Regulating Intermediate Technologies

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Over the last several years, scholars studying health innovation policy have carefully considered the ways in which policymakers regulate different types of technologies to encourage their development and dissemination. Scholars have examined a range of legal incentives, including patents, Food and Drug Administration (FDA) exclusivity periods, taxes, grants, insurance reimbursement, and other tools to promote socially valuable innovations that our current system has structurally disfavored.

However, this research has neglected the temporal dimension of the issue. Specifically, a large set of innovations in the life sciences may be considered to be intermediate innovations. Scientists continue to improve these technologies over time, even as the initial products are made available to patients. Yet the relevant innovation policy levers do not consider whether intermediate technologies ought to be regulated differently from technologies which are further along in the development process.

Whether our existing regulatory frameworks are cognizant of an innovation's stage of development matters. If the regulatory structure around the intermediate technology is not appropriately calibrated, the technology could be frozen in time such that future development does not occur. This failure would be harmful both for public health and for societal welfare. Policy levers that appear targeted at early-stage technologies in fact lack a fit with these considerations.

This Article articulates the problem of regulating intermediate technologies in the life sciences and considers how existing laws and regulations might be altered to accommodate the situation. It argues that some of the FDA's existing regulatory approaches are capable of addressing the

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problem, and others can be altered to do so. Other solutions may lie in the realm of reimbursement, where the stage of a technology could play into the payments made by insurers for that technology.

Introduction

Today, many of us carry around cell phones that have incredible computing and software capabilities. Our phones allow us not only to communicate with each other, but also to record and edit video and audio, use word- and data-processing programs, and play video games.[1] Increasingly, these phones are also able to serve as powerful medical devices, allowing doctors to carry out electrocardiograms, ultrasounds, blood pressure monitoring, and more—all using a device they carry in their pockets.[2]

1. David Pierce, *Your Smartphone Is the Best Computer You Own*, WALL ST. J. (May 23, 2018 10:00 AM), https://www.wsj.com/articles/your-phone-is-the-best-computer-you-ownso-use-it-more-1527084001 [https://perma.cc/VD6H-K2B7].

2. Gaby Loria, *Top 5 Medical Devices for iPad or iPhone*, SOFTWARE ADVICE, https://www.softwareadvice.com/resources/top-5-medical-devices-ipad-iphone [https://perma.cc/UUE6-J6NZ].

One of the reasons cell phone technology has progressed so rapidly over the last several years is the ability of software developers to iterate their products on short timescales and to push updates to users whenever a new version is available. Whether it is Apple or Android pushing their newest operating system update, or a new version of one of our apps, consumers have become accustomed to accepting these frequent updates. These updates are pushed to users at the discretion of companies when they decide it is time to fix a bug or add a feature.

But what about updates to medical software? Updates to the ultrasound software for the iPhone—or the software that runs your implanted pacemaker or insulin pump? These products are not only consumer goods. They are also medical devices, regulated by the Food and Drug Administration (FDA). Companies may need the agency's approval before making updates, even (or perhaps especially) if those updates are needed to address serious safety issues,[3] imposing a barrier to improvements. Alternatively, companies may lack the incentives to develop such improvements if health insurers will not compensate them for those improvements or if there are intellectual property concerns.

This problem—the problem of technologies which are intermediate in nature, but which ought to be improved with time—is not limited to the digital health context. It extends more broadly throughout the health care technologies field and to technologies in other fields as well, such as self-driving cars.[4] Yet it has been largely ignored in the literature. To be sure, there is a large and growing scholarly literature on incentives for innovation in health care technologies, a significant portion of which has focused on institutional actors including the FDA.[5] But this scholarship largely focuses on whether a technology is developed in the first instance, not whether an available technology is subject to improvements over time.

This Article takes up this question of the regulation of intermediate technologies. It contends that the regulation of intermediate technologies poses

3. *See, e.g.*, *Firmware Update to Address Cybersecurity Vulnerabilities Identified in Abbott's (Formerly St. Jude's Medical) Implantable Cardiac Pacemakers: FDA Safety Communication*, FOOD & DRUG ADMIN. (Aug. 29, 2017), https://www.fda.gov/medical-devices/safety-communications/firmware-update-address-cybersecurity-vulnerabilities-identified-abbotts-formerly-st-judes-medicals [https://perma.cc/53VB-2JHY].

4. *See, e.g.*, Tracy Hresko Pearl, *Fast & Furious: The Misregulation of Driverless Cars*, 73 N.Y.U. ANN. SURV. AM. L. 19, 27-29 (2017) (articulating the industry-specified levels of automation and explaining that we are midway through the process and have not yet achieved full automation).

5. *See generally*, Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345 (2007); Yaniv Heled, *Patents vs. Statutory Exclusivities in Biological Pharmaceuticals—Do We Really Need Both?*, 18 MICH. TELECOMM. & TECH. L. REV. 419 (2012); Daniel J. Hemel & Lisa Larrimore Ouellette, *Beyond the Patents-Prizes Debate*, 92 TEX. L. REV. 303 (2013); Lisa Larrimore Ouellette, *Patentable Subject Matter and Nonpatent Innovation Incentives*, 5 U.C. IRVINE L. REV. 1115 (2015); W. Nicholson Price II, *Regulating Black-Box Medicine*, 116 MICH. L. REV. 421 (2017); Arti K. Rai, *Building a Better Innovation System: Combining Facially Neutral Patent Standards with Therapeutics Regulation*, 45 HOUS. L. REV. 1037 (2008); Rachel E. Sachs, *Innovation Law and Policy: Preserving the Future of Personalized Medicine*, 49 U.C. DAVIS L. REV. 1881 (2016).

special concerns, because a poorly calibrated regulatory structure may freeze a technology in time, such that future development does not occur. Importantly, these regulations are likely to be both well-intentioned and critical for consumer protection in most cases. Yet they may still have this side effect, ossifying intermediate health care technologies at an early stage of development, which would be harmful both to public health and societal welfare. Our existing regulatory frameworks largely do not take account of an innovation's stage of development, and existing laws and regulations will need to be altered to accommodate these particular challenges.

