently enacted 21st Century Cures Act, a piece of federal legislation that has been described as “landmark,”³ the

¹ See, e.g., THOMAS E. STARZL, *THE PUZZLE PEOPLE: MEMOIRS OF A TRANSPLANT SURGEON* (2003); *Our Approach for Pacemakers*, STANFORD HEALTH CARE, <https://stanfordhealthcare.org/medical-treatments/p/pacemaker.htm> [<https://perma.cc/VX6X-K9XS>] (last visited June 10, 2018); Michelle Andrews, *FDA’s Approval of a Cheaper Drug for Hepatitis C Will Likely Expand Treatment*, NPR (Oct. 4, 2017, 5:00 AM), <https://www.npr.org/sections/health-shots/2017/10/04/555156577/fdas-approval-of-a-cheaper-drug-for-hepatitis-c-will-likely-expand-treatment> [<https://perma.cc/URJ5-WNJH>]; see also *Medical Milestones: Celebrating Key Advances Since 1840*, BRITISH MED. J. Suppl: S1 (M. Chew and K Sharrock eds., 2007), http://www.bmj.com/content/suppl/2007/01/18/334.suppl_1.DC2/milestones.pdf [<https://perma.cc/EJ84-XJPR>]; *Gene Therapy for Children, Teens and Young Adults*, DANA-FARBER CANCER AND BLOOD DISORDERS CTR., <http://www.danafarberbostonchildrens.org/innovative-approaches/gene-therapy.aspx> [<https://perma.cc/5EJM-N55L>] (last visited June 10, 2018); Dan Childs & Susan Kansagra, *10 Health Advances that Changed the World*, ABC NEWS (Sept. 20, 2007), <http://abcnews.go.com/Health/TenWays/story?id=3605442&page=1> [<https://perma.cc/E6N8-6Z9R>]; *10 Medical Advances in the Last 10 Years*, CNN (June 5, 2013), <http://www.cnn.com/2013/06/05/health/lifework-medical-advances/index.html> [<https://perma.cc/KJ86-CKX3>].

² See, e.g., Gaia Bernstein, *In the Shadow of Innovation*, 31 CARDOZO. L. REV. 2257, 2257–60, 2290 (2010); Mark A. Lemley & R. Anthony Reese, *Reducing Digital Copyright Infringement Without Restricting Innovation*, 56 STAN. L. REV. 1345, 1349–50 (2004) (referring to the “social value” of innovation and how certain legal and regulatory actions may stifle innovation); Arti K. Rai, *The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, and Access in the Post-Genomics Era*, 2001 U. ILL. L. REV. 173 (2001); Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1800 (1996) (“The Medical Device Amendments represented a conscious legislative attempt to avoid what some viewed as the innovation-stifling effects of FDA’s drug approval system.” (citation omitted)).

³ *Remarks by Acting FDA Commissioner Stephen M. Ostroff, M.D. FDLI Annual Conference: May 4, 2017, Washington, DC*, 72 FOOD & DRUG L.J. 378, 381 (2017) (“Let me

“most significant overhaul of the U.S. Food and Drug Administration . . . in decades,”⁴ and a “bipartisan victory,”⁵ uses the word “innovation” sixty-five times.⁶ The 21st Century Cures Act, which was enacted in December 2016, committed \$6.3 billion, to be distributed over seven years, to fund a number of projects, including the Beau Biden Cancer Moonshot, the Precision Medicine Initiative, the BRAIN Initiative, and projects that aim to address the opioid crisis, mental illness, Alzheimer’s disease, and other diseases, in addition to creating an accelerated FDA review process for a new category of drugs that are classified as “regenerative advanced therapies.”⁷

In signing the 21st Century Cures Act into law in December 2016, President Obama stated:

Over the last eight years, one of my highest priorities as President has been to unleash the full force of American innovation to some of the biggest challenges that we face. That meant restoring science to its rightful place. It meant funding the research and development that’s always kept America on the cutting edge It meant investing in the medical

now switch over to medical products. Without question, the biggest change from last year is the 21st Century Cures Act. This is landmark legislation. And like any big change, it took a long time to develop and a lot of hard work by a lot of people inside and outside FDA. And it passed with overwhelming bipartisan support.”)

⁴ Jacob S. Sherkow, *Cancer’s IP*, 96 N.C. L. REV. 297, 299 (2018).

⁵ See, e.g., Norm Ornstein, *A Bipartisan Victory for Medical Research in Congress*, THE ATLANTIC (Jul. 13, 2015), <https://www.theatlantic.com/politics/archive/2015/07/21st-century-cures-act-bipartisan/398369/> [<https://perma.cc/2G59-LTTB>]. See also Gary E. Marchant & Yvonne A. Stevens, *Resilience: A New Tool in the Risk Governance Toolbox for Emerging Technologies*, 51 U.C. DAVIS L. REV. 233, 259 (2017) (“Perhaps, at least within the healthcare industry, the most comprehensive adaptive regulation comes in the form of the 21st Century Cures Act, which came into effect on December 13, 2016.” (citation omitted)); Zachary Liscow & Quentin Karpilow, *Innovation Snowballing and Climate Law*, 95 WASH. U. L. REV. 387, 435 (2017) (“For example, according to the recently-passed 21st Century Cures Act, which includes prizes for innovation in healthcare, experts will pick particular projects.” (citation omitted)).

⁶ The word “innovation” appears 60 times in the 21st Century Cures Act and the word “innovations” appears 5 times in the Act. See 21st Century Cures Act, Pub. L. No. 114-255, 130 Stat. 1033 (2016), available at <https://www.gpo.gov/fdsys/pkg/PLAW-114publ255/pdf/PLAW-114publ255.pdf> (providing the text of the entire statute as signed into law) [<https://perma.cc/T3QK-SASP>].

⁷ See Press Release, White House Office of the Press Secretary, Remarks by the President and the Vice President at the 21st Century Cures Act Bill Signing (Dec. 13, 2016), available at <https://obamawhitehouse.archives.gov/the-press-office/2016/12/13/remarks-president-and-vice-president-21st-century-cures-act-bill-signing> [<https://perma.cc/RW33-WJ3C>] [hereinafter Remarks by the President]; *The 21st Century Cures Act*, NAT’L INSTS. OF HEALTH, <https://www.nih.gov/research-training/medical-research-initiatives/cures> [<https://perma.cc/4RYF-VJNH>] (last visited June 10, 2018). “BRAIN” is an acronym that stands for “Brain Research through Advancing Innovative Neurotechnologies.” *Id.*

breakthroughs that have the power to cure disease and help all of us live healthier, longer lives.⁸

Medical advances are moving away from using pharmaceuticals to treat disease to using parts of the human body to cure or ameliorate harmful conditions.⁹ New medical techniques focus on using a patient's own cells or donor tissue, instead of pharmaceuticals or surgery, to treat ailments.¹⁰ These new treatments have a variety of uses at different periods in the diagnostic process, including: (1) before disease-causing genes can be inherited (such as with mitochondrial transfer, the subject of much media coverage in the United Kingdom); (2) after disease-causing genes have been inherited but before an embryo becomes a fetus (such as with gene editing systems including CRISPR-Cas9, which has been the subject of a well-publicized patent battle); or, (3) after a disease manifests, but often fails to respond to conventional medical treatment (such as with autologous stem cell treatments to treat orthopedic conditions without invasive surgery or fecal transplants to treat *C. difficile*, an antibiotic-resistant infection commonly contracted after hospitalization).¹¹ None of these aforementioned techniques fits clearly within existing legal structures and in spite of their differing disease targets and methods, all of these techniques offer great promise in improving patient health. Yet, all of the aforementioned techniques, in spite of their differing treatment targets, are subject to onerous legal requirements in the United States that are often so stringent that the clinical use of these techniques is effectively banned.¹²

⁸ Remarks by the President, *supra* note 7.

⁹ See *infra* note 11 and accompanying text (discussing new methods of treating ailments that focus on using donor tissue or the use or modification of a patient's own cells or DNA instead of drugs, medical devices, or supplements).

¹⁰ *Id.*

¹¹ See, e.g., Richard A. Epstein, *The FDA's Misguided Regulation of Stem-Cell Procedures: How Administrative Overreach Blocks Medical Innovation*, MANHATTAN INST. (Sept. 24, 2013), <https://www.manhattan-institute.org/html/fdas-misguided-regulation-stem-cell-procedures-how-administrative-overreach-blocks-medical-5897> [<https://perma.cc/JBW2-QFYJ>]; James Gallagher, *UK scientists edit DNA of human embryos*, BBC (Sept. 20, 2017), <http://www.bbc.com/news/health-41269200> [<https://perma.cc/8VWT-SM3C>]; Maryn McKenna, *Swapping Germs: Should Fecal Transplants Become Routine for Debilitating Diarrhea?*, SCI. AM. (Dec. 1, 2011), <https://www.scientificamerican.com/article/swapping-germs/> [<https://perma.cc/9CCC-5W6B>]. See *infra* Part I for more detail and descriptions of innovative medical technologies.

¹² McKenna, *supra* note 11 (noting that clinical trials involving fecal transplants were underway in Canada, but not the United States); See *FDA Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P's) Product List*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/RegulationofTissues/ucm150485.htm> [<https://perma.cc/G4FG-BAKG>] (last updated Feb. 2, 2018) (listing “. . . cell nuclei, oocyte nuclei, mitochondrial genetic material in ooplasm, [and] genetic material contained in a genetic vector” as products that are regulated under “Section 351 of the [Public Health Service] Act and/or the [Food, Drug & Cosmetic] Act” without explaining how the communicable disease provision of the Public Health Service Act

The FDA is using a regulatory framework that was created for drugs to regulate the practice of medicine.¹³ While the practice of medicine is subject to the state police power, the FDA has been continually encroaching on the practice of medicine by effectively banning new medical techniques through agency-issued letters or by pursuing litigation against physicians based on an over-expansive view of “commerce.”¹⁴ When doing so, the FDA often states that these techniques are within the FDA’s jurisdiction or “regulatory authority,” without explaining how the FDA has jurisdiction over these medical techniques or how political motivations may be affecting the agency’s decision-making.¹⁵ The FDA impedes the use of innovative

“and/or” the Food, Drug, and Cosmetic Act applies to these “products.”); *infra* note 132 (providing text from the FDA’s response to FOIA Request 2016-4882 and the associated shareholder lawsuit that highlighted the FDA’s actions.); *see also* Ariana Eunjung Cha, *FDA cracks down on company marketing ‘three-parent’ babies*, WASH. POST (Aug. 8, 2017), https://www.washingtonpost.com/news/to-your-health/wp/2017/08/07/fda-cracks-down-on-company-marketing-three-parent-babies/?utm_term=.0562ad833f54 [<https://perma.cc/9GYZ-3HMQ>] (citing Letter from Mary A. Malarkey, Director of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, to Dr. John Zhang, CEO, Darwin Life, Inc. and New Hope Fertility Center (Aug. 4, 2017) (on file at the Washington Post)) (noting that not only does the FDA state that an investigational new drug application is required for techniques such as Dr. Zhang’s (a type of mitochondrial transfer), but such an attempt to obtain a pre-investigational new drug application would not be successful due to a federal appropriations rider); discussion *infra* Part II.B.2.b of fecal transplants with an emphasis on those patients who are driven to pursue “Do-it-yourself” fecal transplants; discussion *infra* Part III.

¹³ *See generally* Myrisha S. Lewis, *How Subterranean Regulation Hinders Innovation in Assisted Reproductive Technology*, 39 CARDOZO L. REV. 1239 (2018) (providing more information on the process through which the FDA regulates such innovative medical treatments (with an emphasis on those that implicate fraught ethical areas)). In this article, after submitting Freedom of Information Act (FOIA) requests and examining primary source documents, I observed that the FDA has been consistently regulating forms of assisted reproductive technology that involve genetic modifications in a “subterranean” manner that effectively prevents their use in the United States. “Subterranean regulation” generally has four qualities: (1) contested agency jurisdiction; (2) the assertion of wrongdoing in an atypical manner; (3) obfuscation of the agency’s action, by not including addressees or all correspondence in publicly available databases (or FOIA requests); and (4) chilling effects on research. The term “subterranean” refers to the fact that the FDA’s jurisdiction over these techniques is questionable and also that the agency uses non-legislative rules, specifically letters sent on agency letterhead, to inform physicians that if they continue using those techniques, that they must participate in the agency’s new drug approval process; these letters have a chilling effect on research as physicians stop providing these techniques to patients after receiving these letters from the FDA, with one physician explaining that he felt “threatened” after receiving the letter.

¹⁴ *See* *Gonzales v. Oregon*, 546 U.S. 243, 270 (2006) (discussing the state’s historic police power over the practice of medicine); *See also infra* Section II.B.2.c for discussion of the *U.S. v. Regenerative Sciences* litigation and the FDA’s use of subterranean regulation to target forms of assisted reproductive technology involving genetic modifications.

¹⁵ *See infra* Section II.B.2.c for discussion of the *U.S. v. Regenerative Sciences*

medical technologies, in spite of the existence of laws that already protect patients, medical promise, and, in the case of at least one technique, the recommendations of the National Academies of Sciences, Engineering, and Medicine (National Academies).¹⁶ In this way, contrary to the prevalent belief that increased FDA regulation improves patient health, the administrative state is halting the use of these innovations in medical treatment to the potential detriment of patient care.¹⁷

In spite of Executive Branch statements and the recent passage of legislation encouraging medical innovation, the current regulatory framework not only infringes on state jurisdiction over the practice of medicine but also uses a process that is not structured to regulate the life sciences.¹⁸ This Article argues that the current federal regulatory scheme actually has the effect of hindering innovation in the life sciences. The current federal regulatory scheme has this effect for at least two reasons. First, even with the passage of the 21st Century Cures Act, the current federal regulatory regime does not permit the FDA to exert such extensive jurisdiction—as the FDA now does—over the regulation of the life sciences.¹⁹ Furthermore, the nature of life sciences innovations and their clinical use actually renders state regulation a critical piece of the regulatory puzzle as these innovations implicate the practice of medicine which is an area subject to the state’s historic police powers.²⁰ Additionally, the federal regulatory scheme is not structured to regulate the life sciences, as evidenced by its historical roots and the manner in which the FDA has constructed an *ad hoc* regime to regulate such innovations over at least the past twenty years.²¹

This Article’s main claim is that the FDA should not be regulating innovative new medical techniques in the current manner. Instead, the life sciences can only be adequately regulated through a regulatory scheme that is specifically created for

litigation.

¹⁶ See THE NAT’L ACADS. OF SCIS., ENG’G, & MED., MITOCHONDRIAL REPLACEMENT TECHNIQUES: ETHICAL, SOCIAL, AND POLICY CONSIDERATIONS (ANNE CLAIBORNE ET AL., 2016). In the foregoing report, the Committee on the Ethical and Social Policy Considerations of Novel Techniques for Prevention of Maternal Transmission of Mitochondrial DNA Diseases provided a limited recommendation for the use of mitochondrial transfer in the United States. *Id.* at xv. The Committee was assembled at the request of the FDA and the National Academies of Sciences, Engineering, and Medicine. *Id.* at xiii.

¹⁷ See, e.g., DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION 1–2 (2010); see also *infra* Parts II and III.

¹⁸ See Remarks by the President, *supra* note 7 and accompanying text; see also KEAN BIRCH, INNOVATION, REGIONAL DEVELOPMENT AND THE LIFE SCIENCES: BEYOND CLUSTERS 7 (2016) (discussing the definition of “life sciences”).

¹⁹ See *infra* Part II.B.2 (discussing how the FDA regulates innovations in the life sciences even though those innovations do not fall wholly within federal jurisdiction).

²⁰ See *Gonzales v. Oregon*, 546 U.S. 243, 270 (2006) (discussing the state’s historic police power over the practice of medicine).

²¹ See generally Lewis, *supra* note 13 (explaining how the FDA has exerted jurisdiction over human cellular and tissue-based products on an *ad hoc* basis).

them and that involves a greater role for state governments.²² This Article makes several contributions to the literature. First, the health law (and the life sciences) legal literature is marked by fragmentation.²³ This Article takes a synthetic approach by examining multiple agency targets in one article.²⁴ Furthermore, often these agency targets are the subject of separate legal disciplines. For example, articles focused on intellectual property tend to focus on CRISPR-Cas9 and gene editing; articles from the family law discipline focus on assisted reproductive technology (ART); articles categorized as health law consider innovations in insurance markets; and administrative law scholarship focuses on the use of non-legislative rules.²⁵ This Article contributes to the literature by revealing a common problem: the FDA's regulation of products that are likely outside of its jurisdiction.²⁶ Moreover, this

²² State governments have experience encouraging innovation in the life sciences. *See, e.g.*, CAL. INST. FOR REGENERATIVE MED., CIRM STRATEGIC PLAN: 2016 AND BEYOND 4, https://www.cirm.ca.gov/sites/default/files/CIRM_StrategicPlan_2016.pdf [<https://perma.cc/4NJP-DFX5>] (last visited June 10, 2018) [hereinafter CIRM STRATEGIC PLAN] (noting that “[o]n November 2, 2004, 59% of the voters approved Proposition 71, which amended the California Constitution to establish the right to conduct stem cell research in California and authorize[d] \$3 billion to fund stem cell research.”).

²³ Lawrence A. Gostin, Scott Burris & Zita Lazzarini, *The Law and the Public's Health: A Study of Infectious Disease Law in the United States*, 99 COLUM. L. REV. 59, 118 (1999) (“Our review of public health legislation suggests that state public health law remains fragmented both within and among states.”); *see also* Mark A. Hall, *Law, Medicine, and Trust*, 55 STAN. L. REV. 463, 464 (2002) (“Scholars have long noted that the field of health care law lacks cohesion. They speak in terms of the ‘pathologies’ of health law, or its contradictory and competing ‘paradigms,’ which constitute a ‘chaotic, dysfunctional patchwork.’ This conceptual disarray exists because, unlike other areas of law, no unifying principle or animating concern has yet been identified for the law of health care delivery. For example, family law is concerned with rights and obligations arising from intimate relationships, environmental law is built around a set of core statutes, and intellectual property law applies general property principles to intangible constructs. The field of health care law, in contrast, is largely a creature of happenstance.” (citations omitted)).

