INNOVATING FEDERALISM IN THE LIFE SCIENCES

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ABSTRACT

This Article challenges the view that the U.S. Food and Drug Administration (FDA) has exclusive jurisdiction over life sciences innovations. Many current and forthcoming life sciences innovations are "innovative therapies" such as gene editing, gene therapy, and regenerative stem cell treatments, which are actually "hybrids" of state and federal jurisdiction. Thus, both state and federal jurisdiction coexist: federal jurisdiction exists to the extent that these medical innovations use drugs or biologics, but state jurisdiction exists to the extent that these innovations are procedures regulated by states as the practice of medicine.

This Article argues that the regulation of numerous current and forthcoming innovative therapies requires the recognition of a state-federal partnership—not only because both federal and state jurisdiction already coexist but also because a cooperative form of shared governance would improve the transparency and quality of regulation. This Article provides a structural framework for that shared governance that draws on existing federal-state cooperative programs and applies the advantages of cooperative federalism, with an emphasis on often neglected actors in the realm of regulating innovative therapies: states. Incorporating this Article's cooperative structural framework would (1) curtail the federal usurpation of state jurisdiction, (2) minimize the significance of the FDA's resource shortage by complementing federal regulation, and (3) reduce the likelihood that the FDA would continue to unlawfully incorporate political and social motivations into its decision-making process. Applying this Article's cooperative framework would also serve to recognize the continued existence of both state and federal jurisdiction over innovative therapies.

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INTRODUCTION

While a professional athlete, Kobe Bryant had several injuries that threatened to derail his career.[1] After several surgeries on his right knee, Kobe Bryant often underwent a treatment, Regenokine, that used his own blood to aid his recovery and to maintain the health of his knee.[2] While this treatment arguably prolonged his career, one problematic aspect of this treatment was that, at the time Kobe Bryant began using it, he had to travel to Germany to obtain it.[3] According to the U.S Food and Drug Administration (FDA), even though the procedure used Bryant's own blood, the fact that additives were combined with Bryant's own blood before it was injected back into him meant that the product was subject to the FDA's approval process, which would lengthen the amount of time that would pass before the treatment would become available in the United States.[4] While this regulatory delay is not as problematic for individuals like Kobe Bryant who could simply travel to Germany where the procedure was pioneered, Americans without Kobe Bryant's resources or sophisticated medical team might be tempted to travel to a less reputable domestic provider or to an unregulated clinic in another country without Germany's or the United States' regulatory standards, which could lead to significant harm.[5]

The United States' federal regulatory structure continues to be challenged by innovations in medicine.[6] This Article focuses on what it refers to as "innovative

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1. *See* Joshua Sexton, *A Gruesome Look at Kobe Bryant's Injury History*, BLEACHER REP. (Jan. 9, 2012), http://bleacherreport.com/articles/1015940-a-gruesome-look-at-kobe-bryants-injury-history [https://perma.cc/2XSH-V6XQ].

2. *See id.* See also *infra* note 9 for an explanation of the Regenokine treatment, including the process involved and how it is regulated in the United States.

3. Will Carroll, *What Is This Knee Treatment Kobe Bryant Goes All the Way to Germany For?*, BLEACHER REP. (Oct. 4, 2013), http://bleacherreport.com/articles/1798763-what-is-this-knee-treatment-kobe-bryant-goes-all-the-way-to-germany-for [https://perma.cc/DF3R-DA7D].

4. *Id.*

5. *See* Liz Kowalczyk, *He Went Abroad for Stem Cell Treatment. Now He's a Cautionary Tale*, BOS. GLOBE (June 22, 2016), http://www.bostonglobe.com/metro/2016/06/22/went-abroad-for-stem-cell-treatment-now-cautionary-tale/wH8d9uLejaDvSwWRt91w5L/story.html [https://perma.cc/B2NN-33RD] (detailing the case of Jim Gass who traveled to Argentina, China, and Mexico for stem cell treatments and is now "more disabled than he was prior to stem cell therapy").

6. *See, e.g.*, U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-16-432, FDA NEEDS MORE STRATEGIC PLANNING TO GUIDE ITS SCIENTIFIC INITIATIVES (2016), http://www.gao.gov/assets/680/677116.pdf [https://perma.cc/Y8XH-5FDJ] ("FDA has faced challenges regulating medical products [("drugs, devices, and biologic products . . . which include[s] vaccines, blood products, and proteins," *id.* at 1 n.1)], owing in part to rapid changes in science and technology."); Barbara J. Evans, *The Limits of FDA's Authority To Regulate Clinical Research Involving High-Throughput DNA Sequencing*, 70 FOOD & DRUG L.J. 259, 259 & n.5 (2015) ("These [proposed FDA regulatory efforts to regulate laboratory developed tests] sparked heated debates about whether FDA has authority to regulate genomic testing and the potential impact such regulation may have on genomic discovery and innovation."); Diane Hoffmann et al., *Improving Regulation of Microbiota Transplants*, 358 SCI. 1390, 1390 (2017) ("The advent of these applications for [microbiota transplants] poses challenges for regulatory bodies. The transplanted material is not a 'typical' drug, and thus may not be appropriate for the drug regulatory pathway. The material consists of a community of highly dynamic, metabolically active organisms. . . . Each batch of 'product' is different, making characterization of the transplanted material problematic."); Insoo Hyun, *Allowing Innovative Stem Cell-Based Therapies Outside of Clinical Trials: Ethical and Policy Challenges*, 38 J.L. MED. & ETHICS 277, 279–80 (2010) (discussing the ethical and regulatory challenges that accompany stem-cell based innovative therapies); Gary E. Marchant & Yvonne A. Stevens, *Resilience: A New*

therapies." In this Article, "innovative therapies" are life sciences innovations that combine federally regulated products and state-regulated procedures, as states regulate the practice of medicine and the federal government regulates medical products.[7] Examples of innovative therapies include regenerative stem cell treatments and treatments that target defective genes, including gene therapies and gene editing.[8]

Overregulation motivates Americans to travel abroad in search of innovative therapies. For example, during their professional careers, Kobe Bryant, Alex Rodriguez, Peyton Manning, and other professional athletes traveled to Europe for medical treatments that were not (and are still not) approved by the FDA, including certain regenerative stem cell treatments.[9] While these treatments may be successful (or at least not harmful) for professional athletes, results may be less positive for members of the general public who, lacking the resources of professional athletes, also travel in pursuit of these treatments but to countries with far less regulation, or lately, due to

Tool in the Risk Governance Toolbox for Emerging Technologies, 51 U.C. DAVIS L. REV. 233, 237 (2017) ("Emerging technologies such as nanotechnology, synthetic biology, artificial intelligence/robotics, CRISPR gene editing, and applied neuroscience present significant governance challenges."); Jordan Paradise, *Cultivating Innovation in Precision Medicine Through Regulatory Flexibility at the FDA*, 11 N.Y.U. J.L. & LIBERTY 672, 675 (2017) [hereinafter Paradise, *Cultivating Innovation*] ("Precision medicine poses challenges to traditional FDA regulatory paradigms."); Rachel E. Sachs & Carolyn A. Edelstein, *Ensuring the Safe and Effective FDA Regulation of Fecal Microbiota Transplantation*, 2 J.L. & BIOSCIENCES 396, 415 n.116 (2015) ("The FDA has undoubtedly faced numerous new challenges throughout its history, and it has had to consider how it might adapt old statutes to new problems.").

7. See *infra* Section I for more on the practice-products divide in the regulation of medicine. See also *infra* notes 43–47 and accompanying text for more on innovative therapies, including common characteristics such as their failure to fit clearly within FDA-regulated categories and their designation as "combination products" by the FDA.

8. See *infra* Part I.C for a discussion of such therapies.

9. Regenokine is a technique in which a patient's blood is combined with other substances, including anti-inflammatory agents, in a laboratory before that blood is injected back into a patient. *See* Carroll, *supra* note 3. Regenokine is referred to as a "blood spinning therapy." *See id.* Due to the mixture of a patient's blood with other substances, however, the FDA's regulatory position is that such a treatment is a mixture that constitutes "more than minimal manipulation" under the FDA's Human Cellular and Tissue-Based Products regulatory scheme, thus requiring the submission of an investigational new drug application. FDA, REGULATORY CONSIDERATIONS FOR HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS: MINIMAL MANIPULATION AND HOMOLOGOUS USE: GUIDANCE FOR INDUSTRY AND FOOD AND DRUG ADMINISTRATION STAFF 1, 4 (2017), http://www.fda.gov/media/124138/download [https://perma.cc/7KBL-VRZL]. Even though Regenokine is reportedly available now in the United States, athletes continue to travel abroad to obtain it. *See, e.g.*, Marc Carig, *Yankees Slugger Alex Rodriguez Reportedly Goes to Germany for Knee Treatment*, NJ.COM (Dec. 28, 2011), http://www.nj.com/yankees/index.ssf/2011/12/yankees_slugger_alex_rodriguez_8.html [https://perma.cc/XD85-BASD]. For more on the availability of Regenokine in the United States, see Lloyd Sederer, *An Arthritis Treatment Worthy of the Pope and Kobe*, ATLANTIC (Oct. 15, 2012), http://www.theatlantic.com/health/archive/2012/10/an-arthritis-treatment-worthy-of-the-pope-and-kobe/261606/ [https://perma.cc/MEL4-K2GV]; see also Antonio Regalado, *The NFL Has a Problem with Stem Cell Treatments*, MIT TECH. REV. (Dec. 10, 2014), http://www.technologyreview.com/s/533171/the-nfl-has-a-problem-with-stem-cell-treatments/ [https://perma.cc/7DQE-A5KJ]; Jenny Vrentas, *Stem Cell Treatment: Out from the Shadows, onto the Cutting Edge*, SPORTS ILLUSTRATED (July 30, 2014), http://www.si.com/2014/07/30/stem-cell-treatment-nfl-sports-medicine [https://perma.cc/5TBZ-JYS8]. For more on the minimal manipulation standard in FDA regulations, which establishes when the use of a patient's own cells or tissues are subject to FDA approval, see, for example, Myrisha S. Lewis, *Halted Innovation: The Expansion of Federal Jurisdiction over Medicine and the Human Body*, 2018 UTAH L. REV. 1073, 1098 [hereinafter Lewis, *Halted Innovation*].

underregulation, to domestic states with less restrictive regulatory regimes.[10] How does one improve the U.S. scheme of regulating life sciences so that athletes and other individuals do not have to travel internationally or seek the services of those governed by less restrictive regulatory regimes that may not adequately regulate therapies for their safety and effectiveness?[11]

Recently, the now-former FDA commissioner observed, regarding regenerative stem cell therapies, that "[t]he FDA must advance an efficient and least burdensome framework as a way to help new products remain compliant with the law through a regulatory structure that does not become a barrier to beneficial new innovation."[12] This Article responds to that call and simultaneously extends it to other innovative therapies: this Article argues that efficiently (and transparently) regulating forthcoming innovative therapies requires a larger role for individual states.

This Article also builds on previous scholarship that explains how the FDA does not have exclusive jurisdiction over innovative life sciences techniques and also how the FDA's regime is inadequate to regulate these techniques.[13] There are several problems with the current way the FDA exercises jurisdiction. First, the current method of regulation fails to recognize the longstanding "practice-products distinction" in the state-federal regulatory system, where states regulate the practice of medicine and the federal government regulates the products used in the practice of medicine.[14] Not only is the line between medical practice and medical products blurring over time but also scholars question whether the FDA should be regulating innovative technologies in the current manner because those "products" do not fit within the FDA's regulatory scheme, in spite of the agency's assertions of jurisdiction.[15]

Within the realm of life sciences innovations, this Article focuses on innovative therapies that it labels as "hybrids" of federal and state jurisdiction because they involve federally regulated products and the state-regulated practice of medicine. As a

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10. *See, e.g.*, Kowalczyk, *supra* note 5 (discussing "stem cell tourism" due at least in part to publicity surrounding professional athletes' pursuit of stem cell treatments abroad). See also *infra* Part I.C.3 for a discussion of stem cell treatments and their availability in certain states.

11. *See* Kirstin R.W. Matthews & Maude L. Cuchiara, *U.S. National Football League Athletes Seeking Unproven Stem Cell Treatments*, 23 STEM CELLS & DEV. 60, 60 (2014) ("The majority of patients journey from industrialized countries to developing ones where federal regulations may be more lenient or nonexistent."); *see also* 21 U.S.C. § 393(b)(2) (2018); Barbara J. Evans, *Seven Pillars of a New Evidentiary Paradigm: The Food, Drug, and Cosmetic Act Enters the Genomic Era*, 85 NOTRE DAME L. REV. 419, 425–26 (2010) [hereinafter Evans, *Seven Pillars*] (discussing "safety and efficacy" in the context of FDA regulation).

12. *See* Press Release, U.S. Food & Drug Admin., Statement from FDA Commissioner Scott Gottlieb, M.D. on the FDA's New Policy Steps and Enforcement Efforts To Ensure Proper Oversight of Stem Cell Therapies and Regenerative Medicine (Aug. 28, 2017), http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573443.htm [https://perma.cc/PJF9-Y79K]. Scott Gottlieb was the FDA Commissioner until April 5, 2019. *See Scott Gottlieb, M.D.*, FDA, http://www.fda.gov/node/373545 [https://perma.cc/P6BS-F6UP] (last updated Apr. 19, 2019).

13. *See supra* notes 6–7, *infra* note 14 and accompanying text.

14. *See infra* Section I; *see also, e.g.*, Barbara J. Evans, *Distinguishing Product and Practice Regulation in Personalized Medicine*, 81 CLINICAL PHARMACOLOGY & THERAPEUTICS 288, 288 (2007) ("Targeted drug therapies and the screening tests that support them raise thorny issues of how to draw the line between regulation of medical products and regulation of medical practice. Careful line-drawing has always been important, lest product regulations limit physicians' discretion to use products as they deem best for the individual patient.").

15. See *infra* Section I for an analysis of the FDA's regulatory scheme.

jurisdictional matter, forthcoming innovative therapies such as gene editing (including CRISPR-Cas9, which has received a significant amount of media attention), gene therapy, and autologous stem cell therapies involve state jurisdiction over the practice of medicine and federal jurisdiction over the approval of specific categories of products that the FDA regulates.[16] Nevertheless, the federal government continues to regulate these innovations without adequate statutory authority.[17] Recently, for example, a former chief counsel of the FDA expressed doubt as to whether the FDA's current statutes enabled the FDA to regulate gene therapy, one of the innovative therapies this Article addresses.[18]

Second, precedent shows that although representatives of the FDA acknowledge jurisdictional limitations in statements to the public and Congress, a close analysis of the agency's actual decisionmaking reveals that the agency does include political and social considerations in its decision-making process, which are outside of its statutory mandate and contrary to administrative law's goals of transparency and accountability.[19]

16. See *infra* Part I.C for an analysis of these forthcoming innovative therapies.

17. *See infra* Part I.C; *supra* notes 6–7; *see also* Myrisha S. Lewis, *How Subterranean Regulation Hinders Innovation in Assisted Reproductive Technology*, 39 CARDOZO L. REV. 1239, 1243 (2018) [hereinafter Lewis, *How Subterranean*] (arguing that forms of assisted reproductive technology involve genetic modifications that fall outside of the FDA's jurisdiction). For support of the FDA's method of asserting jurisdiction, see Peter Barton Hutt, *Philosophy of Regulation Under the Federal Food, Drug and Cosmetic Act*, 50 FOOD & DRUG L.J. 101, 102 (1995). Peter Barton Hutt is a former chief counsel of the FDA. *See id.* at 103. For criticism of the FDA's method of asserting jurisdiction, see 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, 1202 & n.4 (citing Richard A. Merrill & Bryan J. Rose, *FDA Regulation of Human Cloning: Usurpation or Statesmanship?*, 15 HARV. J.L. & TECH. 85, 100, 124 (2001) (Richard A. Merrill was a former chief counsel of the FDA)); Lewis, *Halted Innovation*, *supra* note 9, at 1073. Nonetheless, generally, most scholars write from the position that the FDA has jurisdiction over these techniques. Similarly, the position of FDA employees, even in congressional testimony, is that the FDA has jurisdiction over such innovations. *See, e.g.*, Lewis, *How Subterranean*, *supra*, at 1273–74.

18. *See FDA Conference Videos: Plenary Session 2: A Discussion with Former FDA Chief Counsels*, AM. U. WASH. C. L. (Oct. 19, 2018), http://www.wcl.american.edu/impact/initiatives-programs/health/events/fdaconf18/videos/ [https://perma.cc/ZG7A-F3J4] [hereinafter *Plenary Session 2*] (containing remarks of Daniel Troy, former chief counsel of the FDA).

19. *See, e.g.*, Nina A. Mendelson, *Disclosing "Political" Oversight of Agency Decision Making*, 108 MICH. L. REV. 1127, 1130–31, 1141 (2010) [hereinafter Mendelson, *Disclosing "Political" Oversight*] ("[I]n a 2009 decision invalidating a Food and Drug Administration . . . decision to make the emergency contraceptive Plan B available only to women eighteen and older, a federal judge found that contact between the White House and the agency was a factor weighing *against* upholding the agency action." (citing Tummino v. Torti, 603 F. Supp. 2d 519, 547 (E.D.N.Y. 2009))); *id.* at 1141 n.66 ("Whether or not it was permissible . . . these discussions were not the norm for the FDA with respect to this type of decision." (omission in original) (quoting *Tummino*, 603 F. Supp. 2d at 547)); *see also* Daniel A. Farber & Anne Joseph O'Connell, *The Lost World of Administrative Law*, 92 TEX. L. REV. 1137, 1168 (2014) ("Agencies rarely acknowledge these political considerations explicitly, though few commentators and scholars dispute their importance."); *id.* (also discussing the impact of political considerations on the FDA's Plan B decision); Catherine M. Sharkey, *Federalism Accountability: "Agency-Forcing" Measures*, 58 DUKE L.J. 2125, 2128, 2131–43 (2009) [hereinafter Sharkey, *Federalism Accountability*] (discussing "federal agencies' dismal track record on accountability"); *id.* at 2190 (observing, while discussing the Supreme Court's decision in *Wyeth v. Levine*, 555 U.S. 555 (2009), which addressed the interface between federal regulations and state law, "[l]urking just beneath the surface of the *Wyeth* majority opinion is deep suspicion that the FDA changed its position on preemption for political as opposed to scientific or risk management reasons"). See *infra* Part I.A for a discussion of the FDA's use of informal tools to regulate innovative therapies. *See also* Lewis, *How Subterranean*, *supra* note 17, at 1273–74 (discussing the

Sometimes, overregulation results when regulators introduce concerns such as politics into regulatory decisionmaking, as evidenced by the delay in the conversion of emergency contraception from a prescription drug product to an over-the-counter drug.[20] Further, when the FDA makes decisions for reasons other than safety or effectiveness, the administrative state is not structured so that the public and the judicial system can easily ascertain those underlying motivations.[21] By strengthening the role of states in the regulation of innovative therapies, the significance of improperly motivated regulatory decisions may be minimized.

This Article contributes to the health law, administrative law, federalism, and innovation literatures by focusing on the significance of the sometimes neglected states in the regulatory system.[22] Increasing the role of the states in the regulatory process adds another "check" on administrative agencies other than the judiciary.[23] This Article argues that the regulation of numerous current and forthcoming innovative therapies requires the recognition of a state-federal partnership not only because both federal and state jurisdiction already coexist but also because a cooperative form of shared governance would improve the transparency and quality of regulation.

Drawing on the literatures of federalism, administrative law, and health law, this Article offers a structural solution for a specific subset of life sciences innovations: innovative therapies. Because state and federal jurisdiction coexist, improvements to the scheme for regulating innovative therapies should include both state

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role of social and ethical issues in agency decisionmaking on topics such as human reproductive cloning and forms of assisted reproductive technology involving genetic modifications).

20. *See generally* Lisa Heinzerling, *The FDA's Plan B Fiasco: Lessons for Administrative Law*, 102 GEO. L.J. 927, 928–76 (2014) ("With every new stratagem, the FDA dug itself deeper into an administrative law hole: inventing policies on the fly, grasping at tangents, shrouding the truth, and cowering before illegitimate political demands.").

21. *See, e.g.*, Mendelson, *Disclosing "Political" Oversight*, *supra* note 19, at 1128–29.

22. *See, e.g.*, Jessica Bulman-Pozen, *Preemption and Commandeering Without Congress*, 70 STAN. L. REV. 2029, 2031 (2018) [hereinafter Bulman-Pozen, *Preemption*]; Gillian E. Metzger, *The Constitutional Duty To Supervise*, 124 YALE L.J. 1836, 1852 (2015) [hereinafter Metzger, *The Constitutional Duty*] ("Cooperative federalism denotes instances in which state and local governments undertake primary responsibility for implementing federal programs or enforcing federal law under the supervision and oversight of federal agencies." (citing Jessica Bulman-Pozen, *Federalism as a Safeguard of the Separation of Powers*, 112 COLUM. L. REV. 459, 472–75 (2012) [hereinafter Bulman-Pozen, *Federalism as a Safeguard*])); *id.* at 1853 ("Major legislative and administrative initiatives of the last few years have significantly increased the scope of such federal-state cooperation. Not only is the federal government asking states to play new roles in federal programs, but it is also giving states broader discretion and control over the shape of their participation. The Affordable Care Act is a prime example."); Miriam Seifter, *States as Interest Groups in the Administrative Process*, 100 VA. L. REV. 953, 954–55, 981–84 (2014); Philip J. Weiser, *Towards a Constitutional Architecture for Cooperative Federalism*, 79 N.C. L. REV. 663, 665, 671 (2001). See *infra* Sections II and III for more on federalism in health law.

23. *See* Roderick M. Hills, Jr., *The Political Economy of Cooperative Federalism: Why State Autonomy Makes Sense and "Dual Sovereignty" Doesn't*, 96 MICH. L. REV. 813, 859–62, 883 (1998) (noting that overlapping jurisdiction between states and the federal government "allows Congress to play state and federal officials off of each other to avoid dishonesty or corruption by either"); *see also* Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1782 (1996) [hereinafter Merrill, *The Architecture*] ("In sum, in the new drug approval process—as in most administrative licensing regimes—FDA exercises effectively unchallengeable authority to dictate the number and kinds of studies required to support approval and nearly unreviewable discretion to interpret the results.").

and federal governments. Thus, this Article argues for the recognition of separate state and federal spheres for the regulation of innovative therapies. Doing so would facilitate and strengthen an overlooked aspect of innovative therapies, which is that states also play an important regulatory role. Specifically, this Article's cooperative framework draws on the concept of "cooperative federalism."

Cooperative federalism, as will be further detailed in Section III, is a form of governance in which, instead of situating all authority for regulation of a particular area in the federal government, states are able to experiment subject to the existence of federal baselines, federal agency oversight, and federal judicial review.[24] Section III also explains the criteria that would trigger the use of this Article's cooperative framework, which are the existence of state jurisdiction, an innovative therapy that would implicate state jurisdiction, a "combination product" under the FDA's regulatory scheme, and the FDA's assertion of jurisdiction via guidance documents.[25] An additional criterion that might exist for some therapies but not others includes the likelihood that the therapy's use would be accompanied by political or social controversy. Although the traditional tools of cooperative federalism do not completely solve the problem of adequately regulating innovative therapies, those traditional tools provide some structures that could serve as a starting point to resolving the issue this Article identifies.[26] This Article builds upon those traditions in its proposed structural solution, "A Cooperative Framework for Regulating Innovative Therapies," outlined in Section III, which would tailor the regulatory system to regulating innovative therapies. The structural solution emphasizes increasing the role of states in the regulation of innovative therapies by using a number of aspects of cooperative federalism programs, including a state-federal committee and increasing the role of the states in monitoring innovative therapies.

This Article proceeds as follows: Section I provides legal background on the current regulation of innovative therapies, with an emphasis on the jurisdictional boundaries of federal and state regulation and the complexities of regulating innovative therapies that are hybrids of state and federal jurisdiction. Section II assesses the weaknesses of the current regulatory system and examines alternative options available for improving the regulation of life sciences innovation. Section III provides background on the concept of cooperative federalism and examines existing state and federal cooperative schemes in medicine and related areas, including Medicaid, communicable disease prevention, food regulation, and nuclear medicine. Ultimately, Section III proposes a novel, cooperative

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24. *See, e.g.*, City of Rancho Palos Verdes v. Abrams, 544 U.S. 113, 128–29 (2005) (Breyer, J., concurring) ("Congress initially considered a single national solution, namely, a Federal Communications Commission wireless tower siting policy that would pre-empt state and local authority. But Congress ultimately rejected the national approach and substituted a system based on cooperative federalism. State and local authorities would remain free to make siting decisions. They would do so, however, subject to minimum federal standards—both substantive and procedural—as well as federal judicial review." (citations omitted)); *see also* Dave Owen, *Cooperative Subfederalism*, 9 U.C. IRVINE L. REV. 177, 179 (2018).

25. See *infra* Parts I.A and II.A for a discussion of federal regulation and the weaknesses of the current regime.

26. *See infra* Part III.A; *see also* Metzger, *The Constitutional Duty*, *supra* note 22, at 1852–54 (noting the usefulness of federal funding in cooperative federalism and programs providing increased state-federal cooperation such as the Affordable Care Act's "state-run health benefit exchanges, expanded federally funded state Medicaid programs, and state enforcement of its insurance requirements"). For a criticism of cooperative federalism, see Michael S. Greve, *Against Cooperative Federalism*, 70 MISS. L.J. 557, 559 (2000).

regulatory solution that could significantly improve the regulation of innovations in medicine, especially as innovative therapies continue to evolve past standard legal classifications.

I. REGULATION OF INNOVATIVE THERAPIES: THE PRACTICE-PRODUCTS DISTINCTION

Traditionally, the line between state and federal jurisdiction relies on the distinction between medical practice, which is regulated by individual states, and medical products, which are regulated by the federal government. However, that line has been "blurring" over time.[27] As medical innovations move toward more individualized therapies, the line between what is the practice of medicine and what is the use of a federally regulated product becomes less clear.[28] Nevertheless, as this Article argues, even if a "bright line" cannot be drawn between medical practice and federally regulated products, both state and federal jurisdiction apply to the innovative therapies this Article discusses.[29]

This Section provides an overview of the current system for regulating innovation in medicine. Part I.A provides an overview of the federal regulation of products used in the practice of medicine. Part I.B provides an overview of state jurisdiction over the practice of medicine. Part I.C illustrates how the practice-products distinction operates in the context of innovative therapies, such as gene therapy, gene editing, and regenerative medicine therapies, which are "hybrids" of state and federal jurisdiction and how, due to jurisdictional constraints and regulatory goals, increased state-federal cooperation is required in the regulation of innovative therapies.