Part I of this Article answers two fundamental questions: what exactly *is* an intermediate technology, and what might we learn from other scholars about it? Legal and economic scholars have asked questions about the process of research and development that are related to but distinct from this problem, and those strands of the literature reveal helpful information in addressing this issue. Further, the range of examples of intermediate health care technologies is quite broad. Using examples of genetic testing, pharmaceutical manufacturing, and the microbiome, Part I demonstrates the diversity of intermediate technologies, expanding the potential scope of the problem. Part I closes by addressing the question of whether this broad scope is unlimited—in other words, whether *everything* is an intermediate technology, and if so, what that would mean for this inquiry.

Part II examines the ways in which different doctrines within innovation policy have dealt with the question of intermediacy or sequential innovation. A set of doctrines within patent law is explicitly designed to mediate between the interests of first inventors and subsequent improvers, but these doctrines typically envision clashes between multiple parties, rather than envisioning an initial creator who seeks to improve their own product. Food and drug law has more recently considered the problem of intermediacy, but specifically in the context of health care software, a development that provides insight into how a flexible strategy can allow an agency to leverage old statutes in service of new problems.[6] Finally, literature in administrative law and environmental law has developed a theory of adaptive management, in which agencies are able to alter their regulations in the face of new information or changing conditions.

Part III applies these lessons to consider how existing laws might be altered to accommodate the problem of intermediate technologies. It chiefly argues that some of the FDA's existing regulatory approaches around devices or biologic products are already capable of addressing the problem (even if they were designed for other purposes), and others can be altered to do so. Other solutions may lie in the realm of reimbursement, in which the stage of a technology could play into the payments made by insurers for that technology, either through the use of existing policy levers or through the creation of new

6. *See generally* Jody Freeman & David B. Spence, *Old Statutes, New Problems*, 163 U. PA. L. REV. 1 (2014).

ones. It is somewhat more pessimistic about patent law's ability to deal with these problems, however.

Part IV widens the Article's scope, considering whether the problem of intermediacy in health care technologies has implications beyond the health care field. It argues that, for technologies embedded within an existing regulatory framework (such as self-driving cars), the principles articulated in Part III can easily be translated. However, for technologies largely untethered from existing regulation (such as many web-based technologies), the "intermediate technologies" framing is a poor fit for the true concerns at issue.

I. Defining the Problem

Some examples of intermediate technologies, like the self-driving car innovations mentioned above, will be immediately identifiable and broadly understandable. Others, like the pharmaceutical technologies described *infra* in Section I.B, require more explanation and may not be apparent upon first glance. As such, it is critical to attempt to define more precisely what is meant by an "intermediate technology." Essentially all technologies are intermediate in some ways—innovators always strive for improvement over time—but my focus here is more specific.

It may be easiest to define the concept of "intermediate technologies" by reference to the problem this Article seeks to solve. Specifically, it is concerned with the set of technologies where, if the existing regulatory structure is not appropriately calibrated, the technology will be frozen at an early stage of commercialization such that future development does not occur. To put it slightly differently, the essential concern is that if the regulation around the *intermediate* technology is not appropriately calibrated, the *end-stage* technology will not be developed.

In my view, this framing of the concern has two corollaries. First, this would be a bad thing. It would be harmful—for public health, for societal welfare—if these technologies were not developed further. Although this proposition is not highly controversial, it is certainly contestable. It is difficult if not impossible to determine whether the level of innovation in any particular area is optimal.[7] Even the concept of innovation itself is amorphous, although here I adhere to the framework I have adopted in previous work: my focus is on the promotion of innovation in health technologies "where private market signals are not likely to be reflective of social value,"[8] here because of the existing regulatory barriers.

7. It is highly likely that in some areas of health care technologies there is too much investment, and in others there is not enough.

8. Rachel E. Sachs, *Administering Health Innovation*, 39 CARDOZO L. REV. 1991, 1996 (2018).

Second, though, we would not obviously be able to identify such occurrences. By definition, the concern is that the existing regulatory framework will stifle future innovation along a particular path, so we as a society do not observe the innovation that is never developed.[9] It is not easy to identify the invisible innovation that could have but never took place, even where it might have proven socially valuable.

A version of this argument is commonly made by technology companies that are currently not subject to significant governmental regulation (most notably internet companies like Facebook or Google) in an attempt to forestall the imposition of such regulation, a topic to which I return in Section IV.B. But it is also made by companies that are already subject to more significant governmental regulation, although that regulation varies by technological area. These latter companies and technological areas are the primary focus of this Article.

In this Part, I consider this formulation of the problem—one concerned about technological ossification driven by regulatory structures—and examine different aspects of it. First, I situate it within the existing literature on innovation and regulation, explaining how it both resembles and differs from existing problems already identified. Second, I provide examples of intermediate technologies, explaining how their temporal qualities are mediated by existing regulation and what scientists hope to accomplish in the future. Finally, I consider whether there are any true limiting principles associated with this formulation of the problem, and if not, what implications that may have for its force and generalizability.