²⁴ Many scholars have written analyses of specific, individual areas in which the FDA is hindering medical innovation. For example, other scholars have written articles that focus on the FDA's questionable jurisdiction over other innovative techniques such as the use of autologous stem cells as an alternative to orthopedic surgery and heart surgery. *See, e.g.*, Epstein, *supra* note 11; *see also* Lewis, *supra* note 13.

²⁵ *See, e.g.*, Jorge L. Contreras & Jacob S. Sherkow, *CRISPR, Surrogate Licensing, and Scientific Discovery*, 355 SCIENCE 698, 698 (2017); Abbe R. Gluck, *Federalism from Federal Statutes: Health Reform, Medicaid, and the Old-Fashioned Federalists' Gamble*, 81 FORDHAM L. REV. 1749, 1749–51 (2013); Nicole Huberfeld, *Federalizing Medicaid*, 14 U. PA. J. CONST. L. 431, 435–36 (2011); John F. Manning, *Non-legislative Rules*, 72 GEO. WASH. L. REV. 893, 893 (2004); Radikha Rao, *Assisted Reproductive Technology and the Threat to the Traditional Family*, 47 HASTINGS L.J. 951, 952 (1996); John A. Robertson, *Assisted Reproductive Technology and the Family*, 47 HASTINGS L.J. 911, 913 (1996); Mark Seidenfeld, *Substituting Substantive for Procedural Review of Guidance Documents*, 90 TEX. L. REV. 331, 333 (2011).

²⁶ *See infra* Part II.A (providing the definitions of the terms “biologics” and “drugs” in

jurisdictional overreaching corresponds to an over-regulation that will continue to pose a barrier to the clinical use of innovative procedures. Additionally, this Article examines newer fields that have been the subject of less attention in the legal literature such as fecal microbiota transplants.²⁷ The Article also reveals that while regulatory capture has been a criticism of the FDA's relationship with the pharmaceutical industry in the past, recent medical innovations exist in a regulatory space that is both outside of the pharmaceutical industry and less amenable to regulatory capture.²⁸

This Article proceeds in four Parts. Part I provides an overview of innovative medical techniques that are currently being regulated by the FDA including techniques of ART involving the use of donor material in order to prevent the transmission of harmful genetic diseases to offspring, gene editing, methods of ART that use a woman's own cells, fecal microbiota transplants, and autologous stem cell treatments. Part II begins with the National Academies' observation that many new biotechnological innovations do not fall within federal jurisdiction and then examines the tension between the federal administrative state and the practice of medicine. This Article specifically addresses what the 2017 National Academies' report did not: jurisdictional gaps that do not permit the FDA to regulate many of the innovative medical techniques discussed in Part I.²⁹ Part III of the Article examines the broader implications of the agency's regulatory actions including how federal interference has hindered innovation without adequate statutory authorization. Part III also explains why the current *ad hoc* federal regime is not only

the context of FDA regulation).

²⁷ See *infra* Part II.B.2.b (noting that physicians must rely on promises from the FDA to exercise its enforcement discretion in favor of those physicians, in the context of fecal microbiota transplants, which leads to an unpredictable legal situation); see, e.g., *FMT demonstrates consistently high success rates for recurrent CDI*, MAYO CLINIC, <http://www.mayoclinic.org/medical-professionals/clinical-updates/digestive-diseases/fmt-demonstrates-consistently-high-success-rates-for-recurrent-cdi> [https://perma.cc/Q6VG-TW89] (last visited June 10, 2018) ("Maria I. Vazquez Roque, M.D., a gastroenterologist at Mayo Clinic's campus in Jacksonville, Florida, observes that the Food and Drug Administration (FDA) initially proposed requiring investigational new drug (IND) status for FMT procedures. That stance would have denied access to the procedure for many, if not most, patients and was later changed. For the time being, the FDA exercises enforced discretion."). A Westlaw search of "fecal/p transplant" revealed 9 articles in the Journals and Law Review Search Engine as of February 13, 2018. *But see* Rachel E. Sachs & Carolyn A. Edelstein, *Ensuring the safe and effective FDA regulation of fecal microbiota transplantation*, 2 J.L. & BIOSCIENCES 396, 396 (2015) ("... examin[ing] the nature of the regulatory challenges the FDA will face in deciding to regulate [fecal microbiota transplantation] as a biologic drug . . .").

²⁸ See Nicholas Bagley & Richard L. Revesz, *Centralized Oversight of the Regulatory State*, 106 COLUM. L. REV. 1260, 1289 (2006) (observing that the "FDA has recently been the subject of searing criticism because of its cozy relationship with the pharmaceutical industry" (citation omitted)).

²⁹ See discussion *infra* Part II.

inapplicable to the life sciences but also not structured to regulate the life sciences.³⁰ After explaining why states actually retain jurisdiction over a critical aspect of life sciences regulation, Part IV proposes several ways in which life sciences regulation could be improved with an emphasis on methods that would emphasize the increased regulatory involvement of individual states. The Article then concludes.

I. SCIENTIFIC BACKGROUND ON INNOVATIVE MEDICAL TECHNIQUES

While the term “life sciences” traditionally has “refer[red] to biomedical research and innovation,” many techniques that compose the “innovation” part of the life sciences definition are a part of medical practice as opposed to discoveries resulting from laboratory research.³¹ The case studies in this Part emphasize innovations in the life sciences that use the human body in order to treat ailments.

A. *Genetic Modifications of the Human Body: Mitochondrial Transfer, CRISPR-Cas9, Gene Editing, and Cloning*

With the addition of genetic modifications, ART has moved from being an area of state regulation and experimentation to an area of federal regulation, which entails additional regulatory barriers.³² For example, using ART that involves genetic modifications has been prevented by the exercise of FDA power through non-legislative rules.³³ While ART techniques were originally used to treat infertile couples, a new form of ART, mitochondrial transfer, has received significant attention recently due to its ability to prevent the transmission of harmful genetic

³⁰ See THE NAT’L ACADS. OF SCIS., ENG’G, & MED., PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY 10 (2017), <http://www.nap.edu/24605> [<https://perma.cc/EQ N6-PYWF>].

³¹ BIRCH, *supra* note 18.

³² See e.g., Michele Goodwin, *A View from the Cradle: Tort Law and the Private Regulation of Assisted Reproduction*, 59 EMORY L.J. 1039, 1071–72, 1079 (2010) (discussing the state-based regulation of assisted reproductive technology and the lack of federal oversight over “traditional” forms of assisted reproductive technology such as artificial insemination and *in vitro* fertilization not involving genetic modification); see generally CHARLES P. KINDREGAN, JR. & MAUREEN MCBRIEN, *ASSISTED REPRODUCTIVE TECHNOLOGY: A LAWYER’S GUIDE TO EMERGING LAW AND SCIENCE* (2d ed. 2011) (discussing the state-by-state regulation of assisted reproductive technology).

³³ See *infra* Part II.B; see, e.g., *Advisory on Legal Restrictions on the Use of Mitochondrial Replacement Techniques to Introduce Donor Mitochondria into Reproductive Cells Intended for Transfer into a Human Recipient*, U.S. FOOD & DRUG ADMIN. (Aug. 4, 2017), <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm570185.htm> [<https://perma.cc/4FQA-SYWS>] [hereinafter *Restrictions on Mitochondrial Replacement Techniques*].

diseases from parents to their children.³⁴ Mitochondria provide energy to the cell; however, the inheritance of defective mitochondria can cause genetic disease.³⁵

Mitochondrial transfer is a form of ART that combines *in vitro* fertilization and genetic modification to prevent the transmission of harmful genetic disease.³⁶ Clinical trials are underway in the United Kingdom where the “Newcastle Group” (as the scientists who developed the technique are called)

uses a modified version of [*in vitro* fertilization] to combine the healthy mitochondria of a donor woman with DNA of the two parents.³⁷

It results in babies with 0.1% of their DNA from the second woman and is a permanent change that would echo down through the generations.³⁸

An American scientist, Dr. Shoukhrat Mitalipov, has also pioneered a mitochondrial transfer technique; however, as discussed *infra* in Parts II and III, while human clinical trials go forward in the United Kingdom, mitochondrial transfer has been subjected to burdensome regulatory requirements and a congressional funding restriction in the United States.³⁹

Similarly, Autologous Germline Mitochondrial Energy Transfer (AUGMENT) is another technique that has rarely been explored in the legal literature.⁴⁰ AUGMENT is another technique that uses the human body to address infertility; however, due to the FDA’s use of regulatory tools, as explored in Part II, this

³⁴ See, e.g., Paula Amato, et. al., *Three-Parent IVF: Gene Replacement for the Prevention of Inherited Mitochondrial Diseases*, 101 FERTILITY AND STERILITY 31 (2014); see also *Letter to Sponsors / Researchers - Human Cells Used in Therapy Involving the Transfer of Genetic Material By Means Other than the Union of Gamete Nuclei*, U.S. FOOD & DRUG ADMIN. (Jul. 6, 2001), <https://wayback.archive-it.org/7993/20170404210748/https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ucm105852.htm> [<https://perma.cc/978M-BZCN>] [hereinafter *Human Cells Used in Therapy*].

³⁵ See, e.g., James Gallagher, *UK Approves Three-Person Babies*, BBC (Feb. 24, 2015), <http://www.bbc.com/news/health-31594856> [<https://perma.cc/TY6V-W4AG>]; see also Marni J. Falk et al., *Mitochondrial Replacement Techniques — Implications for the Clinical Community*, 374 NEW ENG. J. MED. 1103, 1103 (2016) (“[P]ersons [affected with mitochondrial disease] may present at any age with some combination of severe, often progressive, and sometimes fatal neurologic, musculoskeletal, cardiac, gastrointestinal, renal, ophthalmologic, and audiologic involvement. No cures or therapies have been approved by the Food and Drug Administration (FDA) for any [mitochondrial] DNA disease, although symptom-based clinical management can be beneficial.”).

³⁶ See *supra* note 35.

³⁷ James Gallagher, *UK Approves Three-Person Babies*, BBC (Feb. 24, 2015), <http://www.bbc.com/news/health-31594856> [<https://perma.cc/TY6V-W4AG>].

³⁸ *Id.*

³⁹ See discussion *infra* Part II.B.2.a, Part III.A.

⁴⁰ See Karen Weintraub, *Rejuvenating the Chance of Motherhood?*, MIT TECH. REV. (Dec. 9, 2016), <https://www.technologyreview.com/s/603065/rejuvenating-the-chance-of-motherhood/> [<https://perma.cc/NY8U-DWVE>].

treatment—created by an American company—“is so far available only in Canada and Japan”⁴¹ Genome- or gene-editing technologies

allow genetic material to be added, removed, or altered at particular locations in the genome. Several approaches to genome editing have been developed. A recent one is known as CRISPR-Cas9, which is short for clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9. The CRISPR-Cas9 system has generated a lot of excitement in the scientific community because it is faster, cheaper, more accurate, and more efficient than other existing genome editing methods.⁴²

Human reproductive cloning, as opposed to cloning for human research, is a “process[] that can be used to produce genetically identical copies of a biological entity. The copied material, which has the same genetic makeup as the original, is referred to as a clone.”⁴³ Human reproductive cloning is not currently a medical treatment; however, it is briefly mentioned because the method that the federal government has used to regulate it is similar to that used to regulate innovative medical techniques as noted *infra* in Part II.⁴⁴

B. Fecal Microbiota Transplants

Fecal transplants have received an increasing amount of medical and media attention lately; yet, the subject has been largely neglected by the legal literature.⁴⁵

⁴¹ *Id.*

⁴² See *What Are Genome Editing and CRISPR-Cas9?*, NAT’L INSTS. OF HEALTH (Jan. 16, 2018), <https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting> [<https://perma.cc/NYY4-RB5B>].

⁴³ *Cloning*, NAT’L INSTS. OF HEALTH (Mar. 21, 2017), <https://www.genome.gov/25020028/cloning-fact-sheet/> [<https://perma.cc/QH4Q-3QEA>] (“The term cloning describes a number of different processes that can be used to produce genetically identical copies of a biological entity. The copied material, which has the same genetic makeup as the original, is referred to as a clone.”).

⁴⁴ See, e.g., Gail H. Javitt & Kathy Hudson, *Regulating (for the Benefit of) Future Persons: A Different Perspective on the FDA’s Jurisdiction to Regulate Human Reproductive Cloning*, 2003 UTAH L. REV. 1201, 1207–08 (2003) (“CBER’s claim that reproductive cloning is not reproduction, along with its failure to identify the component of cloning that constitutes a drug, underscores the fact that the FDA has, in all of its iterations of what might be termed policy, assiduously avoided answering the central question of what precisely is the subject of its jurisdiction, or, in statutory parlance, the article that it seeks to regulate Thus far, the FDA appears to be floundering for a regulatory hook; it is positing a desired regulatory result that is in search of a cogent legal theory.”).

⁴⁵ See *supra* note 27 and accompanying text; see also Ciaran P. Kelly, *Fecal Microbiota Transplantation — An Old Therapy Comes of Age*, 368 N. ENGL. J. MED. 474, 474–75 (2013); David Salisbury, *These days, fecal transplantation is no joke*, VANDERBILT UNIV. (July 12, 2016), <https://news.vanderbilt.edu/2016/07/12/these-days-fecal-transplantation-is-no-joke/> [<https://perma.cc/7DC8-WCMB>]; Carl Zimmer, *Fecal Transplants can be Life-*

Fecal transplants can minimize patient suffering caused by certain medical conditions, especially drug-resistant infections of *Clostridium difficile*, commonly referred to as “C. diff,” which can be acquired during hospital stays, typically after use of antibiotic medication.⁴⁶ “Fecal transplantation (or bacteriotherapy) is the transfer of stool from a healthy donor into the gastrointestinal tract for the purpose of treating recurrent *C. difficile colitis*” when antibiotics have proven ineffective.⁴⁷ A recent study showed that just one fecal transplant was 81% effective among those suffering from colitis caused by *Clostridium difficile*.⁴⁸ As explained in Part II, *infra*, due to the FDA’s assertion of jurisdiction over this medical treatment, it is only available under very limited circumstances to patients in the United States.⁴⁹

C. Stem Cell Treatments

Stem cells have been a part of the American scientific, legal, and medical discourse since at least the 1960s.⁵⁰ Stem cells are so versatile and varied that the

Saving, but How?, N.Y. TIMES (July 15, 2016), https://www.nytimes.com/2016/07/15/science/fecal-transplants-bacteria-viruses.html?mcubz=0&_r=0 [<https://perma.cc/Q6EM-F223>].

⁴⁶ See, e.g., Fernanda C. Lessa *et al.*, *Burden of Clostridium difficile Infection in the United States*, 372 N. ENG. J. MED. 825, 827 (2015) (“*C. difficile* has become the most common cause of health care–associated infections in U.S. hospitals, and the excess health care costs related to *C. difficile* infection are estimated to be as much as \$4.8 billion for acute care facilities alone.” (citations omitted)); *C. difficile infection*, MAYO CLINIC, <https://www.mayoclinic.org/diseases-conditions/c-difficile/symptoms-causes/syc-2035> 1691 [<https://perma.cc/M45J-XSFJ>]; *FDA struggles to regulate fecal transplants*, CBS NEWS (June 26, 2014), <http://www.cbsnews.com/news/fda-struggles-to-regulate-fecal-transplants/> [<https://perma.cc/6JHP-5WD6>] [hereinafter *FDA struggles*]; see also Kenneth A. Young, *Of Poops and Parasites: Unethical FDA Overregulation*, 69 FOOD & DRUG L.J. 555, 562–63 (2014); *How Doctors are Using Fecal Transplants to Treat Deadly Disease*, VICE NEWS (June 22, 2016), https://www.vice.com/en_us/article/vice-on-hbo-student-debt-fecal-transplant [<https://perma.cc/6JHP-5WD6>] [hereinafter *Doctors Using Fecal Transplants*]; Woo Jung Lee *et al.*, *Fecal Microbiota Transplantation: A Review of Emerging Indications Beyond Relapsing Clostridium difficile Toxin Colitis*, 11 GASTROENTEROLOGY & HEPATOLOGY 24, 25 (2015), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4836576/pdf/GH-11-24.pdf> [<https://perma.cc/2676-UN2F>].

⁴⁷ *Fecal Transplantation (Bacteriotherapy)*, JOHNS HOPKINS MED. https://www.hopkinsmedicine.org/gastroenterology_hepatology/clinical_services/advanced_endoscopy/fecal_transplantation.html [<https://perma.cc/V7Y2-UDJR>] (last visited June 10, 2018).

⁴⁸ See Andi L. Shane, *The Problem of DIY Fecal Transplants* THE ATLANTIC (Jul. 16, 2013), <https://www.theatlantic.com/health/archive/2013/07/the-problem-of-diy-fecal-transplants/277813/> [<https://perma.cc/87A4-BPM7>]; Hyun Choi & Young-Seok Cho, *Fecal Microbiota Transplantation: Current Applications, Effectiveness, and Future Perspectives*, 49 CLIN. ENDOSC. 257, 258 (2016).

⁴⁹ See *infra* Part II.B.2.b.

⁵⁰ See, e.g., Leonardo M. R. Ferreira, *Stem Cells: A Brief History and Outlook*, HARV. (Jan. 2, 2014), <http://sitn.hms.harvard.edu/flash/2014/stem-cells-a-brief-history-and->

possibilities surrounding their use have been characterized as “endless.”⁵¹ Unlike with fecal transplants, which involve the use of a donor’s material, autologous stem cell treatments use an individual’s own tissue.⁵² While “stem cells” in general have received significant media treatment, not all stem cells are the same and often the public discourse does not acknowledge this difference.⁵³ Autologous stem cells, as opposed to allogeneic stem cells, are stem cells that come from a patient’s *own* body.⁵⁴ The medical promise of stem cells has been discussed for years, with discussion moving from the topic of embryonic stem cells (and associated discourse which often includes a political discussion of abortion) to that of adult stem cells.⁵⁵ Adult stem cells are also referred to as “autologous stem cells” and have been used as an alternative to knee replacements, to treat cardiac conditions, and to alleviate the symptoms of Parkinson’s disease.⁵⁶

* * *

The techniques examined in this Part are all innovative medical treatments that tackle medical ailments in different ways. Even though some of these techniques use the material of a donor, whereas others use a patient’s own cells to tackle ailments that pharmaceuticals and medical devices have been unable to resolve successfully, these innovative techniques should all be studied together because their clinical use faces a common challenge: FDA regulatory hurdles. The techniques examined in this Part are all alike insofar as they are innovative medical treatments that hold great promise for patient health yet, as explained in the next Part, none of these techniques clearly fits within the categories of products whose regulation is statutorily assigned to the FDA.

outlook-2/ [https://perma.cc/3GVV-KYZC].