A. Federal Regulation of the Products Used in the Practice of Medicine

The FDA regulates a number of products for safety and effectiveness, including drugs, biologics, food, medical devices, cosmetics, and tobacco, through a regime that emphasizes information disclosure, with a focus on providing the information on the

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27. *See, e.g.*, Sarah Duranske, *Reforming Regenerative Medicine Regulation*, 34 GA. ST. U. L. REV. 631, 639–40 (2018); Evans, *Seven Pillars*, *supra* note 11, at 500–03, 509–10, 517–18; Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845, 892 (2017) [hereinafter Zettler, *Pharmaceutical Federalism*]; *see also* Lars Noah, *State Affronts to Federal Primacy in the Licensure of Pharmaceutical Products*, 2016 MICH. ST. L. REV. 1, 15 [hereinafter Noah, *State Affronts*] ("Congress['s] repeated[] . . . assurances that the FDA's authority to license therapeutic products would not interfere with the practice of medicine.").

28. *See* Zettler, *Pharmaceutical Federalism*, *supra* note 27, at 888–92 ("The blurriness of the practice-products distinction revealed by recent state drug regulation may have significance . . . . And this line drawing may be particularly difficult when the FDA is faced with questions about whether, and how, to regulate new medical technologies that may not fit comfortably within the agency's existing framework.").

29. *See* Press Release, U.S. Food & Drug Admin., *supra* note 12.

> At the same time, it's incumbent upon the FDA to make sure that this existing framework is properly defined, with bright lines separating new treatments that are medical products subject to the FDA's regulation from those therapies that are individualized by surgeons in such a way that they are not subject to FDA regulation. The field of regenerative medicine, because of the very nature of the science and the rapidly evolving clinical developments, not infrequently lends itself to often close calls between what constitutes an individualized treatment being performed by a doctor within the scope of his medical practice on the one hand, and what constitutes a medical product that is currently subject to the authorities Congress has already charged the FDA with exercising.

Id.

risks and benefits of approved products.[30] In 1938, the Food, Drug, and Cosmetic Act (FDCA) created a new system of drug regulation requiring federal approval by the FDA before marketing begins.[31] The FDA bases its approval on a number of statutory factors including "safety and effectiveness."[32]

The FDA also operates with the goal of encouraging medical innovation and hastening the speed through which innovations are approved, which requires an efficient and effective regulatory process.[33] This goal has been furthered through various congressional enactments. First, recently, the 21st Century Cures Act instituted a number of reforms to hasten the FDA approval of certain products, namely those designated as "regenerative advanced therapies."[34] Second, before the 21st Century Cures Act, other legislation also aimed to accelerate the drug approval process, including the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, which created a process for the accelerated approval of generic drugs.[35] Third, just as Congress created regimes to expedite the approval of

30. *See What Does FDA Regulate?*, FDA, http://www.fda.gov/AboutFDA/Transparency/Basics/ucm194879.htm [https://perma.cc/2BCH-FRBD] (last updated Mar. 28, 2018); *see also* Merrill, *The Architecture*, *supra* note 23, at 1801–36 (discussing federal medical-device regulation); Patricia J. Zettler, *The Indirect Consequences of Expanded Off-Label Promotion*, 78 OHIO ST. L.J. 1053, 1059 (2017) [hereinafter Zettler, *Indirect Consequences*]. For scholarly assessments of the federal drug approval process, see, for example, Noah, *State Affronts*, *supra* note 27, at 9; Lars Noah, *Triage in the Nation's Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs*, 54 S.C. L. REV. 741, 748 (2003); Christina Sandefur, *Safeguarding the Right To Try*, 49 ARIZ. ST. L.J. 513, 514–15 (2017); Kara W. Swanson, *Food and Drug Law as Intellectual Property Law: Historical Reflections*, 2011 WIS. L. REV. 331, 332–37.

31. *Milestones in U.S. Food and Drug Law History*, FDA, http://www.fda.gov/about-fda/fdas-evolving-regulatory-powers/milestones-us-food-and-drug-law-history [https://perma.cc/4ZSX-6LEN] (last updated Jan. 31, 2018). For more on the FDA's drug-approval process, see, for example, Zettler, *Indirect Consequences*, *supra* note 30, at 1061, 1086; *see also* 21 U.S.C. § 355(a) (2018); Stacey B. Lee, PLIVA v. Mensing*: Generic Consumers' Unfortunate Hand*, 12 YALE J. HEALTH POL'Y, L., & ETHICS 209, 214 (2012); Merrill, *The Architecture*, *supra* note 23, at 1764–68, 1776–92 (discussing the 1962 FDCA amendments).

32. *See* 21 U.S.C. § 393(b)(2)(C).

33. *See, e.g.*, Amy Kapczynski, *Dangerous Times: The FDA's Role in Information Production, Past and Future*, 102 MINN. L. REV. 2357, 2379 (2018).

34. *See* 21st Century Cures Act, Pub. L. No. 114-255, 130 Stat. 1033, 1033 (2016), http://www.gpo.gov/fdsys/pkg/PLAW-114publ255/pdf/PLAW-114publ255.pdf [https://perma.cc/F5R4-7Q4U] (stating the purpose of the Act is "[t]o accelerate the discovery, development, and delivery of 21st century cures, and for other purposes"). For more on existing processes and legislation providing accelerated product approval, see, for example, Jordan Paradise, *21st Century Citizen Pharma: The FDA & Patient-Focused Product Development*, 44 AM. J.L. & MED. 309, 323–26 (2018) [hereinafter Paradise, *21st Century Citizen Pharma*]; *supra* note 12 and accompanying text for the statement of former FDA Commissioner Scott Gottlieb on the relationship between the FDA's regulatory framework and innovation; see also Kapczynski, *supra* note 33, at 2379.

35. *See Examining the Senate and House Versions of the 'Greater Access to Affordable Pharmaceuticals Act'*: *Hearing Before S. Comm. on the Judiciary*, 108th Cong. 7–10 (2003) (statement of Daniel E. Troy, Chief Counsel, U.S. Food & Drug Admin.), http://www.govinfo.gov/content/pkg/CHRG-108shrg91832/pdf/CHRG-108shrg91832.pdf [https://perma.cc/LY7Q-BKS9]; FDA, A HISTORY OF THE FDA AND DRUG REGULATION IN THE UNITED STATES (2006), http://www.fda.gov/media/73549/download [https://perma.cc/VL63-V9WM]. The abbreviated drug approval process for generic drugs is codified at 21 U.S.C. § 355(j). For information on new brand-name drug applications, see 21 C.F.R. §§ 314.50–314.90 (2019); Merrill, *The Architecture*, *supra* note 23, at 1792–1800 (discussing congressional amendments to the Federal Food, Drug, and Cosmetic Act in 1984 and 1992). For more on the role of patents within the FDA's regulatory regime, see, for example, *Frequently Asked Questions on Patents and Exclusivity*, FDA, http://www.fda.gov/drugs/development-approval-process-

pharmaceuticals, especially generic pharmaceuticals, Congress also "created a significant new abbreviated approval process for biological products."[36] Fourth, while the practical effectiveness of the recently enacted federal "right to try" legislation, which was based on state legislation allowing patients to access pharmaceuticals at the clinical trial state before those pharmaceuticals are FDA approved, remains to be seen, the legislation had the goal of accelerating patient access to pharmaceuticals.[37] Additionally, statements by former FDA Commissioner Scott Gottlieb, while in office, also emphasized the importance of efficient and effective regulatory processes.[38]

The FDA's system of regulation is structured to regulate products that fall within clearly defined categories, namely food, drugs, biologics, medical devices, and tobacco.[39] A device is "an instrument, apparatus, implement, machine, contrivance,

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drugs/frequently-asked-questions-patents-and-exclusivity [https://perma.cc/6BAW-WDSW] (last updated May 2, 2018).

36. *See* Paradise, *Cultivating Innovation*, *supra* note 6, at 691 (citing 42 U.S.C. § 262(k) (2018)); *see also* 21 U.S.C. § 356(c) (containing the provision regarding expedited approval of drugs for serious or life-threatening diseases or conditions); Jonathan J. Darrow et al., *The FDA Breakthrough-Drug Designation—Four Years of Experience*, 378 NEW ENG. J. MED. 1444, 1444 (2018) (discussing the implementation of the expedited approval process for breakthrough therapies); Susan Bartlett Foote & Robert J. Berlin, *Can Regulation Be As Innovative As Science and Technology? The FDA's Regulation of Combination Products*, 6 MINN. J.L. SCI. & TECH. 619, 630 (2017) (citing 42 U.S.C. § 262); *Implementation of the Biologics Price Competition and Innovation Act of 2009*, FDA, http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/ucm215089.htm [https://perma.cc/HGB4-HLWL] (last updated Feb. 12, 2016).

37. While the FDA has an "expanded access" program in which those who are not participants in clinical trials can gain access to the pharmaceuticals being tested in those trials, "advocates seeking less restrictive rules have [historically] turned to state legislatures," often through "right to try" laws. Rebecca Dresser, *The "Right to Try" Investigational Drugs: Science and Stories in the Access Debate*, 93 TEX. L. REV. 1631, 1640 (2015); *see also* 21 U.S.C. § 360bbb (outlining expanded access to unapproved therapies and diagnostics); Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, Pub. L. No. 115-176, § 2, 132 Stat. 1372, 1372 (2017) (codified at 21 U.S.C. § 360bbb-0a); Abigail All. for Better Access to Developmental Drugs v. von Eschenbach, 495 F.3d 695, 697–99 (D.C. Cir. 2007) (en banc); Sam Adriance, *Fighting for the "Right To Try" Unapproved Drugs: Law as Persuasion*, 124 YALE L.J.F. 148, 148–52 (2014) (describing the origins of the "right to try" movement); Holly Fernandez Lynch et al., *Promoting Patient Interests in Implementing the Federal Right to Try Act*, 320 JAMA 869, 869 (2018), http://jamanetwork.com/journals/jama/article-abstract/2697358 [https://perma.cc/5FBY-7HFA] (discussing the FDA's Expanded Access Program); Kapczynski, *supra* note 33, at 2374–76; *id.* at 2361 (noting that state right-to-try laws "had little practical effect, because their main provisions were preempted by federal FDA law"); *id.* at 2367–68, 2368 n.56 (explaining that the FDA "allows individuals who are seriously ill to choose to take experimental drugs via its compassionate-use program, and it approves nearly all such requests"); Morten Wendelbo & Timothy Callaghan, *What Is "Right to Try" and Will It Help Terminally Ill Patients?*, CBS NEWS (May 30, 2018, 2:35 PM), http://www.cbsnews.com/news/right-to-try-bill-trump-signing-will-it-help-terminally-ill-patients-today-2018-05-30/ [https://perma.cc/2WLW-ZUA2] (observing that (1) right to try legislation does not require pharmaceutical companies to provide experimental medications to patients; and (2) despite the legislation, there are many disadvantages to providing access to unapproved experimental medications to patients, including cost to patients, possible legal liability for pharmaceutical companies, and the potential that the eventual approval of the drugs by the FDA might be delayed due to the data collected (and the manner in which it was collected)).

38. See *supra* note 12 and accompanying text for the statement of former FDA Commissioner Gottlieb; see also *supra* note 29 for an analysis of the FDA's existing regulatory framework.

39. See *supra* note 27 for information about the FDA's authority to regulate medicine and its relationship with the practice of medicine. *See also* 21 U.S.C. § 321; Riegel v. Medtronic, Inc., 552 U.S. 312, 315 (2008); *Is The Product A Medical Device?*, FDA, http://www.fda.gov/medical-devices/classify-your-medical-

implant, in vitro reagent, or other similar or related article . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals."[40] Under the FDCA, a "drug" is defined as follows:

> (A) articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia 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 animals.[41]

Under the Public Health Service Act (PHSA), which also provides the FDA with jurisdiction, a "biologic" or "biological product" is

> 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.[42]

Nonetheless, although the FDA's system of regulation is category driven, many innovative therapies either do not fit within the categories of regulated products or fall in between categories. The FDA addresses this situation under the rubric of "combination products"; "innovative therapies," as the term is used in this Article, often implicate combination products.[43] Combination products can include various combinations, and a combination product could be any combination of drug, device, or biologic product.[44] For example, a combination product could be both a drug and a device, such as a prefilled syringe, both a drug and a biologic, such as a "[m]onoclonal antibody combined with a therapeutic drug," or even a combination of all three categories of products.[45] For

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device/product-medical-device [https://perma.cc/3GRS-T6ZX] (last updated Mar. 22, 2018) ("Medical devices range from simple tongue depressors and bedpans to complex programmable pacemakers with micro-chip technology and laser surgical devices. In addition, medical devices include in vitro diagnostic products, such as general purpose lab equipment, reagents, and test kits . . . ."). While medical devices are not implicated in the innovative therapies at issue in this Article, they are relevant to this Article's arguments on preemption.

40. 21 U.S.C. § 321(h).

41. *Id.* § 321(g)(1).

42. 42 U.S.C. § 262(i)(1) (2018); *see also* Paradise, *Cultivating Innovation*, *supra* note 6, at 692 (explaining that "a biological product is distinct from a drug because of its source (as biological rather than chemically synthesized)").

43. 21 U.S.C. § 353(g)(1)(A) ("The Secretary shall, in accordance with this subsection, assign a primary agency center to regulate products that constitute a combination of a drug, device, or biological product."); *see also* Foote & Berlin, *supra* note 36, at 621 (identifying tissue engineering, nanomedicine, and gene therapy as "growth area[s] for combination product research").

44. 21 U.S.C. § 353(g).

45. *See, e.g.*, *id.*; Bracco Diagnostics, Inc. v. Shalala, 963 F. Supp. 20, 28 (D.D.C. 1997) ("The . . . products all likely meet both the definition of a drug and the definition of a device under the Federal Food, Drug and Cosmetic Act, and the FDA therefore has discretion in determining how to treat them." (citing 21 U.S.C. § 353(g))); *see also* FDA Regulation of Combination Products; Public Hearing, 67 Fed. Reg. 65,801, 65,801–04 (Oct. 28, 2002), http://www.govinfo.gov/content/pkg/FR-2002-10-28/pdf/02-27267.pdf [https://perma.cc/GH8G-QPRA]; Matthew Avery & Dan Liu, *Bringing Smart Pills to Market: FDA Regulation of Ingestible Drug/Device Combination Products*, 66 FOOD & DRUG L.J. 329, 330 n.14 (2011); *Frequently Asked*

combination products, the FDA Office of Combination Products determines a product's "primary mode of action."[46] Next, the Office of Combination Products assigns "primary jurisdiction" for a combination product to the FDA center that corresponds with the product's "primary mode of action."[47]

In spite of the existence of "combination products," many recent innovations in medicine, including those that are classified as combination products, still do not wholly fall within the categories of products traditionally FDA regulated.[48] The FDA also uses guidance documents and other agency-issued documents to explain agency regulatory policy and to assert jurisdiction over various therapies that also tend to be therapies over which the FDA's jurisdiction is uncertain.[49] The literature on emerging technologies has emphasized the use of flexibility instead of traditional regulation to address emerging technologies; however, guidance documents are not the only method of regulating innovative therapies.[50] The FDA characterizes guidance documents, which are nonbinding agency pronouncements, as "describ[ing the] FDA's interpretation of [its] policy on a regulatory issue" although guidance documents go much further than simply interpreting the FDA's policy, with many of these documents proclaiming the FDA's jurisdiction over innovative therapies.[51]

The many guidance documents and assertions of jurisdiction, often explaining how the agency's statutory categories will apply to new technologies, also indicate how the

Questions About Combination Products, FDA, http://www.fda.gov/combination-products/about-combination-products/frequently-asked-questions-about-combination-products [https://perma.cc/L7TU-RQ24] (last updated Sept. 4, 2019).

46. 21 U.S.C. § 353(g)(1)(C); *Frequently Asked Questions About Combination Products*, *supra* note 45.

47. *Frequently Asked Questions About Combination Products*, *supra* note 45; *see also Office of Combination Products*, FDA, http://www.fda.gov/about-fda/office-special-medical-programs/office-combination-products [https://perma.cc/S2Z7-RM6D] (last updated Sept. 19, 2018).

48. *See, e.g.*, Foote & Berlin, *supra* note 36, at 631, 637–41 ("Combination products continue to present challenges to the regulatory structure of the FDA. How to regulate innovative combinations raises issues that are similar to those that arose around the emergence of innovative drugs, devices, and biologics in the last century.").

49. *See* Lewis, *Halted Innovation*, *supra* note 9, at 1096–1108; *infra* notes 55–57 and accompanying text; *see also* Colleen R. Kelly et al., *Guidance on Preparing an Investigational New Drug Application for Fecal Microbiota Transplantation Studies*, 12 CLINICAL GASTROENTEROLOGY & HEPATOLOGY 283, 283 (2014) (noting that while the FDA will exercise enforcement discretion for the use of fecal microbiota transplantation to treat *clostridium difficile*, the positions of the FDA and the NIH remain that an investigational new drug application is still required for research; as such, without the requisite documentation, federal funding through the NIH would not be available); *Information About Self-Administration of Gene Therapy*, FDA, http://www.fda.gov/biologicsbloodvaccines/cellulargenetherapyproducts/ucm586343.htm [https://perma.cc/W45N-E4N8] (last updated Nov. 21, 2017) ("FDA considers any use of CRISPR/Cas9 gene editing in humans to be gene therapy. . . . Clinical studies of gene therapy in humans require the submission of an investigational new drug application (IND) prior to their initiation in the United States, and marketing of a gene therapy product requires submission and approval of a biologics license application (BLA). . . . [Additionally, t]he sale of ['do it yourself' gene therapy 'kits'] is against the law. FDA is concerned about the safety risks involved."). *See generally* Lewis, *How Subterranean*, *supra* note 17, at 1241 ("The FDA uses subterranean regulation to regulate medical techniques that are accompanied by ethical controversy including cloning, advanced assisted reproductive technologies, and unconventional methods of enhancing fertility.").

50. *See* Marchant & Stevens, *supra* note 6, at 252–53; Paradise, *Cultivating Innovation*, *supra* note 6, at 676.

51. *See Guidances*, FDA, http://www.fda.gov/industry/fda-basics-industry/guidances [https://perma.cc/9U5H-6Z9X] (last updated May 24, 2018).

FDA has developed an ad hoc system of regulating innovations in medicine over the years.[52] While the issuance of guidance documents can benefit regulated entities (and their attorneys) who would like a preview of how the agency plans to apply a statute or exercise its enforcement discretion, there are also disadvantages. For example, there is a "consensus" in administrative law that "guidance documents should be tolerated only grudgingly" as there is a "concern that agencies routinely use guidance documents to establish binding rules while evading the procedural obstacles that might otherwise deter them from acting."[53] Although guidance documents generally do not go through the notice and comment process typically used to generate binding rules, they may achieve practically binding effect in spite of prominent disclaimers of their nonbinding nature.[54]

These FDA-centric agency pronouncements focus on informing the public that the FDA has jurisdiction over certain innovations, without acknowledging the limitations of the FDA's jurisdiction and the existence of state authority.[55] As a practical matter, these agency proclamations are especially problematic because they often coincide with the agency imposing regulatory burdens that effectively ban or significantly curtail access to

52. Lewis, *How Subterranean*, *supra* note 17, at 1239, 1255, 1257–62. *See generally* Merrill & Rose, *supra* note 17, at 88 ("The FDA's claims of jurisdiction over human cloning have nonetheless created a de facto, if possibly hollow, regulatory regime. Rather than a thoughtful strategy for meeting a novel regulatory challenge, the Agency's repeated assertions apparently represent a response to public and congressional demands concerning cloning."); Lars Noah, *Governance by the Backdoor: Administrative Law(lessness?) at the FDA*, 93 NEB. L. REV. 89, 97 (2014) [hereinafter Noah, *Governance by the Backdoor*] (discussing the FDA's use of guidance documents).

53. Nicholas Bagley & Helen Levy, *Essential Health Benefits and the Affordable Care Act: Law and Process*, 39 J. HEALTH POL., POL'Y, & L. 441, 459 (2014); *see also* Merrill, *The Architecture*, *supra* note 23, at 1864. *But see* Bagley & Levy, *supra*, at 459–60 ("This consensus, however, rests on an unflattering view of administrative motivation.").

54. *See, e.g.*, 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 (2016), http://www.fda.gov/media/96562/download [https://perma.cc/VS6H-MBXU]. This March 2016 Draft Guidance contains a header that reads "Contains Nonbinding Recommendations." *Id.* at 1 ("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."). For more FDA documents containing similar language emphasizing their nonbinding effect, see also FDA, QUESTIONS AND ANSWERS ON BIOSIMILAR DEVELOPMENT AND THE BPCI ACT: GUIDANCE FOR INDUSTRY 1 (2018), http://www.fda.gov/media/119258/download [https://perma.cc/UW5C-4CNF]; FDA, *supra* note 9, at 1; FDA, SAME SURGICAL PROCEDURE EXCEPTION UNDER 21 CFR 1271.15(B): QUESTIONS AND ANSWERS REGARDING THE SCOPE OF THE EXCEPTION: GUIDANCE FOR INDUSTRY 1 (2017), http://www.fda.gov/media/89920/download [https://perma.cc/G8RZ-YR5R]. See *supra* note 9 for more on the term "minimal manipulation" as used in FDA regulations, FDA actions (including the regulation of autologous stem cell treatments), and FDA guidance documents. The FDA does have a process for soliciting public input on certain guidance documents; however, many of the FDA's assertions of jurisdiction over certain innovative therapies are not announced through documents that are labeled as "guidance documents" even though they are not regulations. *See, e.g.*, *Opportunities for Input into Guidance Development*, FDA, http://www.fda.gov/media/82966/download [https://perma.cc/R5SL-UTCX] (last visited Feb. 1, 2020). For more on the FDA's use of guidance documents and how that use minimizes the strength of procedural safeguards, see, for example, Noah, *Governance by the Backdoor*, *supra* note 52, at 90–93.

55. *See supra* notes 49–50. For more on the FDA actions to expand its jurisdiction, see generally Lars Noah, *The Little Agency That Could (Act with Indifference to Constitutional and Statutory Strictures*), 93 CORNELL L. REV. 901, 902 (2008) [hereinafter Noah, *Little Agency That Could*].

technologies in the United States.[56] Further, sometimes these effective bans occur during the development stage so as to limit innovation in the first place.[57] Such limitations tend to lead to the medical tourism described in the introduction of this Article; this medical tourism imposes significant costs financially, informationally, and in terms of access to healthcare. Overall, as Part II.A discusses, at least two problems plague the federal regulatory regime: (1) motivations based on political objections to certain forms of experimentation, such as those related to human embryos; and (2) failure to acknowledge the existence of a medical procedure that would thus be subject to state jurisdiction.[58]

Although the FDA is statutorily empowered to regulate products, it does not have that same statutory jurisdiction over the practice of medicine.[59] As the next Part describes, the regulation of the practice of medicine has traditionally fallen within the province of individual states.

B. State Jurisdiction over the Practice of Medicine

This Part builds upon the prevailing view of "courts, medical practitioners, and Congress [who] have not viewed the federal government—and the one-size-fits-all approach that may come with it—as a natural fit for regulating medical practice" because states regulate the practice of medicine.[60] The primacy of states in the regulation of medicine and the repeated statements that Congress did not intend the FDCA to regulate the practice of medicine can be found throughout the legislative histories of various amendments to the FDCA.[61]

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56. *See, e.g.*, Merrill & Rose, *supra* note 17, at 88.

57. In prior works, I have focused on the FDA's continued regulation of certain forms of assisted reproductive technology as medical products, even though the FDA does not regulate in vitro fertilization, the method of assisted reproductive technology that is common to all of these procedures. *See* Lewis, *Halted Innovation*, *supra* note 9, at 1086–1110; Lewis, *How Subterranean*, *supra* note 17, at 1251–65 (explaining the limits on FDA authority over assisted reproductive technology methods that combine in vitro fertilization with genetic modification and tracing the FDA's expansion of jurisdiction over various reproductive technology techniques).

58. *See infra* note 84.

59. *See, e.g.*, Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 350 (2001) ("Indeed, a recent amendment to the FDCA expressly states in part that '[n]othing in this chapter shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship.' Thus, the FDA is charged with the difficult task of regulating the marketing and distribution of medical devices without intruding upon decisions statutorily committed to the discretion of health care professionals." (alteration in original) (citation omitted)); *see also infra* notes 62–65.

60. Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 SAN DIEGO L. REV. 427, 438 (2015) [hereinafter Zettler, *Toward Coherent*]. For examples of state statutes regulating the practice of medicine, see CAL. BUS. & PROF. CODE § 2052 (West 2019); FLA. STAT. ANN. § 458.311 (West 2019); MASS. GEN. LAWS ANN. ch. 112, § 6 (West 2019). See *infra* notes 66–68 and accompanying text for an overview of state statutes regulating the practice of medicine.

61. *See, e.g.*, *Regulation of Diethylstilbestrol (DES) (Its Use as a Drug for Humans and in Animal Feeds): Hearings Before the Subcomm. of the H. Comm. on Gov't Operations*, 92d Cong. 103 (1971) (statement of then General Counsel of the FDA, Peter Barton Hutt) ("There is no question that FDA is authorized to approve the safety and effectiveness for all drugs. . . . On the other hand, the legislative history of both [the 1938 Food, Drug, and Cosmetic Act and the 1962 amendments] flatly states that FDA is not authorized to regulate the practice of medicine by requiring that physicians do or do not use specific drugs only in specific ways.").

States have a longstanding role as regulators for the benefit of the public health, including through the regulation of the practice of medicine.[62] Historically, as the U.S. Supreme Court has noted, "the several States have exercised their police powers to protect the health and safety of their citizens . . . [b]ecause these are 'primarily, and historically, . . . matter[s] of local concern.'"[63] In the states, "[t]he application of police power has traditionally implied a capacity to . . . promote the public health, morals, or safety, and the general well-being of the community" and to "enact and enforce laws" to that end.[64] In light of these longstanding duties, for example, all states and the District of Columbia have medical boards and health departments.[65]

As such, the "practice of medicine" is a part of the historic state police powers over public health and safety.[66] Over time, states have defined "the practice of medicine" statutorily, especially in connection with statutes that identify who may or may not legally "practice medicine."[67] While each state has its own statute defining the "practice of medicine," statutory definitions typically include:

> (1) diagnosing, preventing, treating, and curing disease; (2) holding oneself out to the public as able to perform the above; (3) intending to receive a gift, fee, or compensation for the above; (4) attaching such titles as "M.D." to one's name; (5) maintaining an office for reception, examination, and treatment; (6) performing surgery; and (7) using, administering, or prescribing drugs or medicinal preparations.[68]

1. States as Patient Protectors and Gatekeepers to the Medical Profession

States govern the practice of medicine by imposing requirements for the licensing of medical professionals and administering malpractice regimes.[69] For example, all states

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62. *See* Ross D. Silverman, *Regulating Medical Practice in the Cyber Age: Issues and Challenges for State Medical Boards*, 26 AM. J.L. & MED. 255, 256 (2000).