A. Contextualizing the Temporal Aspects of the Literature

The existing literature on innovation policy has grappled with three sets of policy concerns that resemble the problem of intermediate technologies in some important ways, but differ in others. Considering the similarities and differences of these policy concerns not only provides a fuller appreciation of the existing literature and its scope but also reveals aspects of those policy concerns that remain unexplored by scholars.

First, there is a significant and growing strand of scholarship that considers how different legal incentives shape the kinds of new technologies that are developed. Scholars have considered the roles played by general incentives including patents,[10] grants,[11] tax credits,[12] prizes,[13] and other legal

9. It is here that international comparisons become relevant. Other countries may adopt different balances of innovation incentives, meaning that these technologies could be developed elsewhere.

10. *See, e.g.*, Eric Budish et al., *Do Firms Underinvest in Long-Term Research? Evidence from Cancer Clinical Trials*, 105 AM. ECON. REV. 2044 (2015); Ted M. Sichelman, *Commercializing Patents*, 62 STAN. L. REV. 341 (2010).

11. *See, e.g.*, W. Nicholson Price II, *Grants*, 34 BERKELEY TECH. L.J. 1(2019).

tools[14] in encouraging the development of new technologies of all kinds, and they have also considered the ways in which technology-specific incentives like FDA exclusivity periods also serve these goals.[15] The goal of much of this scholarship is to consider not only how these incentives promote innovation, but also what innovations they might be leaving on the table, and how we might alter or support existing law to encourage the development of those innovations.

One article by Professors Amy Kapczynski and Talha Syed[16] is emblematic of this line of scholarship. They argue that patents "will predictably and systematically distort private investment decisions" by "overstating the value of highly excludable information goods and understating the value of highly nonexcludable ones."[17] In short, private firms will be more likely to invest in the development of highly excludable goods like novel pharmaceuticals rather than much less excludable information goods with similar or even greater social value, such as the development of negative information about existing drugs[18] or innovations in health care quality such as a surgical checklist.[19] Kapczynski & Syed use their analysis to bolster existing arguments about the importance of public funding of informational goods like these, arguing that the output of much of this research will be "highly nonexcludable and hence particularly ill-suited to be generated by markets and patents,"[20] even if it is of high social value.

The authors writing in this line of scholarship have focused on the types of technologies that are incentivized under existing law, and the types of technologies that are left out. Does the fact that patents must be applied for early in the drug development process disadvantage pharmaceuticals whose development can be expected to be particularly lengthy, such as those that prevent disease rather than treat it?[21] Should we expect investment in diagnostic tests to stagnate after the Supreme Court made it more difficult to

12. *See, e.g.*, Daniel J. Hemel & Lisa Larrimore Ouellette, *Beyond the Patents-Prizes Debate*, 92 TEX. L. REV. 303 (2013).

13. *See, e.g.*, Michael Abramowicz, *Perfecting Patent Prizes*, 56 VAND. L. REV. 115 (2003); Benjamin N. Roin, *Intellectual Property Versus Prizes: Reframing the Debate*, 81 U. CHI. L. REV. 999, 1013 (2014).

14. *See, e.g.*, Rachel E. Sachs, *Prizing Insurance: Prescription Drug Insurance as Innovation Incentive*, 30 HARV. J.L. & TECH. 153 (2016).

15. *See, e.g.*, Eisenberg, *supra* note 5; Heled, *supra* note 5; Ouellette, *supra* note 5.

16. Amy Kapczynski & Talha Syed, *The Continuum of Excludability and the Limits of Patents*, 122 YALE L.J. 1900 (2013).

17. *Id*. at 1942.

18. *Id*. at 1923-26; *see also id*. at 1903 (noting that excludability is not a "binary quality" but is instead highly variable along a spectrum).

19. *Id*. at 1937.

20. *Id*. at 1951.

21. *See, e.g.*, Budish et al., *supra* note 10.

obtain patents on these technologies,[22] or can we expect other innovation incentives to fill the gaps?[23] Does the fact that private insurance pays more for drugs than does Medicaid discourage drug companies from developing drugs for low-income populations?[24]

Importantly, at its core this is the same question I address in this Article. My question is whether existing regulatory structures incentivize the development of an intermediate technology but disincentivize the development of a more advanced, end-stage version of that technology. Both this Article and this line of scholarship are fundamentally looking for invisible technologies, whose absence is difficult to detect. But these articles generally consider whether a technology is developed at all—not what stage of the technology is brought to market, or whether the technology is then prone to improvements later on. In short, they do not consider the temporal nature or intermediacy of the technology.

A second strand of literature has focused more heavily on the staged development of health care technologies. This literature examines the evocatively named "Valley of Death," which "separates upstream research on promising genes, proteins, and biological pathways from downstream drug candidates."[25] The concern is that the initial academic research that articulates disease pathways and identifies potential drug compounds that might be brought to bear on those pathways will not translate to the necessary commercial development of a pharmaceutical product, even if the science is promising. Making sure that promising health care technologies can traverse the "Valley of Death" is critical to ensuring that basic research discoveries translate into real health benefits for patients.

Scholars like Professors Rebecca Eisenberg and Arti Rai have written about the ways in which the "Valley of Death" problem stems from and can be addressed through innovation-policy levers. The failure to translate academic discoveries into private-sector development efforts was a key driver in the passage of the Bayh-Dole Act,[26] which permitted universities to retain patent

22. *See, e.g.*, Rebecca S. Eisenberg, *Diagnostics Need Not Apply*, 21 B.U. J. SCI. & TECH. L. 256, 256 (2015) ("[M]ost important advances in [diagnostic testing] lie outside the boundaries of patent-eligible subject matter." (footnote omitted)).