⁵¹ See *Coaxing Cells*, JOHNS HOPKINS MED. http://www.hopkinsmedicine.org/stem_cell_research/coaxing_cells/index.html [https://perma.cc/P6DZ-P6EJ] (last visited June 10, 2018).

⁵² See NAT’L INSTS. OF HEALTH, *Hematopoietic Stem Cells*, in *STEM CELLS: SCIENTIFIC PROGRESS AND FUTURE RESEARCH DIRECTIONS* 46 (2001), <https://stemcells.nih.gov/info/2001report/chapter5.htm> [https://perma.cc/MU4W-YPDJ].

⁵³ See, e.g., *Stem Cell Basics III: What are embryonic stem cells?*, NAT’L INSTS. OF HEALTH, <https://stemcells.nih.gov/info/basics/3.htm> [https://perma.cc/JA9E-Y3TB] (last visited June 10, 2018); *Stem Cell Basics I: Introduction: What are stem cells, and why are they important?*, NAT’L INSTS. OF HEALTH, <https://stemcells.nih.gov/info/basics/1.htm> [https://perma.cc/992F-7LP8] (last visited December 3, 2018). Much of the controversy over stem cells stems from discussions of research on embryonic stem cells. *Stem Cells Fast Facts*, CNN (July 17, 2018, 4:36 PM), <http://www.cnn.com/2013/07/05/health/stem-cells-fast-facts/index.html> [https://perma.cc/CZJ8-M355].

⁵⁴ *Supra* note 53.

⁵⁵ *Id.*

⁵⁶ See Epstein, *supra* note 11; *infra* Part II.B.2.c

II. THE TENSION BETWEEN THE ADMINISTRATIVE STATE AND THE PRACTICE OF MEDICINE

Biotechnology specifically presents a challenge for regulation because, as stated by the National Academies in a 2017 report, *Preparing for the Future Products of Biotechnology*, there are several aspects of biotechnology that do not fall within the current purview of federal jurisdiction.⁵⁷ There are limits to this 2017 National Academies report; for example, human drugs and medical devices were specifically excluded from the study at a “sponsor’s request.”⁵⁸ While the report did not identify who that sponsor was, presumably, the sponsor was the FDA who was a sponsor of the 2017 report and is also the only agency that would regulate drugs and medical devices intended for human use.⁵⁹ As noted in the Introduction, this Article specifically addresses what the 2017 National Academies’ report did not. As this Part will show, when jurisdictional “gaps” occur, as they do in the regulatory space surrounding innovative treatments in the life sciences, the FDA often asserts jurisdiction and regulates that area anyway, even in the absence of statutory authorization.

This Part provides background on the intersection between federal statutory law, federal agency regulations, and the regulation of innovations in the life sciences. Current regulatory practices have created a tension between federal regulation and state jurisdiction.⁶⁰ That tension, more specifically, is one between state jurisdiction over the practice of medicine and the FDA’s continued usurpation of that state jurisdiction, which it does by regulating in areas outside of its jurisdiction. This Part explains how the FDA’s approach to these treatments that use the human body to treat illness, instead of traditional “drugs” or other “articles” is to expand federal jurisdiction over the human body, without statutory authorization, often to the detriment of innovation. There is also a tension between innovation and regulation that the FDA resolves by using a heavy-handed, risk-averse approach as opposed to one that balances jurisdictions and aims to increase the availability of life-saving treatments.

⁵⁷ See THE NAT’L ACADS. OF SCIS., ENG’G, & MED., PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY 10 (2017), available at <http://www.nap.edu/24605> [<https://perma.cc/EQN6-PYWF>].

⁵⁸ *Id.* at 2 (“Human drugs and medical devices will not be included in the purview of the study per a sponsor’s request.”).

⁵⁹ *Id.* at 17 (listing the U.S. Food and Drug Administration, U.S. Department of Agriculture, and U.S. Environmental Protection Agency as the sponsors of the report).

⁶⁰ See Lewis, *supra* note 13, at 1252.

A. Definitional Background

1. *The Practice of Medicine, Research, and Innovation*

While the pharmaceutical industry is clearly within the FDA's jurisdiction, medicine is not. As noted earlier, the practice of medicine is regulated by states.⁶¹ As indicated by the Supreme Court's ruling in *Gonzales v. Oregon*, for example, the federal government does have a role to play in affecting the practice of medicine as, for example, physicians have to obtain clearance through the Drug Enforcement Administration to prescribe certain drugs (that have been approved by the FDA).⁶² However, there are limits to the federal government's jurisdiction over the practice of medicine as the federal government cannot, for example, criminalize the actions of physicians who aid in state-approved, physician-assisted suicide because the U.S. Attorney General does not approve of such a regime.⁶³ In other words, there is some overlap between the practice of medicine and articles that are regulated by the federal government, including controlled substances and pharmaceuticals, but that overlap does not allow the federal government to regulate the practice of medicine.⁶⁴

The current FDA Commissioner (who previously worked at the FDA as Deputy Commissioner for Medical and Scientific Affairs), Scott Gottlieb, M.D.,⁶⁵ criticized the FDA's use of Risk Evaluation and Mitigation Strategies (REMS) to impose conditions on drug approvals (and ultimately physicians), while he was a Resident Fellow at the American Enterprise Institute.⁶⁶ While criticizing the REMS process, Dr. Gottlieb observed:

Too many of the [FDA]'s decisions and judgments are starting to turn on FDA's desire to regulate aspects of the practice of medicine. The agency wants to make sure that doctors conform to the FDA's judgment about how new products should be used. But FDA's control over medical practice is tenuous, and will remain so

. . . [The FDA's] judgment should not stand in for the considerations that get made in real world medical practice, where doctors and patients

⁶¹ See, e.g., Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845, 885 (2017) ("Conventional wisdom in health law and policy holds that states regulate the practice of medicine, while the federal government—specifically the FDA—regulates drugs.").

⁶² *Gonzales v. Oregon*, 546 U.S. 243, 252 (2006).

⁶³ See *Gonzales*, 546 U.S. 243.

⁶⁴ *Id.*

⁶⁵ *Meet Scott Gottlieb, M.D., Commissioner of Food and Drugs*, U.S. FOOD & DRUG ADMIN. (May 11, 2017), <https://www.fda.gov/aboutfda/centersoffices/ucm557569.htm> [<https://perma.cc/C85A-YD2Y>] [hereinafter *Meet Scott Gottlieb*].

⁶⁶ Scott Gottlieb, *FDA Safety Regs Faulted for Lax Oversight*, FORBES (Feb. 12, 2013, 3:12 PM), <https://www.forbes.com/sites/scottgottlieb/2013/02/13/fda-safety-regulations-faulted-for-lax-oversight/#503be0a64004> [<https://perma.cc/XT25-6WPC>].

have to balance difficult issues to tailor treatments to each person's unique circumstances and needs.⁶⁷

Today, five years after that criticism, Dr. Gottlieb leads an agency that continues to use the previously criticized REMS process and continues to target innovative medical treatments for onerous legal treatment.⁶⁸

Contrary to the FDA's regulatory position, using human tissue to treat patient ailments is properly categorized within the practice of medicine and not the regulation of drugs.⁶⁹ Different states have different definitions of the practice of medicine; however, it is generally seen as "the art of healing."⁷⁰ Additionally, national standards of care exist in connection with medical malpractice and the licensing of physicians.⁷¹ Medical techniques are a part of the practice of medicine, while pharmaceuticals, biologics, and vaccines, for example, are tools that are used as a part of the practice of medicine.⁷² Thus, the FDA has jurisdiction over contact

⁶⁷ *Id.* But see Press Release, U.S. Food & Drug Admin., Statement from FDA Commissioner Scott Gottlieb, M.D. on new steps to improve FDA review of shared Risk Evaluation and Mitigation Strategies to improve generic drug access (Nov. 8, 2017), <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm584259.htm> [<https://perma.cc/83LC-FKXM>].

⁶⁸ *Meet Scott Gottlieb*, *supra* note 65 ("Dr. Scott Gottlieb was sworn in as the 23rd Commissioner of Food and Drugs on May 11, 2017."); see Ariana Eunjung Cha, *FDA Cracks Down on Company Marketing 'Three-Parent' Babies*, WASH. POST (Aug. 8, 2017), https://www.washingtonpost.com/news/to-your-health/wp/2017/08/07/fda-cracks-down-on-company-marketing-three-parent-babies/?utm_term=.0562ad833f54 [<https://perma.cc/9GYZ-3HMQ>]; Letter from Mary A. Malarkey, Dir. of Office of Compliance & Biologics Quality, U.S. Food & Drug Admin., to John Zhang, PhD, MD, Chief Exec. Officer, Darwin Life, Inc. & New Hope Fertility Ctr. (Aug. 4, 2017), <https://www.fda.gov/downloads/BioLogicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ComplianceActivities/Enforcement/UntitledLetters/UCM570225.pdf> [<https://perma.cc/M28W-C4ST>].

⁶⁹ For the FDA's regulatory position, see for example *Human Cells Used in Therapy*, *supra* note 34.

⁷⁰ See *JAMA 100 Years Ago: What Constitutes the Practice of Medicine?*, 299 J. AMER. MED. ASS'N 463 (reprinted Jan. 30, 2008); see also Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 SAN DIEGO L. REV. 427, 435–36, 451 (2015).

⁷¹ See, e.g., Nicole Huberfeld, *Federalizing Medicaid*, 14 U. PA. J. CONST. L. 431, 476–79 (2011).

⁷² See, e.g., *Pharmaceutical products*, WHO, http://www.who.int/topics/pharmaceutical_products/en/ [<https://perma.cc/85RU-UQRQ>] (last visited June 10, 2018) ("Pharmaceutical products—more commonly known as medicines or drugs—are a fundamental component of both modern and traditional medicine. It is essential that such products are safe, effective, and of good quality, and are prescribed and used rationally."); see also *FDA's Role in Regulating Medical Devices*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/HomeHealthandConsumer/HomeUseDevices/ucm204884.htm> [<https://perma.cc/Q2K5-N7W2>] (last visited June 10, 2018); see also *What does FDA regulate?*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/AboutFDA/Transparency/Basics/ucm194879.htm> [<https://perma.cc/N7RE-LSFE>] (last visited June 10, 2018).

lenses and LASIK surgery machines, but it does not have jurisdiction over LASIK surgery itself, other surgical techniques, or the licensing of ophthalmologists.⁷³

Just as the line between medical practice and the tools used to practice medicine is blurring, the line between research and clinical innovation has been hazy for some time. Nonetheless, it is a significant line as it marks a limit between federal and state regulatory authority. The federal “Common Rule,” which is “heavily influenced by the Belmont Report, written in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research,” is a part of the legal foundation of the FDA’s jurisdiction over research.⁷⁴ The term “Common Rule” is a term that refers to a number of regulations promulgated by the U.S. Department of Health and Human Services that address human subjects research.⁷⁵ However, the federal government does not have regulatory authority over all research. Instead, the federal government’s authority over research is limited to categories such as research “conducted or supported by a federal department or agency” and “[r]esearch subject to regulation,” which includes research for which the government “has specific responsibility.”⁷⁶ Thus, the example offered in the regulations of “[r]esearch subject to regulation” is “Investigational New Drug requirements administered by the Food and Drug Administration” as those submitting applications for marketing approval from the FDA have to adhere to

⁷³ See, e.g., *LASIK: FDA’s Role*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/ucm061319.htm> [<https://perma.cc/XM5F-E2N7>] (last visited June 10, 2018) (“FDA regulates the sale of medical devices in the U.S. and monitors the safety of all regulated medical devices. In the U.S., FDA regulates the sale of medical devices such as the lasers used for LASIK. Before a medical device can be legally sold in the U.S., the person or company that wants to sell the device must seek approval from the FDA. To gain approval, they must present evidence that the device is reasonably safe and effective for a particular use.”).

The FDA does not have the authority to:

- Regulate a doctor’s practice. In other words, FDA does not tell doctors what to do when running their business or what they can or cannot tell their patients.
- Set the amount a doctor can charge for LASIK eye surgery.
- “Insist” the patient information booklet from the laser manufacturer be provided to the potential patient.
- Make recommendations for individual doctors, clinics, or eye centers. FDA does not maintain nor have access to any such list of doctors performing LASIK eye surgery.
- Conduct or provide a rating system on any medical device it regulates.”).

⁷⁴ *Federal Policy for the Protection of Human Subjects (‘Common Rule’)*, U.S. DEP’T HEALTH & HUM. SERVS. (Mar. 18, 2016), <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html> [<https://perma.cc/4LVY-KQ2E>].

⁷⁵ *Id.*

⁷⁶ 45 C.F.R. §§ 46.101(a), 46.102(e) (2009). For more on the limits on the federal government’s ability to regulate research, see BARRY R. FURROW ET AL., *HEALTH LAW: CASES, MATERIALS AND PROBLEMS* 1746–56 (7th ed. 2013).

those requirements.⁷⁷ Beyond that, “research” is defined by the U.S. Department of Health and Human Services (which contains the FDA) as “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”⁷⁸

Furthermore, physician efforts to aid one patient, as opposed to an investigation to aid many, are classified as “clinical innovation” or “practice” as opposed to human research or experimentation.⁷⁹ The term “medical practice” is a part of the states’ historic “police powers to legislate as to the protection of the lives, limbs, health, comfort, and quiet of all persons.”⁸⁰ The Belmont Report, for example, when distinguishing between medical practice and medical research, noted:

For the most part, the term “practice” refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals. By contrast, the term “research[.]” designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships)

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is “experimental,” in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility

⁷⁷ 45 C.F.R. § 46.102(e).

⁷⁸ 45 C.F.R. § 46.102(d). The U.S. Food and Drug Administration is a part of the U.S. Department of Health and Human Services. See *Food and Drug Administration*, U.S. DEP’T OF HEALTH & HUM. SERVS., (Mar. 18, 2016), <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/fda/index.html> [<https://perma.cc/9QTK-CC34>] (“The Food and Drug Administration (FDA) is an HHS agency that regulates clinical investigations of products under its jurisdiction, such as drugs, biological products, and medical devices.”).

⁷⁹ See, e.g., Nancy M. P. King, *The Line Between Clinical Innovation and Human Experimentation*, 32 SETON HALL L. REV. 573, 573–74 (2002); see also U.S. DEP’T OF HEALTH & HUM. SERVS., BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR PROTECTION OF HUMAN SUBJECTS OF RESEARCH (1979), <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html> [<https://perma.cc/K55Q-AHTP>] [hereinafter BELMONT REPORT].

⁸⁰ See *Gonzales v. Oregon*, 546 U.S. 243, 270 (2006) (citing *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 475 (1996) (quoting *Metro. Life Ins. Co. v. Massachusetts*, 471 U.S. 724, 756 (1985))).

*of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.*⁸¹

More specifically, Professor Nancy King observes that “specialties such as surgery, emergency and trauma medicine, and brain and spinal cord injury and rehabilitation” have been “historically exempted from standardized research pathways.”⁸² Thus, even though novel techniques are incorporated in surgery, the surgical realm of medical practice is not regulated by the FDA and is minimally regulated by individual states (to the extent that medical malpractice laws would apply *ex post* in the case of a harmful surgical procedure).⁸³ As such, novel heart surgeries, for example, are part of the practice of medicine and are not submitted to the FDA for premarket approval.⁸⁴ Similarly, even if one looks at the history of organ transplantation, while pharmaceutical protocols involved in antirejection measures, for example, might involve the action of the FDA, the transplantation techniques themselves are not subject to federal regulation.⁸⁵ Thus, even though surgery involves innovative techniques (and the use of pharmaceuticals and medical devices before, during, and after surgical procedures), this area of medical practice is not subject to the FDA’s jurisdiction.⁸⁶

⁸¹ BELMONT REPORT, *supra* note 79, at 5 (emphasis added) (citations omitted).

⁸² King, *supra* note 79, at 575.

⁸³ See, e.g., Jonathan J. Darrow, *Explaining the Absence of Surgical Procedure Regulation*, 27 CORNELL J.L. & PUB. POL’Y 189, 190 (2017) (“Yet, notwithstanding the frequency of surgical procedures and their often critical importance to patient health, no state or federal agency either approves the use of new surgical procedures or directly regulates existing procedures.”) (citing Robert S. Rhodes, *Should Surgery Have an FDA?*, AMA J. ETHICS (Oct. 2004), <https://journalofethics.ama-assn.org/2004/10/pfor2-0410.html>); Anna C. Mastroianni, *Liability, Regulation and Policy in Surgical Innovation: The Cutting Edge of Research and Therapy*, 16 HEALTH MATRIX 351, 353–54, 357–59 (2006).

⁸⁴ Mastroianni, *supra* note 83, at 372–98.

⁸⁵ See STARZL, *supra* note 1, at 212, 222, 240 (discussing the process of obtaining cyclosporine for use in liver transplantation). *But see id.* at 295 (“No week goes by without a newspaper or television story about overregulation by the FDA that has prevented the orderly development of a drug or device, or about under-regulation and release of an unsafe product. We were astonished at what we found. Each of the FDA scientists was an expert in his or her own right and understood perfectly what we had to report. When we finished, they pointed out the gaps in our research (mostly toxicology), what safeguards they thought would be necessary if clinical trials ever were to be considered, and how our work so far did or did not fulfill FDA requirements. They invited us to return when we had more results to report.”); *id.* (lauding especially the work of Dr. Gregory Burke at the U.S. Food and Drug Administration during the time that Dr. Thomas Starzl and others were developing research and treatment protocols related to the use of cyclosporine to prevent the rejection of newly transplanted human livers).

⁸⁶ King, *supra* note 79, at 575.