63. Medtronic, Inc. v. Lohr, 518 U.S. 470, 475 (1996) (second alteration and second omission in original) (quoting Hillsborough Cty. v. Automated Med. Labs., Inc., 471 U.S. 707, 719 (1985)); *see also id.* at 485; Silverman, *supra* note 62, at 256.

64. Jorge E. Galva et al., *Public Health Strategy and the Police Power of the State,* 120 PUB. HEALTH REP. 1, 20 (Supp. 1 2005); *see also* Jacobson v. Massachusetts, 197 U.S. 11, 25 (1905). For more on the American medical profession and the origins of the physician licensure regime, see PAUL STARR, THE SOCIAL TRANSFORMATION OF AMERICAN MEDICINE 39–47, 57–59 (1982).

65. James N. Thompson & Lisa A. Robin, *State Medical Boards: Future Challenges for Regulation and Quality Enhancement of Medical Care*, 33 J. LEGAL MED. 93, 94 (2012); *State Health Departments*, U.S. DEP'T HEALTH & HUM. SERVS., http://healthfinder.gov/FindServices/SearchContext.aspx?show=1&topic=820 [https://perma.cc/E56A-TN8L] (last visited Feb. 1, 2020).

66. BARRY R. FURROW ET AL., HEALTH LAW: CASES, MATERIALS, AND PROBLEMS 87 (7th ed. 2013).

67. *See, e.g.*, Michael H. Cohen, *Holistic Health Care: Including Alternative and Complementary Medicine in Insurance and Regulatory Schemes*, 38 ARIZ. L. REV. 83, 90 (1996).

68. *Id.* (citing Michael H. Cohen, *A Fixed Star in Health Care Reform: The Emerging Paradigm of Holistic Healing*, 27 ARIZ. ST. L.J. 79, 97–98, 157–59 app. I tbl.2 (1995) (providing state statutes defining the practice of medicine and categorizing state statutes by the provisions contained in their definitions of the "practice of medicine")).

69. *See, e.g.*, FURROW ET AL., *supra* note 66, at 87; *see also* Lori B. Andrews, *The Shadow Health Care System: Regulation of Alternative Health Care Providers*, 32 HOUS. L. REV. 1273, 1298–1308 (1996) (discussing state definitions of the "practice of medicine" and prosecutions for the unauthorized practice of medicine).

have physician licensure statutes, generally administered through state medical boards.[70] Licensed physicians are then able to prescribe drugs that the federal government has approved.[71] Individuals who the state has not licensed to practice medicine are therefore subject to prosecution for the unauthorized practice of medicine.[72] State medical boards also discipline medical practitioners "that cease to be competent" as identified through various methods, including complaints by members of the public.[73] In addition to licensing healthcare professionals, states also license hospitals and other institutions that provide healthcare.[74]

Medical malpractice regimes allow patients to hold physicians liable under state tort law for breaches of the standard of care in their treatment.[75] Medical malpractice reform continues to be a topic of discussion at both the state and federal levels of government, although medical malpractice liability only exists at the state level.[76]

Although states still face difficulties in characterizing actions as part of (or outside of) the "practice of medicine," such as when determining whether alternative medicine practitioners or healthcare professionals subordinate to physicians are practicing medicine, the "practice of medicine" marks a general demarcation of state jurisdiction in the context of current and forthcoming innovative therapies and medicine in general.[77]

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70. FURROW ET AL., *supra* note 66, at 87; *see also* Timothy Stoltzfus Jost, *Oversight of the Quality of Medical Care: Regulation, Management, or the Market?*, 37 ARIZ. L. REV. 825, 828, 833, 862 (1995).

71. *See* Cohen, *supra* note 67, at 90.

72. *See, e.g.*, *id.* at 85.

73. *See* Jost, *supra* note 70, at 861, 867.

74. *See, e.g.*, Nicole Huberfeld, *Tackling the "Evils" of Interlocking Directorates in Healthcare Nonprofits*, 85 NEB. L. REV. 681, 687–89, 705–06 (2007); Sandra H. Johnson, *Quality-Control Regulation of Home Health Care*, 26 HOUS. L. REV. 901, 922–41 (1989).

75. *See* David M. Studdert et al., *Medical Malpractice*, 350 NEW ENG. J. MED. 283, 283, 287 (2004); *see also* Catherine M. Sharkey, *Unintended Consequences of Medical Malpractice Damages Caps*, 80 N.Y.U. L. REV. 391, 398–99 (2005) (discussing state medical malpractice awards).

76. *See, e.g.*, Beverly Cohen, *Disentangling EMTALA from Medical Malpractice: Revising EMTALA's Screening Standard To Differentiate Between Ordinary Negligence and Discriminatory Denials of Care*, 82 TUL. L. REV. 645, 661–62 (2007) ("Courts have unanimously agreed that [the Emergency Medical Treatment and Active Labor Act's (EMTALA)] screening requirement does not create a federal cause of action akin to medical malpractice. . . . Further, EMTALA expressly states that it is not intended to preempt state laws unless they directly conflict with EMTALA. This preemption provision forecloses any argument that EMTALA is intended to preempt state malpractice law." (footnote omitted)); Michelle M. Mello et al., *Medical Liability—Prospects for Federal Reform*, 376 NEW ENG. J. MED. 1806, 1806 (2017). *See generally* Karen Stockley, *How Do Changes in Medical Malpractice Liability Laws Affect Health Care Spending and the Federal Budget?* (Cong. Budget Office, Working Paper No. 2019-03, 2019), http://www.cbo.gov/system/files/2019-04/55104-Medical%20Malpractice_WP.pdf [https://perma.cc/GAA2-L88F] (discussing the impact of medical malpractice reform on federal spending).

77. *See* FURROW ET AL., *supra* note 66, at 104–24; Lars Noah, *Ambivalent Commitments to Federalism in Controlling the Practice of Medicine*, 53 U. KAN. L. REV. 149, 161–65 (2004) (discussing the difficulties that arise in defining the "practice of medicine," including determining whether physicians who work in administrative capacities, such as for health insurers or as expert witnesses, are engaged in the practice of medicine, and whether nonphysicians, including laypeople or "[u]nless they are exempted under separate scope-of-practice legislation, nurses, pharmacists, and other licensed health care professionals whose conduct crosses the line into the practice of medicine," are engaged in the unauthorized practice of medicine); *see also* Elizabeth Y. McCuskey, *Body of Preemption: Health Law Traditions and the Presumption Against Preemption*, 89 TEMP. L. REV. 95, 108 (2016) [hereinafter McCuskey, *Body of Preemption*] ("Courts have a distinct presumption against preemption for topics covered by state police powers, based on an ostensible tradition of state regulatory

Additionally, even though pharmaceuticals and medical devices must obtain premarket approval from the FDA before they can be legally marketed and sold in the United States, state law protects patients by providing tort remedies for failure-to-warn and design-defect claims, with limitations imposed by Supreme Court decisions related to brand name and generic drugs.[78] These state law protections are necessary complements to federal regulation because, as the Supreme Court majority in *Wyeth v. Levine*[79] noted,

> [t]he FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge. State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly.[80]

Thus, state law complements federal law, which focuses on premarketing approval, by focusing on the adverse consequences of using FDA-approved products after they are on the market.

Even with the FDA's jurisdiction over the products used in the practice of medicine, various statutory provisions (and regulations repeating those directives) state that the current federal regulatory structure does not overrule state jurisdiction over the practice of medicine.[81] Similar restrictions exist in other federal statutes related to healthcare, including those governing Medicaid, Medicare, and fertility clinic success rate reporting requirements.[82] Against that backdrop, physicians, within the practice of medicine, can

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primacy over those topics." (citing Cipollone v. Liggett Grp., Inc., 505 U.S. 504, 518 (1992))); Zettler, *Toward Coherent*, *supra* note 60, at 435–37.

78. *See* Catherine M. Sharkey, *States Versus FDA*, 83 GEO. WASH. L. REV. 1609, 1613–14 (2015) [hereinafter Sharkey, *States Versus FDA*]; *see also* Wyeth v. Levine, 555 U.S. 555, 578–79, 581 (2009) (holding that Levine's failure-to-warn claims under state tort law, for her injury by the brand-name drug Phenergan, were not preempted by federal FDA approvals). *But see* Mut. Pharm. Co. v. Bartlett, 570 U.S. 472, 475–76 (2013) (holding the state law was without effect because it imposed a duty "*not* to comply with federal law"); PLIVA, Inc. v. Mensing, 564 U.S. 604, 617–18 (2011). The current tension between federal labeling regulations and state tort law, as a result of state preemption doctrine and the FDA's labeling regulations, is a topic large enough for a separate article.

79. 555 U.S. 555 (2009).

80. *Wyeth*, 555 U.S. at 578–79 (footnote omitted).

81. *See, e.g.*, 21 U.S.C. § 396 (2018) ("Nothing in this chapter [of the Federal Food, Drug, and Cosmetic Act] shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship."); *id.* § 903 ("No provision of this subchapter shall be construed as indicating an intent on the part of the Congress to occupy the field in which that provision operates, including criminal penalties, to the exclusion of any State law on the same subject matter which would otherwise be within the authority of the State, unless there is a positive conflict between that provision of this subchapter and that State law so that the two cannot consistently stand together.").

82. 42 U.S.C. § 1395 (2018) ("Nothing in this subchapter shall be construed to authorize any Federal officer or employee to exercise any supervision or control over the practice of medicine or the manner in which medical services are provided, or over the selection, tenure, or compensation of any officer or employee of any institution, agency, or person providing health services; or to exercise any supervision or control over the administration or operation of any such institution, agency, or person."); *see also id.* § 263a-2(i)(1)–(2) ("In developing the certification program, the Secretary may not establish any regulation, standard, or requirement which has the effect of exercising supervision or control over the practice of medicine in assisted reproductive technology programs."); *id.* § 416 ("Nothing in this subchapter shall be construed as authorizing the Commissioner of Social Security or any other officer or employee of the United States to interfere in any way

prescribe FDA-approved drugs for off-label uses (although manufacturers cannot market them for those uses). States are not, however, permitted to overrule the FDA's approval of products, and historical state efforts to "limit or entirely bar access" to contraceptives that were FDA approved, for example, have been invalidated by the Supreme Court.[83]

2. State Interests in Medical Innovation

States already innovate in the absence of federal government action or in response to federal governmental action that is contrary to the preferences of states' citizenries.[84] For example, in response to a ban on the federal funding of research involving human embryos, California specifically enacted legislation to regulate and fund stem cell research that could not obtain federal funding.[85] In 2017, California also enacted a new law outlining informed consent requirements that were specifically applicable to stem cell treatments that had not been FDA approved.[86] Additionally, many states that house centers for biotechnology innovation or research centers that receive significant amounts of federal and private funding, like Maryland, which is the site of Johns Hopkins University, have robust human subjects research regimes that supplement the federal government's human subjects protection regulations.[87] Maryland also has a Stem Cell Research Fund, which was created by statute in 2006 in response to federal funding restrictions on stem cell research announced during President George W. Bush's administration.[88] Thus, state regulation and funding are important complements to federal regulation.

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with the practice of medicine or with relationships between practitioners of medicine and their patients, or to exercise any supervision or control over the administration or operation of any hospital.").

83. *See, e.g.*, Noah, *State Affronts*, *supra* note 27, at 16; *see id.* at 17–23 (describing state efforts to limit access to products approved by the FDA); *id.* at 3–16 (describing Massachusetts's effort to limit access to Zohydro, an opioid, without an "abuse-resistant formulation"); *see also* Sharkey, *States Versus FDA*, *supra* note 78, at 1615–24.

84. For more on the state interest in accelerating access to pharmaceuticals, see *supra* note 37, discussing state right-to-try laws, which preceded federal right-to-try legislation.

85. *See* June Carbone, *Negating the Genetic Tie: Does the Law Encourage Unnecessary Risks?*, 79 UMKC L. REV. 333, 360 (2010). For more on the federal limitations on embryonic stem cell research, see generally *Sherley v. Sebelius*, 689 F.3d 776, 779–80 (D.C. Cir. 2012) (comparing the federal treatment of embryonic stem cell research funding in the George W. Bush and Barack Obama presidential administrations).

86. *See* CAL. BUS. & PROF. CODE § 684(b)(1) (West 2019) ("A health care practitioner licensed under this division who performs a stem cell therapy that is not FDA-approved shall communicate to a patient seeking stem cell therapy the following information in English: 'THIS NOTICE MUST BE PROVIDED TO YOU UNDER CALIFORNIA LAW. This health care practitioner performs one or more stem cell therapies that have not yet been approved by the United States Food and Drug Administration. You are encouraged to consult with your primary care physician prior to undergoing a stem cell therapy.'"). This law also involves monetary penalties for multiple instances of noncompliance and a requirement that the Medical Board of California publish information related to legal and disciplinary action applicable to licensed health care practitioners who provide stem cell therapies. *Id.* § 684(d).

87. *See, e.g.*, MD. CODE ANN., HEALTH-GEN. § 13-2002 (West 2019); *see also* CAL. HEALTH & SAFETY CODE § 111525 (West 2019) (requiring and defining the role of consent "[p]rior to prescribing or administering an experimental drug"); Barbara A. Noah, *Bioethical Malpractice: Risk and Responsibility in Human Research*, 7 J. HEALTH CARE L. & POL'Y 175, 214 n.168 (2004).

88. *See About Us*, MD. STEM CELL RESEARCH FUND, http://www.mscrf.org/about-us [https://perma.cc/F8HS-4Q6N] (last visited Feb. 1, 2020) ("[Established b]y the Governor and the Maryland General Assembly through the Maryland Stem Cell Research Act of 2006 . . . . The purpose of the Fund is to

C. Hybrid Jurisdiction: The Practice-Products Distinction in the Context of Innovative Therapies

A hybrid regime of life sciences regulation, as opposed to a federally focused one, would better regulate many current and forthcoming innovations. This Part provides brief overviews of innovative therapies that would be amenable to a cooperative governance structure. The innovative therapies discussed in this Part all require state regulation over the practice of medicine and federal regulation of the drugs, biologics, and/or combination products used in those innovative therapies.

1. Gene Therapy

Gene therapy targets disease-causing genetic variations in an effort to "treat, cure or prevent a disease or medical condition."[89] Specifically, gene therapy uses "vectors," such as viruses, to target genes that are defective or missing by inserting new genes into a cell.[90] The first human gene therapy clinical trial in the United States began in 1990.[91] The trial included two patients, and scientists concluded after the completion of the trial that "'gene therapy can be a safe and effective addition to treatment' for some people born with severe combined immunodeficiency disease (SCID)."[92] A number of other human gene therapy trials ensued with many revealing medical promise and others revealing safety concerns that scientists and researchers drew upon when developing subsequent gene therapy protocols.[93]

On September 17, 1999, four days after beginning a gene therapy treatment in a clinical trial at the University of Pennsylvania to ascertain the safety and effectiveness of using a specific gene therapy protocol to treat babies with a fatal form of ornithine transcarbamylase (OTC) deficiency, Jesse Gelsinger died.[94] At least one commentator noted that this marked the beginning of a "perilous time for gene therapy," and it was not

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promote state-funded stem cell research and cures through grants and loans to public and private entities in the state. To date we supported 460 awards with $156 million."); *see also* O. Carter Snead, *The Pedagogical Significance of the Bush Stem Cell Policy: A Window into Bioethical Regulation in the United States*, 5 YALE J. HEALTH POL'Y, L., & ETHICS 491, 492 & n.4 (2005) (describing the reaction of states to President Bush's stem cell research funding policy).

89. *What Is Gene Therapy? How Does It Work?*, FDA, http://www.fda.gov/consumers/consumer-updates/what-gene-therapy-how-does-it-work [https://perma.cc/AU6A-YXL4] (last updated Dec. 22, 2017).

90. *Id.*; *see also How Does Gene Therapy Work?*, NAT'L INSTS. HEALTH (Oct. 1, 2019), http://ghr.nlm.nih.gov/primer/therapy/procedures [https://perma.cc/Z8NJ-H4MB].

91. *Results from First Human Gene Therapy Clinical Trial*, NAT'L HUM. GENOME RES. INST. (Oct. 19, 1995), http://www.genome.gov/10000521/1995-release-first-human-gene-therapy-results [https://perma.cc/K5EB-BTHM].

92. *Id.*

93. *See, e.g.*, Sheryl Gay Stolberg, *The Biotech Death of Jesse Gelsinger*, N.Y. TIMES MAG. (Nov. 28, 1999), http://www.nytimes.com/1999/11/28/magazine/the-biotech-death-of-jesse-gelsinger.html [https://perma.cc/JPW8-UR7S].

94. *See id.* ("Typically, newborns [with severe OTC deficiency] slip into a coma within 72 hours of birth. Most suffer severe brain damage. Half die in the first month, and half of the survivors die by age 5."). For more on the Jesse Gelsinger gene therapy trial, see Melinda Wenner, *Gene Therapy: An Interview with an Unfortunate Pioneer*, SCI. AM. (Sept. 1, 2009), http://www.scientificamerican.com/article/gene-therapy-an-interview/?redirect=1 [https://perma.cc/WMU8-YK6Z].

until 2017 that the FDA approved the first gene therapy product for marketing and use in humans.[95]

In October 2018, at a plenary session held during the "FDA: Past, Present, and Future" Conference at American University, former chief counsels of the FDA discussed their opinions on "controversial topics," including what they thought "about the agency and its efforts . . . in gene therapy."[96] Two of the former chief counsels had laudatory views on the FDA's work, with one noting that the FDA was doing a "good job" with these (and other) modern technologies in general and the other praising the agency's work in approving CAR-T therapies, a type of gene therapy.[97] Another, however, noted the commissioner was wrestling with

> the jurisdictional and practical challenges of selling gene therapy . . . . [W]hen you're talking about individual therapy . . . for a particular person that is not a conventional drug or biologic, . . . I'm not sure that the current authorities and the current statute are really adequate to . . . enable the agency to wrestle with those issues. [The FDA] has done the best it can . . . and obviously it had to respond when there was a death . . . at the University of Pennsylvania [in reference to Jesse Gelsinger], . . . early . . . [in] gene therapy [research,] . . . but I do think that all of these emerging technologies are a real challenge for an agency.[98]

The jurisdictional challenges of gene therapy have become more prevalent due to recent scientific promise (as opposed to previously failed trials) and recent approvals.[99]

In 1993, the FDA announced through the Federal Register that it would regulate gene therapy as a biological product or drug.[100] In spite of the federally focused regime

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95. *See* News Release, U.S. Food & Drug Admin., FDA Approval Brings First Gene Therapy to the United States (Aug. 30, 2017), http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm [https://perma.cc/4J9W-TNRP]; Stolberg, *supra* note 93; *see also Gene-Therapy Trials Must Proceed with Caution*, 534 NATURE 590, 590 (2016).

96. *Plenary Session 2*, *supra* note 18, at 48:14; *see FDA: Past, Present, and Future*, AM. U. WASH. C.L. (Oct. 19, 2018), http://www.wcl.american.edu/impact/initiatives-programs/health/events/fdaconf18/agenda/ [https://perma.cc/3LC9-EBMP] (listing the four participating former chief counsels in Plenary Session 2 as Richard Cooper, Peter Barton Hutt, Gerald Masoudi, and Daniel Troy). For more on the role of the FDA Office of the Chief Counsel, see *Office of the Chief Counsel*, FDA, http://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeoftheChiefCounsel/default.htm [https://perma.cc/A5KK-8Q4F] (last updated Mar. 28, 2018).

97. *Plenary Session 2*, *supra* note 18, at 48:18 (containing comments of Peter Barton Hutt, former Chief Counsel of the FDA and stating, in response to the question of how the FDA was handling the issue of gene therapy: "[W]e can go through all modern technology and say the same thing: I think they're doing a good job"); *see also id.* at 49:35 (containing comments of Gerald Masoudi, former Chief Counsel of the FDA, lauding the FDA's actions in relation to CAR-T therapies). For more on CAR-T therapies, which are types of immunotherapy that "collect[] and us[e] patients' own immune cells to treat their cancer," see *CAR T Cells: Engineering Patients' Immune Cells To Treat Their Cancers*, NAT'L INSTS. HEALTH, NAT'L CANCER INST., http://www.cancer.gov/about-cancer/treatment/research/car-t-cells [https://perma.cc/TW9G-4WJT] (last updated July 30, 2019).

98. *See Plenary Session 2*, *supra* note 18, at 48:27 (providing comments of Daniel Troy, former Chief Counsel of the FDA).

99. See *infra* notes 102–107 and accompanying text for a discussion of several gene therapy products the FDA recently approved.

100. Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53,248, 53,251 (Oct. 14, 1993), http://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/UCM148113.pdf [https://perma.cc/687W-3DS9] ("Gene therapy is

used to regulate gene therapy, gene therapy involves both a federally regulated product and the state-regulated practice of medicine due to the combination of a gene-modifying product with a therapy tailored for an individual patient.[101] Until recently, there had been little debate over the FDA's jurisdiction over gene therapy, possibly because it was not necessary due to its various failures—including, most notably, the death of Jesse Gelsinger.[102] It was not until 2017 when the FDA approved the first gene therapy product, Kymriah, for marketing in the United States.[103] Ultimately, the FDA approved a total of three gene therapy products in 2017: (1) Kymriah, to treat "certain pediatric and young adult patients with a form of acute lymphoblastic leukemia";[104] (2) Yescarta, "to treat adult patients with certain types of large B-cell lymphoma who have not responded to or who have relapsed after at least two other kinds of treatment";[105] and (3) Luxturna, to treat "inherited form of vision loss that may result in blindness."[106] Scientists expect that new gene therapies can improve the treatment of leukemia and potentially cure certain forms of blindness and inherited blood disorders.[107]

The aforementioned approved gene therapy products were all approved as biologics.[108] The gene therapy of the infamous, failed clinical trial that Jesse Gelsinger

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a medical intervention based on modification of the genetic material of living cells. Cells may be modified ex vivo for subsequent administration or may be altered in vivo by gene therapy products given directly to the subject. . . . The genetic manipulation may be intended to prevent, treat, cure, diagnose, or mitigate disease or injuries in humans. . . . Final products containing the genetic material intended for gene therapy are regulated as biological products requiring PLA's (e.g., viral vectors containing genetic material to be transferred, ex vivo transduced cells and analogous products) or as drugs requiring NDA's (e.g., synthetic products) . . . .").

101. *See* Francis S. Collins & Scott Gottlieb, *The Next Phase of Human Gene-Therapy Oversight*, 379 NEW ENG. J. MED. 1393, 1393–95 (2018) (detailing the role of the FDA and the NIH, each a federal body, in regulation of gene therapy products). See *supra* notes 59–67 and accompanying text for an overview of the state's regulatory authority over the practice of medicine.

102. *See, e.g.*, Collins & Gottlieb, *supra* note 101, at 1393–95; Robin Fretwell Wilson, *The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research*, 36 AM. J.L. & MED. 295, 301 (2010); *Gene-Therapy Trials Must Proceed with Caution*, *supra* note 95, at 590. *But see* Jacob S. Sherkow et al., *Is It 'Gene Therapy'?*, 5 J.L. & BIOSCIENCES 786, 789 (2018) (discussing the difficulties of defining gene therapy and noting that "[a]ttempts to define 'gene therapy' waned after the 1999 death of Jesse Gelsinger, a clinical trial subject" (citing Jennifer Couzin & Jocelyn Kaiser, *As Gelsinger Case Ends, Gene Therapy Suffers Another Blow*, 307 SCI. 1028, 1028 (2005))); *id.* ("Second, other definitions of gene therapy—such as FDA's—are so broad as to be essentially meaningless.").

103. *See* News Release, U.S. Food & Drug Admin., *supra* note 95.

104. *Id.*

105. News Release, U.S. Food & Drug Admin., FDA Approves CAR-T Cell Therapy To Treat Adults with Certain Types of Large B-cell Lymphoma (Oct. 18, 2017), http://www.fda.gov/news-events/press-announcements/fda-approves-car-t-cell-therapy-treat-adults-certain-types-large-b-cell-lymphoma [https://perma.cc/2VSQ-5EYC].

106. News Release, U.S. Food & Drug Admin., FDA Approves Novel Gene Therapy To Treat Patients with a Rare Form of Inherited Vision Loss (Dec. 18, 2017), http://www.fda.gov/news-events/press-announcements/fda-approves-novel-gene-therapy-treat-patients-rare-form-inherited-vision-loss [https://perma.cc/G854-E3FU].

107. *See, e.g.*, Rob Stein, *Gene Therapy for Inherited Blood Disorder Reduced Transfusions*, NPR (Apr. 18, 2018, 5:01 PM), http://www.npr.org/sections/health-shots/2018/04/18/602914728/gene-therapy-for-inherited-blood-disorder-reduced-transfusions [https://perma.cc/U6WR-GM6W].

108. *See* Letter from Wilson W. Bryan, Dir., Ctr. for Biologics Evaluation & Research, U.S. Food & Drug Admin., to Dr. Manisha Patel, Novartis Pharm. Corp. (Aug. 30, 2017), http://www.fda.gov/media/106989/download [https://perma.cc/Q9GS-BLVD] (granting Biologics License

participated in involved the use of a viral vector to "deliver corrective genes" in order to test the safety (and not the efficacy) of gene therapy to treat "a [rare] liver deficiency."[109] Just as with pharmaceutical products, monitoring is essential in gene therapy trials: "Monitoring lies 'at the heart of the matter,' sa[id] Dr. Philip Noguchi, the FDA's [former] director of the Division of Cellular and Gene Therapies. 'And that's not something the FDA can do alone.'"[110] Additionally, the FDA admitted that its monitoring was "sometimes 'less than adequate'" in the past.[111]

Of the innovative therapies discussed in this Article, gene therapy has existed for the longest time.[112] The regulation of gene therapy could provide a "floor" for the federal regulation of forthcoming innovative therapies although the regulation of gene therapy still suffers from the problem that politics could still manifest in the regulatory process.[113]

2. Gene Editing, Including CRISPR-Cas9

Gene editing is a versatile technology that is the subject of much attention and excitement due to the possibility that it could cure or prevent the inheritance of genetic

Application (BLA) approval for Kymriah); Letter from Mary A. Malarkey & Wilson W. Bryan, Dirs., Ctr. for Biologics Evaluation & Research, U.S. Food & Drug Admin., to Rizwana F. Sproule, Kite Pharma, Inc. (Oct. 18, 2017), http://www.fda.gov/media/108458/download [https://perma.cc/7V6P-CZJP] (granting BLA approval for Yescarta); Letter from Mary A. Malarkey & Wilson W. Bryan, Dirs., Ctr. for Biologics Evaluation & Research, U.S. Food & Drug Admin., to Jim Wang, Spark Therapeutics, Inc. (Dec. 19, 2017), http://www.fda.gov/media/109487/download [https://perma.cc/4SH4-ABJM] (granting BLA approval for Luxturna).