23. *See* Ouellette, *supra* note 5, at 1128.

24. *See* Sachs, *supra* note 5, at 200.

25. Arti K. Rai et al., *Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discovery*, 8 YALE J. HEALTH POL'Y, L. & ETHICS 1, 4 (2008); *see also* Rochelle Cooper Dreyfuss, *Tailoring Incentives: A Comment on Hemel and Ouellette's Beyond the Patents-Prizes Debate*, 92 TEX. L. REV. 131, 134 (2014) (describing federal research as a potential solution to the "valley of death" problem). Although much of this literature has focused on healthcare technologies, some of it has been applied more generally. *See, e.g.*, F. Scott Kieff, *IP Transactions: On the Theory & Practice of Commercializing Innovation*, 42 HOUS. L. REV. 727, 744 (2005); Liza Vertinsky, *Making Knowledge and Making Drugs? Experimenting with University Innovation Capacity*, 62 EMORY L.J. 741, 821 n.10 (2013).

26. *See* Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 VA. L. REV. 1663, 1698-99 (1996); Arti

rights in the technologies they developed. In theory, those patents then facilitate transactions between universities and private firms looking to develop those technologies.[27] However, patents alone may be insufficient to ensure that translational research occurs, and Rai and others have proposed more intensive collaborations between academics and industry as one possible catalyst for scientific advancements.[28]

This line of scholarship focuses far more on the temporal nature of research and development than does the innovation-policy literature, which focuses on the kinds of technologies that are advantaged and disadvantaged by the current set of policy levers. The temporal aspect of the research question provides a useful analogy for the problem of intermediate technologies. In a way, the problem of intermediate technologies articulates a second Valley of Death, one that appears only after a technology is initially developed and erects barriers to its final state. The question then can be reframed around how to traverse that second Valley and promote more complete development of the relevant technology.

The focus of the Valley of Death literature on the development process, rather than on the binary question of whether the technology is developed or not developed, is a frame that carries over to the question of intermediate technologies. Its focus on not only innovation-policy levers but also on institutional relationships among different actors in the innovation ecosystem is helpful as well. But there is still a gap between the Valley of Death scholarship and the question posed in this Article. The primary concern for scholars writing on the Valley of Death is ultimately whether a particular product comes to market at all, not whether a product, once it is available, is improved over time. But the intermediate technologies question also incorporates questions about iterating improvement over time.

Third, this question of cumulative or sequential innovation has been taken up squarely in the intellectual property scholarship.[29] Some of this work

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Kaur Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77, 95-96 (1999).

27. *See* Kenneth J. Arrow, *Economic Welfare and the Allocation of Resources for Invention*, *in* THE RATE AND DIRECTION OF INVENTIVE ACTIVITY 609, 615 (Nat'l Bureau of Econ. Research ed., 1962); Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEX. L. REV. 989, 1050-51 (1997). *But see* Michael J. Burstein, *Exchanging Information Without Intellectual Property*, 91 TEX. L. REV. 227 (2012) (arguing that patents are not essential to facilitate these types of transactions).

28. Rai et al., *supra* note 25, at 4-6. Industry has indeed begun forming financial partnerships with universities of this type, dedicated to discovering potential new therapies and advancing them through the development process. *See, e.g.*, Jonathan D. Rockoff, *Big Pharma, Short on Blockbusters, Outsources the Science*, WALL ST. J. (Dec. 6, 2016), http://www.wsj.com/articles/big-pharma-short-on-blockbusters-outsources-the-science-1481042583 [https://perma.cc/DY2C-9HLS]; Brigid Sweeney, *In Era of Research Cuts, Romance Blossoming Much Earlier Between Universities and Big Pharma*, CRAIN'S CHI. BUS. (June 10, 2017), http://www.chicagobusiness.com/article/20170610/ISSUE01/170609858/in-era-of-research-cuts-romance-blossoming-much-earlier-betweenuniversities-and-big-pharma [https://perma.cc/B5D5-7W3X].

29. I discuss some of these doctrinal moves in more detail in Section II.A, *infra*.

examines particular doctrines designed to encourage successive innovators to improve existing technologies, such as blocking patents.[30] But much of it considers the scope of intellectual property rights and whether granting broad or narrow rights, or granting rights early or late in the development process, will most effectively serve the goals of promoting scientific progress.[31] The essential inquiry is "how patent scope decisions influence the *development* of a technology, both in the sense of an individual invention and that of a future line of improvements extending from it."[32] The concern is that granting broad patents to initial inventors may discourage follow-on research that leads to "something not simply slightly different but significantly better than the patented technology."[33]

One of the foundational articles on this subject, Professors Robert Merges and Richard Nelson's *On the Complex Economics of Patent Scope*,[34] illustrates the difficulty of this inquiry but also reveals how it has not yet been applied fully to the health technologies sphere. Merges and Nelson contrast technologies whose development fits the "discrete invention model," in which the invention "does not point the way to wide ranging subsequent technical advances" and may be understood largely as an end-stage technology,[35] with technologies following the cumulative innovation model, "in the sense that today's advances build on and interact with many other features of existing technology."[36] They argue that broad, early patents may cause problems for innovation in cumulative technologies, while they are less likely to be of concern for discrete technologies.[37] Merges and Nelson contend that "many new pharmaceuticals" fit the discrete invention model,[38] but note that the processes for manufacturing these drugs may fit the cumulative technology model more closely.[39] Initially, this would seem to suggest that any problems of intermediacy would more strongly affect pharmaceutical manufacturing than it would pharmaceutical development as a distinct process.