2. *Drugs*

As its name suggests, the FDA has jurisdiction over food and drugs, in addition to medical devices, tobacco, and a broader category of tools called “biologics,” but not the practice of medicine, which is within the jurisdiction of the states.⁸⁷ Medical innovations are not drugs as they are not “articles,” which is a term used multiple times in the definition of “drug.”⁸⁸ The Federal Food, Drug, and Cosmetic Act defines a “drug”:

The term “drug” means (A) articles recognized in the official United States Pharmacopœia, official Homœopathic Pharmacopœia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals⁸⁹

The definition of drug was crafted in 1938 and even with amendments, the definition has failed to keep pace with the innovations of today.⁹⁰ For example, “[w]hereas the prototypical drug in the late nineteenth century was a natural remedy whose safety and effectiveness were established through longstanding practice and traditional knowledge, today’s prototypical drug is a synthetic, laboratory-developed substance that has been subjected to intensive scientific research and approved by the government.”⁹¹

While much of the analysis of innovative medical techniques focuses on the idea that they may cure, mitigate, or treat disease, it is important not to neglect the term “article” in the definition.⁹² The word “article” matters because, as the FDA

⁸⁷ 21 U.S.C. § 321(g)(1) (2018); 42 U.S.C. § 262(2)(c) (2018); *see also* *Gonzales v. Oregon*, 546 U.S. 243, 270 (2006) (discussing the state’s historic police power over the practice of medicine).

⁸⁸ 21 U.S.C. § 321(g)(1); *see, e.g.*, Elizabeth C. Price, *Does the FDA Have Authority to Regulate Cloning?*, 11 HARV. J.L. & TECH. 619, 629–34 (1998) (discussing the importance of the word “article” in the definition of “drug”).

⁸⁹ 21 U.S.C. § 321(g)(1).

⁹⁰ *See, e.g.* MICHELLE MEADOWS, PROMOTING SAFE AND EFFECTIVE DRUGS FOR 100 YEARS, FDA CONSUMER MAG. (2006); *see also* Javitt & Hudson, *supra* note 44, at 1219 (“The [Food Drug & Cosmetic] Act has been amended eighty-eight times since its enactment in 1938.”).

⁹¹ Lewis A. Grossman, *Food, Drugs, and Droids: A Historical Consideration of Definitions and Categories in American Food and Drug Law*, 93 CORNELL L. REV. 1091, 1095–96 (2008).

⁹² *Id.*

and many commentators have indicated,⁹³ the FDA does not have jurisdiction over the practice of medicine.⁹⁴ Whereas “drugs” are “articles” or “items,” techniques are procedures that are a part of the practice of medicine, and thus not subject to the FDA’s jurisdiction.⁹⁵ Thus, traditional ART techniques such as *in vitro* fertilization or artificial insemination, for example, are not regulated by the FDA because they are procedures and not “articles.”⁹⁶ Extending that analogy, innovative techniques such as fecal transplants or stem cell treatments are also procedures as opposed to articles. Similarly, while CRISPR-Cas9 will likely involve a delivery method (so as to deliver the “product” that will edit the relevant gene(s)), the gene editing itself would not be an “article”; as such the entire technique would not fall within the FDA’s jurisdiction.⁹⁷ Instead, as emphasized *infra* in Part IV, a hybrid method of state–federal regulation (to the extent that any federal regulation is involved) would likely be required to regulate adequately new innovations in the life sciences.

3. *Biologics*

While the definition of “biologic,” another category of product regulated by the FDA, is a broad one, innovative new medical techniques studied in this Article likely do not fall within that classification either. A “biological product” is defined as

a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.⁹⁸

⁹³ See 21 U.S.C. § 321(g)(1) (providing the definition of “drug” which uses the word “articles” four times); see also Price, *supra* note 88, at 630 (“As an initial matter, it is important to note that both of these definitions are limited to ‘articles.’ Thus, if the FDA wishes to assert jurisdiction over human cloning under the drug definition of the FDCA, it must first identify the requisite ‘article’ to regulate. Although the term ‘article’ is not defined in the FDCA itself, the ordinary meaning of the word is ‘a member of a class of things; *esp.*: a piece of goods.’”).

⁹⁴ See, e.g., Zettler, *supra* note 61, at 885 (“Conventional wisdom in health law and policy holds that states regulate the practice of medicine, while the federal government—specifically the FDA—regulates drugs.”).

⁹⁵ See 21 U.S.C. § 321(g)(1) (providing the definition of “drug” in the Federal Food, Drug, and Cosmetic Act).

⁹⁶ See *supra* note 32 and accompanying text; see also Lewis, *supra* note 13, at 1252–53 nn. 49–53.

⁹⁷ See, e.g., Emily Mullen, *Five Ways to Get CRISPR into the Body*, MIT TECH. REV. (Sept. 22, 2017), <https://www.technologyreview.com/s/608898/five-ways-to-get-crispr-into-the-body/> [<https://perma.cc/24CJ-E57P>].

⁹⁸ 42 U.S.C. § 262(B)(i)(1) (2018).

As the definition indicates, “blood,” a “bodily fluid,” merited a specific reference in the statute, whereas other parts of the human body are not mentioned.⁹⁹ Biologics, like drugs, have existed for some time in the medical sphere although their nature has changed: “Biologics are not new; development of human growth hormone, insulin, and red-blood cell stimulating agents occurred decades ago, but the targets have increased exponentially with new genetic information and new understanding of subcellular cascades and disease processes.”¹⁰⁰ So, for example, the human growth hormone is not created from an individual’s own hormones, nor is insulin, and “red-blood cell stimulating agents” are similarly manufactured hormones that are provided in “drug” form.¹⁰¹ Unlike the conventional biologics that often involve the use of external material to create what the body lacks, innovative medical treatments focus on using the patient’s own tissues or another person’s tissues as a treatment.

4. *Regenerative Advanced Therapies*

Congress had the opportunity to clarify the definition of “drug” within the 21st Century Cures Act, and while the Act accelerated the approval process for certain innovations, the statutory classifications created by the Act failed to increase the statutory scope of products regulated by the FDA. The 21st Century Cures Act identified a new category of products, called “regenerative advanced therapies,” yet the addition of this new statutorily recognized category does not resolve the jurisdictional challenges that this Article addresses. A “regenerative advanced therapy” is a type of “drug.” Thus, while the 21st Century Cures Act has added a term to the FDA’s regulatory repertoire, it does not provide an additional definition. Regenerative advanced therapies are significant because any drug that is classified as a regenerative advanced therapy is eligible for expedited review; yet, it is still a “drug.”¹⁰² According to the 21st Century Cures Act (as incorporated into the Federal Food, Drug, and Cosmetic Act),

⁹⁹ See *Blood*, PUBMED HEALTH, (Sept. 2004) <https://www.ncbi.nlm.nih.gov/pubmed/health/PMHT0022037/> [<https://perma.cc/DQ5V-DBEP>].

¹⁰⁰ Thomas Morrow & Linda H. Felcone, *Defining the Difference: What Makes Biologics Unique*, BIOTECHNOLOGY HEALTHCARE 24, 24–29 (2004), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3564302/> [<https://perma.cc/YPZ8-Q9ZG>].

¹⁰¹ See, e.g., *Erythropoietin-Stimulating Agents*, CLEVELAND CLINIC (Sept. 9, 2014), <https://my.clevelandclinic.org/health/drugs/14573-erythropoietin-stimulating-agents> [<https://perma.cc/RJC8-PAHB>] (“In order to make red blood cells, the body maintains an adequate supply of erythropoietin (EPO), a hormone that is produced by the kidney Having more red blood cells raises your hemoglobin levels Anemia is a disorder that occurs when there is not enough hemoglobin in a person’s blood Anemia can be caused by the body’s inability to produce enough EPO. . . . [In some cases], it may be necessary to give the patient recombinant erythropoietin[,] . . . a man-made version of natural erythropoietin.”).

¹⁰² 21 U.S.C. § 356 (g)(2) (2016).

A drug is eligible for designation as a regenerative advanced therapy under this subsection if--

(A) the drug is a regenerative medicine therapy (as defined in paragraph (8));

(B) the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and

(C) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition.¹⁰³

Section 356 of the Food, Drug, and Cosmetic Act (as amended by the 21st Century Cures Act) explains that

For purposes of this section, the term “regenerative medicine therapy” includes cell therapy, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products, except for those regulated solely under section 361 of the Public Health Service Act and part 1271 of title 21, Code of Federal Regulations.¹⁰⁴

Thus, as indicated, “regenerative medicine therapy” is a term whose definition is provided for the purposes of Section 356 (referred to as “this section” in the above-quoted language) of the Federal Food, Drug, and Cosmetic Act, which is entitled “Expedited approval of drugs for serious or life-threatening diseases or conditions.”¹⁰⁵ Yet, the statutory provision did not define the terms used in the definition of “regenerative medicine therapy.” Instead, the terms used in the definition of “regenerative medicine therapy” remain vaguely defined in FDA regulations; furthermore, these unclear definitions are accompanied by similarly vague, non-binding guidance documents that attempt to explain what these terms mean in the FDA’s regulatory space.¹⁰⁶ As such, instead of clarifying what a drug is, which is defined in Section 321 of the Federal Food, Drug, and Cosmetic Act, legislators made an administrative determination in the 21st Century Cures Act as to which “drugs” merit priority review by a federal agency.¹⁰⁷

¹⁰³ *Id.*

¹⁰⁴ 21 U.S.C. § 356 (g)(6) (2016). The term “regenerative medicine therapy” is also used in Section 506(g) of the 21st Century Cures Act, “Standards for Regenerative Medicine and Regenerative Advanced Therapies” (codified at 21 USC § 356(g) (2016)) which addresses evidentiary standards for the approval of such therapies, along with Sec. 3034. Guidance regarding devices used in the recovery, isolation, or delivery of regenerative advanced therapies (codified at 21 USC § 356(g). and Sec. 3035. Report on regenerative advanced therapies (codified at 21 USC § 356).

¹⁰⁵ 21 U.S.C. § 356.

¹⁰⁶ *See, e.g., infra* Part II.B.1 (discussing the FDA’s Human Cellular and Tissue-Based Products Rule).

¹⁰⁷ Section 321 of the Federal Food, Drug, and Cosmetic Act is codified at 21 U.S.C. §

* * *

The statutory language of the Federal Food, Drug, and Cosmetic Act does not permit an extensive construction of the terms “drug” or “biologic” so as to incorporate the human body. Furthermore, the 21st Century Cures Act does not provide additional jurisdictional authority, even though proponents and authors of the legislation knew of forthcoming innovative life sciences, with an emphasis on the use of autologous stem cells.¹⁰⁸ Thus, the FDA’s regulatory perspective is based on an unreasonable construction of the statute as the FDA has yet to explain how the human body is an article subject to regulation. Second, it is impermissible to construe the statute so as to cover genetic modifications and unforeseen inventions. The next Section provides background on the *ad hoc* regulatory structure that the FDA has created in order to apply the Federal Food, Drug, and Cosmetic Act to the unforeseen inventions of the life sciences. It then explains how the FDA has specifically targeted many life-sciences innovations for federal regulation even though an agency should not govern in the absence of statutory direction.

B. FDA Regulations and Guidance Documents

The FDA regulates techniques involving genetic modifications in a subterranean manner.¹⁰⁹ Subterranean regulation is characterized by (1) a lack of jurisdiction; (2) regulation through letters instead of clearly applicable rules; and (3) a chilling effect on research.¹¹⁰ This Article has demonstrated that subterranean regulation is not limited to ART, but that it indeed extends to a number of innovations in the life sciences. Specifically, the FDA references its rule on human cells, tissues, and cellular and tissue-based products (Human Cellular and Tissue-Based Products Rule) in communications that it issues to physicians and researchers that aim to hinder the clinical use of innovative medical techniques.¹¹¹

321(g)(1) (2018).

¹⁰⁸ See, e.g., 21st Century Cures Act, Beau Biden Cancer Moonshot and NIH Innovation Projects, Pub. L. No. 114–255, § 1001(b)(D), available at <https://www.congress.gov/bill/114th-congress/house-bill/34/> [<https://perma.cc/6AEF-9FCT>] (“For the National Institutes of Health, in coordination with the Food and Drug Administration, to award grants and contracts for clinical research to further the field of *regenerative medicine using adult stem cells, including autologous stem cells*, for which grants and contracts shall be contingent upon the recipient making available non-Federal contributions toward the costs of such research in an amount not less than \$1 for each \$1 of Federal funds provided in the award, not to exceed a total of \$30,000,000, as follows” (emphasis added)).

¹⁰⁹ See Lewis, *supra* note 13, at 1272–73.

¹¹⁰ *Id.* at 1254–56.

¹¹¹ *Id.* at 1266–71.

1. Human Cellular and Tissue-Based Products Rule

Notice-and-comment rulemaking, has been described as a method to allay the negative aspects of regulatory decision-making; however, it is not without fault.¹¹² The FDA bases its regulation of innovative medical techniques, especially those involving genetic modifications, on the agency's Human Cellular and Tissue-Based Products Rule.¹¹³ While the regulation was subject to the notice-and-comment process, it still suffers from various shortcomings. For example, the regulation itself is written unclearly, despite public comments suggesting modification.¹¹⁴

The FDA's Human Cellular and Tissue-Based Products Rule uses the term "minimally manipulated,"¹¹⁵ which has a counter-intuitive meaning.¹¹⁶ The term surfaces not only in the FDA's communications with researchers that the agency sees as operating without its approval but also in at least one federal court decision addressing the legality of the actions of physicians and researchers.¹¹⁷ "Minimal manipulation" is "processing that does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement . . . [or] the relevant biological characteristics of cells or tissues."¹¹⁸ The regulation does not further define the other terms used in the definition of "minimal manipulation" such as "original relevant characteristics," "relevant biological characteristics," or "utility."¹¹⁹ During the notice-and-comment process (prior to the finalization of the rule), various public commenters objected to the use of the term "minimal manipulation"; however, the FDA still retained the term.¹²⁰

¹¹² Mark Seidenfeld, *Who Decides Who Decides: Federal Regulatory Preemption of State Tort Law*, 65 N.Y.U. ANN SURV. AM. L. 611, 645 (2010) [hereinafter Seidenfeld, *Who Decides Who Decides*]; see also *id.* at 649 ("In addition, scholars have reported that in several instances, agencies have abused the notice-and-comment process by sneaking preemption provisions into the preamble to rules thereby avoiding the notice-and-comment process altogether." (citing Catherine Sharkey, *Federalism Accountability: "Agency-Forcing" Measures*, 58 DUKE L.J. 2125, 2131–34 (2009)).

¹¹³ See Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. 5447 (Jan. 19, 2001) (codified at 21 C.F.R. pts. 207, 807, 1271 (2018)), available at <https://www.gpo.gov/fdsys/pkg/FR-2001-01-19/pdf/01-1126.pdf> [<https://perma.cc/DWB8-QEN5>] [hereinafter Human Cells].

¹¹⁴ See *id.* at 5450–62.

¹¹⁵ *Id.* at 5457.

¹¹⁶ *Id.* (discussing submitted comments which described the term as "vague and open to subjective interpretation").

¹¹⁷ See discussion *infra* Part II.B.2.c. (discussing *U.S. v. Regenerative Sciences* and the FDA's letters to other providers of innovative techniques such as OvaScience and Celltex).

¹¹⁸ Human Cells, *supra* note 113, at 5467.

¹¹⁹ *Id.*

¹²⁰ See *id.* at 5457 ("We disagree that the term should be eliminated . . ."); see also *United States v. Regenerative Scis., LLC*, 741 F.3d 1314, 1321–22 (2014); Lewis, *supra* note 13, at 1241–44 (discussing the FDA's issuance of Untitled Letters to providers of cytoplasmic transfer).

While non-legislative documents have been lauded for providing benefits such as flexibility in nascent industries, the FDA uses them to *hinder* the clinical use of innovations in the life sciences. The FDA accomplishes this by subjecting those innovations to burdensome regulatory requirements, which has a “chilling effect” on their clinical use.¹²¹ Other scholars have criticized federal agencies’ overuse of guidance documents, with some specifically criticizing the FDA’s overuse of non-legislative rules, including guidance documents.¹²² On the other hand, those in favor of increased deference to federal agencies often note the specialization of agency employees.¹²³ Yet, as noted *infra*, while the FDA certainly has specialists in pharmaceutical regulation—especially in regulating drugs, to the extent that drugs are pharmaceuticals like analgesics or antidepressants—the deference to agency specialization is more difficult to support when it comes to innovative medical techniques.¹²⁴ Considering the recentness of new techniques that focus on using the human body to cure ailments and the FDA’s historical role in regulating pharmaceuticals as opposed to the practice of medicine, it is less likely that the appropriate area of regulatory specialization rests solely with the FDA.

¹²¹ See, e.g., Lewis, *supra* note 13, at 1241–44 (discussing the FDA’s issuance of Untitled Letters to providers of cytoplasmic transfer which ultimately led to the technique becoming unavailable in the United States); see also *United States v. Regenerative Scis., LLC*, 878 F. Supp.2d 248, 252 (D.D.C. 2012), *aff’d*, 741 F.3d 1314 (D.C. Cir. 2014) (noting that the FDA sent a letter to Regenerative Sciences in which it “notified Regenerative that the FDA believed that the cell product used in the Regenexx™ Procedure constituted a drug under the FFDCRA and a biological product under the Public Health Service Act, 42 U.S.C. § 262 (‘PHSA’). Further, the FDA stated that because Regenerative had not obtained the necessary approvals for the cell product, its actions in this regard were possibly unlawful.”). For more on the *Regenerative Sciences* litigation, see discussion *infra* Part II.B.2.c; see also Tim Wu, *Agency Threats*, 60 DUKE L.J. 1841, 1850–54 (2011).

¹²² For more on guidance documents in general, see generally Seidenfeld, *supra* note 25. For FDA-specific criticisms, see generally Lars Noah, *Governance by the Backdoor: Administrative Law (Lessness?) at the FDA*, 93 NEB. L. REV. 89 (2014). See also Nina A. Mendelson, *Regulatory Beneficiaries and Informal Agency Policymaking*, 92 CORNELL L. REV. 397, 408 (2007) (“[B]y issuing a guidance document, an agency can obtain a rule-like effect while minimizing political oversight and avoiding the procedural discipline, public participation, and judicial accountability required by the APA. The prospect of ‘compliance for less’ is almost certainly among the reasons that agencies use guidance documents rather than go through the effort of notice-and-comment rulemaking.”).