109. Wilson, *supra* note 102, at 298; *see also* Stolberg, *supra* note 93.

110. Barbara Sibbald, *Death but One Unintended Consequence of Gene-Therapy Trial*, 164 CAN. MED. ASS'N J. 1612, 1612 (2001); *see also* Nina A. Mendelson, *A Presumption Against Agency Preemption*, 102 NW. U. L. REV. 695, 698 (2008).

111. Sibbald, *supra* note 110, at 1612; *see also* U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-06-402, DRUG SAFETY: IMPROVEMENT NEEDED IN FDA'S POSTMARKET DECISION-MAKING AND OVERSIGHT PROCESS 1 (2006), http://www.gao.gov/new.items/d06402.pdf [https://perma.cc/8CFA-JQQL] ("FDA lacks clear and effective processes for making decisions about, and providing management oversight of, postmarket safety issues."); Gillian E. Metzger, *Federalism and Federal Agency Reform*, 111 COLUM. L. REV. 1, 29–31 (2011) [hereinafter Metzger, *Federalism*]; *supra* notes 19–21 (discussing political and social influences on FDA regulatory decisions).

112. *See, e.g.*, NAT'L ACADS. SCIS., ENG'G, & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 65 (2017), http://www.ncbi.nlm.nih.gov/books/NBK447268/ [https://perma.cc/PE6R-MYV5] ("The past 5 years have seen the development of a completely novel system, known as CRISPR/Cas9 (CRISPR stands for clustered regularly interspaced short palindromic repeats)."); Angelo S. Mao & David J. Mooney, *Regenerative Medicine: Current Therapies and Future Directions*, 112 PROC. NAT'L ACAD. SCI. U.S. 14,452, 14,452 (2015) (observing that "tissue engineering and regenerative medicine emerged as an industry about two decades ago"); *Gene Therapy*, NAT'L INSTS. HEALTH, http://history.nih.gov/exhibits/genetics/sect4.htm [https://perma.cc/2MP7-L73K] (last visited Feb. 1, 2020) (providing the NIH's timeline, "Timeline Telling the Story of Developing the First Human Gene Therapy," a timeline of the development of gene therapy treatments, which began in 1985). See also *infra* note 131 for the statement of former commissioner Gottlieb on regenerative medicine therapies.

113. *See, e.g.*, Javitt & Hudson, *supra* note 17, at 1214–15; *see also What Are the Ethical Concerns of Genome Editing?*, NAT'L HUM. GENOME RES. INST., http://www.genome.gov/27569225/what-are-the-ethical-concerns-about-genome-editing/ [https://perma.cc/85HC-6RDX] (last updated Aug. 3, 2017) (discussing the ethical concerns that arise as a result of human germline editing).

disease instead of only treating disease symptoms.[114] Beyond its medical treatment uses, gene editing is a technology with a myriad of uses, ranging from medical care to the modification of animals, plants, and even "do-it-yourself" glow-in-the-dark beer.[115] Gene (or genome) editing "technologies . . . give scientists the ability to change an organism's DNA. These technologies allow genetic material to be added, removed, or altered at particular locations in the genome."[116] As the National Institutes of Health (NIH) noted, "[t]he CRISPR-Cas9 system [of gene editing] 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."[117] Similarly, in a jointly authored article in the *New England Journal of Medicine*, the NIH Director and the now-former FDA Commissioner observed that CRISPR-Cas9 was a "quantum leap forward" in the ability of scientists to edit genes.[118] CRISPR-Cas9 could possibly cure or prohibit the inheritance of a vast array of diseases with genetic causes, including Tay-Sachs disease, sickle cell anemia, muscular dystrophy, neurofibromatosis, and cystic fibrosis.[119] CRISPR-Cas9 could also target certain genetic mutations that increase the risk of individuals contracting diseases such as cancer and Alzheimer's.[120]

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114. *See* George Q. Daley et al., *After the Storm—A Responsible Path for Genome Editing*, 380 NEW ENG. J. MED. 897, 899 (2019); Donald B. Kohn et al., *Ethical and Regulatory Aspects of Genome Editing*, 127 BLOOD 2553, 2553, 2556 (2016).

115. *See, e.g.*, Klaus Rajewsky, *The Historical Scientific Context*, *in* INTERNATIONAL SUMMIT ON HUMAN GENE EDITING 6–8 (2015), http://nationalacademies.org/cs/groups/pgasite/documents/webpage/pga_170455.pdf [https://perma.cc/YUR5-YQWS]; Molly Olmstead, *The Fuzzy Regulations Surrounding DIY Synthetic Biology*, SLATE (May 4, 2017, 10:52 AM), http://slate.com/technology/2017/05/the-fuzzy-regulations-surrounding-diy-synthetic-biology.html [https://perma.cc/2CMC-UH8D].

116. *See What Are Genome Editing and CRISPR-Cas9?*, NAT'L INSTS. HEALTH (Oct. 1, 2019), http://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting [https://perma.cc/CXT7-4B7X].

117. *Id.*; *see also* Henry T. Greely, *Neuroscience, Artificial Intelligence, CRISPR—and Dogs and Cats*, 51 U.C. DAVIS L. REV. 2303, 2327–28 (2018) (referring to CRISPR-Cas9 as "the Model T of DNA editing"). The NIH explains the CRISPR-Cas9 method of genome editing as follows:

> CRISPR-Cas9 . . . is short for clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9. . . .
>
> . . . .
>
> . . . [With t]he CRISPR-Cas9 system . . . [, r]esearchers create a small piece of RNA with a short "guide" sequence that attaches (binds) to a specific target sequence of DNA in a genome. The RNA also binds to the Cas9 enzyme. As in bacteria, the modified RNA is used to recognize the DNA sequence, and the Cas9 enzyme cuts the DNA at the targeted location. Although Cas9 is the enzyme that is used most often, other enzymes (for example Cpf1) can also be used. Once the DNA is cut, researchers use the cell's own DNA repair machinery to add or delete pieces of genetic material, or to make changes to the DNA by replacing an existing segment with a customized DNA sequence.

What Are Genome Editing and CRISPR-Cas9?, *supra* note 116.

118. *See, e.g.*, Collins & Gottlieb, *supra* note 101, at 1394.

119. *See, e.g.*, Sharon Begley, *Scientists Unveil the 'Most Clever CRISPR Gadget' So Far*, STAT (Apr. 20, 2016), http://www.statnews.com/2016/04/20/clever-crispr-advance-unveiled/ [https://perma.cc/4T3T-YMGG]; Berly McCoy, *CRISPR Gene-Editing 'Eliminates' HIV in Some Mice. What Does It Mean for Humans?*, PBS (July 2, 2019, 5:40 AM), http://www.pbs.org/newshour/science/crispr-gene-editing-eliminates-hiv-in-some-mice-what-does-it-mean-for-humans [https://perma.cc/668C-6SFK]. *But see* Eric S. Lander, *What We Don't Know*, *in* INTERNATIONAL SUMMIT ON HUMAN GENE EDITING, *supra* note 115, at 20–27 ("[I]f we really care about helping parents avoid cases of genetic disease, germline editing is not the first, second, third, or fourth thing that we should be thinking about.").

120. *See, e.g.*, Begley, *supra* note 119.

Current options for delivering CRISPR-Cas9 into the human body include a topical gel, "a drinkable or edible CRISPR probiotic," direct injections, skin grafts, or an injection of modified cells into the human body.[121] Viral vectors are commonly used, and nanotechnology, another developing field, has also been proposed as a method of delivering the CRISPR-Cas9 gene editing system into the body.[122] A physician would have to administer or prescribe all of these aforementioned techniques of delivering CRISPR-Cas9 into the body, thus involving the practice of medicine. The use of CRISPR-Cas9 would also still require significant monitoring.[123]

Although CRISPR-Cas9 offers promise, it also has potential disadvantages, which include off-target effects in which the editing of one gene leads to the unexpected alteration of another gene that was not the target of the technology and the possibility of an increased cancer risk.[124] While scientists continue to make advances that would minimize some of the unintended negative consequences of using CRISPR-Cas9, the discovery of additional possible negative impacts of gene editing is similar to the side effects that are experienced by some users of pharmaceuticals but are addressed through an information disclosure regime. Thus, just as with gene therapy, "monitoring lies 'at the heart of the matter.'"[125]

CRISPR-Cas9 is an excellent candidate for state and federal regulation because it will implicate both state and federal regulation due to its combination of the practice of medicine and the use of federally regulated products. The gene editing system itself implicates the state's regulatory authority over the practice of medicine, but the method of "delivering" CRISPR-Cas9 into the human body would be subject to federal

121. Emily Mullin, *Five Ways To Get CRISPR into the Body*, MIT TECH. REV. (Sept. 22, 2017), http://www.technologyreview.com/s/608898/five-ways-to-get-crispr-into-the-body/ [https://perma.cc/E4BL-U43N].

122. *See* Anne Trafton, *CRISPR-Carrying Nanoparticles Edit the Genome*, MIT NEWS (Nov. 13, 2017), http://news.mit.edu/2017/crispr-carrying-nanoparticles-edit-genome-1113 [https://perma.cc/54T4-VQQZ]; *FDA's Approach to Regulation of Nanotechnology Products*, FDA, http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/ucm301114.htm [https://perma.cc/LAB6-9PJ9] (last updated Mar. 23, 2018).

123. CRISPR-Cas9 would differ from other non-over-the-counter pharmaceuticals as it would eventually replace physicians in the treatment of many diseases by providing a cure instead of providing one of many treatment tools that would require ongoing physician involvement. *See, e.g.*, McCoy, *supra* note 119. A future article will focus on arguing for the regulatory treatment of gene editing similar to that of in vitro fertilization, another treatment that physicians carry out and that often requires prescribed pharmaceuticals but that is generally not regulated by the federal government.

124. *See, e.g.*, Sharon Begley, *CRISPR-Edited Cells Linked to Cancer Risk in 2 Studies*, SCI. AM. (June 12, 2018), http://www.scientificamerican.com/article/crispr-edited-cells-linked-to-cancer-risk-in-2-studies/ [https://perma.cc/S72U-4JS4] (republished from STAT News); Sharon Begley, *CRISPR 'Gone Wild' Has Made Stocks Swoon, but Studies Show How To Limit Off-Target Editing*, STAT (Mar. 5, 2018), http://www.statnews.com/2018/03/05/crispr-off-target-editing/ [https://perma.cc/HSW7-9MZ7] ("The basic reason for such 'off-target effects' is that CRISPR's guide molecule, which is usually 20 genetic letters long, isn't as precise as often advertised."). *But see id.* ("'Progress is being made at a pretty stunning rate' . . . . A parade of new discoveries . . . 'suggests that it's possible to use these genome-editing tools and not make unintended edits.'").

125. Sibbald, *supra* note 110, at 1612. See also *supra* notes 111–113 and accompanying text for an analysis of the role of federal monitoring in the use of gene therapy.

regulation as the method would require federally regulated products.[126] As the definition of "biological product" includes a "virus, . . . vaccine, . . . or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings," viral methods of delivering CRISPR-Cas9 would fall at least partially within the jurisdiction of the FDA.[127] Similarly, the definition of "drug," which includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and . . . articles (other than food) intended to affect the structure or any function of the body of man or other animals"[128] would also likely cover other CRISPR-Cas9 delivery methods such as a "drinkable or edible CRISPR probiotic."[129]

Additionally, gene editing is another technology that leads to extensive debate related to the propriety of using assisted reproductive technology and also whether the federal government and other governments should aim to prevent the actual clinical use of the technology when it would be used to modify embryos.[130] Thus, gene editing is another innovative therapy that might lend itself toward nontransparent regulation by the regulatory state based on political concerns as opposed to scientific concerns, in addition to risk-averse regulation that could preclude innovation.

3. Regenerative Medicine Therapies

Regenerative medicine is a broad "interdisciplinary field that applies engineering and life science principles to promote regeneration, [which] can potentially restore diseased and injured tissues and whole organs."[131] The use of stem cells, especially a patient's own adult stem cells (autologous stem cells), as opposed to embryonic stem cells, could aid in the treatment of various medical conditions including macular degeneration, "regenerating bone . . . , developing insulin-producing cells for type 1 diabetes, and repairing damaged heart muscle following a heart attack with cardiac muscle cells."[132]

Even though the 21st Century Cures Act recognized a new category of "drug" called a "regenerative advanced therapy," which is subject to an expedited approval pathway, the FDA's "regenerative medicine advanced therapies" pathway still aims to fit

126. See *supra* Part I.B for a discussion of state regulation of the practice of medicine. *See also* Mullin, *supra* note 121 (discussing the various delivery techniques for CRISPR-Cas9).

127. 42 U.S.C. § 262(i)(1) (2018).

128. 21 U.S.C. § 321(g)(1) (2018).

129. Mullin, *supra* note 121.

130. *See, e.g.*, Eric S. Lander et al., *Adopt a Moratorium on Heritable Genome Editing*, 567 NATURE 165, 168 (2019) (acknowledging scientific and ethical divisions over human germline editing and advocating for stricter regulation of the practice). A future article will discuss the bioethical debates related to assisted reproductive technology (both at its inception and today), in addition to the bioethical debates that accompany the regulation and use of gene editing.

131. *See* Mao & Mooney, *supra* note 112, at 14,452.

132. *Stem Cell Information*, NAT'L INSTS. HEALTH, http://stemcells.nih.gov/info/basics/4.htm [https://perma.cc/ZU9R-WMHS] (last visited Feb. 1, 2020); *see also, e.g.*, Michiko Mandai et al., *Autologous Induced Stem-Cell-Derived Retinal Cells for Macular Degeneration*, 376 NEW ENG. J. MED. 1038, 1038 (2017). Autologous stem cell treatments involve the use of a person's own stem cells as opposed to embryonic stem cells.

regenerative therapies into the category of a drug.[133] Thus, the FDA (and Congress) continue to apply an older regulatory system to products that the system was not created to regulate (even with amendments).[134]

As former FDA Commissioner Gottlieb noted in August 2017, most cell therapies as used in regenerative medicine "are in early stages of development."[135] Like the other innovative therapies this Article discusses, regenerative stem cell therapies involve both state and federal jurisdiction. Commissioner Gottlieb publicly acknowledged this aspect of their regulation and noted that "it's incumbent upon the FDA to make sure that this existing framework is properly defined, with bright lines separating new treatments that are medical products subject to the FDA's regulation from those therapies that are individualized by surgeons in such a way that they are not subject to FDA regulation."[136] Commissioner Gottlieb's statement thus alludes to the regulatory state in which the FDA neither regulates surgeries nor therapies that surgeons individualize, as they are instead subject to state regulation based on the state's police powers over the practice of medicine.[137] Commissioner Gottlieb also acknowledged the "close calls" inherent in drawing the line between medical practice and medical products in relation to regenerative therapies.[138]

Subterranean regulatory methods and slow-moving pathways have characterized FDA regulation of innovative life sciences techniques.[139] The use of adult stem cells in medical treatments (or other treatments advertised as stem cell therapies) has also led to FDA enforcement actions against clinics providing those therapies that are harming patients (along with express or implied threats of doing the same to other clinics).[140] In

133. *See* 21 U.S.C. § 356(g)(2) (stating that "[a] drug is eligible for designation as a regenerative advanced therapy under this subsection if" the drug meets certain statutorily delineated conditions); *id.* § 356(g)(8) ("For purposes of this section [providing expedited approval for regenerative advanced therapies], 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 [42 U.S.C. § 264] and part 1271 of title 21, Code of Federal Regulations." (alteration in original)); *Regenerative Medicine Advanced Therapy Designation*, FDA, http://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/regenerative-medicine-advanced-therapy-designation [https://perma.cc/FTA7-RW8X] (last updated May 17, 2019); *see also* FDA, EXPEDITED PROGRAMS FOR REGENERATIVE MEDICINE THERAPIES FOR SERIOUS CONDITIONS: GUIDANCE FOR INDUSTRY 2–3 (2017), http://www.fda.gov/media/120267/download [https://perma.cc/2D4B-MDQM].

134. *See* 21 U.S.C. § 356(g)(2) (allowing expedited review for drugs that are designated as regenerative advanced therapies, as added by the 21st Century Cures Act); Hoffmann et al., *supra* note 6, at 1390; *Regenerative Medicine Advanced Therapy Designation*, *supra* note 133.

135. Press Release, U.S. Food & Drug Admin., *supra* note 12 (noting that those "technologies . . . hold significant promise for transformative and potentially curative treatments for some of humanity's most troubling and intractable maladies").

136. *Id.*

137. *See, e.g.*, Nancy M. P. King, *The Line Between Clinical Innovation and Human Experimentation*, 32 SETON HALL L. REV. 573, 573–74, 580 (2002); *see also* Order on Motions for Summary Judgment at 8–10, United States v. U.S. Stem Cell Clinic, LLC, No. 18-61047 (S.D. Fla. June 3, 2019) (discussing the "'same surgical procedure' exception" in FDA regulation (citing 21 C.F.R. § 1271.15(b) (2019))).

138. Press Release, U.S. Food & Drug Admin., *supra* note 12.

139. Lewis, *Halted Innovation*, *supra* note 9, at 1077, 1096.

140. *See, e.g.*, George Q. Daley, *Polar Extremes in the Clinical Use of Stem Cells*, 376 NEW ENG. J. MED. 1075, 1075–77 (2017) (discussing the Mandai study and the harms of many for-profit stem cell clinics in the United States); Mandai et al., *supra* note 132, at 1038. One autologous stem cell treatment, Cultured Regenexx,

these enforcement actions, the FDA targets clinics for selling or marketing adulterated drugs and biologics under the FDCA and PHSA.[141] Nonetheless, clinics providing autologous stem cell treatments continue to flourish in the United States, especially in Florida, California, and Texas.[142]

* * *

The hybrid innovative therapies discussed in this Section involve both state and federal jurisdiction. This Article embraces the practice-products distinction and uses that distinction as the basis for exploring a new regulatory structure for the life sciences: state-federal cooperation as opposed to the current regime in which the federal government has usurped jurisdiction over the life sciences, thus ignoring state jurisdiction.[143] Further, even if the practice-products distinction cannot be clearly made in all cases, at least some aspect of innovative therapies involves the practice of medicine, and cooperative federalism would be a useful governance structure as medicine continues to evolve past its pharmaceutical- and physician-based foundations.

II. WEAKNESSES OF THE CURRENT REGIME AND NONCOOPERATIVE ALTERNATIVES TO THE REGULATION OF INNOVATIVE THERAPIES

This Section builds upon the preceding Section by explaining the weaknesses of the current regime as applied to innovative therapies and the weaknesses of noncooperative alternatives to the regulation of innovative therapies. Part II.A explains the weaknesses

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was the subject of federal court litigation in 2014 that concluded that such an autologous stem cell treatment in which a patient's own stem cells were combined with an antibiotic mixture was a mixture, subject to FDA regulation, and not a procedure (which would fall wholly within the practice of medicine). *See* United States v. Regenerative Scis., LLC, 741 F.3d 1314, 1317, 1321 (D.C. Cir. 2014); *see also* Lewis, *Halted Innovation*, *supra* note 9, at 1098, 1105–08 (discussing *United States v. Regenerative Sciences*). For more on express and implied threats in administrative law, see Lars Noah, *Administrative Arm-Twisting in the Shadow of Congressional Delegations of Authority*, 1997 WIS. L. REV. 873, 876–98 [hereinafter Noah, *Administrative Arm-Twisting*]; Tim Wu, *Agency Threats*, 60 DUKE L.J. 1841, 1842–43 (2011). For more on the FDA's use of threats as a regulatory tool, see Noah, *Administrative Arm-Twisting*, *supra*, at 888–97.

141. *See, e.g.*, Order on Motions for Summary Judgment, *supra* note 137, at 6–7; News Release, U.S. Food & Drug Admin., FDA Acts To Remove Unproven, Potentially Harmful Treatment Used in 'Stem Cell' Centers Targeting Vulnerable Patients (Aug. 28, 2017), http://www.fda.gov/news-events/press-announcements/fda-acts-remove-unproven-potentially-harmful-treatment-used-stem-cell-centers-targeting-vulnerable [https://perma.cc/CGH2-QPEL] (discussing the seizure of a vaccine "reserved only for people at high risk of smallpox" from the StemImmune stem cell clinic).

142. *See* Diane C. Lade, *Florida a Destination for Desperate Patients Buying Unproven Stem Cell Treatments*, S. FLA. SUN SENTINEL (Dec. 2, 2017), http://www.sun-sentinel.com/health/fl-fea-florida-stem-cell-clinics-20171130-story.html [https://perma.cc/3NRK-VGC4] ("Of 570 for-profit stem cell clinics counted in the United States last year, 113 were found in California and 104 in Florida, far outpacing other states, according to a report in the peer-reviewed journal, Cell Stem Cell."); *see also* Todd Ackerman, *Critics Wary of Stem Cell Clinics That Promise Big Results but Have Little Regulation*, HOUS. CHRON. (Nov. 26, 2017), http://www.houstonchronicle.com/news/houston-texas/houston/article/Critics-wary-of-stem-cell-clinics-that-promise-12384995.php [https://perma.cc/YV9B-67P4] (offering criticisms of stem cell treatments available in Texas and an overview of the motivation for Texas's statute increasing access to stem cell treatments in the state).

143. See *supra* note 17 for more on the debate over the FDA's jurisdiction over innovations in the life sciences (and the author's views in this debate).

of the current federally focused regime. Part II.B explores noncooperative alternatives such as allocating additional power to the FDA, redesigning the FDA, or devolving all jurisdiction over innovative therapies (including jurisdiction over currently federally regulated products such as drugs and biologics) to states. Part II.C then explains why these noncooperative alternatives would not adequately improve the regulation of innovative therapies.

A. Weaknesses of the Current Regime

The current federally focused regime for the regulation of innovative therapies suffers from a number of shortcomings. The traditional literature on the FDA's regulatory scheme emphasizes the "command and control" model of regulation in which the FDA and regulated entities engage in a "strictly" exclusive relationship;[144] however, states play an important role in the regulation of medicine. First, federal regulation does not prohibit the marketing approval of all products that could operate counter to the agency's goals of furthering the public health and safety, as evidenced by (1) the many unexpected side effects of approved products; (2) products that are recalled voluntarily after other entities, including physicians, discover significant adverse effects of those products; and (3) the lack of comparative effectiveness research used in the United States.[145] Second, the FDA has been vulnerable to risk-averse decisionmaking and capture by anti-innovation special interest groups, which sometimes overlap with those who are opposed to certain innovations based on political and social considerations, without adequate transparency or public deliberation.[146]

Beyond the ad hoc nature of regulating through guidance documents, a significant problem will continue to arise: a significant amount of recent medical innovation involves political and social issues, which the FDA, a regulatory agency within the executive branch, is not only unequipped to objectively assess but also should not assess based on its lack of transparency when regulating based on political or social views.[147]

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144. *See* Paradise, *21st Century Citizen Pharma*, *supra* note 34, at 312.

145. *See, e.g.*, Kapczynski, *supra* note 33, at 2364, 2368–71, 2373, 2380; *see also* Mary J. Davis, *The Battle over Implied Preemption: Product Liability and the FDA*, 48 B.C. L. REV. 1089, 1151 (2007) (showing that labeling regulations combined with the FDA's policy of negotiating with manufacturers over labeling changes resulted in a years-long delay in implementing that change, which even extended past the date the drug was voluntarily recalled); Evans, *Seven Pillars*, *supra* note 11, at 429–31 (discussing "a spate of incidents where serious risks came to light after drugs were approved"); *Vioxx Risk Lingers At Least 1 Year After Using Drug*, NBC NEWS (Oct. 13, 2008), http://www.nbcnews.com/id/27169441/#.USBLMGfg4S4 [https://perma.cc/GHN6-38LW].

146. *See, e.g.*, Arti K. Rai, *Intellectual Property Rights in Biotechnology: Addressing New Technology*, 34 WAKE FOREST L. REV. 827, 842 (1999) ("Economic and legal theorists prominent in the public choice movement have long lamented the undue susceptibility of the political process to small, politically active interest groups."); *see also* William W. Buzbee, *Preemption Hard Look Review, Regulatory Interaction, and the Quest for Stewardship and Intergenerational Equity*, 77 GEO. WASH. L. REV. 1521, 1539–40, 1548 (2009) [Buzbee, *Preemption Hard Look Review*]; Mark Seidenfeld, *Who Decides Who Decides: Federal Regulatory Preemption of State Tort Law*, 65 N.Y.U. ANN. SURV. AM. L. 611, 627 (2010) [hereinafter Seidenfeld, *Who Decides*] ("Outside of the notice-and-comment rulemaking paradigm, transparency of agency standard setting declines, potentially precipitously.").

147. *See supra* notes 20–21 and accompanying text. For more on the inappropriateness of considering political concerns in medical regulatory decisionmaking, especially as it relates to the reproductive sphere, which would be implicated by gene editing, see, for example, Myrisha S. Lewis, *The American Democratic Deficit in*

Yet, the specter of decisionmaking based on politics as opposed to science looms. To the extent that those political reasons are disguised as scientific concerns or ethical views, "political reasons prompting an agency to decide based on factors irrelevant under the authorizing statute are clearly out-of-bounds."[148]

Past regulatory actions reveal that the agency sometimes includes outside considerations in its regulatory process. Examples of these outside considerations influencing the regulatory process include the FDA's decisionmaking in the approval and conversion of emergency contraception, notably "Plan B," from a prescription to an over-the-counter drug, and recently, concerns about the role of patient involvement in FDA decisionmaking, especially when the agency is tasked with regulating for safety and effectiveness.[149] Current and forthcoming technologies implicate political and social issues, namely ones related to genetic modification, that the FDA is not structured to regulate due to its status as an executive branch agency (as opposed to an independent regulatory agency) and how it has routinely prohibited public discussion of the ethical (or social or political) issues that may arise in the regulation of various innovative technologies (even though those same political issues may have surfaced in the agency's decisions related to the FDA's effective banning of human cloning and forms of assisted reproductive technology involving genetic modification).[150] Furthermore, the FDA should not regulate these issues. Historically, these issues have involved concerns related to reproductive rights, which an agency that is subject to political pressure should not subject itself to.[151]

Assisted Reproductive Technology Innovation, 45 AM. J.L. & MED. 130 (2019) [hereinafter Lewis, *The American Democratic Deficit*].