30. *See, e.g.*, Kevin Emerson Collins, *Getting into the "Spirit" of Innovative Things: Looking to Complementary and Substitute Properties to Shape Patent Protection for Improvements*, 26 BERKELEY TECH. L.J. 1217, 1271-72 (2011); Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEX. L. REV. 989, 991-92 (1997).

31. *See* Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265 (1977); Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. ECON. PERSP. 29, 33-35 (1991).

32. Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 843 (1990).

33. *Id*. at 870.

34. 90 COLUM. L. REV. 839 (1990).

35. *Id*. at 880.

36. *Id*. at 881.

37. *Id*. at 882.

38. *Id*. at 880, 882 ("[P]articular chemical product innovations seldom are the keystones to the development of large numbers of other chemicals.").

39. *Id*. at 883, 898.

However, Merges and Nelson also carve out a third category of technologies, in addition to those that are either discrete or cumulative: those that are science-based.[40] Science-based technologies are those "whose advance is predominantly driven by such developments,"[41] where granting early broad patents has the potential to stifle the development of the field as a whole. [42] Merges and Nelson place the then-emerging field of biotechnology in this category.[43] Importantly, as the science in a field becomes more established, Merges and Nelson envision that innovation will become either discrete or cumulative, such that the "issues involved in setting appropriate patent scope changes as an industry advances."[44] Publishing in 1990, the authors did not advance a view as to how the field of biotechnology would evolve. Now, when seven out of the ten best-selling drugs in the world are biologic products,[45] it may be time to revisit this question.

The intellectual-property literature on cumulative innovation is an easy fit with the idea of intermediate technologies, and therefore provides a theoretical grounding for the investigation in this Article. However, its application to health care technologies has yet to be fully explored. First, health care technologies today are different in kind from the technologies that were prominent when much of this foundational literature was written. The rise of biologic products, in which the product is defined more by its manufacturing process than by its chemical formula,[46] suggests that pharmaceuticals today may share more similarities with the cumulative innovation model than the discrete-innovation model, with the resulting implications for patent scope that Merges and Nelson articulate. At the same time, the literature's focus on intellectual property has sidelined the role of other regulatory regimes that are critical to the development of health care technologies: safety and efficacy regulations imposed by the FDA and the Centers for Medicare and Medicaid Services (CMS), and regulations regarding insurance reimbursement for these technologies. This Article not only updates the patent literature for our current understanding of technological intermediacy, but also explores patent law's interaction with FDA regulations and insurance reimbursement in this space.

40. *Id*. at 880, 883-84.

41. *Id*. at 883.

42. *Id*. at 883-84.

43. *Id*. at 904.

44. *Id*. at 908.

45. Rupali Mukherjee, *Biologics Enter Top Selling Drugs' List*, TIMES OF INDIA (Dec. 28, 2016), https://timesofindia.indiatimes.com/business/india-business/Biologics-enter-top-selling-drugs-list/articleshow/56209425.cms [https://perma.cc/6DZH-UPEW].

46. W. Nicholson Price II & Arti K. Rai, *Manufacturing Barriers to Biologics Competition and Innovation*, 101 IOWA L. REV. 1023, 1028 (2016).

B. Illustrating the Scope of Intermediate Technologies

With this background in mind, the search for intermediate technologies—those where the existing regulatory structure threatens to ossify the technology at the stage when it is ready for public consumption, but before its full potential is reached—begins to yield results. Examples of intermediate technologies can be found readily, and three examples from the health care field are instructive: diagnostic testing, manufacturing process improvements, and tissue platform technologies.

These three examples helpfully reveal both the different ways in which technologies can have intermediate qualities and the different ways in which technologies can be rendered "stuck" by the regulatory framework. However, they are by no means intended to exhaust the possible set of intermediate technologies or even to represent the only three categories of such technologies (products, processes, and platform technologies). Instead, they are particularly useful because they are all examples in which scientists could or can foresee with at least some clarity the future direction of the technology—that is, their intermediacy is readily apparent.

1. Learning from Genetic Testing

A core example comes from the world of diagnostic tests. Scholars have written a great deal about Myriad Genetics' tests for mutations in the BRCA genes, which can predispose women to an increased risk of breast and ovarian cancer.[47] Women with family histories of these diseases often want to determine whether they have inherited harmful genetic mutations so that they can take precautions to mitigate their risk.[48] For many years, Myriad was the only commercial provider of such a test in the United States,[49] due to their portfolio of patents surrounding the test.[50]

A woman obtaining BRCA testing from Myriad typically receives one of three straightforward results: her genes either are normal, contain sequence variations which are harmless, or contain a clearly harmful mutation.[51] But in some cases, the genetic sequence is difficult to interpret, and a test returns a

47. *See* Mary-Claire King, *"The Race" to Clone BRCA1*, 343 SCI. 1462, 1462 (2014).

48. These precautions may include everything from increased screening to a prophylactic double mastectomy. *See, e.g.*, Angelina Jolie, *My Medical Choice*, N.Y. TIMES (May 14, 2013), https://www.nytimes.com/2013/05/14/opinion/my-medical-choice.html [https://perma.cc/4RTL-XS6N].

49. King, *supra* note 47, at 1465.

50. Robert Cook-Deegan et al., The Next Controversy in Genetic Testing: Clinical Data as Trade Secrets?, 21 EUR. J. HUM. GENETICS 585, 585 (2013) ("[Myriad's] status as the sole commercial provider of BRCA testing in the United States is a consequence of its exclusive US patent rights.").