¹²³ See, e.g., Seidenfeld, *Who Decides Who Decides*, *supra* note 112, at 618.

¹²⁴ See, e.g., Centers for Disease Control and Prevention, *Therapeutic Drug Use*, NAT’L CENTER FOR HEALTH STATISTICS, <https://www.cdc.gov/nchs/fastats/drug-use-therapeutic.htm> [<https://perma.cc/7DVK-V9XE>] (last visited June 10, 2018).

2. *Non-legislative Rules: The FDA's Current Method of Regulating Innovative Medical Techniques*

(a) *Genetic Modifications of the Human Body*

With the addition of genetic modifications, ART has moved from being an area of state regulation and experimentation to an area of federal regulation, resulting in additional regulatory barriers.¹²⁵ For example, the clinical use of forms of ART that involve genetic modifications has been hindered by the exercise of agency power through non-legislative rules.¹²⁶ While ART was originally used to aid couples dealing with fertility difficulties, a new form of ART, mitochondrial transfer, has received significant attention recently due to its ability to prevent the transmission of harmful genetic diseases from parents to their children.¹²⁷ As noted in Part I, clinical trials related to mitochondrial transfer are underway in the United Kingdom, while in the United States, the technique has been subjected to burdensome regulatory requirements, resulting in a chilling effect on research and clinical use of the technique.¹²⁸ For years, the FDA would send letters to physicians and researchers stating that in order for those individuals to continue using innovative techniques like mitochondrial transfer and a related technique, cytoplasmic transfer, they would have to submit an investigational new drug application as a part of the FDA's extensive (and expensive) drug-approval process.¹²⁹ As a result, U.S.-based physicians have provided the technique abroad, most notably in Mexico, in order to avoid the restrictive regime created by the FDA.¹³⁰

¹²⁵ For an overview of state laws related to assisted reproductive technology, see generally CHARLES P. KINDREGAN, JR. & MAUREEN MCBRIEN, *ASSISTED REPRODUCTIVE TECHNOLOGY: A LAWYER'S GUIDE TO EMERGING LAW AND SCIENCE* (2d ed. 2011) (chronicling the ongoing legal developments within the field of ART).

¹²⁶ See, e.g., *Restrictions on Mitochondrial Replacement Techniques*, *supra* note 33.

¹²⁷ See, e.g., *Doctors given approval for UK's first 'three-person babies'*, BBC NEWS (Feb. 2, 2018), <http://www.bbc.com/news/health-42918341> [<https://perma.cc/3ECL-SA7W>]; Paula Amato et. al., *Three-Parent IVF: Gene Replacement for the Prevention of Inherited Mitochondrial Diseases*, FERTILITY AND STERILITY (2014), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4005382/pdf/nihms-571742.pdf> [<https://perma.cc/EY9Z-62A4>]; *Human Cells Used in Therapy*, *supra* note 34.

¹²⁸ See, e.g., James Masters, "Three-parent" babies approved in the UK, CNN (Dec. 15, 2016), <http://www.cnn.com/2016/12/15/health/babies-three-people-embryos/index.html> [<https://perma.cc/K3UU-DJVH>].

¹²⁹ *Id.*; see also Jason Millman, *Does it really cost \$2.6 billion to develop a new drug?*, WASH. POST (Nov. 18, 2014), https://www.washingtonpost.com/news/wonk/wp/2014/11/18/does-it-really-cost-2-6-billion-to-develop-a-new-drug/?utm_term=.45ffc90434b4 [<https://perma.cc/DZE3-Q7XZ>].

¹³⁰ Michelle Roberts, *First 'three person baby' born using new method*, BBC (Sept. 27, 2016), <http://www.bbc.com/news/health-37485263> [<https://perma.cc/GQX9-9EXN>] (noting also that the provision of mitochondrial transfer to a Jordanian family in Mexico by U.S. based physicians aimed to avoid maternal transmission of Leigh Syndrome: "Leigh

AUGMENT—a method that uses a woman’s own genetic material to improve her fertility—is another innovative technique that has been the subject of the FDA’s subterranean regulation.¹³¹ After telling its shareholders for some time that the technique would not have to go through the FDA’s extensive regulatory process for premarket approval, OvaScience, the creator of AUGMENT, received a letter from the FDA informing the company otherwise: If OvaScience wished to continue providing AUGMENT in the United States, then it would need to be approved through the FDA’s extensive investigational new drug application and approval process.¹³² Now, OvaScience only provides AUGMENT to patients outside the United States.¹³³ While it is certainly useful for companies to discover that the FDA

syndrome . . . would have proved fatal to any baby conceived. The family had already experienced the heartache of four miscarriages as well as the death of two children—one at eight months and the other at six years of age.”)

¹³¹ See 21st Century Cures Act, *supra* note 6 and accompanying text.

¹³² See FOIA REQUEST 2016-4882 (on file with author) (The FDA’s letter noted, in pertinent part:

Our understanding is that your autologous mitochondrial transfer product, AUGMENT, consists of cells isolated from a biopsy of ovarian tissue, which are processed to extract mitochondria that are then introduced into other reproductive tissues during the IVF process. The removal of mitochondria and introduction into other reproductive tissue appears to be more than minimal manipulation. This is based on the limited information available; please note that the addition of mitochondrial DNA to other reproductive tissue may raise additional regulatory concerns.

See also Complaint at 2, *Ratner v. OvaScience Inc.*, 134 F.Supp. 3d 621 (D. Mass. 2013) (No. 14-12412) (“Throughout the Class Period, Ova[S]cience represented to the FDA and investors that it believed that Augment qualified for designation as a 361 HCT/P, which allows human cellular and tissue based products to be tested and marketed without FDA licensure. Under FDA guidelines, organisms can only achieve this designation if they are ‘only minimally manipulated,’ i.e., the process does not alter ‘the relevant biological characteristics of the cells or tissue.’ . . . Ultimately, the FDA rejected OvaScience’s faulty designation. On September 10, 2013, the Company disclosed that it was suspending enrollment of AUGMENT in the U.S. after receiving an ‘untitled’ letter from the FDA ‘questioning the status of AUGMENT as a 361 HCT/P and advising the Company to file an Investigational New Drug (IND) application.’”).

¹³³ *Id.*; see also OVASCIENCE, INC, FORM 10-K 14 (2016), <http://ir.ovascience.com/static-files/0b856624-270a-4dc6-be45-b337e3317092> [<https://perma.cc/6DCG-QF84>] (“The United States does not have a fertility regulatory body separate and apart from the FDA. In September 2013, we received an ‘untitled’ letter from the FDA advising us to file an IND application for the AUGMENT treatment. Following the receipt of the FDA letter, we chose to suspend the availability of the AUGMENT treatment in the United States. We plan to meet with the FDA in the first half of 2017, as part of our ongoing exploration of potential entry into the U.S. market.”); *Pipeline and Treatments*, OVASCIENCE, <http://www.ovascience.com/treatments/> [<https://perma.cc/YCL5-TFRE>] (last visited June 10, 2018).

has “flagged” their techniques for potential enforcement action, it does not resolve the crucial issue of whether the FDA should target them for enforcement action in the first place, based on its statutory mandate.

The FDA took a similar approach to cloning in 1998, which does not receive in-depth treatment in this Article because human reproductive cloning has not been identified as a treatment for any ailments.¹³⁴ The FDA took this approach even though members of Congress had tried (and failed) multiple times to pass legislation that would specifically prohibit human reproductive cloning in the United States, suggesting that at least some of those individuals responsible for defining the FDA’s jurisdiction were concerned that the current regime was insufficient.¹³⁵

(b) *Fecal Microbiota Transplants*

Fecal microbiota transplants should not be subject to FDA regulation as they are not “drugs” or “biologics.” Further, the FDA has not explained what about these techniques renders them “drugs” or “biologics.” Nonetheless, the FDA has asserted that it has jurisdiction over these procedures through guidance documents, another way of regulating in a confusing manner.¹³⁶ Guidance documents represent a confusing way of regulating because they are not binding upon the agencies that issue them, and—as illustrated by changes in the FDA’s guidance documents related

¹³⁴ Stuart L. Nightingale, *Letter About Human Cloning*, U.S. FOOD & DRUG ADMIN. (Oct. 26, 1998), <https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm150508.htm> [<https://perma.cc/3NQJ-UQAM>] (“The purpose of this letter is to confirm to institutional review boards (IRBs) that the Food and Drug Administration (FDA) has jurisdiction over clinical research using cloning technology to create a human being, and to inform IRBs of the FDA regulatory process that is required before any investigator can proceed with such a clinical investigation.”).

¹³⁵ Richard A. Merrill & Bryan J. Rose, *FDA Regulation of Human Cloning: Usurpation or Statesmanship?*, 15 HARV. J.L. & TECH. 85, 98–99 (2001); *See also The Great Cloning Debate*, ECONOMIST, May 9, 2002, <https://www.economist.com/node/1125284> [<https://perma.cc/BH5H-BTGB>].

¹³⁶ *See* FDA, ENFORCEMENT POLICY REGARDING INVESTIGATIONAL NEW DRUG REQUIREMENTS FOR USE OF FECAL MICROBIOTA FOR TRANSPLANTATION TO TREAT *CLOSTRIDIUM DIFFICILE* INFECTION NOT RESPONSIVE TO STANDARD THERAPIES: DRAFT GUIDANCE FOR INDUSTRY, 1 (2016), *available at* <https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/vaccines/ucm488223.pdf> [<https://perma.cc/CSC6-FJ8N>] [hereinafter 2016 GUIDANCE]; *see also* FDA, GUIDANCE FOR INDUSTRY: ENFORCEMENT POLICY REGARDING INVESTIGATIONAL NEW DRUG REQUIREMENTS FOR USE OF FECAL MICROBIOTA FOR TRANSPLANTATION TO TREAT *CLOSTRIDIUM DIFFICILE* INFECTION NOT RESPONSIVE TO STANDARD THERAPIES 1 (2013), *available at* <https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/UCM361393.pdf> (explaining prior enforcement guidance on the use of fecal microbiota transplants in the United States) [<https://perma.cc/PK95-6T9A>] [hereinafter 2013 GUIDANCE].

to fecal microbiota transplants—they can be withdrawn and replaced far more easily than agency regulations.¹³⁷

The FDA’s interpretation of the law is that an investigational new drug application is necessary in order to carry out a fecal microbiota transplant in the United States.¹³⁸ Initially, just as with the use of forms of ART that involve genetic modifications, the FDA stated that physicians performing fecal transplants must submit an investigational new drug application similar to that which pharmaceutical companies must submit to have a new drug approved.¹³⁹ Ultimately, the FDA changed its policy for fecal transplants involving known, but not unknown, donors.¹⁴⁰ Specifically, the agency has stated that it “intend[s] to exercise enforcement discretion under limited conditions, regarding the investigational new drug (IND) requirements for the use of fecal microbiota for transplantation (FMT) to treat *Clostridium difficile* (*C. difficile*) infection not responding to standard therapies.”¹⁴¹ In other words, the FDA will not pursue legal action against physicians who comply with the provisions outlined in the guidance document; however, there is no guarantee of continued enforcement discretion as the agency’s statement comes through a nonbinding document.¹⁴²

The FDA announced this policy change through a guidance document which includes a prominent disclaimer on the first page, stating:

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.¹⁴³

As indicated by the FDA’s language, guidance documents are not legally enforceable; the agency could implement a different policy in enforcement actions, and those acting in accordance with the guidance document would have no legal protection by “relying” on the agency’s expressed position. Additionally, stool banks are not beneficiaries of the FDA’s intent to exercise enforcement discretion.¹⁴⁴ By targeting stool banks, the guidance document, to the extent that it is binding (or

¹³⁷ See 2013 GUIDANCE, *supra* note 136 (“FDA’s guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA’s current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.”).

¹³⁸ *Id.*

¹³⁹ *Id.*

¹⁴⁰ 2016 GUIDANCE, *supra* note 136, at 3.

¹⁴¹ *Id.* at 1.

¹⁴² *Id.*

¹⁴³ *Id.*

¹⁴⁴ *Id.* at 3.

influences decision-making in the way that binding guidance would), minimizes the number of available donors.¹⁴⁵

As a result, the limited options available to physicians and patients are (1) to submit an investigational new drug application, which comes with extremely high costs (both in time and in research funding) or (2) to follow a guidance document that clearly states it is not final and that limits the availability of donors to aid patients, as based on an FDA assertion of “jurisdiction.”¹⁴⁶ The FDA has exerted authority over another aspect of the practice of medicine—fecal transplants—to the chagrin of many patients who travel to other States to find sympathetic physicians after their primary physicians refuse to perform the procedure or watch YouTube videos to prepare for their own at-home attempts of procedures that their physicians will not perform.¹⁴⁷ Similarly, the websites of major academic hospitals offering fecal transplants indicate that physicians understand that they must proceed relying upon the FDA’s enforcement discretion, which is unpredictable.¹⁴⁸

(c) *Stem Cell Treatments*

The promise of stem cell research is being stymied by FDA regulation. In spite of an FDA employee-authored article in the *New England Journal of Medicine* asserting at the outset that the agency shared the “current excitement over the

¹⁴⁵ See *id.* at 1 (“The consent should include, at a minimum, a statement that the use of FMT products to treat *C. difficile* is investigational and a discussion of its reasonably foreseeable risks; 2) the FMT product is not obtained from a stool bank; and 3) the stool donor and stool are qualified by screening and testing performed under the direction of the licensed health care provider for the purpose of providing the FMT product for treatment of the patient.”).

¹⁴⁶ But see *id.* at 3 (stating that waivers may be available for investigational new drug application sponsors who are “within” or “affiliated with a stool bank”). Nonetheless, the guidance is still non-binding and there is no guarantee that a waiver will be granted. See *FDA Struggles*, *supra* note 46 (“Duff says the unresolved status of FDA’s oversight discourages more doctors from offering the treatment. ‘There are so many doctors who are suspicious that the FDA could change their mind at any given moment and decide to not exercise discretion,’ Duff says.”); Maryn McKenna, *Fecal Transplants: They Work, the Regulations Don’t*, WIRED (Dec. 9, 2011 6:20 AM) <https://www.wired.com/2011/12/fecal-transplants-work/> [<https://perma.cc/CT3A-5DRD>] (noting that an investigational new drug application is necessary for NIH Funding of fecal transplantation); Millman, *supra* note 129.

¹⁴⁷ See, e.g., *Doctors Using Fecal Transplants*, *supra* note 46; see also *FDA Struggles*, *supra* note 46; Mary Brophy Marcus, *Fecal transplants need better regulation, experts say*, CBS NEWS (Oct. 23, 2015 6:00 AM) <https://www.cbsnews.com/news/fecal-transplants-need-better-regulation-experts-say/> [<https://perma.cc/8FBT-AY8E>].

¹⁴⁸ See, e.g., MAYO CLINIC, *supra* note 27 (“Maria I. Vazquez Roque, M.D., a gastroenterologist at Mayo Clinic’s campus in Jacksonville, Florida, observes that the Food and Drug Administration (FDA) initially proposed requiring investigational new drug (IND) status for FMT procedures. That stance would have denied access to the procedure for many, if not most, patients and was later changed. For the time being, the FDA exercises enforced discretion.”) [<https://perma.cc/Q6VG-TW89>].

potential for stem cell therapy to improve patient outcomes or even cure diseases,” the agency’s actions are somewhat contrary to that message.¹⁴⁹ Instead, the agency’s position, as indicated by the content of its publication in the *New England Journal of Medicine*, is that there is a “lack of evidence” as it relates to the “effectiveness of stem-cell treatments.”¹⁵⁰ The use of stem cells as an alternative to open heart surgery (and, in at least one case, after open heart surgery had failed) has also been hindered due to the FDA’s action.¹⁵¹ Thus, the use of autologous stem cells represents another area in which clinical innovation—which has generally occurred without federal involvement—is stymied through the current regulatory apparatus.¹⁵²

Consequently, those physicians who want to use these innovative procedures in their practice must await research trials related to the use of stem cells in the treatment of cardiac problems such as cardiomyopathy (a disease that can cause heart failure), even if such treatments would be the only option to save a patient.¹⁵³ In the meantime, clinical trials have been taking place abroad and at certain U.S. research hospitals.¹⁵⁴

¹⁴⁹ Peter W. Marks, Cella M. Witten & Robert M. Califf, *Clarifying Stem-Cell Therapy’s Benefits and Risks*, 376 N. ENGL. J. MED. 1007, 1007 (2017) (the author affiliation note at the end of the article indicates that the article is “[f]rom the Food and Drug Administration, Silver Spring, MD”). FDA documents confirm the employment of the authors, with Robert Califf (the third listed author) having served as the agency’s Commissioner from February 2016 until January 2017. *See Biography of Robert M. Califf, M.D.*, U.S. FOOD & DRUG ADMIN. (Jan. 26, 2017) <https://www.fda.gov/AboutFDA/History/FOrgsHistory/Leaders/ucm537751.htm> [<https://perma.cc/9PVX-7UTT>]; *Meet Peter Marks, M.D., Ph.D., Director, Center for Biologics Evaluation and Research*, U.S. FOOD & DRUG ADMIN. (Jan. 15, 2016) <https://www.fda.gov/AboutFDA/CentersOffices/ucm481936.htm> [<https://perma.cc/X2AN-KB7V>]; *CBER: Key Staff Directory*, U.S. FOOD & DRUG ADMIN. (May 14, 2018) <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm123224.htm> [<https://perma.cc/5QYL-PBQN>].

¹⁵⁰ Marks, Witten & Califf, *supra* note 149, at 1008.

¹⁵¹ *See* Epstein, *supra* note 11, at 1–2.

¹⁵² *See* Wash. Legal Found. v. Kessler, 800 F. Supp. 26, 35–36 (D.D.C. 1995) (“Although the FDA characterizes the ‘regulatory letters’ and other statements of FDA officials as merely ‘advisory,’ the court must not be blind to the practical effects of these letters and other statements.”).