148. Mendelson, *Disclosing "Political" Oversight*, *supra* note 19, at 1141 (discussing this exception as the sole exception to the general rule that "courts have not offered clear guidance on whether political reasons, if offered, can serve as an adequate basis for an agency's decision").

149. *See* Heinzerling, *supra* note 20, at 928 (discussing how the delay in the approval of Plan B as an over-the-counter drug was not based on safety or efficacy but rather political motivations); Lewis, *How Subterranean*, *supra* note 17, at 1273–75 (discussing how political or social considerations can impact federal regulatory decisions in the realm of assisted reproductive technology); *see also* Lars Noah, *A Miscarriage in the Drug Approval Process?: Mifepristone Embroils the FDA in Abortion Politics*, 36 WAKE FOREST L. REV. 571, 573–74 (2001) ("This Article concludes that the FDA's decisionmaking process [related to mifepristone (RU-486), a drug that is used to induce abortion,] was and probably will continue to be distorted by an inappropriate preoccupation with achieving a politically predetermined outcome."); Susan Pulliam and Brody Mullins, *How the FDA Approved a $300,000-a-Year Drug Its Own Experts Didn't Believe Worked*, WALL STREET J. (May 18, 2017, 10:43 AM), http://www.wsj.com/articles/how-the-fda-approved-a-300-000-a-year-drug-its-own-experts-didnt-believe-worked-1495116544 [https://perma.cc/WNS2-4A2E]; Sabrina Tavernise, *F.D.A. Approves Muscular Dystrophy Drug That Patients Lobbied For*, N.Y. TIMES (Sept. 19, 2016), http://www.nytimes.com/2016/09/20/business/fda-approves-muscular-dystrophy-drug-that-patients-lobbied-for.html [https://perma.cc/KMB9-9HRP].

150. For background on independent regulatory agencies as compared to executive branch agencies, see, for example, Lisa Schultz Bressman & Robert B. Thompson, *The Future of Agency Independence*, 63 VAND. L. REV. 599, 600 (2010). For more on the impact of social and political concerns on agency decisionmaking, see, for example, Lewis, *How Subterranean*, *supra* note 17, at 1271–79; Lewis, *The American Democratic Deficit*, *supra* note 147, at 167–68.

151. *See, e.g.*, Carbone, *supra* note 85, at 354 ("Given the . . . [d]eep-seated religious opposition to assisted reproduction, substantive regulation is likely to shut down promising innovations rather than provide a safer way to test their impact."); *see also* Mendelson, *Disclosing "Political" Oversight*, *supra* note 19, at 1143.

B. Noncooperative Alternatives

To illustrate the limitations of a noncooperative framework, this Part provides an overview of singularly state-based and federally based options and assesses their usefulness in regulating innovative therapies against the above-mentioned criteria. Part II.B.1 examines options for statutory changes to the FDA's method of regulating innovative medical techniques and preemption doctrine. Part II.B.2 discusses the option of state-by-state regulation of the life sciences (similar to how states address the results of assisted reproductive technology or have enacted laws banning human reproductive cloning).

1. Congressional Action To Allocate Jurisdiction or Redesign the FDA

Congress could undertake various efforts to improve the regulation of innovative therapies. One solution to the challenge of regulating the life sciences is one in which Congress crafts a new category and definition of product that the U.S. Department of Health and Human Services (HHS) regulates. Based on the current distribution of jurisdiction within the HHS, the FDA would likely be the agency that would federally regulate these innovative therapies.[152] As noted in Part II.A, "the FDA's system of regulation is category driven"; however, some products do not fall solely within one specific category of FDA-regulated product.[153] With this legislative solution, Congress would introduce another category of a FDA-regulated product, thus filling the gap between drugs and biologics—two categories that innovative therapies in the life sciences tend to fall in between.

Such an approach would be similar to Congress's action after the FDA lost to the tobacco industry, subsequent to the FDA asserting jurisdiction over cigarettes and smokeless tobacco as "'combination products' that deliver nicotine to the body."[154] In *FDA v. Brown & Williamson Tobacco Co.*,[155] the Supreme Court held that tobacco products did not fall within the jurisdiction of the FDA;[156] subsequently, Congress passed

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152. *See Food & Drug Administration*, U.S. DEP'T HEALTH & HUM. SERVS., http://www.hhs.gov/ohrp/regulations-and-policy/regulations/fda/index.html [https://perma.cc/79GM-6V4N] (last updated Mar. 18, 2016) ("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.").

153. *See* Javitt & Hudson*, supra* note 17, at 1213.

154. FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 125–26 (2000), *superseded by statute*, Family Smoking Prevention and Tobacco Control Act, Pub. L. No. 111-31, § 101, 123 Stat. 1776, 1783 (2009) (codified as amended at 21 U.S.C. § 387 (2018)).

155. 529 U.S. 120 (2000).

156. *Brown & Williamson*, 529 U.S. at 125–26 ("Regardless of how serious the problem an administrative agency seeks to address, however, it may not exercise its authority 'in a manner that is inconsistent with the administrative structure that Congress enacted into law.' . . . In this case, we believe that Congress has clearly precluded the FDA from asserting jurisdiction to regulate tobacco products. Such authority is inconsistent with the intent that Congress has expressed in the FDCA's overall regulatory scheme and in the tobacco-specific legislation that it has enacted subsequent to the FDCA. In light of this clear intent, the FDA's assertion of jurisdiction is impermissible."); *see also* WILLIAM N. ESKRIDGE JR. ET AL., STATUTES, REGULATION, AND INTERPRETATION: LEGISLATION AND ADMINISTRATION IN THE REPUBLIC OF STATUTES 210 (2014); Foote & Berlin, *supra* note 36, at 643; Richard A. Merrill, *The FDA May Not Regulate Tobacco Products as "Drugs" or as "Medical Devices*,*"* 47 DUKE L.J. 1071, 1074–94 (1998).

legislation that statutorily empowered the FDA to regulate tobacco products.[157] The advantage of such an approach is that the federal government could create a statutory definition that encompasses all innovative therapies, although such a statutory creation could reduce state jurisdiction. A clearer definition of federal authority, which would also involve broadening the FDA's authority, could resolve jurisdictional concerns, although it likely would have to be revised again. At the same time, such a definition might be difficult to create and potentially short-lived as innovative therapies move towards being more personalized to various patients and thus are not amenable to large-scale manufacturing (and broad categorizations).[158] In addition to these prospective disadvantages, expanding federal jurisdiction would possibly lead to greater preemption of state authority in the traditionally state-regulated field of medical practice.[159]

A second federally based solution could focus on preemption. Preemption is a doctrine whose foundation lies in the Supremacy Clause of the Constitution.[160] The Supremacy Clause establishes that in case of conflict between state and federal law, federal law applies.[161]

A discussion of preemption doctrine inevitably arises in the context of regulation of the life sciences because, to the extent that the FDA has jurisdiction over the life sciences, its regulations and statutes will generally preempt conflicting state law.[162] Yet, preemption doctrine also operates based on a presumption against preemption.[163] Even though "[f]ederal and state regulatory powers overlap enormously when it comes to

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157. Family Smoking Prevention and Tobacco Control Act § 101; *see also* ESKRIDGE ET AL., *supra* note 156, at 210.

158. See *supra* notes 28–29 and accompanying text for a discussion of the jurisdictional challenges brought on by the popularity of individualized treatments.

159. See *supra* Section I for a discussion of the dual jurisdictional nature of innovative therapies. *See also infra* notes 160–163 and accompanying text.

160. *See* PLIVA, Inc. v. Mensing, 564 U.S. 604, 617–18 (2011) ("The Supremacy Clause establishes that federal law 'shall be the supreme Law of the Land . . . any Thing in the Constitution or Laws of any State to the Contrary notwithstanding.' Where state and federal law 'directly conflict,' state law must give way." (omission in original) (citations omitted)); Ashutosh Bhagwat, Wyeth v. Levine *and Agency Preemption: More Muddle, or Creeping To Clarify?*, 45 TULSA L. REV. 197, 198–99 (2009) ("By its terms, the Supremacy Clause says very little about state law and certainly does not explicitly authorize Congress to displace state law. . . . Instead, current preemption doctrine . . . presumes that the Supremacy Clause is the source of all preemption.").

161. *PLIVA*, 564 U.S. at 617–18; Hillsborough Cty. v. Automated Med. Labs., Inc., 471 U.S. 707, 712–14 (1985). Federal regulations are equated with federal statutes in Supremacy Clause analysis by virtue of the federal statute empowering the agency to make those regulations. *See* Bhagwat, *supra* note 160, at 201 ("The conventional wisdom, as stated by the Supreme Court, is that '[f]ederal regulations have no less pre-emptive effect than federal statutes." (alteration in original) (quoting Fidelity Fed. Sav. & Loan Ass'n v. de la Cuesta, 458 U.S. 141, 153 (1982))).

162. *See* Noah, *State Affronts*, *supra* note 27, at 28–35 (discussing preemption in the context of pharmaceutical licensing and the ability of plaintiffs to recover under state tort law for harms suffered due to the use of FDA-approved pharmaceuticals); Sharkey, *States Versus FDA*, *supra* note 78, at 1611; *see also* McCuskey, *Body of Preemption*, *supra* note 77, at 96, 110 ("And, where the state attempts to regulate in an area where federal regulation already exists, 'the federal scheme prevails though it is a more modest, less pervasive regulatory plan than that of the State.'" (quoting Rice v. Santa Fe Elevator Corp., 331 U.S. 218, 236 (1947))).

163. *See* McCuskey, *Body of Preemption*, *supra* note 77, at 95, 98 ("Unlike the general presumption against preemption on federalism grounds, courts base this tradition presumption on a notion of 'state primacy' that is rooted in tradition and unique to health regulation. Therefore, courts assume it is unlikely in most cases that Congress intended to preempt state health laws.").

regulating health," there are areas in which the powers do not overlap at all,[164] which the National Academies of Sciences, Engineering, and Medicine acknowledged in a report commissioned by a number of federal agencies, including the FDA.[165] In those areas in which jurisdiction does not overlap and federal law does not provide jurisdiction over an aspect of innovative therapy, the jurisdictional default is for those "reserved powers" to go to the states.[166] Preemption doctrine would expand federal jurisdiction at the expense of state jurisdiction, which, as outlined in the next Part, would deprive American patients of the current benefits of state regulation. These benefits include complementing federal regulation by aiding in the discovery of adverse effects of FDA-approved products and ensuring Americans have proper access to the regulatory structures that have been created due to the state's historic police powers.

A preemption-based solution could also use a waiver to allow states to opt back into the regulatory system after the expansion of federal jurisdiction, where interested states obtain the approval of the FDA to regulate innovative therapies. To have a waiver-based system, however, the federal government would still, as a foundational matter, have to preempt or supersede the authority of the states.[167] A natural inclination, especially in light of the use of waivers in other areas of health regulation, namely health insurance regulation, might be to create a statutory waiver for jurisdictional issues related to scientific innovation;[168] however, this Article does not recommend that approach for several reasons, as outlined in Part II.C.[169]

Another congressional action could focus on the deficiencies in the FDA's jurisdiction or method of exercising jurisdiction by transforming the nature of the agency. Other scholars have explored transforming the FDA, or part of it, into an independent regulatory agency.[170] While transforming the FDA into an independent regulatory

164. Elizabeth Y. McCuskey, *Agency Imprimatur & Health Reform Preemption*, 78 OHIO ST. L.J. 1099, 1101 (2017) [hereinafter McCuskey, *Agency Imprimatur*].

165. NAT'L ACADS. OF SCIS., ENG'G, & MED., PREPARING FOR FUTURE PRODUCTS OF BIOTECHNOLOGY 1, 10–11 (2017), http://www.nap.edu/24605 [https://perma.cc/58M7-C237].

166. *See* Lawrence O. Gostin, *The Model State Emergency Health Powers Act: Public Health and Civil Liberties in a Time of Terrorism*, 13 HEALTH MATRIX 3, 24 (2003) ("However, states have 'plenary' authority to protect the public's health under their reserved powers in the Tenth Amendment. The Supreme Court has made clear that states have a deep reservoir of public health powers, conceiving of state police powers as an 'immense mass of legislation [in which] [i]nspection laws, quarantine laws, [and] health laws of every description . . . are component[s] of this mass.' The Supreme Court, moreover, has regarded Federal police powers as constitutionally limited, and has curtailed the expansion of national public health authority." (omission in original) (alterations in original) (footnote omitted)); *see also* U.S. CONST. amend. X ("The powers not delegated to the United States by the Constitution, nor prohibited by it to the states, are reserved to the states respectively, or to the people.").

167. *See, e.g.*, Hills, *supra* note 23, at 866 ("Congress can also 'hire' the states to carry out federal programs through the use of conditional preemption. Under this system, Congress enacts a general regulatory scheme, delegating implementation to the states on the condition that the states submit an acceptable implementation plan to the federal government.").

168. *See, e.g.*, McCuskey, *Agency Imprimatur*, *supra* note 164, at 1102–03 (introducing the Section 1332 waiver program that "applies to the ACA's core [insurance] provisions").

169. *See infra* Part II.C.

170. See *supra* notes 15–18 and accompanying text for more on the jurisdictional limits of the federal government over innovative therapies. Scholars have proposed other options, including an independent regulatory agency for a number of innovative technologies; however, to the extent that these innovative therapies

agency could reduce the executive branch's influence on access to innovation and might increase the scientific quality of decisionmaking, changing the nature of the FDA, however, still would not solve the underlying problem of how to recognize and address federal and state jurisdiction.

2. State-by-State Regulation of the Life Sciences

While this Article does not advocate for a state-by-state approach, an analysis of a state-by-state approach is useful insofar as some states might opt into a cooperative system and others might not. Broadly, state regulation of innovative therapies could result in both a "race to the bottom" and a "race to the top." A race-to-the-bottom approach could involve some states adopting a regulatory structure that permits any sort of therapy, which may result in patient harm, whereas a race-to-the-top approach could lead to a restrictive regime that is similar to the FDA's current regulation of pharmaceuticals in one specific state. Such a restrictive regime could cause innovators to have to comply with multiple state-based regulatory regimes.

To the extent that innovative medical techniques constitute the practice of medicine and are not "articles" subject to the regulation of the FDA, a state-by-state approach to regulating the life sciences would operate similarly to how states address the results of assisted reproductive technology or have enacted laws banning human reproductive cloning.[171] Similarly, in the current regime, the federal government serves as a "gatekeeper" to the pharmaceutical market, and state regulation provides a regime that patients can use when physicians improperly administer those federally approved products.[172] Thus, federal assertions of jurisdiction aim to prevent certain types of harms (or, at the very least, to inform the public of potential harms), but state-regulated entities, namely physicians, work to determine which "safe and effective" treatments are best to use. It is also possible that states would not want to involve themselves in the regulation of innovative medical techniques in a robust manner or in a manner different from how a state regulates other instances of medical malpractice or access to markets. For example, in spite of state statutes governing the treatment of the results of assisted reproductive technology, namely the parentage of children conceived using assisted reproductive technology, scholars and commentators continue to regard traditional assisted reproductive technology as "unregulated" or "minimally regulated" by the states and the federal government.[173]

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would involve both state and federal jurisdiction, an independent regulatory agency could improve federal jurisdiction as a matter of scientific assessment but that still does not resolve the issue of shared jurisdiction. *See, e.g.*, Barry R. Furrow, *The CRISPR-Cas9 Tool of Gene Editing: Cheaper, Faster, Riskier?*, 26 ANNALS HEALTH L. 33, 49–51 (2018); *see also* Robert M. Califf et al., *Seven Former FDA Commissioners: The FDA Should Be an Independent Federal Agency*, 38 HEALTH AFFAIRS 84, 84 (2019).

171. *See* Lewis, *How Subterranean*, *supra* note 17, at 1251–53.

172. *See supra* Section I.

173. *See* Brenda Reddix-Smalls, *Assessing the Market for Human Reproductive Tissue Alienability: Why Can We Sell Our Eggs but Not Our Livers?*, 10 VAND. J. ENT. & TECH. L. 643, 655, 689 (2008) ("Additionally, states have also neglected to enter into the regulation of the reproductive marketplace."); *see also* Lewis, *How Subterranean*, *supra* note 17, at 1241 & n.1 (providing citations to the conventional view that assisted reproductive technology is unregulated or "minimally regulated"). *But see State Laws Related to Insurance Coverage for Infertility Treatments*, NAT'L CONF. STATE LEGISLATURES (June 12, 2019),

C. Insufficiency of Noncooperative Alternatives

Both singularly federal and singularly state-based approaches suffer from significant weaknesses. Drawing on the experience of states in the regulation of assisted reproductive technology, it remains possible that some states will want to continue not being involved in the regulation of certain current and forthcoming innovations.[174] Even if all states choose not to participate, such a regulatory regime would be no different than the current state of federally based regulation but would at least recognize state jurisdiction.[175] A state-by-state approach would be inconsistent as different states would likely choose different regulatory approaches, whereas the current method of federal regulation indicates that the federal regulatory system is predictably hostile to certain innovations in medicine.[176] In a state-by-state regime, a variety of regulatory systems would likely emerge.[177] This variety of regulatory systems might include certain systems that increase the rate of patient access to developed innovative therapies or that encourage the development of innovative therapies, which would ultimately lead to patients being able to access innovative therapies more quickly. A purely state-based system, moreover, would require states to replace the current regulatory role of the FDA so as to still maintain a baseline level of patient safety.

At the same time, this Article does not advocate for any increase in the scope of federal power. First, the preemption doctrine fails to resolve the difficulty of regulating innovative therapies as innovative therapies straddle traditional areas of federal and state jurisdiction.[178] Further, by using preemption instead of a shared regulatory approach, the regulatory system is deprived of a meaningful dialogue between states and the federal government on emerging innovations and regulatory changes. Creating a cooperative regime that facilitates debate and discussion among the states and the federal government

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http://www.ncsl.org/research/health/insurance-coverage-for-infertility-laws.aspx [https://perma.cc/6VJP-SSBW] (identifying states with statutes addressing insurance coverage of assisted reproductive technology).

174. *See* Lewis, *How Subterranean*, supra note 17, at 1251–53 (reviewing state legislation related to the regulation of assisted reproductive technology and noting that "[s]tate law generally does not restrict the mechanics of assisted reproductive technology"); *see also* Lewis, *The American Democratic Deficit*, *supra* note 147, at 149 ("Historically, there has been little state or federal regulation of ART, which allowed the industry to develop with little regulatory oversight.").

175. See *supra* Part I.A for a discussion of federal regulation over products used in the practice of medicine.

176. The federal government both regulates innovation through federal agencies (e.g., the FDA) and funds research in medicine and other areas (e.g., grants provided by the NIH). As such, there is sometimes a difference between the approaches taken by federal regulatory agencies and participants in the federal regulatory structure and the research initiatives undertaken by or funded by the federal government. *Compare* Lewis, *How Subterranean*, *supra* note 17, at 1274 (discussing the federal hostility to innovation in assisted reproductive technology involving genetic modification), *with Budget*, NAT'L INSTS. HEALTH, http://www.nih.gov/about-nih/what-we-do/budget [https://perma.cc/A2CL-TAQ3] (last updated Jan. 24, 2019) ("The NIH invests nearly $39.2 billion annually in medical research for the American people." (footnote omitted)).

177. *See, e.g.*, Carbone, *supra* note 85, at 359 ("If, on the other hand, the issue arises in the context of state legislation, the legislature may be indifferent, if not downright hostile, to the concerns of a lesbian couple."); *see also* Reddix-Smalls, *supra* note 173, at 655 ("Thus, the lack of initial federal funding for embryonic and genetic research created a vacuum of federally sponsored research that was filled by private entrepreneurs, private research facilities, and medical universities in the fertility industry.").

178. *See* McCuskey, *Body of Preemption*, *supra* note 77, at 96 ("Preemption generally describes the displacement of state law by federal law.").

promotes a number of federalism's values, with an emphasis on participation and transparency.[179]

This Article also does not recommend a preemption-based solution that would combine preemption with a waiver. First, a waiver would likely involve the FDA deciding whether to grant a waiver to states that apply, which would not be preferable in light of the agency's previous regulation without jurisdiction.[180] Second, a waiver would imply that the federal government was approving the exercise of state jurisdiction only in certain instances, which would not fully recognize concurrent state and federal jurisdiction, especially in the absence of additional federal grants.[181] Third, to the extent that a waiver was created that did preserve judicial review of agency action, a judge might assume that the FDA had the requisite (and superior) "[s]cientific and technical expertise" in the area of regulation, thus leading to increased judicial deference to the agency's decision.[182] In sum, a waiver would likely empower the FDA to continue imposing additional regulatory requirements on U.S. entities and also on states that would participate in the regulation of innovative therapies in a waiver-based system.[183]

Based on this analysis, this Article's cooperative framework further discourages both explicit and implicit federal preemption of state jurisdiction. Specifically, this Article is most concerned by implied preemption, for which states (and patients) may not have notice.[184] In the absence of an explicit preemption provision, similar to the one that Congress provided with the 1976 Medical Device Amendments to the FDCA, the FDA may unexpectedly act to preempt state authority, in spite of the promises and acknowledgments of members of Congress and past FDA employees about the lack of FDA jurisdiction over the practice of medicine.[185] This Article also does not advocate

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179. *See, e.g.*, Robert A. Schapiro, *Toward a Theory of Interactive Federalism*, 91 IOWA L. REV. 243, 249 (2005) ("[I]t is the dynamic interaction among states and the national government that forms the true sound of federalism."); *see also* Metzger, *Federalism*, *supra* note 111, at 24–25.

180. *See* David J. Barron & Todd D. Rakoff, *In Defense of Big Waiver*, 113 COLUM. L. REV. 265, 301 (2013) (citing 42 U.S.C. § 18052 (2018)) (discussing the Secretary of Health and Human Services's ability to grant waivers to states that apply); *see also* Susan Bartlett Foote, *Administrative Preemption: An Experiment in Regulatory Federalism*, 70 VA. L. REV. 1429, 1441 (1984) ("Granting exemptions or waivers for more protective state provisions thus requires the agency to acknowledge the limitations of its own decisionmaking.").

181. While not discussed in this Article, another form of cooperative federalism in health law, Section 1332 waivers, also tends to focus on insurance programs. *See, e.g.*, Elizabeth Y. McCuskey, *Big Waiver Under Statutory Sabotage*, 45 OHIO N.U. L. REV. 213, 214–18 (2019).

182. McCuskey, *Agency Imprimatur*, *supra* note 164, at 1156; *see also* Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521, 551 (2012) [hereinafter Sharkey, *Inside Agency Preemption*] ("FDA claims that its interpretations of its regulations governing drug labeling are entitled to deference.").

183. *See, e.g.*, Barron & Rakoff, *supra* note 180, at 325 ("The more power the agency has to establish the substantive criteria that will trigger its willingness to waive, the more authority it has to impose a new set of regulatory requirements in the course of 'waiving' those on the books.").

184. Express preemption is authorized by an explicit statutory provision, whereas implied preemption is not. *See* Sharkey, *Inside Agency Preemption*, *supra* note 182, at 525 n.11. For more on the complexities of preemption, including explicit, implicit, and implied preemption and the limits of the "presumption against preemption," see generally Daniel J. Meltzer, *Preemption and Textualism*, 112 MICH. L. REV. 1 (2013); Caleb Nelson, *Preemption*, 86 VA. L. REV. 225 (2000).

185. For more on the regulation of medical devices and the evolution of that regime, see Merrill, *The Architecture*, *supra* note 23, at 1800–35. For more on the operation of preemption doctrine within the context of the Medical Devices Amendments, see generally Lars Noah, *Amplification of Federal Preemption in Medical Device Cases*, 49 FOOD & DRUG L.J. 183 (1994).

for the addition of an explicit preemption provision for innovative therapies, as doing so, even with a procedure for requesting an exemption, would minimize experimentation and a dialogue between states and the federal government on the regulation of innovative therapies. Such a procedure would also subjugate state jurisdiction to federal jurisdiction and minimize the significance of additional actors in the regulatory process. The next Section aims to incorporate the most advantageous aspects of the noncooperative alternatives explored in this Section and the cooperative programs discussed later in Part III.B, while at the same time aiming to minimize the disadvantages of all of those options.

III. A COOPERATIVE FRAMEWORK FOR REGULATING INNOVATIVE THERAPIES

There are a number of options that could improve the regulation of innovative therapies. The current federally focused system is not the best way to regulate life sciences innovations, and a singularly state-based regime would also suffer from significant limitations. As previously noted, the current, federally focused regulatory system has failed to adequately regulate a number of innovative therapies and is not adequately structured to accommodate those innovative therapies including gene editing, gene therapy, and regenerative medicine therapies with a focus on autologous stem cell treatments.[186] The current system suffers from at least three shortcomings: (1) failure to recognize the existence of state jurisdiction; (2) regulatory gaps in which innovative therapies do not fit wholly within the FDA-regulated categories, even with the combination products statute; and (3) the possibility that the executive branch is making decisions based on political views involving certain social or ethical controversies without disclosing those views to the public or soliciting public input.

A shared, hybrid system of jurisdiction could also be useful for life sciences innovations involving unresolved controversies, innovative therapies that are classified as "riskier" than current techniques in use in medical treatment, or biologics and drugs that are currently approved by the FDA.[187] A cooperative system would offer more flexibility than the current federally focused regime. A cooperative regulatory scheme would also improve patient health, especially since states already have some jurisdiction over the life sciences through the practice of medicine.[188] There are a number of criteria that would trigger this Article's framework for regulating innovative therapies, including the existence of an innovative therapy (generally these innovative therapies are designated as "combination products" by the FDA),[189] the existence of state jurisdiction (as is the case with innovative therapies which are hybrids of state and federal jurisdiction),[190] and FDA governance and assertion of jurisdiction via guidance documents.[191] Additionally, while this is not the case for all of the innovative therapies

186. *See supra* Parts I.A and I.C.

187. See *supra* note 145 for examples of FDA-approved products that have been withdrawn from the market after adverse side effects come to light.

188. See *supra* Part I.B for an analysis of state jurisdiction over the practice of medicine.

189. See *supra* notes 43–48 and accompanying text and Part I.C for a discussion on innovative therapies and their amenability to a cooperative governance structure.

190. For more on federalism in the regulation of food and drugs, see, for example, Sharkey, *States Versus FDA*, *supra* note 78, at 1610–15.