51. John M. Conley et. al., *Myriad After Myriad: The Proprietary Data Dilemma*, 15 N.C. J. L. & TECH. 597, 613-14 (2014).

"VUS" result: a variant of unknown significance.[52] A VUS results when a woman's BRCA gene has a mutation, but the clinical importance of that mutation is not known.[53] Perhaps it will be harmless, or perhaps it suggests an increased risk of developing breast cancer.

When Myriad's first tests came on the market in 1996, over 40% of tests returned a VUS result.[54] By 2002, the numbers had dropped, but 12.8% of all Myriad's tests still returned VUS results, a figure that was as high as 38.6% for African-American women.[55] But by 2012, the overall VUS rate had declined to just 2.9%, and to 5.0% among African-American women.[56] Myriad was able to leverage its large, proprietary database of genetic sequences to improve its ability to interpret VUS. John Conley and others have explained the lengths to which Myriad will go to understand the importance of a VUS:

> When Myriad finds a new VUS—or one previously identified but whose clinical significance is not yet understood—it offers free testing to the patient's family members in an effort to help determine the variant's significance. Myriad encourages the person with the VUS to contact others in their family, providing a model letter that patients can send their relatives. Myriad collects data regarding the clinical outcome associated with that VUS, and a VUS may ultimately be reclassified as deleterious or neutral as more is learned.[57]

From an innovation-policy perspective (returning to the significant access concerns *infra*), the improvements in Myriad's tests over the years are a success story of an intermediate technology. Myriad was able to bring its test to market when the product was still an intermediate one: it had some predictive value, but significant improvements were still needed, and were foreseen. It had clinical value at the time for some patients, but for nearly half of women receiving the test, their results were inconclusive. However, that very act of coming to market was necessary to enable Myriad to construct the database of genetic test results it used to bring down the VUS rate. If regulators had required a lower VUS rate before Myriad came to market, it is not clear when (if ever) Myriad would have been able to aggregate the kind of information necessary to meet that goal.

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52. Brenda M. Simon & Ted Sichelman, *Data-Generating Patents*, 111 NW. U. L. REV. 377, 394 (2017). These are sometimes referred to as variants of uncertain significance. *See, e.g.*, Amelia Smith Rinehart, *Myriad Lessons Learned*, 5 U.C. IRVINE L. REV. 1147, 1157 (2015).

53. Barbara J. Evans, *Economic Regulation of Next-Generation Sequencing*, 42 J.L. MED. & ETHICS 51, 53-54 (2014).

54. Julie M. Eggington et al., *Current Variant of Uncertain Significance Rates in BRCA1/2 and Lynch Syndrome Testing*, AM. C. OF MED. GENETICS (Mar. 2012), http://myriad-library.s3.amazonaws.com/posters/VUS-Rate-ACMG.pdf [https://perma.cc/EC5H-CT69].

55. *Id*.

56. *Id*. This number continues to decline, according to Myriad's own reporting. *Rapid Decline in VUS Rates*, MYRIAD GENETICS (2016), https://new.myriadpro.com/products/myriad-myrisk/myriad-myrisk-variant-classification/rapid-decline-in-vus-rates [https://perma.cc/TZ9M-9V65].

57. Conley et al., *supra* note 51, at 615 (citations omitted).

Myriad was able to bring its test to market as early as it did because of the much less onerous regulatory pathway facing most diagnostic tests. Unlike prescription drugs, the majority of genetic tests do not receive FDA scrutiny before coming to market,[58] meaning that they can avoid the expensive, lengthy FDA clinical trial process. These tests do receive some regulatory examination, most notably through CMS, which oversees laboratory tests under authority established by the Clinical Laboratory Improvement Amendments of 1988 (CLIA).[59] But CMS' examination is limited to questions of *analytical* validity, i.e., whether the test finds what it is supposed to find. In other words, CMS asks whether Myriad's test accurately detects the presence or absence of those specific mutations in her genes.[60] CMS does not ask about the test's *clinical* validity, i.e., whether Myriad's test provides the woman with any information about the likelihood that she may develop breast or ovarian cancer.[61]

Not only was Myriad able to come to market early in the development process of the technology, but the patents it held over its tests enabled it to exclude other BRCA test providers from the market and thereby to aggregate the data it used to improve its test over time.[62] Myriad's patents on the BRCA genes were largely struck down by the Supreme Court in 2013,[63] enabling competitors to enter the market. However, Myriad's already aggregated database of test results[64] and its lower VUS rate[65] have allowed it to retain much of its clinical superiority.

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58. SEC'Y'S ADVISORY COMM. ON GENETICS, HEALTH & SOC'Y, U.S. DEP'T OF HEALTH & HUMAN SERVS., GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 61 (2010). In 2014, the FDA took steps toward regulating these tests, *see* Draft Guidance Framework for Regulatory Oversight of Laboratory Developed Tests, 79 Fed. Reg. 59776, 59776 (Oct. 3, 2014), but it later abandoned that initiative. More recently, the FDA and CMS have created a Task Force on LDT Quality Requirements, the output of which remains to be seen. Jeffrey Shuren & Patrick H. Conway, *FDA and CMS Form Task Force on LDT Quality Requirements*, CMS BLOG (Apr. 17, 2015), https://www.cms.gov/blog/fda-and-cms-form-task-force-ldt-quality-requirements [https://perma.cc/42J3-AXDX].

59. Clinical Laboratory Improvement Amendments of 1988, Pub. L. No. 100-578, 102 Stat. 2903 (codified as amended at 42 U.S.C. § 263a (2018)).