¹⁵³ *See* Kristen R. W. Matthews & Ana S. Iltis, *Unproven Stem Cell-Based Interventions and Achieving a Compromise Policy Among the Multiple Stakeholders*, 16 BMC MEDICAL ETHICS, no. 69, 2015, at 1, 1–2; Shigeru Miyagawa, *Phase I Clinical Trial of Autologous Stem Cell—Sheet Transplantation Therapy for Treating Cardiomyopathy*, 6 J. AM. HEART ASSOC., Apr. 2017, at 1 [<https://perma.cc/T4G7-CLCZ>] (this study concluding that stem-cell treatment is feasible for treating cardiomyopathy); News Release, JOHNS HOPKINS MED., Stem Cell Therapy Safely Repairs Damaged Heart Muscle in Chronic Heart Failure Patients, Study Shows (Nov. 6, 2012), http://www.hopkinsmedicine.org/news/media/releases/stem_cell_therapy_safely_repairs_damaged_heart_muscle_in_chronic_heart_failure_patients_study_shows [<https://perma.cc/LQC6-TQPX>]; *see also* *Cardiomyopathy*, MAYO CLINIC, <https://www.mayoclinic.org/diseases-conditions/cardiomyopathy/symptoms-causes/syc-20370709> [<https://perma.cc/BBQ8-VTQE>] (last visited June 10, 2018).

¹⁵⁴ Miyagawa, *supra* note 153, at 2 (referring to clinical research taking place in Japan);

The use of autologous stem cells in the treatment of patients has been hindered by the FDA. In 2013, based on a combination of the Federal Food, Drug & Cosmetic Act, Public Health Service Act, and deference to agency interpretations of FDA regulations related to human cells and tissue, the U.S. Court of Appeals for the D.C. Circuit upheld a district court ruling that combining a patient's own stem cells with an antibiotic must be approved by the FDA.¹⁵⁵ *Gonzales v. Raich*, the aforementioned 2005 Supreme Court decision holding that the Controlled Substances Act did not exceed Congress's power under the Commerce Clause, was also cited to in the federal case that held that the FDA's prohibition of autologous stem cells as an alternative to orthopedic surgery was not outside of the agency's jurisdiction.¹⁵⁶

U.S. v. Regenerative Sciences, Inc. addressed whether autologous stem cell uses were subject to FDA regulation.¹⁵⁷ The stem cell treatment at issue, the "Cultured Regenexx Procedure," was "jointly developed" by two physicians as a "treatment [for] orthopedic injuries and arthritis' and for 'musculoskeletal and spinal injury.'"¹⁵⁸ While the physician recipients of untitled letters from the FDA often cease their offerings of "controversial" techniques after receiving the letters, the story of the FDA's ban of these Colorado physicians' practice of using of autologous stem cells is comparatively complete.¹⁵⁹ This is because, instead of ceasing their practice after receiving the notice from the FDA as physicians tend to do (or moving their practice abroad), Regenerative Sciences litigated the case.¹⁶⁰

JOHNS HOPKINS MED., *supra* note 153 (referring to a "preliminary study by researchers at the Johns Hopkins University School of Medicine and the University of Miami Miller School of Medicine."); Matthews & Iltis, *supra* note 153, at 2 ("While some patients find clinics within the US offering unproven [stem cell-based interventions], many travel abroad, often to countries with less developed medical infrastructures and regulatory oversight, a concept or practice often referred to as [stem cell] tourism.").

¹⁵⁵ *United States v. Regenerative Scis., LLC*, 741 F.3d 1314, 1317, 1326 (D.C. Cir. 2014).

¹⁵⁶ *Id.* at 1320 (citing to *Gonzales v. Raich*, 545 U.S. 1, 17 (2005)).

¹⁵⁷ *Id.* at 1318.

¹⁵⁸ *Id.* at 1317–18 ("The Procedure begins with the extraction of a sample of a patient's bone marrow or synovial fluid. From that sample, Regenerative Sciences isolates mesenchymal stem cells (MSCs), which are capable of differentiating into bone and cartilage cells. The MSCs are then placed in a solution to culture them—that is, to cause them to divide and proliferate. Other substances are sometimes added to the solution that affect the MSCs' differentiation. The culturing process determines the growth and biological characteristics of the resulting cell population. When the MSCs are sufficiently numerous for re-injection, they are combined with doxycycline, an antibiotic obtained in interstate commerce and used to prevent bacterial contamination of the MSCs. The resulting mixture (the Mixture) is injected into the patient from whom the stem cell sample was initially taken, at the site of the damaged tissue.").

¹⁵⁹ See, e.g., Lewis, *supra* note 13, at 1241–42 (noting the impact of FDA "Untitled Letters" on physicians practicing in the field of assisted reproductive technology involving genetic modifications in the United States).

¹⁶⁰ *Regenerative Scis.*, 741 F.3d at 1314.

In *Regenerative Sciences*, the appellants' federalism-based argument, which focused on the "practice of medicine," failed.¹⁶¹ The D.C. Circuit held that the FDA was targeting the *mixture* of stem cells and an antibiotic and not a *procedure* and also that the argument related to what constituted the practice of medicine in Colorado failed.¹⁶² As the Regenexx litigation focused on a federal agency and an alleged infraction involving interstate commerce, the Administrative Procedure Act and associated federal regulations were critical to the court's analysis.¹⁶³ More specifically, the aforementioned "minimal manipulation," an imprecise term that the FDA continues to use to regulate human tissue (from ART to stem cell research) was central to the court's analysis.¹⁶⁴ The court cited to the FDA's regulations and definition of "minimal manipulation," which is "processing that does not alter the relevant biological characteristics."¹⁶⁵ As noted by members of the public during the comment period, the term is "vague"; there is no definition of "relevant biological characteristics."¹⁶⁶ However, the appellants did not contest the meaning of "minimal manipulation."¹⁶⁷ The court stated that it did not defer to the FDA's statement in the Preamble of the Part 1271 regulations; however, it at least agreed with that interpretation.¹⁶⁸ Ultimately, the physicians were unsuccessful in the Regenexx litigation,¹⁶⁹ however, the litigation provides insight into the difficulties of regulating novel medical techniques and the perils of deference to the FDA.

Despite the physicians' failure in *Regenerative Sciences*, it is still possible for future litigation to succeed. First, the physicians did not contest the applicability of the plain language of the statutes, thus leaving room for a successful argument based on this issue.¹⁷⁰ Second, the physicians did not challenge the definition and use of the term "minimal manipulation." While one could argue that the relevant biological characteristics were not altered and that the Regenexx procedure simply increased the number of stem cells in a way that did not result in FDA jurisdiction, this issue was never raised. Similarly, on the subject of the mesenchymal stem cells isolated in the Regenexx procedure, there were some claims that the physicians did not

¹⁶¹ *Id.* at 1319.

¹⁶² *Id.*

¹⁶³ *Id.* at 1321–24.

¹⁶⁴ *Id.*

¹⁶⁵ *Id.* at 1321 (citing 21 C.F.R. §1271.3(f)(2) (2016)).

¹⁶⁶ See Human Cells, *supra* note 113 ("Eight comments asserted that 'minimal manipulation' is vague and open to subjective interpretation, and should be eliminated. Two comments asserted that it is difficult to draw a meaningful distinction between tissues that are minimally manipulated and those that are more than minimally manipulated. One of these comments suggested that instead of the minimal manipulation criterion, FDA should propose that tissue products labeled or promoted for tissue replacement, reconstruction, or restoration of function be regulated as tissue. Another comment requested the development of guidance and noted that, in light of future technological advances, a broader definition of minimal manipulation may be more appropriate.").

¹⁶⁷ *Regenerative Scis.*, 741 F.3d at 1322.

¹⁶⁸ *Id.*

¹⁶⁹ *Id.* at 1325–26.

¹⁷⁰ *Id.* at 1319.

respond to during the litigation.¹⁷¹ Furthermore, there were manufacturing violations in the *Regenerative Sciences* case that other physician–defendants’ practices may not have.¹⁷²

Regenexx is not the only stem cell treatment that the FDA has targeted. In addition to targeting Regenexx, the FDA has targeted other treatments involving the use of autologous stem cells; similarly, those uses of autologous stem cells have been deterred through the receipt of an FDA-issued untitled letter.¹⁷³ For example, one of the amicus briefs in *Regenerative Sciences* was filed by an attorney for William Timothy Moore.¹⁷⁴ Mr. Moore “received three intravenous infusions (once a month for three months) of 200,000,000 of his [own] stem cells” to alleviate symptoms related to Parkinson’s disease using a procedure provided by a company called Celltex.¹⁷⁵ However, as he was preparing to undergo another treatment involving the Celltex protocol, Mr. Moore discovered that the FDA had sent a warning letter to Celltex, and the company “stopped replicating any cells and would not begin again until matters were resolved with the FDA.”¹⁷⁶ After being targeted by the agency for an inspection (and receiving a warning letter), Celltex has since commenced servicing its patients in Mexico.¹⁷⁷

Yet, the federal regulation of stem cell treatments has not automatically resulted in harm to patients. For example, the treatments cited to in the *New England Journal of Medicine* article by FDA employees certainly harmed the patients who received

¹⁷¹ *Id.* at 1322; see also *Stem Cell Information*, NAT’L INSTS. OF HEALTH, (2016) <https://stemcells.nih.gov/glossary.htm#mesenchymal> [<https://perma.cc/YRW3-SZKM>] (“Mesenchymal stem cells - A term that is currently used to define non-blood adult stem cells from a variety of tissues, although it is not clear that mesenchymal stem cells from different tissues are the same.”).

¹⁷² *Regenerative Scis.*, 741 F.3d at 1325 (The court mentioned the violations and concluded that “[t]he fact that the FDA found violations on two separate occasions and that appellants refused to take corrective action even after multiple FDA notices suggests a pattern of deliberate, even flagrant violations.”).

¹⁷³ See, e.g., Letter from Mary A. Malarkey, Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, To David G. Eller, Chief Executive Officer & President, CellTex Therapeutics (Sep. 24, 2012), available at <https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm323853.htm> [<https://perma.cc/KQM9-58CM>].

¹⁷⁴ Brief for Tim Moore as Amicus Curiae Supporting Appellants, *Regenerative Scis.*, et al v. United States, No. 12-5254, 2012 WL 6604723 (D.C. Cir. Dec. 17, 2012).

¹⁷⁵ *Id.* at *viii-ix.

¹⁷⁶ *Id.* at *ix.

¹⁷⁷ See David Cyranoski, *Controversial Stem-Cell Company Moves Treatment Out of the United States*, NATURE.COM: NEWS (Jan. 30, 2013) <https://www.nature.com/news/controversial-stem-cell-company-moves-treatment-out-of-the-united-states-1.12332> [<https://perma.cc/6GYA-RQAT>]; see also David Cyranoski, *Texas Stem-Cell Provider Under FDA Gun*, NATURE.COM: NEWS BLOG (Oct. 18, 2012) <http://blogs.nature.com/news/2012/10/texas-stem-cell-provider-under-fda-gun.html> [<https://perma.cc/2K9Q-2N7W>].

them.¹⁷⁸ Similarly, the FDA's actions in shutting down harmful stem cell treatment providers have been called "spectacular" and "the right thing to do" by individuals such as George Daley, the Dean of Harvard Medical School, who is recognized as a "leading stem cell researcher."¹⁷⁹ While the full protocols involved in the treatments targeted by the FDA (with the support of the U.S. Marshals) were not provided, in at least one of these aforementioned enforcement actions, at least one of those targeted stem cell "treatments" involved the injection of a live vaccine—intended for individuals "at high risk for smallpox"—into patients "intravenously and directly into [their] tumors."¹⁸⁰ These techniques differ from the techniques involving the combination of an antibiotic with a patient's own stem cells (as occurs with Regenxx). Furthermore, shifting all or part of the regulation of innovative techniques from the federal government to the States does not mean that all enforcement activity will cease. For example, the Federal Trade Commission pursues enforcement action against providers who falsely advertise the safety or efficacy of medical products and techniques, including fertility treatments.¹⁸¹ Additionally, state law creates enforcement mechanisms that can be used against those who falsely advertise the efficacy or safety of products or services.¹⁸²

¹⁷⁸ See Marks, Witten & Califf, *supra* note 149, at 1008.

¹⁷⁹ See Rob Stein, *FDA Cracks Down on Stem-Cell Clinics Selling Unapproved Treatments*, NPR (Aug. 28, 2017, 2:31 PM) <http://www.npr.org/sections/health-shots/2017/08/28/546719842/fda-cracks-down-on-stem-cell-clinics-selling-unapproved-treatments> [<https://perma.cc/8A3W-8W97>]; see also *New Dean for Faculty of Medicine*, HARVARD GAZETTE (Aug. 9, 2016) <https://news.harvard.edu/gazette/story/2016/08/new-dean-for-faculty-of-medicine/> [<https://perma.cc/B5FV-RLRW>].

¹⁸⁰ Stein, *supra* note 179; see also FDA Acts to Remove Unproven, Potentially Harmful Treatment Used in 'Stem Cell' Centers Targeting Vulnerable Patients, U.S. Food & Drug Admin. (Aug. 28, 2017) <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573427.htm> [<https://perma.cc/R96V-NPET>] ("On behalf of the FDA, on Friday, Aug. 25, 2017 the U.S. Marshals Service seized five vials of Vaccinia Virus Vaccine (Live) – a vaccine that is reserved only for people at high risk for smallpox, such as some members of the military. Each of the vials originally contained 100 doses of the vaccine, and although one vial was partially used, four of the vials were intact.

As the vaccine is not commercially available, the FDA has serious concerns about how StemImmune obtained the product for use as part of an unapproved and potentially dangerous treatment. The FDA is actively investigating the circumstances by which StemImmune came to possess the vaccine.").

¹⁸¹ See, e.g., Sarah Duranske, *This Article Makes You Smarter! (Or, Regulating Health and Wellness Claims)*, 43 AM. J.L. & MED. 7, 34, 40–41 (2017); see also NAOMI CAHN, TEST TUBE FAMILIES: WHY THE FERTILITY MARKET NEEDS LEGAL REGULATION 193 (2009) ("The Federal Trade Commission, which is the federal agency responsible for consumer protection and the prevention of anticompetitive practices, has brought complaints against fertility clinics for misrepresenting their success rates.").

¹⁸² See, e.g., Duranske, *supra* note 181.

* * *

This Part has provided the background on how administrative agencies, with an emphasis on the FDA, regulate health care and how the line between medical practice—an area historically regulated by States—and drugs and devices—an area historically regulated by the FDA—has become blurred. This blurring, combined with the FDA’s assertion of power outside its jurisdiction, has often operated to the detriment of state jurisdiction and patient care.¹⁸³ There are several statutory definitions that could apply to the regulation of the life sciences. The problem, however, is that the characteristics of these innovative medical techniques cause these techniques to not fit squarely within one category of statutorily defined product regulated by the FDA. Furthermore, an integral piece of life sciences jurisdiction includes state authority over the regulation of medicine, with an emphasis on clinical innovation.

When it regulates in areas of medical innovation, the federal government is infringing in an area in which there is a federal regulatory gap. As a matter of practice, instead of the default rule for addressing the regulatory gap being state regulation or a cooperative regulatory effort between the federal government and States, the federal government encumbers state regulation. And insofar as there has been regulation by the state that fails to prevent innovation in these areas, the federal government is directly stepping on state power.

This Part has examined the jurisdictional difficulties of regulating the life sciences in general, along with the federal government’s approach to regulating the life sciences. Some scholars and policymakers have argued in favor of increased federal oversight of medicine, pharmaceuticals, and the health sciences, whereas this Article takes the opposite view.¹⁸⁴ Instead, after examining the doctrines and statutory provisions that could apply to the life sciences, this Article has concluded that emergent areas of innovation do not fall within the ambit of federal jurisdiction and, alternatively, if they do, the regulatory structure needs significant improvements as it was structured to address historical “tools” used in the practice of medicine such as pharmaceuticals and medical devices. Furthermore, those regulatory improvements are necessary for two significant reasons. First, the current regulatory apparatus is minimizing the availability of medical innovations to patients in the United States. Second, States own a critical piece of the jurisdictional puzzle such that the only method of accurately and adequately regulating the life sciences must include the States. The next Part looks at the implications of the current regulatory regime, which include jurisdictional overstepping and a risk-averse regulatory approach that can be remedied only by a more cooperative regulatory apparatus.

¹⁸³ *But see supra* notes 178–181 and accompanying text (discussing the FDA’s targeting of harmful stem cell treatments).

¹⁸⁴ *See, e.g.,* Mary Agnes Cary, *Feds v. states: Who should run health market?*, NBC NEWS (Jan. 15, 2010), http://www.nbcnews.com/id/34868472/ns/health-health_care/t/feds-vs-states-who-should-run-health-market/#.WS9LdmjyIU [<https://perma.cc/528D-NGXT>].

III. FUTURE IMPLICATIONS: JURISDICTIONAL GAPS AND NASCENT INDUSTRIES

This Section examines the future implications of the continued federal regulation of the life sciences before noting that States should play a larger role in the regulation of the life sciences. Subsections A and B of this Section explore some implications of the current federal regime. Subsection C then asserts that States should exert a larger role in the regulation of the life sciences just as they have exerted with the legalization of marijuana, which has occurred in the face of federal regulation of controlled substances. As explored in Part IV, the federal government is not the only actor that should exert jurisdiction over the life sciences.

A. A Lack of Regulatory Capture

Innovative medical techniques raise different regulatory concerns than pharmaceuticals do in the context of FDA regulation. For example, while regulatory capture is a concern when analyzing the FDA regulation of pharmaceuticals, it seems that the opposite is occurring in the life sciences, where physicians are increasingly unable to use innovative medical techniques.¹⁸⁵ Instead, physicians and researchers make progress only to be told that the “investigational new drug” requirements (which are specifically referred to in the Common Rule) also apply to clinical innovations.¹⁸⁶ The creation of medical innovations by physicians and university researchers as opposed to pharmaceutical companies likely contributes to reduced regulatory capture. This is because physicians and academic medical centers have less contact with the agency, and less lobbying power than pharmaceutical companies. In turn, the comparatively lower number of interactions between physicians and university researchers and the FDA likely reduces their ability to sway the decisions of agency employees (although physicians and university employees have certainly created pharmaceuticals and medical devices that are subject to the FDA’s jurisdiction).¹⁸⁷ Additionally, the number of individuals involved in creating innovative medical techniques possibly generates a coordination problem amongst the various groups who might seek to “capture” an administrative agency.¹⁸⁸

¹⁸⁵ See Bagley & Revesz, *supra* note 28, at 1289.