191. Continued assertions of jurisdiction via guidance documents connect not only to concerns that the FDA may be regulating outside of its jurisdiction but also to the transparency of regulation. *See, e.g.*, Seidenfeld,

studied in this Article, the possibility that the therapy will be accompanied by ethical controversy greater than that of traditionally FDA-regulated products weighs in favor of the application of this Article's cooperative framework, as it would increase the number of regulatory actions and reduce the possibility that the ethical controversy might manifest as ethically or socially motivated regulatory decisionmaking by the FDA.

This Article's proposed cooperative framework aims to minimize the likelihood that, due to overregulation in the United States, people leave the country to either receive safe and effective therapies in places like Germany or receive risky therapies in countries (and even some states) that underregulate. While recent legislative efforts, including notably the 21st Century Cures Act, have improved the pace of regulation, especially, as this Article indicates, in the area of regenerative medicine with the increased funding to the FDA and to federally funded researchers, an additional challenge that the agency faces is the increasing complexity of the products that it must regulate.[192] Part III.A provides background on the concept of cooperative federalism. Part III.B focuses on four areas in which cooperative programs are used to balance state and federal interests. Part III.C describes the goals, advantages, and disadvantages of a cooperative system for regulating innovative therapies. Part III.D provides specific structures that encompass the goals of the cooperative system for regulating innovative therapies.

A. Cooperative Federalism

This Article draws upon cooperative federalism programs in constructing its cooperative framework for the regulation of innovative therapies. Cooperative federalism originated in 1938 as commentators noted a shift in governmental behavior in "classical" federal countries, such as the United States and Canada, after the Great Depression.[193] The first use of cooperative federalism in American legal literature was also in 1938, as part of an *Iowa Law Review* symposium on the subject.[194] The term "cooperative federalism" eventually appeared in a reported federal decision in 1950 and has since appeared in numerous Supreme Court and other federal court decisions.[195] Historically, cooperative federalism has been characterized as "largely an invention of the Progressives, who attempted to reconcile their nationalist ambitions with their affection for local government."[196]

Who Decides, *supra* note 146, at 627 ("Outside of the notice-and-comment rulemaking paradigm, transparency of agency standard setting declines, potentially precipitously.").

192. *See* Kapczynski, *supra* note 33, at 2382.

193. *See* Ronald L. Watts, *Origins of Cooperative and Competitive Federalism*, *in* TERRITORY, DEMOCRACY AND JUSTICE 201, 204–05 (Scott L. Greer ed., 2006).

194. *Id.* at 204; *see also Symposium on Cooperative Federalism*, 23 IOWA L. REV. 455, 456 (1938) ("Comparatively recently, however, there has developed an entirely new field of experiment characterized by the participation of several governments in cooperative legislative or administrative action. The interaction may be between the National Government and one or more of the states or among the states themselves. This realm of 'Cooperative Federalism' it is the purpose of this Symposium to explore.").

195. Robert L. Glicksman, *From Cooperative to Inoperative Federalism: The Perverse Mutation of Environmental Law and Policy*, 41 WAKE FOREST L. REV. 719, 725 (2006).

196. Greve, *supra* note 26, at 576. For more on the historical evolution of cooperative federalism, see *id.* at 576–84.

Since its inception, cooperative federalism has led to a "voluminous" literature that focuses on cooperation between federal, state, and local governments.[197] While cooperative federalism does not have an exact definition, it is generally viewed as a form of regulation involving the "sharing of regulatory authority between the federal government and the states that allows states to regulate within a framework delineated by federal law."[198] Thus, cooperative federalism programs often arise in areas where jurisdiction is concurrent or shared, and much of the literature focuses on shared jurisdiction between state or local and federal governments.[199] Often, cooperative federalism involves the use of federal funding, especially "conditional grants" as an inducement for state regulatory action.[200] States can choose whether to participate in cooperative federalism programs.[201]

Cooperative federalism offers the benefit of combining federal oversight of issues of national importance with local tailoring of programs by state and local governmental officials.[202] Through cooperative federalism programs, states can shape national policies.[203] Within a cooperative federalism framework, states are able to experiment with various regulatory regimes subject to a federal minimum.[204] States and the federal government also interact more often in cooperative frameworks.[205] Further, federal agencies with cooperative federalism programs tend to be more receptive to federalism concerns.[206] This Article focuses on the sharing aspect of that regulatory approach in constructing a shared framework for the regulation of innovative therapies.

Cooperative federalism has a number of advantages and disadvantages, similar to other forms of governance. Cooperative federalism is often contrasted with dual federalism, which envisions "separate and distinct spheres of [state and federal] authority"; however, scholars have noted that such a clean separation between the

197. Hills, *supra* note 23, at 815. For more on cooperative federalism, broadly, and on cooperative federalism in healthcare and the Affordable Care Act, specifically, see Abbe R. Gluck, *Intrastatutory Federalism and Statutory Interpretation: State Implementation of Federal Law in Health Reform and Beyond*, 121 YALE L.J. 534, 537–40, 548–52 (2011).

198. Weiser, *supra* note 22, at 665; *id.* at 668 ("Although there is no precise definition for which regimes fit the cooperative federalism model, the Supreme Court has suggested that this term best describes those instances in which a federal statute provides for state regulation or implementation to achieve federally proscribed policy goals."). For more on the origins of the term "cooperative federalism," see Glicksman, *supra* note 195, at 719, 728–29.

199. *See, e.g.*, Glicksman, *supra* note 195, at 719–20.

200. Hills, *supra* note 23, at 858–61.

201. *See* Weiser, *supra* note 22, at 704–05.

202. David Schleicher, *Vermont Is a Constitutional Problem*, 61 ARIZ. L. REV. 253, 278 (2019).

203. *Id.*

204. *See* William W. Buzbee, *Brownfields, Environmental Federalism, and Institutional Determinism*, 21 WM. & MARY ENVTL. L. & POL'Y REV. 1, 12, 25 (1997).

205. *See, e.g.*, Erin Ryan, *Negotiating Federalism*, 52 B.C. L. REV. 1, 31 (2011) (discussing negotiations between state and federal governments related to enforcement in areas of overlapping jurisdiction).

206. *Id.* at 18 ("Professor Catherine Sharkey . . . also observes that agencies engaged in programs of cooperative federalism with state partners better heed federalism concerns than those administering programs without state collaboration. For example, the Environmental Protection Agency (EPA), which works closely with states in administering the Clean Air and Water Acts, has shown much greater deference to state interests than the Federal Drug Administration, whose regulations have preempted state common law without much sensitivity." (footnotes omitted) (citing Sharkey, *Federalism Accountability*, *supra* note 19, at 2155–72)).

spheres is difficult.[207] In light of the blurring of the line of authority in the regulation of the hybrid innovative therapies, cooperative federalism is a useful regime to examine in the context of innovative therapies, which are hybrids of state and federal jurisdiction.

Nevertheless, cooperative federalism has incited many criticisms and concerns. One concern with the existence of cooperative federalism programs is that it may prove difficult to ensure accountability due to the difficulty in ascertaining which political level—state or federal—is responsible for a decision.[208] In a similar vein, opponents of cooperative federalism argue that it also leads to a "loss of transparency."[209] Others have noted that cooperative federalism can minimize the effectiveness of state elections and reduce accountability as voters will not know who to credit (or blame) for the outcomes of cooperative federalism programs.[210] Another criticism is that cooperative federalism "reliably produces . . . a big, sprawling government."[211] Some scholars view cooperative federalism as a system of governance that reduces state autonomy as states often act as "faithful agents implementing federal programs" as opposed to strongly autonomous sovereigns.[212] This concern is particularly prevalent in regimes where the federal government has provided funds to states. Other commentators have noted that an alternative to cooperative federalism could be simply to have federal governmental agencies with branch offices that implement federal law, similar to the regional offices of the Environmental Protection Agency or Offices of the U.S. Attorneys.[213] Part III.C explains why, in spite of these concerns, this Article still advocates for a cooperative approach.

B. Examples of Cooperative Federalism

Systems for state and federal cooperation often use waivers, exemptions, and opt-in programs in order to balance state and federal interests and improve regulation.[214] Many of these cooperative programs fall under the guise of cooperative federalism, especially those programs that involve the expenditure of federal funds, which are used in state-administered programs.[215] Cooperative federalism is used to regulate in a number

207. Weiser, *supra* note 22, at 665, 693.

208. Hills, *supra* note 23, at 826–27; *see also* Weiser, *supra* note 22, at 696–97.

209. Greve, *supra* note 26, at 567, 575.

210. Schleicher, *supra* note 202, at 281.

211. Greve, *supra* note 26, at 592.

212. Jessica Bulman-Pozen & Heather K. Gerken, *Uncooperative Federalism*, 118 YALE L.J. 1256, 1262 (2009).

213. Schleicher, *supra* note 202, at 278–79.

214. *See* Metzger, *The Constitutional Duty*, *supra* note 22, at 1853; *Vehicle Emissions California Waivers and Authorizations*, EPA, http://www.epa.gov/state-and-local-transportation/vehicle-emissions-california-waivers-and-authorizations [https://perma.cc/J22J-6LQS] (last updated June 23, 2017). For example, section 209 of the Clean Air Act "allows California to seek a waiver of the preemption which prohibits states from enacting emission standards for new motor vehicles." *Id.* Section 209 of the Clean Air Act is codified at 42 U.S.C. § 7543 (2018). For discussions of waivers in other areas, see Derek W. Black, *Federalizing Education by Waiver?*, 68 VAND. L. REV. 607, 611 (2015) (waiver of failure to comply with No Child Left Behind); Jessica Bulman-Pozen, *Executive Federalism Comes to America*, 102 VA. L. REV. 953, 1003–09 (2016) [hereinafter Bulman-Pozen, *Executive Federalism*] (waivers to jumpstart Medicaid expansion). *See generally* Barron & Rakoff, *supra* note 180, at 265 (exploring agencies' ability to waive Congress's rules).

215. *See* Greve, *supra* note 26, at 566; Weiser, *supra* note 22, at 665.

of areas in the law including environmental, education, and welfare.[216] This Part provides an overview of some cooperative federalism programs that relate to healthcare, which this Article then draws upon in constructing a structural framework for the regulation of innovative therapies. While the examples in this Part are not perfect parallels to the regulation of innovative therapies, each cooperative regime provides a relevant lesson or insight that could improve the regulation of innovative therapies.

1. Medicaid

Medicaid is an example of a cooperative framework that uses waivers and federal funding.[217] Medicaid, which was enacted in 1965, provides payment for the healthcare needs of "eligible low-income adults, children, pregnant women, elderly adults and people with disabilities."[218] Medicaid is a joint state-federal program in which "[f]ederal law outlines broad mandatory requirements that state Medicaid programs must follow, but states retain considerable flexibility to cover additional eligibility groups and benefits."[219] Within Medicaid, the federal government provides grants to states, which in turn must comply with federal statutory and regulatory requirements.[220] In spite of those federal requirements, states retain flexibility in a number of areas, including "provider qualification, participation and compensation."[221] Individual states administer and also provide funding to their own Medicaid programs.[222]

The Medicaid program also permits state flexibility through section 1115 waivers.[223] Section 1115 waivers permit states to submit applications for "experimental, pilot, or demonstration project[s]" that would likely further specified goals outlined in the Medicaid statute.[224] A recent study found that as of January 16, 2020, forty-two states had fifty-three approved section 1115 waivers, and twenty-two states had twenty-six pending waivers.[225] Medicaid waivers cover a number of policy innovations including

216. Weiser, *supra* note 22, at 668–70; *see also* Glicksman, *supra* note 195, at 719–20, 723–25; Greve, *supra* note 26, at 558.

217. *See* Bulman-Pozen, *Executive Federalism*, *supra* note 214, at 1003–09; Weiser, *supra* note 22, at 668.

218. *See Medicaid*, MEDICAID.GOV, http://www.medicaid.gov/medicaid/index.html [https://perma.cc/VXN9-YR6S] (last visited Feb. 1, 2020); *Program History*, MEDICAID.GOV, http://www.medicaid.gov/about-us/program-history/index.html [https://perma.cc/8TLQ-83Y7] (last visited Feb. 1, 2020).

219. Sidney D. Watson, *Out of the Black Box and into the Light: Using Section 1115 Medicaid Waivers To Implement the Affordable Care Act's Medicaid Expansion*, 15 YALE J. HEALTH POL'Y, L., & ETHICS 213, 214 (2015); *see also, e.g.*, *Prescription Drugs*, MEDICAID.GOV, http://www.medicaid.gov/medicaid/prescription-drugs/index.html [https://perma.cc/5KQP-3778] (last visited Feb. 1, 2020) ("Medicaid is a joint Federal-State program that pays for medical assistance for individuals and families with low incomes and relatively few assets.").

220. *See* Sara Rosenbaum & David Rousseau, *Medicaid at Thirty-Five*, 45 ST. LOUIS U. L.J. 7, 17 (2001); *see also* 42 U.S.C. § 1396a(a) (2018) (listing the requirements for state Medicaid plans).

221. Rosenbaum & Rousseau, *supra* note 220, at 22; *see also* 42 U.S.C. § 1396a.

222. *See* 42 U.S.C. § 1396a; *Medicaid*, *supra* note 218.

223. *See* 42 U.S.C. § 1315.

224. *Id.*; *see also About Section 1115 Demonstrations*, MEDICAID.GOV, http://www.medicaid.gov/medicaid/section-1115-demo/about-1115/index.html [https://perma.cc/M24U-T4QJ] (last visited Feb. 1, 2020).

225. *Medicaid Waiver Tracker: Approved and Pending Section 1115 Waivers by State*, KAISER FAM. FOUND. (Jan. 16, 2020), http://www.kff.org/medicaid/issue-brief/medicaid-waiver-tracker-approved-and-pending-section-1115-waivers-by-state/ [https://perma.cc/EY8Q-MRFS].

expanded healthcare coverage and "advances in coverage, access, health outcomes, efficiencies in delivery of care, or other improvements to the health of beneficiaries (while maintaining budget neutrality)."[226]

Waivers have also surfaced in the context of the Affordable Care Act (ACA). Recently, for example,

> [s]ome states expanded Medicaid eligibility precisely as the ACA's text laid out; others chose not to expand at all; still others negotiated (and renegotiated) waivers to tailor Medicaid to their liking . . . . All of these states experienced autonomy; all of their choices generated policy localism and experimentation. Waiver states arguably cooperated with the federal government and dissented simultaneously.[227]

Medicaid "is fixed in the collective consciousness as a classic example of cooperative federalism" due to its combination of federal funding and requirements, state administration, and the furtherance of state options through statutory waiver provisions.[228] Even though Medicaid addresses policy innovation as opposed to scientific innovation, Medicaid is a joint state-federal program that provides a cooperative structure that could be applied to the regulation of scientific innovation.[229]

The advantage of using cooperative federalism in the Medicaid program instead of, for instance, having no state role is that states are "closer" to the population that Medicaid would serve.[230] As such, states will have valuable insights that the federal government would not. Additionally, states have already created a structure to provide services to those who Medicaid would serve and to administer the program, such as through the enrolling of participants, thus sparing the federal government from exerting the effort of creating an insurance program for those who would be entitled to Medicaid services.[231] Massachusetts, for example, used a Medicaid waiver to provide health insurance coverage to all residents, which ultimately influenced the federal health insurance structure that the ACA provided.[232]

At the same time, Medicaid is a program that has been the subject of numerous criticisms over the years.[233] Further, there is a risk that, through a program such as Medicaid, where the federal government sets a floor, the federal government will try to

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226. Nicole Huberfeld, *Work Requirements + Medicaid = Bad Medicine*, B.U. SCH. PUB. HEALTH (Jan. 23, 2018), http://www.bu.edu/sph/2018/01/23/work-requirements-medicaid-bad-medicine/ [https://perma.cc/9BY6-XHAW]. *But see* Emily Whelan Parento & Nicole Huberfeld, *Trump, Bevin Violate Federal Law with New Medicaid Rules*, LEXINGTON HERALD-LEADER (Jan. 24, 2018, 4:00 PM), http://www.kentucky.com/opinion/op-ed/article196436639.html [https://perma.cc/36S5-BMUB] (discussing the negative impacts of a Section 1115 waiver granted in Kentucky).

227. Abbe R. Gluck & Nicole Huberfeld, *What Is Federalism in Health Care For?*, 70 STAN. L. REV. 1689, 1694–95 (2018).

228. *See* Nicole Huberfeld, *Federalizing Medicaid*, 14 U. PA. J. CONST. L. 431, 434 (2011). *But see id.* (observing that "the program's design is creating more discord than cooperation").

229. *See, e.g.*, Watson, *supra* note 219, at 214.

230. *See* Mark Seidenfeld, *The Bounds of Congress's Spending Power*, 61 ARIZ. L. REV. 1, 24 (2019) [hereinafter Seidenfeld, *The Bounds*].

231. *Id.* at 24–25.

232. Ryan, *supra* note 205, at 64.

233. *See, e.g.*, John V. Jacobi, *Medicaid Evolution for the 21st Century*, 102 KY. L.J. 357, 357–58, 364–69 (2013) (analyzing the criticism that "Medicaid is 'broken'").

force states to undertake certain actions, even when it exceeds the parameters of federal power. In 2012, the Supreme Court ruled that the federal government could not require states to expand their Medicaid programs after the federal government threatened to remove all Medicaid funding from states that refused to expand Medicaid.[234] Thus, cooperative federalism programs can create situations in which the federal government has additional opportunities to exceed its jurisdiction. Nevertheless, similar to how section 1115 waivers permit "experimental, pilot, or demonstration project[s]" that would likely further specified goals outlined in the Medicaid statute, a cooperative program for regulating the life sciences could facilitate experimental projects likely to assist in promoting the objectives of both the FDCA and state statutes related to the practice of medicine, namely public health and safety.[235]

2. Communicable Disease Prevention

Both the states and the federal government share responsibility for preventing the spread of communicable diseases.[236] The most liberty-restricting of those shared responsibilities include isolation, which separates infected individuals from the rest of the population, and quarantine, which restricts the movements of those who may have been exposed to an infectious disease.[237] State jurisdiction over the spread of disease stems from states' historic police powers arising from the Tenth Amendment.[238] All states have statutes related to quarantine or isolation.[239] Local governments have also instituted isolation measures.[240]

States originally instituted quarantine practice exclusively, but Congress eventually enacted federal legislation governing quarantine.[241] Today, the PHSA provides federal quarantine jurisdiction.[242] As a constitutional matter, the federal power over quarantine stems from the Commerce Clause.[243] Currently, the federal government's authority to quarantine individuals lies with the Centers for Disease Control and Prevention

234. Nat'l Fed'n of Indep. Bus. v. Sebelius, 567 U.S. 519, 580–87 (2012).

235. 42 U.S.C. § 1315 (2018); *About Section 1115 Demonstrations*, *supra* note 224.

236. *See* 42 U.S.C. §§ 264(a), 290bb-21(a); Polly J. Price, *Do State Lines Make Public Health Emergencies Worse? Federal Versus State Control of Quarantine*, 67 EMORY L.J. 491, 498 (2018) ("All U.S. states provide for isolation or quarantine by statute.").

237. *See* Price, *supra* note 236, at 496–98.

238. *See, e.g.*, JARED P. COLE, CONG. RESEARCH SERV., RL 33201, FEDERAL AND STATE QUARANTINE AND ISOLATION AUTHORITY 6 (2014) (discussing the "primary authority for quarantine and isolation exists at the state level as an exercise of the state's police power[s,]" derived from the Tenth Amendment of the Constitution).

239. *See* Price, *supra* note 236, at 498.

240. *See, e.g.*, *id.* at 509 (discussing the City of Milford, Connecticut, imposing a ban on a student from elementary school for twenty-one days after a family trip to Nigeria during the 2014 Ebola outbreak although there were no cases of Ebola in Nigeria).

241. *See History of Quarantine*, CTRS. FOR DISEASE CONTROL & PREVENTION, http://www.cdc.gov/quarantine/historyquarantine.html [https://perma.cc/3BL4-6X7J] (last updated Jan. 10, 2012).

242. *See Legal Authorities for Isolation and Quarantine*, CTRS. FOR DISEASE CONTROL & PREVENTION, http://www.cdc.gov/quarantine/aboutlawsregulationsquarantineisolation.html [https://perma.cc/MX34-L434] (last updated Oct. 8, 2014).

243. *Id.*

(CDC).[244] The CDC operates quarantine stations at various points of entry into the United States, including airports, land border crossings, and ports.[245] The last time the federal government instituted large-scale quarantine and isolation measures was in 1918 during an influenza outbreak.[246]

State and federal cooperation is already an important aspect of the public health laws that prevent the transmission of communicable diseases. The PHSA already requires the Secretary of HHS to

> encourage cooperative activities between the States with respect to comprehensive and continuing planning as to their current and future health needs, the establishment and maintenance of adequate public health services, and otherwise carrying out public health activities. The Secretary is also authorized to train personnel for State and local health work.[247]

Moreover, the HHS, which includes a number of federal agencies, including the CDC, FDA, and NIH, is authorized to accept assistance from state and local authorities "in the enforcement of quarantine regulations made pursuant to [United States Code Title 42, Chapter 6A]."[248] Similarly,

> [t]he Secretary [of HHS] shall also assist States and their political subdivisions in the prevention and suppression of communicable diseases and with respect to other public health matters, shall cooperate with and aid State and local authorities in the enforcement of their quarantine and other health regulations, and shall advise the several States on matters relating to the preservation and improvement of the public health.[249]

Beyond the spirit of cooperation in communicable disease prevention, the statute also directs the HHS to cooperate with "[s]tate and local authorities . . . in the enforcement of . . . other health regulations and . . . matters relating to the preservation and improvement of the public health."[250] Moreover, states (and the federal government) regulate blood products, for example, to prevent the spread of disease, an action that has withstood a preemption challenge in the Supreme Court.[251]

Commentators have criticized state governments as being "especially prone" to a politically driven response to an epidemic that might manifest as an "overly restrictive and counterproductive use of quarantine."[252] Recently, the CDC cooperated with state

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244. Price, *supra* note 236, at 514 (citing COLE, *supra* note 238, at 2).

245. *See U.S. Quarantine Stations*, CTRS. FOR DISEASE CONTROL & PREVENTION, http://www.cdc.gov/quarantine/quarantine-stations-us.html [https://perma.cc/V7P5-Y472] (last updated Sept. 29, 2017).

246. *See Legal Authorities for Isolation and Quarantine*, *supra* note 242.

247. 42 U.S.C. § 243(b) (2018); *see also* Price, *supra* note 236, at 512–14 (arguing that the federal government's power over preventing the spread of infectious disease is greater than simply cooperating at a state's request); *id.* at 518–19 (analyzing a preemption clause that was added to the PHSA in 2002).

248. 42 U.S.C. § 243(a); *see also HHS Agencies & Offices*, U.S. DEP'T HEALTH & HUM. SERVS., http://www.hhs.gov/about/agencies/hhs-agencies-and-offices/index.html [https://perma.cc/JT7G-FN3A] (last updated Oct. 27, 2015).

249. 42 U.S.C. § 243(a).

250. *See id.*

251. *See* Hillsborough Cty. v. Automated Med. Labs., Inc., 471 U.S. 707, 714–16 (1985).

252. *See* Price, *supra* note 236, at 500.

governments that instituted quarantine measures during the 2014 Ebola outbreak.[253] Others characterized this as a deference to state governments as the CDC's position was that these quarantine measures were unnecessary.[254]

State police powers also manifest in state statutes related to vaccinations.[255] The FDA approves vaccines on the basis of safety even though vaccines, like other FDA-approved products, are "neither perfectly safe nor perfectly effective."[256] All states impose vaccine requirements on children who will be attending public school.[257] The federal government also provides grants to states that support their childhood vaccination programs.[258] Thus, the federal government approves the tools that are the subjects of state statutes and programs related to public health goals. State and federal cooperation on communicable disease prevention offers a model in which state and federal governments routinely interact in the realm of public health. Ultimately, a cooperative framework for regulating innovative therapies would comport with previously created statutory requirements calling for state and federal cooperation in furtherance of the public health.

3. Food Regulation

The FDA already cooperates with states in the area of food regulation and should apply the cooperative spirit used in food regulation to the regulation of innovative therapies. For example, the National Shellfish Sanitation Program is a "federal/state cooperative program recognized by the U.S. Food and Drug Administration (FDA) and the Interstate Shellfish Sanitation Conference for the sanitary control of shellfish

253. *See id.* at 505; Kyle Edwards et al., *Why the C.D.C.'s Power To Quarantine Should Worry U*s, N.Y. TIMES (Jan. 23, 2017), http://www.nytimes.com/2017/01/23/opinion/why-the-cdcs-power-to-quarantine-should-worry-us.html [https://perma.cc/RJT8-4YTG]; Marc Santora, *First Patient Quarantined Under Strict New Policy Tests Negative for Ebola*, N.Y. TIMES (Oct. 24, 2014), http://www.nytimes.com/2014/10/25/nyregion/new-york-ebola-case-craig-spencer.html [https://perma.cc/LAA5-XB2H].

254. *See* Price, *supra* note 236, at 524.

255. *See, e.g.*, Zucht v. King, 260 U.S. 174, 177 (1922); Jacobson v. Massachusetts, 197 U.S. 11, 25–26, 39 (1905); *id.* at 34 (discussing *Viemeister v. White*, 72 N.E. 97 (N.Y. 1904), a case involving a state statute related to vaccinations in New York).

256. Kevin M. Malone & Alan R. Hinman, *Vaccination Mandates: The Public Health Imperative and Individual Rights*, *in* LAW IN PUBLIC HEALTH PRACTICE 338, 339–41 (Richard A. Goodman et al. eds., 2007); *Vaccines*, FDA, http://www.fda.gov/vaccines-blood-biologics/vaccines [https://perma.cc/LME8-59CF] (last updated July 5, 2019); *see also* 21 U.S.C. § 393(b)(2)(C) (2018); 42 U.S.C. § 262(a)(2)(C)(i)(1) (2018) (noting that approval of biological products is based on whether the product is "safe, pure, and potent").

257. *See* WEN S. SHEN, CONG. RESEARCH SERV., LSB10300, AN OVERVIEW OF STATE AND FEDERAL AUTHORITY TO IMPOSE VACCINATION REQUIREMENTS 2 (2019); James G. Hodge, Jr. & Lawrence O. Gostin, *School Vaccination Requirements: Historical, Social, and Legal Perspectives*, 90 KY. L.J. 831, 833 (2002); *id.* at 869–73 (illustrating the different vaccinations required by statute within each state); Dorit Rubinstein Reiss & Lois A. Weithorn, *Responding to the Childhood Vaccination Crisis: Legal Frameworks and Tools in the Context of Parental Vaccine Refusal*, 63 BUFF. L. REV. 881, 892 (2015).