60. Sachs, *supra* note 5, at 1892.

61. *Id*. New York state has a particularly robust laboratory certification program that does provide some review for clinical validity, *Comprehensive Test Approval Policy and Submission Guidelines*, N.Y. DEP'T OF HEALTH 1 (2013), http://www.wadsworth.org/labcert/TestApproval/forms/Submission_Guidelines_Policy.pdf [https://perma.cc/KCU7-GTEC], but this review is typically based on scientific literature rather than clinical trials, SEC'Y'S ADVISORY COMM. ON GENETICS, HEALTH & SOC'Y, U.S. DEP'T OF HEALTH & HUMAN SERVS., U.S. SYSTEM OF OVERSIGHT OF GENETIC TESTING 36, 98-99 (2008).

62. Simon & Sichelman, *supra* note 52, at 378; Rinehart, *supra* note 52, at 1157.

63. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576 (2013).

64. Professors Brenda Simon and Ted Sichelman have referred to patents like Myriad's as "data-generating patents," which "generate data that is distinct from the operation and use of the invention itself." Simon & Sichelman, *supra* note 52, at 379. That information is then held as a trade secret, *see* Jacob S. Sherkow, *Cancer's IP*, 96 N.C. L. REV. 297, 344-45 (2018), so these patents enable their holders to retain their monopoly position even once the patents expire or are invalidated, Simon & Sichelman, *supra* note 52, at 379-80.

65. *See* Conley et al., *supra* note 51, at 614 ("Myriad has claimed that the fraction of cases resulting in a VUS is 3% in its hands, versus 20% for its European competitors.").

Yet the legal tools that enabled Myriad to come to market early in the development process and establish a monopoly position created a significant social harm: they allowed Myriad to set the price of the test quite high and limit access for many women who wanted the test (either directly or by preventing them from obtaining a second opinion).[66] In the early 2000s, even as more than one-in-ten women received a VUS result, Myriad's BRACAnalysis test retailed for $2,600.[67] The Myriad example raises questions about whether intermediate technologies with known limitations (such as a high VUS rate) should be permitted to exercise unconstrained rights of exclusion, or whether accommodations are needed as a technology improves.

Myriad's test is in many ways a paradigmatic example of an intermediate technology. Although Myriad's test did benefit many women at the time it was initially marketed, for many others the test did not provide them with the information they sought.[68] But as the test was improved over time, the fundamental technology did not change. Myriad is a case of *improving and refining an existing technology*, in contrast to other examples of intermediate technologies. Myriad is not alone in this category. Most obviously, it is joined by the providers of other diagnostic tests, who seek to refine and improve their therapeutic value to patients. But more recently, it is also being joined by the providers of artificial intelligence or machine-learning algorithms and their application to the health care context.[69]

2. Pharmaceutical Manufacturing Processes

A second example is broader in scope than the previous case: pharmaceutical manufacturing processes. As the FDA itself has phrased the situation, "not much has changed in pharmaceutical production over the last 50 or so years."[70] Professor W. Nicholson Price has most thoroughly written about this problem, in which scientific advances in pharmaceutical manufacturing lag behind manufacturing advances in other fields, such as food products or

66. Rinehart, *supra* note 52, at 1175.

67. Jorge L. Contreras, *Narratives of Gene Patenting*, 43 FLA. ST. U. L. REV. 1133, 1147 (2016); *see also* Bryn Williams-Jones, History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing, 10 HEALTH L.J. 123, 134 (2002) (describing history of Myriad's pricing). Myriad now charges over four thousand dollars for this test. Robert Cook-Deegan & Annie Niehaus, *After Myriad: Genetic Testing in the Wake of Recent Supreme Court Decisions About Gene Patents*, 2 CURRENT GENETIC MED. REPS. 223, 228 (2014).

68. Eggington et al., *supra* note 54.

69. *See, e.g.*, W. Nicholson Price II, *Regulating Black-Box Medicine*, 116 MICH. L. REV. 421, 423-24 (2017). Scholars in related fields have noted many of the additional oversight challenges posed by algorithms like these. *See generally*, Pauline T. Kim, *Auditing Algorithms for Discrimination*, 166 U. PA. L. REV. ONLINE 189 (2017).

70. Lawrence Yu, *Continuous Manufacturing Has a Strong Impact on Drug Quality*, R&D (Apr. 13, 2016), https://www.rdmag.com/blog/2016/04/continuous-manufacturing-has-strong-impact-drug-quality [https://perma.cc/NB8A-SGPB].

consumer goods.[71] Even as pharmaceutical companies develop innovative new drugs, they often use "outdated production techniques and old manufacturing plants" in producing those drugs.[72]

One indicator of these outdated techniques is the widespread use of batch manufacturing rather than continuous manufacturing.[73] Even today, the vast majority of the pharmaceutical industry uses batch manufacturing methods,[74] in which drugs are made in a number of discrete steps, after each of which production stops to ensure quality testing can be completed.[75] However, manufacturers could move to a system of *continuous* manufacturing, in which products are made through more of an assembly-line, uninterrupted start-to-finish process.