¹⁸⁶ See *supra* Part II.A.1 (discussing mitochondrial transfer and assisted reproductive technology).

¹⁸⁷ But see Catherine Ho, *Universities opening D.C. offices, hiring in-house lobbyists to raise government relations profile*, WASH. POST (May 27, 2012), https://www.washingtonpost.com/business/capitalbusiness/universities-opening-dc-offices-hiring-in-house-lobbyists-to-raise-government-relations-profile/2012/05/25/gJQAf7Q3uU_story.html?utm_term=.899736eea633 [<https://perma.cc/52L8-LYE3>]; see also *supra* Part II.B.2.b (discussing academic medical centers’ opposition to the FDA’s original method of regulating fecal microbiota transplantation and subsequent changes to that regulatory plan).

¹⁸⁸ See, e.g., Brenda Reddix-Small, *Assessing the Market for Human Reproductive Tissue Alienability: Why Can We Sell Our Eggs But Not Our Livers?*, 10 VAND. J. ENT. &

B. Dual Designations: Biologics and Drugs

While medical practice and the tools used to practice medicine were once separate concepts, today's medical innovations are blurring the line between medical practice and medical devices and drugs, in addition to the difference between categories of products that the FDA has jurisdiction over under its enabling statutes. For example, the FDA designated the aforementioned Regenexx as "both a drug and a biological product."¹⁸⁹ The agency has done the same for a number of new products as the character of the products regulated by the agency (whether with or without jurisdiction) become more complex.¹⁹⁰ The recurring term "minimal manipulation" is also relevant in this determination as it is one criterion that the agency uses "to distinguish between 'section 361 HCT/Ps [Human Cellular and Tissue-Based Products]' and HCT/Ps regulated as drugs, devices, *and/or* biological products."¹⁹¹ According to a former Chief Counsel for the Agency, "[t]he decision as to which Bureau within the FDA handles these products is entirely an administrative matter that raises no legal issue"; yet just as the FDA fails to explain how innovative products fit within singular categories such as "drug" or "biologic," the FDA fails to explain what about innovative medical techniques leads to such a designation.¹⁹²

TECH. L. 643, 681–82 (2008) ("Administrative agencies may be subject to 'capture' by the very forces they are designed to regulate. The dominant market forces in assisted reproductive technology include the fertility clinics, the physicians, the pharmaceutical companies, the suppliers, the representative organizations, the embryo laboratories, the gamete middlemen and brokers, and the infertile consumer."). Similarly, dominant market forces in regenerative stem cell treatments could include physicians, pharmaceutical companies (to the extent that antibiotics for example were used in the treatments), "representative organizations" such as patient advocacy groups, medical suppliers, patients themselves, and the facilities at which these treatments would occur. In the case of fecal microbiota transplants, one might expect the same composition of dominant market forces with the possible removal of pharmaceutical companies and the addition of stool banks.

¹⁸⁹ *United States v. Regenerative Scis., LLC*, 741 F.3d 1314, 1318 (D.C. Cir. 2014) (referring to an August 2010 FDA filing for a permanent injunction against Regenerative Sciences, LLC and associated physicians).

¹⁹⁰ See *infra* notes 194 and 195 and accompanying text; see also *About Combination Products*, U.S. FOOD & DRUG ADMIN. (Mar. 19, 2018), <https://www.fda.gov/CombinationProducts/AboutCombinationProducts/default.htm> [<https://perma.cc/3GEV-AVE4>].

¹⁹¹ See, e.g., PETER BARTON HUTT ET AL., FOOD AND DRUG LAW: CASES AND MATERIALS 1172 (4th ed. 2014) (excerpting Richard A. Merrill, *Human Tissues and Reproductive Cloning: New Technologies Challenge FDA*, 3 HOUS. J. HEALTH. L. & POL'Y 1 (2002)).

¹⁹² *Id.* at 1169 ("In any event, whether human semen, human tissues and organs are or are not biological products, they clearly are drugs when used for therapeutic purposes or to affect any bodily function and accordingly are subject to the requirements of the FD & C Act. The decision as to which Bureau within the FDA handles these products is entirely and administrative matter that raises no legal issue.").

Although there is a statutory provision that permits the dual designation of products, which are also referred to as “combination products,” to the extent that certain innovations do not fall wholly within the categories of drug and biologic for example, Congress will likely need to revisit this statutory provision in the future.¹⁹³ “Dual designation” is less of a concern when it occurs with food and drugs or cosmetics and drugs such as Latisse, an FDA-approved treatment that grows lashes “longer, fuller and darker.”¹⁹⁴ Dual designations in these categories of food and cosmetics do not tend to result in restrictions on medical practice; furthermore, dual designation products like Botox and Latisse are still on the market.¹⁹⁵ While FDA officials have argued that knowing whether something is a drug, a biological product, “and/or” both is just an administrative determination, principles of good governance indicate that such an administrative determination should be clear.¹⁹⁶ The public should know how the FDA is classifying complex innovations and why it is classifying them in that manner. In other words, when it is unclear whether a product falls within the singular designation of “drug” or “biologic product,” a “dual designation” is similarly, if not more, unclear. Furthermore, legally, it is harder to know whether an agency decision is arbitrary and capricious with no clear understanding of why the agency decision (here, the initial classification) was made.¹⁹⁷ Law is built on analogies and in the case of innovative techniques, those analogies are harder to construct; the burden of trying to construct those analogies and understand their applicability falls on the public when it should fall on the agency.

*C. The Case for Regulatory Innovation, Even in the Absence of Jurisdiction:
Marijuana Decriminalization*

As indicated by the above statement of the former Chief Counsel of the FDA, many—including current (and former) FDA employees—will take the position that the FDA does have jurisdiction over innovative techniques.¹⁹⁸ This Section provides the normative basis for regulatory improvements even if the FDA does somehow have jurisdiction (or eventually obtains it through congressional mandate).¹⁹⁹ While the discourse related to marijuana decriminalization currently focuses on issues such

¹⁹³ See 21 U.S.C. 353(g) (2018).

¹⁹⁴ HUTT ET AL., *supra* note 191, at 138–39, 118–121; see also *Hear From the Experts, LATISSE*, <http://www.latisse.com/FAQs.aspx> [<https://perma.cc/T384-45GJ>] (last visited Dec. 3, 2018).

¹⁹⁵ See HUTT ET AL., *supra* note 191, at 117–120; see also *BOTOX*, https://www.botoxcosmetic.com/?cid=tab_lat_c [<https://perma.cc/U4LF-YXJK>] (last visited June 10, 2018).

¹⁹⁶ See HUTT ET AL., *supra* note 191, at 138–39, 118–121.

¹⁹⁷ See 5 U.S.C. § 706 (2016).

¹⁹⁸ See Bagley & Revesz, *supra* note 28.

¹⁹⁹ See *infra* Part IV (listing possible improvements for regulating the life sciences, including Congress creating a statute that clearly applies to the life sciences); *supra* Part II (discussing the FDA’s lack of jurisdiction over innovative life sciences techniques).

as increasing state tax revenues and criminal justice reforms, marijuana decriminalization, in large part, began with innovation related to the use of marijuana for medical purposes.

After *Gonzales v. Raich* there is no doubt that the federal government has jurisdiction over the distribution of marijuana; however, much doubt exists as to whether the federal government *should* continue to regulate marijuana in the way that it does.²⁰⁰ Currently, marijuana is classified by the federal government as a Schedule I Controlled Substance.²⁰¹ Schedule I Controlled Substances are drugs that have “a high potential for abuse,” that have “no currently accepted medical use in treatment in the United States,” and for the use of which “[t]here is a lack of accepted safety . . . under medical supervision.”²⁰² Marijuana is currently categorized as a Schedule I Controlled Substance, despite growing evidence of its usefulness in medical treatment and the fact that no death from marijuana overdose has been reported.²⁰³ Heroin is also a Schedule I Controlled Substance, whereas cocaine, morphine, and opium are Schedule II Controlled Substances.²⁰⁴ Schedule II controlled substances “have a high potential for abuse which may lead to severe psychological or physical dependence.”²⁰⁵ Due to its classification, the possession or use of marijuana remains illegal under federal law in the United States, just as the possession or use of heroin remains criminalized.²⁰⁶

Marijuana remains a Schedule I Controlled Substance even though States continue to decriminalize both medical and recreational marijuana uses. Even cities

²⁰⁰ See *Gonzales v. Raich*, 545 U.S. 1, 9 (2005).

²⁰¹ See 21 U.S.C. § 812 (2018) (referring to the drug as “marihuana” on the list of Controlled Substances).

²⁰² *Id.*

²⁰³ *Id.*; see also U.S. DRUG ENF’T ADMIN., DEA DRUG FACT SHEET: MARIJUANA (2018), https://www.dea.gov/druginfo/drug_data_sheets/Marijuana.pdf [<https://perma.cc/FFT6-TRHL>]; Melina Delkic, *Medical Marijuana’s Main Ingredient Isn’t Dangerous or Addictive*, *World Health Organization Report Says*, NEWSWEEK (Dec. 14, 2017), <http://www.newsweek.com/medical-marijuana-cbd-not-addictive-toxic-who-says-748069> [<https://perma.cc/MU7K-FCXK>]. For more on the medical benefits of marijuana, see, for example, DUKE UNIVERSITY SCHOOL OF MEDICINE, CASARETT GIVES TED TALK ON MEDICAL MARIJUANA (2017), <https://medicine.duke.edu/medicineneeds/casarett-gives-ted-talk-medical-marijuana> [<https://perma.cc/YU6X-39EN>] (providing background information on Dr. Casarett’s research and a link to his TED Talk entitled *A Doctor’s Case for Medical Marijuana*).

²⁰⁴ See U.S. DRUG ENF’T ADMIN., CONTROLLED SUBSTANCES BY CSA SCHEDULE 5, 8–9 (2018), https://www.deadiversion.usdoj.gov/schedules/orangebook/e_cs_sched.pdf [<https://perma.cc/4B5X-NMKQ>]; see also, U.S. DRUG ENF’T ADMIN. DIVERSION CONTROL DIV., CONTROLLED SUBSTANCE SCHEDULES (2018), <https://www.deadiversion.usdoj.gov/schedules/#define> [<https://perma.cc/W2E5-WQWK>] (“Examples of Schedule II narcotics include: hydromorphone (Dilaudid®), methadone (Dolophine®), meperidine (Demerol®), oxycodone (OxyContin®, Percocet®), and fentanyl (Sublimaze®, Duragesic®). Other Schedule II narcotics include: morphine, opium, codeine, and hydrocodone.”).

²⁰⁵ See also U.S. DRUG ENF’T ADMIN. DIVERSION CONTROL DIV., *supra* note 204.

²⁰⁶ 21 U.S.C. §§ 843, 844 (2018).

have been actors in the decriminalization of marijuana.²⁰⁷ In 2005, a majority of the Supreme Court opined in *Gonzales v. Raich*, that California was known as a “pioneer” in marijuana regulation.²⁰⁸ Since then, California, which used to be at the forefront of discussions related to the decriminalization of marijuana due to its regime for medical marijuana use, has been replaced by Colorado.²⁰⁹ Colorado has expanded to decriminalizing the sale and use of marijuana, to the benefit of both commercial businesses and the state’s coffers.²¹⁰ These actions continue despite the federal prohibitions on the possession and use of marijuana.

Nonetheless, while statements of appointees—such as the Attorney General—in the current Presidential administration indicate a hostility to state-based experimentation with medical and recreational marijuana, recently the 2017–18 Secretary of Veterans Affairs “cautiously signaled a willingness to advance medical marijuana for veterans,” thus indicating that state-based experimentation with marijuana decriminalization may be impacting federal decision-making.²¹¹

²⁰⁷ See, e.g., Grace Donnelly, *Atlanta Is the Latest U.S. City to Decriminalize Marijuana. Here’s What that Means*, FORTUNE (Oct. 3, 2017), <http://fortune.com/2017/10/03/list-of-cities-that-decriminalized-marijuana/> [https://perma.cc/LSE9-W8WD]; see also Melanie Eversley, *D.C. Marijuana Decriminalization Law Takes Effect*, USA TODAY (Jul. 17, 2014), <https://www.usatoday.com/story/news/nation/2014/07/17/dc-marijuana-law/12770301/> [https://perma.cc/5WUD-EVVJ].

²⁰⁸ *Gonzales v. Raich*, 545 U.S. 1, 5 (2005).

²⁰⁹ See Steven B. Duke, *The Future of Marijuana in the United States*, 91 OR. L. REV. 1301, 1302 (2013); see, e.g., David Matthews, *Can Legal Marijuana Fund CPS? Lawmakers Learn How It’s Done in Colorado*, DNA INFO (Apr. 19, 2017), <https://www.dnainfo.com/chicago/20170419/downtown/can-legal-weed-help-fund-cps-lawmakers-learn-how-its-done-colorado> [https://perma.cc/G9JJ-V5CF]. (“Colorado is funding public schools and rehab programs with tax revenue from legalized marijuana—and it’s time for Illinois [sic] do the same thing, state lawmakers were told Wednesday.”).

²¹⁰ *Id.* But see Sara Randazzo, *Court Allows Colorado Couple to Sue Marijuana Growers*, WALL ST. J. (June 7, 2017), <https://www.wsj.com/articles/court-allows-colorado-couple-to-sue-marijuana-growers-1496878545> [https://perma.cc/5GKU-ZNQQ] (discussing a federal appeals court in Denver giving “private landowners in Colorado the go-ahead to sue neighboring marijuana growers under a federal law targeting criminal enterprises, a decision that could expose the recreational marijuana industry to more private litigation”).

²¹¹ See Joe Davidson, *Will VA Chief Be Voice of Reason on Climate Change and Medical Marijuana in Trump Administration?*, WASH. POST (June 5, 2017), https://www.washingtonpost.com/news/powerpost/wp/2017/06/05/will-va-chief-be-voice-of-reason-on-climate-change-and-medical-marijuana-in-trump-administration/?hpid=hp_hp-cards_hp-card-fedgov%3Ahomepage%2Fcard&utm_term=.126383db906d [https://perma.cc/HUJ9-8884] (discussing the position of then-Secretary of Veterans Affairs, David Shulkin, on the legalization of medical marijuana and its acceptance as a treatment method for those obtaining health care through the U.S. Department of Veterans Affairs); see also U.S. DEP’T OF VETERANS AFF., ABOUT VA (2018), https://www.va.gov/about_va/vahistory.asp [https://perma.cc/2UMX-GHYV]; see, e.g., Matt Zapotsky, et al., *Use of Legalized Marijuana Threatened as Sessions Rescinds Obama-Era Directive that Eased Federal Enforcement*, WASH. POST (Jan. 4, 2018), <https://www.washingtonpost.com/world/national-security/sessions-is-rescinding-obama->

Here, the example of medical marijuana is also significant because it indicates that even if the FDA does happen to have jurisdiction over certain innovative technologies, the current development of marijuana decriminalization indicates that states may and should continue to create their own regimes to regulate innovative medical techniques, even when federal jurisdiction has been exerted. The next Part offers some suggestions as to how the regulatory apparatus applicable to the life sciences could be improved, with an emphasis on how individual states specifically could be better integrated into the regulatory scheme.

IV. SUGGESTIONS FOR IMPROVING THE REGULATION OF THE LIFE SCIENCES

This Article has identified the shortcomings of the regulatory apparatus that the FDA uses to regulate innovations in the life sciences. There are, of course, many ways, in which this regulatory apparatus could be improved. For example, a regime that increases the role of states in regulating innovation in the life sciences would be an improvement due not only to the acknowledgement of state jurisdiction but also due to the increase in the variety of ethical perspectives that would be introduced into regulation (as opposed to the current singular view provided by the FDA).²¹² In the case of innovations in the biosciences, for example, Texas, Massachusetts, and California—states that are the sites of medical and scientific innovation—may create specific legal regimes in response to certain innovations such as those in stem cell treatments. And as other states see how these regimes are helpful to research, development, and patient care, other states may adopt such permissive regimes.²¹³ For example, as recent controversies—such as those surrounding the switch from prescription to over-the-counter Plan B and recent regulations increasing the number of entities that can opt out of the requirement that the “minimum essential benefits” offered by insurance companies include contraceptive benefits—emphasize, the U.S. Department of Health and Human Services, of which the FDA is a part, is not an independent regulatory agency.²¹⁴ As such, ethical decisions may manifest in the

era-directive-for-feds-to-back-off-marijuana-enforcement-in-states-with-legal-pot/2018/01/04/b1a42746-f157-11e7-b3bf-ab90a706e175_story.html?utm_term=.6a67d03a735d [<https://perma.cc/995S-T29U>].

²¹² See Lewis, *supra* note 13, at 1272–81.

²¹³ Massachusetts and California are known as sites for innovation. See, e.g., Bruce Booth, *Why Biotech's Talent, Capital and Returns are Consolidating into Two Key Clusters*, FORBES (Mar. 21, 2017), <https://www.forbes.com/sites/brucebooth/2017/03/21/inescapable-gravity-of-biotechs-key-clusters-the-great-consolidation-of-talent-capital-returns/#3f025f5552e9> [<https://perma.cc/RS2X-UGCW>] (showing that Boston and San Francisco were the United States' top “biotech clusters”). Colorado is discussed *supra* in the context of the autologous stem cell innovation that was the subject of *U.S. v. Regenerative Sciences* and in the context of marijuana decriminalization. See *supra* notes 209–210 and accompanying text; see also LATTISE, *supra* note 194.

²¹⁴ See, e.g., Robert Pear et. al., *Trump Administration Rolls Back Birth Control Mandate*, N.Y. TIMES (Oct. 6, 2017), <https://www.nytimes.com/2017/10/06/us/politics/trump-contraception-birth-control.html> [<https://perma.cc/RS2X-UGCW>]; Julia Rover,

regulatory process, and they may not reflect the view of the citizenry in a particular state or the country as a whole. Furthermore, a regime in which States operate as laboratories could foster innovation in patient care, whereas the current federally focused regime does the opposite by effectively banning certain innovative medical techniques, both to the detriment of patient health and without adequate legal support.