258. 42 U.S.C. § 247b(a); Malone & Hinman, *supra* note 256, at 343. For more on federal funding of public health initiatives, see, for example, Polly J. Price, *Sovereignty, Citizenship, and Public Health in the United States*, 17 N.Y.U. J. LEGIS. & PUB. POL'Y 919, 950–55 (2014); *Prevention and Public Health Fund*, U.S DEP'T HEALTH & HUM. Servs., http://www.hhs.gov/open/prevention/index.html [https://perma.cc/7BMX-3Z6J] (last updated Dec. 16, 2016).

produced and sold for human consumption."[259] The National Shellfish Sanitation Program also "include[s] program guidelines, State growing area classification and dealer certification programs, and FDA evaluation of State program elements."[260]

Similarly, the FDA maintains a cooperative program in order to aid state agencies with the regulation of retail food providers as over "3,000 state, local and tribal agencies have primary responsibility to regulate the retail food and foodservice industries in the United States."[261] In this program, similar to other federal cooperative programs, the FDA offers model regulations, guidance, "training, program evaluation, and technical assistance."[262] Cooperation in food regulation is another instance of a cooperative program in which the federal government offers its expertise and assistance to state governments in the regulation of a matter of both local and national importance.

4. Nuclear Medicine

States already regulate one of the tools used in the practice of medicine, radioisotopes, through a program in which federal authority is relinquished to the states.[263] While this is not a cooperative program of shared (or concurrent) jurisdiction in the way that other programs related to public health are, many aspects of the program are applicable to the structuring of a state-federal program that would regulate innovative therapies.

Jurisdictional aggrandizement is not the goal of every federal agency, and some agencies aim to include states within the regulatory system.[264] The U.S. Nuclear

259. *National Shellfish Sanitation Program (NSSP)*, FDA, http://www.fda.gov/food/guidanceregulation/federalstatefoodprograms/ucm2006754.htm [https://perma.cc/FUW9-WY6D] (last updated Oct. 17, 2018) ("Participants in the NSSP include agencies from shellfish producing and non-producing States, FDA, EPA, [National Oceanic and Atmospheric Administration], and the shellfish industry. Under international agreements with FDA, foreign governments also participate in the NSSP.").

260. *Id.*

261. *Retail Food Protection*, FDA, http://www.fda.gov/Food/GuidanceRegulation/RetailFoodProtection/default.htm [https://perma.cc/N8EW-ASKU] (last updated May 20, 2019).

262. *Id.*

263. *See, e.g.*, *Agreement State Program*, U.S. NUCLEAR REG. COMMISSION, http://www.nrc.gov/about-nrc/state-tribal/agreement-states.html [https://perma.cc/U2U5-W2Q5] (last updated Dec. 14, 2018) ("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.").

264. *See id.* For more on federal agency efforts, including those of the FDA, to aggrandize their jurisdiction, see, for example, Stephen Breyer, *Judicial Review of Questions of Law and Policy*, 38 ADMIN. L. REV. 363, 371 (1986) ("Courts sometimes fear that certain agencies suffer from 'tunnel vision' and as a result might seek to expand their power beyond the authority that Congress gave them." (citing Hi-Craft Clothing Co. v. NLRB, 660 F.2d 910, 916 (3d Cir. 1981))); Noah, *Administrative Arm-Twisting*, *supra* note 140, at 911–12; Lars Noah, *Interpreting Agency Enabling Acts: Misplaced Metaphors in Administrative Law*, 41 WM. & MARY L. REV. 1463, 1487 (2000) ("Concerns about agency tendencies toward expansion have long existed. . . . [T]he insights of public choice theory suggest that agency officials may act to further their self-interest, whether by aggrandizing their own powers or placating powerful interest groups."); Noah, *Little Agency That Could*, *supra* note 55, at 902–17. *See generally Hi-Craft Clothing*, 660 F.2d at 916 ("The more intense scrutiny that is appropriate when the agency interprets its own authority may be grounded in the unspoken premise that government agencies have a tendency to swell, not shrink, and are likely to have an expansive view of their mission. Not surprisingly, therefore, an agency ruling that broadens its own jurisdiction is examined carefully.").

Regulatory Commission (NRC) relinquishes regulatory authority over certain types of nuclear material to individual states through its Agreement State Program so that those states can regulate civilian uses of nuclear material that have lower proliferation concerns such as the use of isotopes in medical treatment.[265] The goals provided in section 274 of the Atomic Energy Act could be a useful model for changing the system for regulating innovative therapies.[266] The goals of the Agreement State Program include recognizing that states have an interest in civilian uses of nuclear energy even though the federal government mostly regulates the industry, recognizing the necessity of creating cooperative programs between the states and the federal government, "promot[ing] an orderly regulatory pattern," and effectively coordinating state and federal regulatory efforts.[267] While the regulation of nuclear materials differs from the regulation and distribution of jurisdiction over innovative medical techniques, the NRC's Agreement State Program represents an example of how the federal government can cooperatively govern with individual states as it relates to issues that impact the practice of medicine.[268] Further, the NRC created its Agreement State Program in response to state concerns regarding their role in the regulation of radioactive materials in light of the establishment of the NRC.[269]

The NRC's Agreement State Program, created pursuant to section 274b of the Atomic Energy Act, allows states with "adequate and compatible" regulatory programs to regulate "source, byproduct and small quantities of special nuclear material."[270] Legally, the NRC relinquishes or discontinues its "authority over [the] source, byproduct and small quantities of special nuclear material" in an Agreement State and then that

265. *See, e.g.*, *Agreement State Program, supra* note 263.

266. *See* Act of Sept. 23, 1959, Pub. L. No. 86-373, sec. 1, § 274, 73 Stat. 688 (1959) (codified as amended at 42 U.S.C. § 2021 (2018)).

267. *Id.*; *see also Agreement State Program, supra* note 263.

268. *See Agreement States Program*, *supra* note 263; *see also* 42 U.S.C. §§ 2012–14 (providing an overview of federal regulation of the civilian use of nuclear power).

269. *See* Statement of Principles and Policy for the Agreement State Program; Policy Statement on Adequacy and Compatibility of Agreement State Programs, 62 Fed. Reg. 46,517, 46,519 (Sept. 3, 1997), http://www.gpo.gov/fdsys/pkg/FR-1997-09-03/pdf/97-23330.pdf [https://perma.cc/P93C-7QGR] ("The Atomic Energy Act of 1954 did not specify a role for the States in regulating the use of nuclear materials. Many States were concerned as to what their responsibilities in this area might be and expressed interest in seeing that the boundaries of Federal and State authority were clearly defined. This need for clarification was particularly important in view of the fact that although the Federal government retained sole responsibility for protecting public health and safety from the radiation hazards of byproduct, source, and special nuclear material, the responsibility for protecting the public from the radiation hazards of other sources such as x-ray machines and radium had been borne for many years by the States. Consequently, in 1959 Congress enacted Section 274 of the Atomic Energy Act to establish a statutory framework under which States could assume certain regulatory jurisdiction over byproduct, source, and special nuclear material in quantities less than a critical mass.").

270. *Frequently Asked Questions on the Agreement State Program and the Wyoming Agreement State Application*, U.S. NUCLEAR REG. COMMISSION, http://www.nrc.gov/about-nrc/state-tribal/agreement-states/wyoming-faq.html [https://perma.cc/8TRC-2LXN] (last updated Aug. 31, 2017); *see also* 42 U.S.C. § 2021(b), (d). For more on the NRC's evaluation of an Agreement State Program's adequacy and compatibility, see Agreement State Program Policy Statement, 82 Fed. Reg. 46,840, 46,841–43 (Oct. 6, 2017), http://www.gpo.gov/fdsys/pkg/FR-2017-10-06/pdf/2017-21542.pdf [https://perma.cc/6AXR-QDH8]. *See generally* Statement of Principles and Policy for the Agreement State Program; Policy Statement on Adequacy and Compatibility of Agreement State Programs, 62 Fed. Reg. at 46,518–25.

state regulates those categories of radioactive materials.[271] Currently, thirty-seven states participate in the Agreement State Program and those states regulate eighty-six percent of the nation's licenses for "source, byproduct and small quantities of special nuclear material."[272] The NRC periodically reviews those state programs, including "legislation, regulations or other legally binding provisions," for adequacy and compatibility with federal regulations.[273] Agreement States fund their own programs although the NRC does offer training.[274]

The materials used in nuclear medicine, which is "the use of radioactive materials in diagnostic or therapeutic procedures, most notably treatments for various forms of cancer," are eligible for the Agreement State Program.[275] The FDA is already peripherally involved within the NRC's jurisdictional scheme for the regulation of the medical use of nuclear materials as the

> NRC (or the responsible Agreement State) also regulates the manufacture and distribution of these products. The [FDA] oversees the good practices in the manufacturing of radiopharmaceuticals, medical devices, and radiation-producing x-ray machines and accelerators. The states regulate the practices of medicine and pharmacy and administer programs associated with radiation-producing x-ray machines and accelerators.[276]

As such, regulatory authority in the area of nuclear medicine is already shared among federal, state, and local authorities in a necessarily cooperative framework.[277]

Section 274 of the Atomic Energy Act specifically provides for federal cooperation with state governments in the regulation of certain types of nuclear material.[278] Congress added this state-federal regulatory framework to the Atomic Energy Act in response to state concerns "as to what their responsibilities in th[e] area [of "regulating the use of

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271. *See Frequently Asked Questions on the Agreement State Program and the Wyoming Agreement State Application*, *supra* note 270.

272. *Id.*

273. *Id.*

274. *See* Statement of Principles and Policy for the Agreement State Program; Policy Statement on Adequacy and Compatibility of Agreement State Programs, 62 Fed. Reg. at 46,521 ("Currently, Section 274 does not allow federal funding for the administration of Agreement State radiation control programs. Section 274 permits the NRC to offer training and other assistance to a State in anticipation of entering into an Agreement with NRC, however, it is NRC policy not to fund the establishment of new Agreement State programs.").

275. *Frequently Asked Questions on the Agreement State Program and the Wyoming Agreement State Application*, *supra* note 270; *Nuclear Medicine: What It Is—and Isn't*, U.S. NUCLEAR REG. COMMISSION (Oct. 2, 2017), http://www.nrc.gov/about-nrc/radiation/protects-you/nuclear-medicine.html [https://perma.cc/WY7M-BKK9].

276. *Medical Uses of Nuclear Materials*, U.S. NUCLEAR REG. COMMISSION, http://www.nrc.gov/materials/miau/med-use.html [https://perma.cc/VAT7-MX23] (last updated July 7, 2017) (citation omitted) ("Regulatory authority over the medical use of ionizing radiation is shared among several Federal, state, and local government agencies. NRC (or the responsible Agreement State) has regulatory authority over the possession and use of byproduct, source, or special nuclear material in medicine. Byproduct material is used in some calibration sources, radioactive drugs, bone mineral analyzers, portable fluoroscopic imaging devices, brachytherapy sources and devices, gamma stereotactical surgery devices, and teletherapy units used in medicine. Source material is used for radiation shielding and counterweights in medical devices. A few cardiac pacemakers are still powered by special nuclear material batteries.").

277. *Id.*

278. Act of Sept. 23, 1959, Pub. L. No. 86-373, sec. 1, § 274, 73 Stat. 688 (1959) (codified as amended at 42 U.S.C. § 2021 (2018)).

nuclear materials"] might be and [their] expressed interest in seeing that the boundaries of Federal and State authority were clearly defined."[279]

In sum, the example of federal and state cooperation in the regulation of nuclear material offers at least three lessons. First, it was created in response to state concerns about their role in the regulation of an important matter of both local and national concern.[280] Second, the system in which the NRC relinquishes jurisdiction stands in stark contrast to FDA efforts to aggrandize its jurisdiction.[281] Third, as illustrated by the thirty-eight states that participate in the NRC Agreement State Program, states may opt to participate in a state-federal regulatory program once they have the opportunity.[282] The current NRC Agreement States include a number of innovators in medicine, including stem cell research: New York, California, Texas, Maryland, and Florida.[283] Other states might follow the lead of these innovative states and implement their same programs.[284] The NRC Agreement State Program is a state-federal cooperative program that provides a counterargument to the anticipated criticism that states do not have the expertise to regulate complex scientific processes. Further, the NRC Agreement State Program reveals that even if federal jurisdiction is unquestionable, there are benefits in sharing jurisdiction with states for certain regulatory functions.

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The same nuclear regulatory goals of "promot[ing] an orderly regulatory pattern" and effectively coordinating state and federal regulatory efforts also exist with the regulation of innovative life sciences programs.[285] These goals are important not only to life sciences development but also to the orderly transition of safe and effective innovative therapies from the laboratory to clinical use.[286] Recently, healthcare policy has been categorized as "ha[ving] been shaped principally by cooperation and

279. Statement of Principles and Policy for the Agreement State Program; Policy Statement on Adequacy and Compatibility of Agreement State Programs, 62 Fed. Reg. at 46,519; *id.* at 46,523 (discussing the purpose of section 274 in the "federal-State regulatory framework" for radioactive materials).

280. *See* 42 U.S.C. § 2021(a); *supra* note 269 and accompanying text.

281. *Compare* Statement of Principles and Policy for the Agreement State Program, 62 Fed. Reg. at 46,519, *with* Noah, *Administrative Arm-Twisting*, *supra* note 138, at 878–82 (discussing an example of the FDA imposing "apparently unauthorized conditions on applicants").

282. *See Agreement State Program*, *supra* note 263 (noting that the Agreement State Program "provides assistance to States *expressing interest* in establishing programs" (emphasis added)). Kentucky was the first state to join the Agreement States Program in 1962, and today, there are thirty-eight Agreement States. *Id.* Currently, Vermont is pursuing an application to become an Agreement State. *Id.*

283. *See NRC: NMSS—State Regulations and Legislation*, U.S. NUCLEAR REG. COMMISSION, http://scp.nrc.gov/rulemaking.html [https://perma.cc/749L-U9ZD] (last updated Oct. 1, 2019).

284. *See, e.g.*, Michael A. Livermore, *The Perils of Experimentation*, 126 YALE L.J. 636, 650 (2017) ("There are a number of mechanisms through which policy diffusion takes place. Competitive pressures, such as 'races to the bottom' or 'races to the top,' can prompt states to adopt policies that are similar to each other, and policy adoption in one jurisdiction may lead to copycat behavior in other jurisdictions seeking to minimize any competitive disadvantage. Asymmetries in size or influence may allow 'strong' jurisdictions to foist their policy preferences on 'weak' jurisdictions, for example by setting a product standard in a large market that all manufacturers must meet." (footnote omitted)).

285. 42 U.S.C. § 2021(a); *see also* Livermore, *supra* note 284, at 651–52.

286. *See* Livermore, *supra* note 284, 651–52.

contestation between the federal executive branch and different groups of states."[287] A cooperative program for the regulation of innovative therapies would be another state-federal cooperative program that would improve the ability of the agency to efficiently regulate complex scientific processes whose use in medical practice is expanding in scope. As emphasized by the passage and implementation of the ACA and Medicaid, state-federal cooperation, or cooperative federalism, is an integral part of the current healthcare regulatory system.[288] Similarly, it is an integral part of much of public health law, as in many areas, that state and federal jurisdiction overlap.[289] Often such "cooperative" characterizations in the context of healthcare focus on the Medicaid expansion (or nonexpansion, depending on one's state).[290] Health exchanges have also been characterized as "involv[ing] an unanticipated merging of state and federal authority."[291]

The cooperative programs analyzed in this Part provide various options for regulating innovative therapies. The remainder of this Article incorporates the best practices from these cooperative programs into this Article's proposed cooperative framework for the regulation of innovative therapies.

C. Goals of the Cooperative Framework

Legal structures can impact access to innovation and the costs of accessing those innovations once they are on the market.[292] The cooperative framework aims to increase the pace of innovation, improve access to innovation, minimize regulatory hurdles to innovation, increase transparency within the regulatory system, and provide a diversity of inputs into regulatory decisionmaking.

One might ask, "Why not just expand the jurisdiction of the FDA instead of emphasizing the role of the states?" There are at least four reasons to preserve state jurisdiction over the practice of medicine, especially as it relates to innovative therapies. First, states already have the legal infrastructure for regulating the practice of medicine. Second, states serve as an important complement to federal regulation. As noted in Section I, the Supreme Court observed that the FDA lacks the resources to monitor the thousands of products that it approves for marketing in the United States.[293] In this climate "lawyers and their clients often find themselves serving as drug safety researchers of last resort" as they discover harms of products after FDA approval.[294]

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287. Bulman-Pozen, *Preemption*, *supra* note 22, at 2036; *see also* Gluck & Huberfeld, *supra* note 227, at 1733–34.

288. *See* Bulman-Pozen, *Preemption*, *supra* note 22, at 2035–37; *see also Federalism*, BLACK'S LAW DICTIONARY (10th ed. 2014) (defining "cooperative federalism" as the "[d]istribution of power between the federal government and the states whereby each recognizes the powers of the other while jointly engaging in certain governmental functions"); Metzger, *The Constitutional Duty*, *supra* note 22, at 1852–53.

289. McCuskey, *Agency Imprimatur*, *supra* note 164, at 1109.

290. *See, e.g.*, Gluck & Huberfeld, *supra* note 227, at 1694–95.

291. Bulman-Pozen, *Executive Federalism*, *supra* note 214, at 978. For more on healthcare exchanges, see also Gluck & Huberfeld, *supra* note 227, at 1701–02, 1797–98.

292. *See, e.g.*, Merrill, *The Architecture*, *supra* note 23, at 1755.

293. *See supra* notes 79–80 and accompanying text.

294. Aaron S. Kesselheim & Jerry Avorn, *The Role of Litigation in Defining Drug Risks*, 297 JAMA 308, 311 (2007); *see also* Wyeth v. Levine, 555 U.S. 555, 578–79 (2009).

These harms often manifest through state tort lawsuits, which thus serve a valuable role in healthcare.[295] Third, in light of the states' benefit of being "closer" to patients than the federal government, strengthening the state-monitoring role would serve to further patient health.[296] Fourth, to the extent that political or social views manifest in the federal regulatory process, increasing the role of states in that process could create a diversity of views.[297]

In a cooperative system for regulating innovative therapies, states with experience regulating and encouraging innovation in the life sciences, such as California, Massachusetts, and Maryland, would be encouraged to have a larger stake in the regulation of the life sciences.[298] As such, these states might be incentivized to participate in such a system as encouraging innovation in the life sciences would align with the states' current priorities.[299] Further, many of these states' support for innovation in the life sciences became apparent when those states funded research, including stem cell research, that the federal government would not fund.[300] Texas and Florida might opt into such a system as the increased availability of experimental stem cell treatments in those states and the issuance of state legislation addressing stem cell treatments demonstrates.[301] Some states may decide to opt into such a regime after examining the

295. *Wyeth*, 555 U.S. at 578–79 ("State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly. They also serve a distinct compensatory function that may motivate injured persons to come forward with information."); Kesselheim & Avorn, *supra* note 294, at 310–11.

296. *See* Seidenfeld, *The Bounds*, *supra* note 230, at 24 ("[T]he federal government does not have detailed knowledge of the specific populations it would have to serve, and unlike states, the federal government does not have an extensive system in place to provide social services to the poor, and hence would have to invest in creating such a system.").

297. *See* Bulman-Pozen, *Preemption*, *supra* note 22, at 2031.

298. *See supra* notes 86, 88, 133 and accompanying text; *see also, e.g.*, *Investing in the State of Innovation*, MASS. LIFE SCI. CTR., http://www.masslifesciences.com/about/ [https://perma.cc/BYM7-5ZFF] (last visited Feb. 1, 2020). Additionally, California is one of "[a] few states" that already has agencies "that complement the FDA through inspection, research, and regulation of drugs and devices within the state." Sharkey, *Federalism Accountability*, *supra* note 19, at 2160.

299. See *supra* notes 84–88 and accompanying text for a discussion of states' interests in medical innovation.

300. *See supra* notes 85, 88 and accompanying text. For more on state initiatives funding stem cell research, see JUDITH A. JOHNSON & ERIN D. WILLIAMS, CONG. RESEARCH SERV., RL33524, STEM CELL RESEARCH: STATE INITIATIVES 2–8 (2006), http://stemcells.nih.gov/staticresources/research/GW-State-Funding.pdf [https://perma.cc/83TK-E8VD]; *State Initiatives for Stem Cell Research*, NAT'L INSTS. HEALTH, http://stemcells.nih.gov/research/state-research.htm [https://perma.cc/EP2V-YX8M] (last visited Feb. 1, 2020).

301. *See* TEX. HEALTH & SAFETY CODE ANN. § 1003.002 (West 2019); Bulman-Pozen & Gerken, *supra* note 212, at 1277 (noting that California's goal as a "super-regulator" under the Clean Air Act is "to implement a regulatory regime that will prod national change"); Kelly Servick, *Texas Has Sanctioned Unapproved Stem Cell Therapies. Will It Change Anything?*, SCI. (June 15, 2017, 11:15 AM), http://www.sciencemag.org/news/2017/06/texas-has-sanctioned-unapproved-stem-cell-therapies-will-it-change-anything [https://perma.cc/Y2HH-QJ36]; *see also* Ackerman, *supra* note 142 (offering similar criticisms of stem cell treatments available in Texas and an overview of the motivation for Texas's statute increasing access to stem cell treatments in the state); Lade, *supra* note 142 (criticizing the existence of for profit stem cell clinics in Florida and noting the relative prevalence of stem cell clinics in California and Florida compared to the rest of the United States). At the same time, it is possible that Texas and Florida might also be states that would be opposed to certain medical innovations. *See, e.g.*, Carbone, *supra* note 85, at 356 ("Florida, Illinois, and Texas further restrict the [surrogacy] procedure to those who can demonstrate medical need.").

experiences of other states within the regime, thus allowing for federalism's goals of policy experimentation and diffusion.[302] The results of this experimentation could be relevant not only to other states but also to the federal government, just as it was in the lead up to the creation of the FDCA.[303]

A cooperative system changes the system of federal regulation, although it does not eliminate federal regulation altogether. Instead, the cooperative system of regulation ensures or aims to ensure regulation within appropriate jurisdictional boundaries.[304] As noted in Section I, the regulation of innovation in the life sciences involves both state and federal jurisdiction as, despite the operation of federal law in certain areas, life sciences regulation and public health regulation have yet to become areas of exclusive federal jurisdiction.[305] By capitalizing on the existence of state jurisdiction, the regulatory system can expand the resources available to regulate innovative therapies, which would address a number of concerns related to the resource constraints that the FDA faces.[306] Additionally, states may not necessarily regulate in a manner that is different from the federal government. For example, examining abortion regulation in the United States, the existence of a federal baseline that states can then modify might lead to a regulatory system that is normatively undesirable. Nevertheless, the addition of states into the regulatory system offers, at the very least, a diversity of views.[307] A diversity of views could also lead to increased access to therapies within the United States, as it would differ from the current federal risk-averse (and possibly politically motivated) baseline, which would be significant especially for those who lack the means to travel abroad or the means to thoroughly investigate therapies available in the United States.

While this Article does not argue for waivers per se, this Article draws from certain aspects of waiver-based programs such as Medicaid in constructing its structural framework. Ideally, a cooperative governance structure could remove the political views of the executive and legislative branches from the regulatory process so that federal regulation focuses solely on safety and efficacy and not social views on the acceptability

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302. *See* Livermore, *supra* note 284, at 650 ("[P]olicy adoption in one jurisdiction may lead to copycat behavior in other jurisdictions seeking to minimize any competitive disadvantage.").

303. For more on state statutes related to food and drug regulation before the creation of the 1906 Federal Pure Food and Drug Act, see Frank R. Strong, *Cooperative Federalism*, 23 IOWA L. REV. 459, 479–82 (1938).

304. See *supra* notes 154–156 for a discussion of *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 125–26 (2000), in which the Supreme Court assessed the limits of federal agency jurisdiction.

305. *See, e.g.*, William W. Buzbee, *Asymmetrical Regulation: Risk, Preemption, and the Floor/Ceiling Distinction*, 82 N.Y.U. L. REV. 1547, 1552 (2007) [hereinafter Buzbee, *Asymmetrical Regulation*] ("Outright preemption remains a choice embraced in an array of areas, especially where laws or regulations mandate specific product features or engineering. So-called 'complete preemption' is also found in a few areas where Congress has defined its role as exclusive, often in connection with special solicitude for a particular industry such as nuclear power, or a broad social goal such as childhood vaccination." (footnote omitted)); *id.* at 1554 ("Federal floors preclude less stringent state and local regulation, but allow for additional and more stringent regulation and typically are accompanied by savings clauses and cooperative regulatory structures."); *see also* Hillsborough Cty. v. Automated Med. Labs., Inc., 471 U.S. 707, 709–23 (1985) (rejecting arguments for the federal preemption of local ordinances related to the collection of plasma).

306. See *supra* notes 79–80 and accompanying text regarding the resource constraints that the FDA faces.

307. *See* Nat'l Fed'n of Indep. Bus. v. Sebelius, 567 U.S. 519, 536 (2012) ("Because the police power is controlled by 50 different States instead of one national sovereign, the facets of governing that touch on citizens' daily lives are normally administered by smaller governments closer to the governed.").

of certain therapies. However, even if the cooperative governance structure this Article recommends did not remove those political views, it could supplement the existing federal political views and diversify the political views available to decisionmakers. A regulatory scheme that incorporates state governments before the FDA decides whether to approve a product would not only render the federal regulatory process more transparent by introducing additional actors, but it would also introduce another check on the FDA's executive power.[308] Because creating a structural framework that includes the states would increase the number of actors who would actively participate in the regulatory process, transparency and diversity within the decision-making process would also increase.

For those innovative therapies that would involve ethically controversial products or procedures, the cooperative system would likely require a more transparent discussion of the difference between ethical opposition and the medical risks involved with the use of those technologies, and likely, at the state level.[309] States, in turn, could continue using their expertise in examining social and ethical considerations in regulation, instead of having their assessment foreclosed, as occurs in a federally based process.[310] In doing so, a cooperative process strikes a balance between federal experience with regulating pharmaceuticals, states' jurisdiction over the practice of medicine, and states' historic roles as "laboratories of experimentation."[311] A cooperative system of regulation could also be useful for techniques or medical treatments that are not emerging or the subject of burgeoning media or scientific interest, but still somewhat controversial, including the increased use of medical (and recreational) marijuana in the United States and the possible increase in products containing THC.[312] A cooperative solution also increases the number of parties available to monitor innovative therapies, as prior events have indicated that "[m]onitoring 'lies at the heart of the matter'" of the regulation of innovative therapies, especially where the FDA lacks resources to monitor the products that it already has exclusive jurisdiction over.[313]

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308. As will be detailed later in this Section, the state-federal committee would be a public committee. For more on how states can serve as checks to the federal executive branch, see Bulman-Pozen, *Federalism as a Safeguard*, *supra* note 22, at 486–501.