A natural objection to a regime with a state-based approach or that incorporates States into the federal regulatory process is that States do not have the competence to address issues related to innovative medical techniques and other issues that the FDA routinely addresses such as pharmaceutical and medical device safety. Yet, States have debated and enacted legislation related to scientific and medical research, informed consent, cloning, and ART, in addition to exercising state police powers in areas such as the licensing of physicians and medical personnel, the monitoring of epidemiological conditions, and the provision of health care services in the community.²¹⁵ States are also the source for medical malpractice recovery as

“Plan B” Gets FDA’s Over-Counter Approval, ALL THINGS CONSIDERED, NPR, (Aug. 24, 2006), <https://www.npr.org/templates/story/story.php?storyId=5705260> [<https://perma.cc/YK2H-DJ9B>].

²¹⁵ See, e.g., CAL. HEALTH & SAFETY CODE § 111525 (2018) (“Consent; method and manner of obtaining”); 410 ILL. COMP. STAT. 50/3.1 (2018) (“Subjects of research programs or experimental procedures”); MD. CODE, HEALTH-GEN. § 13-2002 (2018) (“Construction with federal regulations”); NEV. REV. STAT. § 159.0805 (2018) (“Approval of court required before guardian may consent to certain treatment of or experiment on ward; conditions for approval”); N.Y. PUB. HEALTH LAW § 2442 (2018) (“Informed Consent”); 23 R.I. GEN. LAWS § 23-17-19.1 (2018) (“Rights of patients”) (2018); VA. CODE § 32.1-162.18 (2018) (“Informed Consent”); WYO. STAT. § 26-20-301 (2018) (“Clinical trials and studies coverage required”); *Grimes v. Kennedy Krieger Inst. Inc.*, 782 A.2d 807 (Md. 2001) (discussing informed consent in nontherapeutic research); BARRY R. FURROW ET AL., *HEALTH LAW: CASES, MATERIALS, AND PROBLEMS* 87–88 (7th ed. 2013) (providing an overview of state licensing requirements for health care professionals); Adrienne N. Cash, *Attack of the Clones: Legislative Approaches to Human Cloning in the United States*, 4 DUKE L. TECH. REV. 1, 2 (2005) (providing an overview of state statutes that regulate cloning) (“To date, fourteen states have passed legislation pertaining to human cloning. The cloning laws of the fourteen states are similar to one another in that all ban reproductive cloning and impose rather stiff penalties for violators. Arkansas, Indiana, Iowa, Michigan, North Dakota, and South Dakota have extended the ban on cloning to cover therapeutic cloning as well as reproductive cloning. California, Connecticut, Massachusetts, New Jersey, Rhode Island, and Virginia have limited their bans to reproductive cloning. Missouri and Arizona have measures, which address the use of public funds for cloning without specifically prohibiting any form of cloning. Louisiana also enacted legislation prohibiting reproductive cloning; however the law expired in July 2003.” (citations omitted)); see also June Carbone, *Negating the Genetic Tie: Does the Law Encourage Unnecessary Risks?*, 79 UMKC L. REV. 333, 360 (2010) (“Thus, federal oversight of the sciences has often involved federal research funding that sets the standards for industry practices as a condition of eligibility for government grants; with the federal ban on research using embryos, for example, California has authorized funding of stem cell research that has involved the state in creating research protocols that would ordinarily take place at the federal level.”).

there is no federal medical malpractice regime.²¹⁶ States have also instituted product liability regimes that, before a 2011 Supreme Court decision, allowed them to provide greater protections for patients who were harmed by pharmaceuticals than did federal statutes and regulations.²¹⁷ In the realm of life sciences innovation, California, for example, created the California Institute for Regenerative Medicine, after a majority of California voters approved “Proposition 71: the California Stem Cell Research and Cures Initiative.”²¹⁸ The approval of Proposition 71 included the allocation of \$3 billion towards the funding of stem cell research, which is distributed through the California Institute for Regenerative Medicine.²¹⁹ States have also innovated in the legalization of marijuana in spite of now undisputed federal jurisdiction over controlled substances.²²⁰

The decriminalization of medical and recreational marijuana indicates that, even if the FDA has jurisdiction over aspects of the life sciences that are related to the practice of medicine, this does not mean that the FDA *should* regulate innovative life sciences in the way that it currently does; states should continue to experiment in the regulation of these areas, despite federal assertion of jurisdiction, which, in the area of the life sciences, is far less clear than federal jurisdiction over controlled substances.

It is also possible that, after not regulating “drugs” and innovative procedures for decades, states may find it difficult to develop new regulatory regimes due to lack of experience. One could argue that states are skilled at funding innovation but not necessarily at regulating innovation. Any newly developed regimes may, of course, vary in structure, and differing legal regimes may lead to forum shopping or an *intra*-American medical tourism. Yet, uniform statutes might resolve this issue as they have in other areas of innovation such as the Uniform Determination of Death Act.²²¹ And even if not all fifty states adopt permissive regimes (or no States for that matter), this is still preferable to what amounts to a blanket prohibition on certain innovations by the federal government.²²² Also, states share jurisdiction with

²¹⁶ See, e.g., *Baber v. Hosp. Corp. of Am.*, 977 F.2d 872, 880 (4th Cir. 1992) (“[T]he (federal) Emergency Medical Treatment and Active Labor Act is no substitute for state law medical malpractice actions.” citing (42 U.S.C. § 1395dd(f) (2016) (EMTALA does not preempt state law, except to the extent state law directly conflicts with this statute)).

²¹⁷ See *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 608–09 (2011).

²¹⁸ See *History*, CAL. INST. FOR REGENERATIVE MED. (2015), <https://www.cirm.ca.gov/about-cirm/history> (last visited June 12, 2018) [<https://perma.cc/4E6T-A2AZ>].

²¹⁹ See *Where CIRM Funding Goes*, CAL. INST. FOR REGENERATIVE MED. (2015), <https://www.cirm.ca.gov/about/where-cirm-funding-goes> (last visited June 12, 2018) [<https://perma.cc/H2AL-K4D9>].

²²⁰ See discussion *supra* Part III.C.

²²¹ See generally *Legislative Fact Sheet—Determination of Death Act*, UNIF. L. COMM’N (June 20, 2018), <http://www.uniformlaws.org/LegislativeFactSheet.aspx?title=Determination%20of%20Death%20Act> [<https://perma.cc/JSA2-X792>] (noting that 37 states, D.C. and the U.S. Virgin Islands have enacted the Uniform Determination of Death Act).

²²² See, e.g., *Wash. Legal Found. v. Kessler*, 880 F. Supp. 26, 36 (D.D.C. 1995) (“It

the federal government in other “complex” areas. For example, states have jurisdiction over some civilian uses of nuclear power, namely medical isotopes through the U.S. Nuclear Regulatory Commission’s Agreement States Program.²²³ In this process, those states that wish to (and are able to) regulate the use of nuclear material with lowered proliferation concerns are permitted to do so.²²⁴ Any program with an increased role for state-involvement would be preferable because there is at least a chance for innovation, whereas, under the current regime, as indicated in Parts II and III, innovation is being broadly halted.

Yet, there could still be a role for the federal government in the regulation of innovative life sciences. For example, Congress could update the Federal Food, Drug, and Cosmetic Act in a way that adds another definition that clearly applies to the life sciences. Nonetheless, the fact that the terms “biotechnology” and “life sciences” are so broad in scope would render such an effort difficult. Another option would be a system of shared jurisdiction in which jurisdiction is shared between the States and the federal government. Thus, options for an improved regulatory regime include (1) a state-based waiver process²²⁵; (2) a hybrid system of shared

may be true, as FDA argues, that a company which disagrees with the ‘advice’ contained in FDA’s regulatory correspondence may disregard this advice, go ahead with its planned activities, and then challenge the constitutionality of any adverse FDA action in an enforcement proceeding. However, the reality of the situation, as alleged by plaintiff, is that few if any companies are willing to directly challenge the FDA in this manner. In the first instance, the company must expose itself to the FDA’s power to seize an entire product line if the FDA finds the products to be ‘misbranded.’ Although the company can then litigate the validity of the seizure (and therefore the policy pursuant to which the seizure was made), the prospect of lost sales and protracted litigation is understandably discouraging to these companies. In addition, the FDA wields enormous power over drug and medical device manufacturers through its power to grant or deny new product applications. It is evident that manufacturers are most reluctant to arouse the ire of such a powerful agency. The result, according to plaintiff, is that ‘FDA has been able to effectuate its policies without having to resort regularly to formal rulemaking.’”)

²²³ See *Agreement State Program*, U.S. NUCLEAR REG. COMM’N (Aug. 31, 2017), <https://www.nrc.gov/about-nrc/state-tribal/agreement-states.html> [<https://perma.cc/JSA2-X792>] (“NRC provides assistance to States expressing interest in establishing programs to assume NRC regulatory authority under the Atomic Energy Act of 1954, as amended. Section 274 of the Act provides a statutory basis under which NRC relinquishes to the States portions of its regulatory authority to license and regulate byproduct materials (radioisotopes); source materials (uranium and thorium); and certain quantities of special nuclear materials. The mechanism for the transfer of NRC’s authority to a State is an agreement signed by the Governor of the State and the Chairman of the Commission, in accordance with section 274b of the Act.”).

²²⁴ *Id.*

²²⁵ A state-based waiver process could be structured similar to the process that states follow for Medicaid. See *generally About Section 1115 Demonstrations*, MEDICAID.GOV <https://www.medicaid.gov/medicaid/section-1115-demo/about-1115/index.html> [<https://perma.cc/BFR4-3ZW9>] (last visited June 12, 2018).

jurisdiction²²⁶; (3) state-by-state regulation of the life sciences²²⁷; (4) a congressional change in the FDA's method of regulating innovative medical techniques²²⁸; and/or (5) a newly designed regulatory pathway for innovative medical treatments that acknowledges the differences between innovative medical treatments and products that are traditionally regulated by the FDA.²²⁹

²²⁶ A hybrid system of shared jurisdiction could operate similar to the system that the U.S. Nuclear Regulatory Commission has regarding civilian uses of nuclear material that have lower proliferation concerns such as the use of isotopes in medical treatment. *See generally Agreement State Program*, U.S. NUCLEAR REG. COMM'N (Aug. 31, 2017), <https://www.nrc.gov/about-nrc/state-tribal/agreement-states.html> [<https://perma.cc/HS7L-W3FJ>] (“NRC provides assistance to States expressing interest in establishing programs to assume NRC regulatory authority under the Atomic Energy Act of 1954, as amended. Section 274 of the Act provides a statutory basis under which NRC relinquishes to the States portions of its regulatory authority to license and regulate byproduct materials (radioisotopes); source materials (uranium and thorium); and certain quantities of special nuclear materials. The mechanism for the transfer of NRC’s authority to a State is an agreement signed by the Governor of the State and the Chairman of the Commission, in accordance with section 274b of the Act.”).

²²⁷ State-by-state regulation of the life sciences could operate similar to how states address the results of assisted reproductive technology or have enacted laws banning human reproductive cloning. *See generally* CHARLES P. KINDREGAN, JR. & MAUREEN MCBRIEN, *ASSISTED REPRODUCTIVE TECHNOLOGY: A LAWYER’S GUIDE TO EMERGING LAW AND SCIENCE* (2d ed. 2011) (discussing the state-by-state regulation of assisted reproductive technology).

²²⁸ A Congressional change to FDA regulation could involve Congress introducing another definition that would fill the gap between drugs and biologics—two categories that innovative techniques in the life sciences tend to fall “in between.”

²²⁹ *See generally Designating an Orphan Product: Drugs and Biological Products*, FDA (Feb. 16, 2018), <https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/default.htm> [<https://perma.cc/77H3-28YK>] (“The Orphan Drug Act (ODA) provides for granting special status to a drug or biological product (‘drug’) to treat a rare disease or condition upon request of a sponsor. This status is referred to as orphan designation (or sometimes ‘orphan status’). For a drug to qualify for orphan designation both the drug and the disease or condition must meet certain criteria specified in the ODA and FDA’s implementing regulations at 21 CFR Part 316. Orphan designation qualifies the sponsor of the drug for various development incentives of the ODA, including tax credits for qualified clinical testing. A marketing application for a prescription drug product that has received orphan designation is not subject to a prescription drug user fee unless the application includes an indication for other than the rare disease or condition for which the drug was designated.”). As the possible options mentioned in the text draw not only on both the administrative and health law literatures, but also address a number of areas such as innovation in insurance regulation, the FDA’s regulatory process (assuming the FDA has jurisdiction or continues to regulate in the absence of jurisdiction), resource constraints, the Prescription Drug User Fee Acts, and larger federalism concerns, the full consideration of these possible solutions will be the subject of a future article, which will focus on issues related to regulatory best practices and also federalism in the healthcare context.

CONCLUSION

It is becoming increasingly difficult to differentiate between medical practice on the one hand, and drugs, biologics, and medical devices on the other. Procedures using human tissues as medical treatments do not fall within the categories of products that the FDA is empowered to regulate, and the FDA's regulatory scheme is not structured to objectively regulate these innovative uses of human cells and tissues while simultaneously permitting innovation, nor is that regulatory scheme structured to accommodate the resource constraints faced by researchers and physicians in these areas.²³⁰ Although these techniques could treat ailments better than pharmaceuticals and current treatment protocols, patients are largely deprived of these beneficial innovations due to the federal administrative state's encroachment into the practice of medicine.

Much of this Article has focused on the relationships between the FDA, medical providers, and new technologies. The FDA, in spite of criticisms such as those mentioned regarding regulatory capture, generally enjoys a positive reputation in the area of drug regulation.²³¹ This is, of course, not a perfect reputation, as the agency has played a role in a number of imperfect regulatory situations such as delayed action related to Vioxx and a political dispute (with regulatory implications) over the change from prescription to over-the-counter treatment of Plan B.²³² Nonetheless, when thinking of "drug" regulation, individuals tend to think of "drugs" as pharmaceuticals.

The discovery of subterranean regulation in fields outside of ART suggests that FDA officials not only use a particularly risk-averse approach to regulating ethically fraught areas that may also be politically sensitive (*e.g.*, forms of ART that might involve the destruction of embryos which implicate debates about inheritable genetic modifications, eugenics, and embryo destruction), but also to regulating other techniques that may be innovative such that they do not fit within the standard areas that the FDA tends to regulate. The current effect of the FDA regulating these techniques is that innovative techniques are subject to extensive regulation in the United States, often resulting in the chilling of progress or medical tourism, which essentially limits these techniques to individuals who can afford to obtain these treatments abroad.²³³ As commentary focuses on the expedited drug approval

²³⁰ See, *e.g.*, Millman, *supra* note 129 (discussing the costs of drug research and development).

²³¹ David Zaring, *Regulating by Repute*, 110 MICH. L. REV. 1003, 1004–05 (2012) (reviewing DANIEL P. CARPENTER, *REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA* (2010)).

²³² See, *e.g.*, *id.* at 1014, 1009–11 (noting "Carpenter's view of the decline of the agency's reputation during the Bush Administration" and mentioning the discussion of legal issues related to Vioxx).

²³³ See Peter S. Reichertz & Melinda S. Friend, *Hiding Behind Agency Discretion: The Food and Drug Administration's Personal Use Drug Importation Policy*, 9 CORNELL J.L. & PUB. POL'Y 493, 495 (2000) (observing that "during the Laetrile Wars . . . [the] FDA successfully prohibited terminally-ill cancer patients from taking what they believed to be

process and the increased outlay of funds for research, it has largely ignored whether congressional response to the FDA's innovation-hindering "power grabs" has been adequate. In other words, there has been an emphasis on innovation and the processes used by the FDA to approve products without asking whether innovative treatments should be subject to the FDA's regulatory process at all.

While the National Academies has recommended that federal agencies "engage with federal and state consumer- and occupational-safety regulators . . . [in order to address issues] that may confront new biotechnology products in the next 5–10 years," recent events indicate that this recommendation of such a storied body is not enough.²³⁴ "Engagements" are not legally sufficient. The current regime either (1) has an automatic chilling effect on research, or (2) results in lengthy enforcement proceedings and litigation for those who are inclined to challenge the FDA's authority.

Yet the question that should be asked before these engagements, is whether the FDA should be regulating uses of the human body as a treatment for medical ailments. Contrary to the position of various scholars, this Article has argued that it should not.²³⁵ While some scholars believe that agencies and their staff members are "[r]arely . . . interested in simply maximizing the agency budget or jurisdiction,"²³⁶ the case studies in this Article indicate that, at least in the specific field of human tissue as a treatment to human ailments, the FDA has been rapidly expanding its jurisdiction.²³⁷ In light of jurisdictional gaps, the agency could be motivated by the idea that if the agency fails to regulate now, then it may never get to. Yet, regulation without jurisdiction is not the answer—it leads only to a regulatory and clinical environment where medical treatment occurs without innovation that could improve patient health and ultimately save lives.

an effective and perhaps lifesaving unapproved drug," even though some patients ventured to Mexico in order to obtain the drug); see also Barron H. Lerner, *McQueen's Legacy of Laetrile*, N.Y. TIMES (Nov. 15, 2005), <http://www.nytimes.com/2005/11/15/health/mcqueen-legacy-of-laetrile.html> [<https://perma.cc/L6UQ-BK2E>].

²³⁴ See THE NAT'L ACADS. OF SCIS., ENG'G, & MED., PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY 13 (The National Academies Press, 2017), available at <http://www.nap.edu/read/24605/chapter/2> [<https://perma.cc/4YF9-NS53>].

²³⁵ See, e.g., HUTT ET AL., *supra* note 191, at 1169.

²³⁶ Seidenfeld, *Who Decides Who Decides*, *supra* note 112, at 642.

²³⁷ See *id.* at 643 n.136 ("That 'single mission agencies' may have 'dedicated but zealous' staff, which needs to be checked by political oversight outside the agency is a commonly cited excerpt from an administrative law opinion" (citing *Sierra Club v. Costle*, 657 F.2d 298, 406 (D.C. Cir. 1981))).