309. A future article will focus on the use of risk assessments in the regulation of life sciences innovation and pharmaceutical generation. That article will also explore how best to regulate life sciences innovations that involve ethical controversies, especially those involving germline modification of DNA.

310. See *supra* notes 147–151 and accompanying text for a discussion of the impact of social and political concerns in FDA regulation.

311. *See, e.g.*, New State Ice Co. v. Liebmann, 285 U.S. 262, 311 (1932) (Brandeis, J., dissenting); Bulman-Pozen & Gerken, *supra* note 212, at 1261.

312. *See* Rebecca L. Haffajee et al., *Behind Schedule—Reconciling Federal and State Marijuana Policy*, 379 NEW ENG. J. MED. 501, 501–02 (2018) (discussing state regulation of medical and recreational marijuana, federal regulation of marijuana, and the possible tensions between federal criminal law, federal regulatory law, and state decriminalization efforts); *see also FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD)*, FDA, http://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers [https://perma.cc/9XRL-ASPQ] (last updated Oct. 16, 2019) ("[D]elta-9-tetrahydrocannabinol (THC) . . . is considered the psychoactive component of cannabis.").

313. Sibbald, *supra* note 110, at 1612; *supra* note 110 and accompanying text; *see also* Wyeth v. Levine, 555 U.S. 555, 578–79 (2009) ("The FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as

Many of the disadvantages of a solution that incorporates the states, such as resource constraints and the possibility of capture, are similar to those that already exist at the federal level.[314] As such, concerns about regulatory capture, which could be an issue for innovative therapies that pharmaceutical companies create, will not be allayed.[315] Just as regulatory capture is a concern in federal regulation, it is also a concern in state regulation.[316] Thus, state agencies will also be susceptible to regulatory capture. At the same time, from the perspective of preventing capture, recognition of diverse jurisdictional powers might serve as an obstacle to capture by diffusing the targets. Also, states would be able to capture the federal government more easily. It has been suggested that stakeholders in certain debates should "focus their lobbying efforts on agencies and the rulemaking process, not (as is the current dominant strategy) exclusively on Congress."[317] This suggestion stems from the perspective that "[f]ederal agencies now play the dominant role in statutory interpretation."[318] A cooperative solution for regulating innovative therapies would diffuse targets for those seeking to capture decisionmakers in the regulatory process.

Another criticism that may arise is that there might be a race to the bottom in which various companies race to states with the most favorable (and underregulating) legislation in order to avoid regulatory requirements. There are at least two responses to this concern. First, a race to the bottom would still be one in which FDA regulation at the very least provided a "floor" of regulation as the regulation of medical products continues to exist.[319] As such, including states in the hybrid regime does not lead to complete decentralization of the regulation of innovative therapies as federal law persists.[320] Second, a race to the bottom is not the only response to more state regulation. For example, Delaware is well-known for its regulation of large, public corporations; however, that regulation has led to a robust system of regulation that is well regarded by corporate law scholars and most observers as opposed to little regulation or no regulation

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new risks emerge. State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly." (footnote omitted)); Buzbee, *Asymmetrical Regulation*, *supra* note 305, at 1616 ("Little 'learning by monitoring' will go on with no diversity of institutional actors and no reward for such action."); Sharkey, *Federalism Accountability*, *supra* note 19, at 2136 ("More specifically, several House Representatives charged that the FDA 'suffers from a high turnover rate of scientists, an inadequate information technology system, a weak organizational structure, and a rapidly declining inspection force.'").

314. *See, e.g.*, Nicholas Bagley, *Agency Hygiene*, 89 TEX. L. REV. 1, 2 (2010) ("[U]s[ing] the word 'capture' as shorthand for the phenomenon whereby regulated entities wield their superior organizational capacities to secure favorable agency outcomes at the expense of the diffuse public.").

315. *See, e.g.*, Jane R. Bambauer, *Dr. Robot*, 51 U.C. DAVIS L. REV. 383, 398 (2017) ("There is also a risk of anti-competitive maneuvering by the health tech firms themselves, at least the one that come to the table first. IBM's Watson team already has a very close working relationship with the FDA. The two are collaborating on a Blockchain project."); Stuart Minor Benjamin & Arti K. Rai, *Fixing Innovation Policy: A Structural Perspective*, 77 GEO. WASH. L. REV. 1, 40–41 (2008).

316. *See* Owen, *supra* note 24, at 204.

317. Sharkey, *Inside Agency Preemption*, *supra* note 182, at 526.

318. *Id.* at 521.

319. See *supra* Section I for a discussion of the practice-products divide and the federal regulation of medical products.

320. *See* Livermore, *supra* note 284, at 644 ("Managed experimentation in which the federal government provides incentives for policy innovation while setting national baseline standards that mitigate public choice failures at the local level is a better alternative to unfettered decentralization.").

at all.[321] Further, for those who do not view Delaware's regime as a race-to-the-top system of regulation, federal law, as administered through the U.S. Securities and Exchange Commission, still provides a federal floor in the same way that federal law, as administered through the FDA, does.[322] In the realm of innovative therapies, states would have an even stronger interest in patient health, due to the fact that, as state expenditures on Medicaid indicate, states already pay money to treat citizens' health problems. Further, states have an economic interest in life sciences innovation as evidenced through initiatives such as research grants, including those through stem cell funds.[323] Simply because states cooperate in the regulation of a certain technique does not mean that they have to create an entirely new regulatory structure. For example, Maryland has a statute that requires the application of federal research protections to research conducted in its state that would not otherwise fall under the jurisdiction of the federal government.[324] Third, a race-to-the-bottom argument must consider that the race to use innovative new technologies is not U.S.-centric; instead, not only are Americans willing to travel to other states to obtain innovative treatments, but many are willing to travel abroad, often to countries that are known to have little oversight over medical treatment.[325] An improvement in the U.S. regime of regulation could increase the pace with which Americans can access safe, innovative medical treatments here in the United States.

D. Structures that Institute the Goals of the Cooperative Framework

Administrative law scholarship has noted the inadequacies of various executive orders requiring agencies to consult with states throughout the regulatory process and to consider the federalism impacts of their regulatory actions.[326] Similarly,

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321. *See* Mark J. Roe, *Delaware's Competition*, 117 HARV. L. REV. 588, 594 (2003); Roberta Romano, *The States as a Laboratory: Legal Innovation and State Competition for Corporate Charters*, 23 YALE J. ON REG. 209, 212–14 (2006). *But see* William L. Cary, *Federalism and Corporate Law: Reflections upon Delaware*, 83 YALE L.J. 663, 670 (1974) ("Judicial decisions in Delaware illustrate that the courts have undertaken to carry out the 'public policy' of the state and create a 'favorable climate' for management. Consciously or unconsciously, fiduciary standards and the standards of fairness generally have been relaxed. In general, the judicial decisions can best be reconciled on the basis of a desire to foster incorporation in Delaware. It is not clear, however, that the revenue thermometer should replace the chancellor's foot. This trend should be reversed.").

322. *See* Robert B. Thompson & Hillary A. Sale, *Securities Fraud as Corporate Governance: Reflections upon Federalism*, 56 VAND. L. REV. 859, 860 (2003).

323. *See, e.g.*, VA. CODE ANN. § 32.1-162.31 (West 2019) (creating the Christopher Reeve Stem Cell Research Fund). For more on state stem cell initiatives, see JOHNSON & WILLIAMS, *supra* note 300, at 2–8.

324. MD. CODE ANN., HEALTH-GEN. § 13-2002 (West 2019) ("Notwithstanding any provision in the federal regulations on the protection of human subjects that limits the applicability of the federal regulations to certain research, [federal research protections] appl[y] to all research using a human subject.").

325. *See supra* notes 9–11.

326. *See, e.g.*, Exec. Order No. 13,132, 64 Fed. Reg. 43,255 (Aug. 10, 1999); Sharkey, *Federalism Accountability*, *supra* note 19, at 2163–64 (discussing the federalism impact statements (FISs) required by Executive Order 13,132 and agencies' responses, which have "either blithely ignored their responsibility to provide FISs or have gone to great lengths to obfuscate whether their preemption determinations have any federalism impact whatsoever"); *id.* at 2191–92 (noting that "agency disregard of state regulatory interests" has raised questions regarding "the boundaries of federal law and the outcome of clashes with state law"); *see also* Foote, *supra* note 180, at 1431–32 ("[C]onclu[ding] that agencies have failed to protect the states' interests in

notice-and-comment rulemaking is insufficient for the expression, consideration, and inclusion of state regulatory concerns into the regulatory process.[327] Administrative law scholarship often uses the FDA's behavior to illustrate the lack of consideration of federalism values in agency decisionmaking.[328] For example, even in spite of an executive order requiring agencies to consider federalism values, the effect of that order has been cursory statements in regulations.[329] That executive order has only resulted in the FDA making statements in the preamble to regulations such as, "Here, FDA has determined that the exercise of State authority conflicts with the exercise of Federal authority under the act"[330] and "Because we have determined that the act preempts State law because the exercise of State authority conflicts with the exercise of Federal authority under that statute, we need not construe our statutory rulemaking authority as required by section 4(b) of the Executive order."[331] In light of the lack of substantial compliance with previous requests to consider federalism values and the FDA's favoring of preemption, informal methods of including states are insufficient to ensure adequate consideration of state jurisdiction and a more permanent and structured method of including states in the regulation of innovative therapies is necessary.[332]

As many Supreme Court decisions have emphasized, including the recent Medicaid decision in *National Federation of Independent Business v. Sebelius*,[333] there are restraints on federal power and the ability of the federal government to commandeer state jurisdiction and autonomy.[334] The cooperative framework furthers state autonomy by targeting federal power for restriction. In sum, the federal power to hinder innovation and access to innovation should be severely limited in favor of state experimentation in the absence of a very high showing of harm.

To the extent that the FDA's guidance documents and other regulatory decisions that the FDA has undertaken involve a lack of transparency, a cooperative framework should adopt many of the transparency-inducing aspects of cooperative federalism

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health and safety as Congress intended that they do under the administrative preemption provisions."); Greve, *supra* note 26, at 604 (criticizing federalism impact statements).

327. Sharkey, *Federalism Accountability*, *supra* note 19, at 2137, 2139–40.

328. *See id.* See *infra* note 332 and accompanying text for a discussion of the FDA's preference for pro-preemption policies and their impact on the jurisdictional balance in regulating innovative therapies.

329. Sharkey, *Federalism Accountability*, *supra* note 19, at 2163–64. *But see id.* at 2164–68 (detailing other instances of FDA outreach to states although these focused on the solicitation of comments for proposed rules).

330. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3967 (Jan. 24, 2006) (codified at 21 C.F.R. pts. 201, 314, 601 (2019)).

331. *Id.* at 3967 n.10.

332. *See* Buzbee, *Preemption Hard Look Review*, *supra* note 146, at 1527–28 (discussing the FDA's "pro-preemption" position in regulation); *see also* Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3935 (asserting the FDA's view that "[s]tate law actions also threaten FDA's statutorily prescribed role as the expert Federal agency responsible for evaluating and regulating drugs").

333. 567 U.S. 519 (2012).

334. *See, e.g.*, *Sebelius*, 567 U.S. at 579–80; *see also* Strong, *supra* note 305, at 470 ("The Tenth Amendment, however, expressly reaffirms what is implicit in the body of the original Constitution—there is a limit to federal power, beyond which is the province of the states."). For more on the limits of federal jurisdiction, see, for example, Printz v. United States, 521 U.S. 898, 902, 925–36 (1997); New York v. United States, 505 U.S. 144, 149, 161–63 (1992).

programs, which include public hearings and consultations between various stakeholders.[335] Even though states are able to participate in the FDA's decisionmaking through mechanisms such as advisory committee meetings and agency requests for comments, a cooperative framework would acknowledge state jurisdiction and also provide more access to the regulatory decision-making process by rendering decisionmaking more of a joint effort.[336] The hope is that a cooperative regime, especially for those life sciences innovations that would involve ethically controversial methods and/or products, would likely require a more transparent discussion of the difference between ethical opposition and the medical risks involved with the use of those technologies. Further, the cooperative framework would encourage states not just to respond to innovative therapies through retroactive regulation such as through tort regimes (including malpractice laws) as well as through the licensing of professionals who administer those therapies, but also to develop more comprehensive regimes that focus on innovative therapies. The remainder of this Article provides some specific examples that exemplify this Article's cooperative framework.

1. Innovative Therapies Committee

The FDA already has scientific advisory committees; however, the recommendations of experts on these committees are not binding.[337] Building on the existence of these committees, this Article advocates for a type of committee that recognizes state jurisdiction. Environmental law, which contains numerous cooperative frameworks, provides a number of useful lessons for improving the regulation of innovative therapies.[338] In addition to decades of cooperative federalism, often through waivers, there are other statutory provisions from environmental law that would prove useful in acknowledging coexistent state-federal jurisdiction. While federal agencies have generally failed to meaningfully consider the implications of their actions on states and state jurisdiction, the Environmental Protection Agency has been recognized for its incorporation of federalism concerns into its regulatory process.[339] One way to further considerations of federalism is to insert a check into the regulatory structure. A committee similar to the Endangered Species Committee would be helpful.[340] The Endangered Species Committee, which was created by an amendment to the Endangered

335. *See, e.g.*, Hills, *supra* note 23, 887–88.

336. Sharkey, *States Versus FDA*, *supra* note 78, at 1626, 1628 (providing information on state opportunities to participate in the FDA drug approval process).

337. 21 U.S.C. § 355(n) (2018); *see also Advisory Committees*, FDA, http://www.fda.gov/AdvisoryCommittees/default.htm [https://perma.cc/9AC5-NG5R] (last visited Feb. 1, 2020).

338. *See, e.g.*, Owen, *supra* note 24, at 204; Hannah J. Wiseman, *Delegation and Disfunction*, 35 YALE J. ON REG. 233, 236 (2018).

339. *See, e.g.*, Sharkey, *Federalism Accountability*, *supra* note 19, at 2164 n.149 ("The EPA stands as a counterexample. It has been at the forefront in terms of providing internal guidance on how to conduct a suitable FIS consistent with the principles embodied in Executive Order 13,132."); *see also* Sharkey, *Inside Agency Preemption*, *supra* note 182, at 569–70 ("EPA and the states have developed a collaborative relationship as coregulators, particularly over the past twenty years. EPA has an internal Office of Congressional and Intergovernmental Relations ('OCIR') that coordinates a variety of state-EPA performance partnerships, such as the National Environmental Performance Partnership System ('NEPPS')."); *supra* notes 328–332 regarding the FDA and federalism concerns.

340. *See* 16 U.S.C. § 1536(e) (2018).

Species Act, is composed of federal officials from various agencies and "individual[s] from each affected State."[341] While an Innovative Therapies Committee would not operate with the same goals of the Endangered Species Committee, as the Endangered Species Committee can waive the application of federal law, an Innovative Therapies Committee could be structured similarly.[342]

As the Endangered Species Committee is composed of representatives from federal agencies that address issues related to environmental law and economics, an Innovative Therapies Committee could similarly include representatives from relevant operating agencies within the HHS and economic agencies. Thus, the membership of such a committee could include, paralleling the membership of the Endangered Species Committee,

(A) the Secretary of HHS,

(B) the Commissioner of the FDA,

(C) the Director of the NIH,

(D) the Chairman of the Council of Economic Advisors,

(E) the Chairman of the Federal Trade Commission,[343] and

(F) "individual[s] from each affected State."[344]

"[I]ndividual[s] from each affected state" would be defined differently than it is for the Endangered Species Committee, as "affected state" would be different in the case of innovative therapies.[345] Thus, the term "individual[s] from each affected State" could be defined as states that have established entities providing these innovative therapies or could be construed in a way that emphasizes interested state officials, such as those who are housed in state departments of public health or State Attorneys General.[346] If none of these departments were sufficient, in light of the suggestion in Part III.D.3 for state clearinghouses, in keeping with recent trends in state administrative law, states could create a new administrative agency to address the regulation of innovative therapies.[347]

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341. *Id.* § 1536(e)(3) (providing the membership of the Endangered Species Committee); *see also* Kate R. Bowers, *Saying What the Law Isn't: Legislative Delegations of Waiver Authority in Environmental Laws*, 34 HARV. ENVTL. L. REV. 257, 263 (2010).

342. *See* Bowers, *supra* note 341, at 265 (noting that "the Endangered Species Committee . . . normally decides whether waivers of the [Endangered Species Act] are warranted"); *see also* Barron & Rakoff, *supra* note 180, at 304.

343. The Federal Trade Commission (FTC) also exercises regulatory authority related to the use of drugs in the United States. *See, e.g.*, Jody Freeman & Jim Rossi, *Agency Coordination in Shared Regulatory Space*, 125 HARV. L. REV. 1131, 1162 (2012) (discussing a memorandum of understanding between the FDA and the FTC regarding enforcement actions related to prescription drug advertising).

344. *See* 16 U.S.C. § 1536(e).

345. *See id.* § 1536(e)(3)(G).

346. *See, e.g.*, Sharkey, *Federalism Accountability*, *supra* note 19, at 2160 ("In the realm of drugs, California's Department of Public Health has its own Drug Safety Program division, which monitors the drug, cosmetic, and 'other consumer product industries' to ensure that 'products are not adulterated, misbranded or falsely advertised.'"); Sharkey, *Inside Agency Preemption*, *supra* note 182, at 588–90 (proposing "the introduction of a novel notification provision to the state attorneys general and to the National Association of Attorneys General" because of their interest in issues of federal preemption of state law).

347. *See, e.g.*, Miriam Seifter, *Further from the People? The Puzzle of State Administration*, 93 N.Y.U. L. REV. 107, 129–30 (2018) ("States have also created numerous new agencies to respond to emerging problems . . . [such as] for ground water management and hazardous waste[,] . . . campaign finance, recycling, and census

Ultimately, the benefit of such a structured committee is that it requires state and federal cooperation and creates a regime in which the FDA is required to consult with states and recognize their jurisdiction. Such a structure also inserts a check into the FDA's notoriously obscure regulatory process.[348] Further, inserting a check into the regulatory process simultaneously creates a structure that facilitates discussions between the state and federal governments thus providing for increased opportunities to share lessons learned in regulation. The cooperative framework would differ from current avenues for state participation as it would not just involve a state's input solely on matters of federal jurisdiction or product formulation but would also involve a discussion between peer regulators.[349]

2. State Mandatory Disclosure Laws

While state regimes tend to emphasize the ability to avail oneself of legal remedies after an individual has been harmed, there are also simpler solutions that do not disrupt that jurisdictional balance. Just as states can add variety to the regulatory system, the federal government can also influence the states. Federal regulation already exists as a floor in the regulation of innovative medical techniques as they implicate federal jurisdiction based on their use of medical products.[350] Federal jurisdiction already influences state regulation as states borrow definitions from the federal government.[351] As previously mentioned, California enacted a law requiring the communication of specific information related to stem cell treatments that were not approved by the FDA.[352] This law used the federal definition of "human cells, tissues, or cellular or tissue-based products" when defining stem cell therapies.[353] Drawing on California's response to stem cell clinics, which emphasized information disclosure and informed consent, other states could adopt similar measures for innovative therapies.[354]

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data. . . . One way to understand these dual trends is to say that states are taking on new tasks and are able to perform them in a more coordinated and thus effective way. . . . In an evermore complex society, states continually face new challenges; moreover, they are often able to respond more quickly than the national government. Cybersecurity and opiate addiction . . . are recent examples of states breaking new regulatory ground." (footnotes omitted)).

348. *See, e.g.*, Zettler, *Indirect Consequences*, *supra* note 30, at 1092; *see also* Thomas O. McGarity, *Seeds of Distrust: Federal Regulation of Genetically Modified Foods*, 35 U. MICH. J.L. REFORM 403, 477–78 (2002); Laurence Tai, *A Tale of Two Transparency Attempts at FDA*, 68 FOOD & DRUG L.J. 423, 425–26 (2013); Megan S. Wright et al., *When Biomarkers Are Not Enough: FDA Evaluation of Effectiveness of Neuropsychiatric Devices for Disorders of Consciousness*, 21 STAN. TECH. L. REV. 276, 308–09 (2018).

349. *See* Sharkey, *States Versus FDA*, *supra* note 78, at 1621 (noting that Massachusetts was given an opportunity to provide input into the FDA regulatory process before Massachusetts instituted restrictions on the sale of Zohydro, an opioid, within the state).

350. See *supra* Section I for a discussion of current federal regulation of medical products.

351. *See infra* note 353 and accompanying text.

352. *See supra* note 86 and accompanying text.

353. CAL. BUS. & PROF. CODE § 684(a) (West 2019) ("For the purpose of this section: (1) 'FDA' means the United States Food and Drug Administration. (2) 'HCT/Ps' means human cells, tissues, or cellular or tissue-based products, as defined in Section 1271.3 of Title 21 of the Code of Federal Regulations, as amended August 31, 2016, as published in the Federal Register (81 Fed. Reg. 60223). (3) 'Stem cell therapy' means a therapy involving the use of HCT/Ps.").

354. See *supra* note 85–86 for a discussion of California's stem cell research law.

3. State Clearinghouses for Adverse Event Reporting

Innovation is both a scientific and a regulatory goal. In the scientific realm, significant sums continue to be spent on scientific research.[355] Legislatively, Congress has aimed to shorten the time delay between scientific research success and market availability.[356] Often, congressional solutions to innovation that involve states also involve federal funding, which is used to encourage state policy innovation.[357] Scholars have noted that federal incentives, notably federal funding, increase the pace of policy diffusion throughout the states.[358] Other scholars have observed that Congress has instructed the FDA to create adaptive regulations to address medical innovations.[359] One method of strengthening that instruction is to use federal funding to incentivize states to collaborate in the creation of those adaptive regulations, while simultaneously recognizing that states have jurisdiction over some aspects of innovative therapies. The disadvantage of such a solution, however, is that federal grants often come with federal restrictions and oversight.[360]

One cooperative improvement to the regulation of innovative therapies would be strengthening opportunities for states to monitor these innovative therapies.[361] The federal government could provide funds to states in a pilot program for those that would like to establish clearinghouses for adverse event reporting so as to increase state monitoring of the practice of medicine, similar to the post-market surveillance of pharmaceuticals.[362] States could similarly maintain databases addressing clinical trials in their states, similar to the federal government's existing database.[363] States could also use statutory language similar to California's 2017 informed consent provision so as to

355. *See* Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 373 (2007) ("The reason that the budget of the National Institutes of Health (NIH) has grown, even as the budgets of other science agencies have languished, is that health-related innovation enjoys broader political appeal than other scientific pursuits. We value health, and we believe that high quality biomedical science will have public health payoffs. FDA regulation similarly promotes public health by promoting high quality scientific investigation of a particular sort—specifically, the conduct of scientifically rigorous clinical trials of drugs.").

356. See *supra* notes 33–36 and accompanying text for a discussion of the various acts of Congress aimed at hastening the regulatory process for medical innovation.

357. *See, e.g.*, Kristin Madison, *Building a Better Laboratory: The Federal Role in Promoting Health System Experimentation*, 41 PEPP. L. REV. 765, 769 (2014) ("First, the federal government could spur more state policy innovation through funding programs that provide the same sort of financial incentives to states as those currently offered to private health care providers."); *id.* at 788–89 (explaining how federal funding through the ACA has helped promote the states' innovation).

358. *See, e.g.*, Susan Welch & Kay Thompson, *The Impact of Federal Incentives on State Policy Innovation*, 24 AM. J. POL. SCI. 715, 723 (1980).

359. *See supra* note 50 and accompanying text.

360. *See, e.g.*, Madison, *supra* note 357, at 799 ("It is true that federal funding of the ACA's programs will affect state policies, as federal funding directed to states always has. To obtain Medicaid funding, for example, states must comply with federal mandates dictating the structure of their Medicaid programs.").

361. See *supra* notes 110–111 and accompanying text for a discussion of the need for greater monitoring of medical innovation.

362. *See, e.g.*, Sharkey, *States Versus FDA*, *supra* note 78, at 1622 ("[S]tates could plan an enhanced role in the post-approval risk surveillance phase of the drug regulatory process.").

363. *See, e.g.*, U.S. NAT'L LIBR. MED. CLINICALTRIALS.GOV, http://clinicaltrials.gov/ [https://perma.cc/Z7JG-8ZWA] (last visited Feb. 1, 2020).

ensure that patients are adequately warned of the potential adverse impacts of innovative therapies.[364] States are closer to innovative therapies as, in spite of FDA enforcement action in the realm of regenerative therapies, clinics offering them continue to flourish in many states.[365] Just as the structure of the Medicaid program provides "broad mandatory requirements that state Medicaid programs must follow, but states retain considerable flexibility to cover additional eligibility groups and benefits," this Article's cooperative framework provides a floor of broad mandatory requirements, as established through federal product approval, that would apply to innovative therapies.[366]

CONCLUSION

Scientific and technological innovations continue to advance at a faster pace than the law. The tension between innovation, safety, and regulation is longstanding.[367] This Article explores the array of available solutions for improving life sciences regulation before explaining that the cooperative governance structures used in other areas of law could significantly improve the regulation of life sciences innovation, namely innovative therapies, especially as these innovations continue to evolve past standard legal classifications. This Article's proposed solutions to improving the current regulatory system draw on health law and administrative law, among other fields.

The current system of regulation attempts to place innovative therapies within the categories of products that the FDA regulates in an ad hoc fashion that does not fully contemplate their complexities and the existence of state jurisdiction.[368] A system for efficiently regulating those therapies, which do not currently or clearly fit within the FDA's regulatory scheme or the practice of medicine, is inevitable and developing that system before those products are practice ready is an ideal way to regulate.[369] The cooperative framework focuses on a number of criteria that apply for many therapies and also flags areas for concern. In other words, implementing a cooperative system for the regulation of innovative therapies would allow for a regulatory scheme in which the law manages to keep up with science (or to at least avoids being exponentially outpaced by it).

364. See *supra* note 86 and accompanying text for a discussion of the informed consent provision in California's stem cell research law.

365. See *supra* notes 133–135 and accompanying text for a discussion of FDA regulation of regenerative therapies.

366. *See, e.g.*, Watson, *supra* note 219, at 214.

367. *See, e.g.*, *supra* note 6 and accompanying text.

368. *See, e.g.*, Hoffmann et al., *supra* note 6, at 1390 ("The advent of these applications for [microbiota transplants] poses challenges for regulatory bodies. The transplanted material is not a 'typical' drug, and thus may not be appropriate for the drug regulatory pathway. The material consists of a community of highly dynamic, metabolically active organisms. . . . Each batch of 'product' is different, making characterization of the transplanted material problematic.").

369. *See, e.g.*, Javitt & Hudson, *supra* note 17, at 1210.