Pharmaceutical companies' continued reliance on older manufacturing techniques, including batch manufacturing, is concerning for efficiency and cost reasons, and for patient safety reasons. First, the FDA notes that continuous manufacturing "saves time, reduces the likelihood for human error, and can respond more nimbly to market changes."[76] Each break in the batch manufacturing process is an opportunity for "inefficiency and delay, as well as the increased possibility of defects and error."[77] The National Science and Technology Council has estimated that shifting to continuous manufacturing may reduce manufacturing costs "by up to 40 to 50 percent."[78]

Second, manufacturing problems are also closely tied to drug recalls or shortages, which can harm patient care.[79] In 2017, 37% of drug shortages were due to quality issues involving manufacturing,[80] including "bacterial or mold contamination, tablet disintegration, and the presence of foreign particles such

71. *See generally* W. Nicholson Price II, *Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing*, 55 B.C. L. REV. 491 (2014); *see also* Leila Abboud & Scott Hensley, *New Prescription for Drug Makers: Update the Plants*, WALL ST. J. (Sept. 3, 2003, 12:01 AM ET), https://www.wsj.com/articles/SB10625358403931000 [https://perma.cc/FG9T-7LGV] (noting that pharmaceutical manufacturing is "far behind [that] of potato-chip and laundry-soap makers").

72. Price, *supra* note 71, at 493.

73. *Id*. at 502.

74. *See infra* note 85 for the FDA's promotion of rare instances of continuous manufacturing.

75. *Id*.; *see also* Sau Lee, *Modernizing the Way Drugs Are Made: A Transition to Continuous Manufacturing*, SPOTLIGHT ON CDER SCIENCE (May 17, 2017), https://www.fda.gov/Drugs/NewsEvents/ucm557448.htm [https://perma.cc/AF26-9RH8] (describing continuous- vs. batch-manufacturing processes).

76. Lee, *supra* note 75.

77. Yu, *supra* note 70.

78. *Advanced Manufacturing: A Snapshot of Priority Technology Areas Across the Federal Government*, NAT'L SCI. & TECH. COUNCIL 29 (2016), https://www.whitehouse.gov/sites/whitehouse.gov/files/images/Blog/NSTC%20SAM%20technology%20areas%20snapshot.pdf [https://perma.cc/3E6J-EUJX].

79. Hanan Shaban et al., *Impact of Drug Shortages on Patient Safety and Pharmacy Operation Costs*, FED. PRACTITIONER, Jan. 2018, at 24, 31.

80. *Drug Shortages*, FOOD & DRUG ADMIN. (2017), https://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM441583.pdf [https://perma.cc/4SH3-3A95].

as glass or metal in vials."[81] Another 27% of shortages were due to quality issues involving delays,[82] such as when "embedded quality problems with one product forces closure of a production line or facility for repairs, resulting in shortage of other products."[83] These shortages are also costly to our health care system and may result in $230 million in additional costs annually for hospitals.[84]

So why do pharmaceutical companies still use outdated production methods?[85] In short, the regulatory structure. Initially, the patent system does not provide pharmaceutical companies with sufficient incentives to innovate in the development of new manufacturing processes. Although pharmaceutical companies can obtain patents on innovations in manufacturing technologies, those patents are extremely difficult to enforce.[86] A pharmaceutical company typically cannot determine if its competitors are using its patented manufacturing technology just from observing the sale of their finished products, so it is difficult for companies to detect infringement of their method claims.[87] As a result, companies often do not want to incur the costs of disclosing their innovations publicly (as is required to obtain a patent) if they cannot gain the benefits of excluding others from using their technologies.[88]

Further, the FDA approval process both encourages companies to begin production using older manufacturing techniques and makes it costly for companies to update those processes later in a drug's life cycle. When seeking

81. Sandra L. Kweder & S. Dill, Drug Shortages: The Cycle of Quantity and Quality, 93 CLINICAL PHARMACOLOGY THERAPEUTICS 245, 247 (2013).

82. *Drug Shortages*, *supra* note 80.

83. Kweder & Dill, *supra* note 81, at 247.

84. *Drug Shortages*, PEW CHARITABLE TRUSTS 5 (2017), http://www.pewtrusts.org/-/media/assets/2017/01/drug_shortages.pdf [https://perma.cc/T5UY-FQD7].

85. Because of the dynamics described here involving manufacturing and trade secrecy, it is difficult to determine exactly how many companies are actually using continuous-manufacturing methods. However, the FDA itself continues to note that "most drug makers" still use older manufacturing methods. *See* Scott Gottlieb, *FDA Budget Matters: Investing in Advanced Domestic Manufacturing*, FDA VOICE (July 13, 2018), https://www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/fda-budget-matters-investing-advanced-domestic-manufacturing [https://perma.cc/DP8H-S6LK]. To date, the FDA publicly cites only two examples of companies using continuous manufacturing methods: Vertex, which has used continuous manufacturing for its cystic-fibrosis product Orkambi since its approval in 2015, and Janssen, which received FDA approval in 2016 to change the production of its HIV product Prezista from batch to continuous manufacturing. *See* Yu, *supra* note 70; Michael Kopcha, *Continuous Manufacturing - Common Guiding Principles Can Help Ensure Progress*, AM. PHARMACEUTICAL REV. (Sept. 13, 2017), https://www.americanpharmaceuticalreview.com/2727-Blog/342223-Continuous-Manufacturing-Common-Guiding-Principles-Can-Help-Ensure-Progress [https://perma.cc/RML2-ZC5L]. Although there may be others, the agency portrays these two as notable exceptions to the general practice of batch manufacturing.

86. Price, *supra* note 71, at 526. This is true for a variety of reasons, including that process patents are often easier to design around than are product patents, since each step of the process must be performed to qualify as infringement. *See, e.g.*, Limelight Networks, Inc. v. Akamai Techs., Inc., 572 U.S. 915, 921-22 (2014).

87. Price, *supra* note 71, at 526.

88. *Id.*; *see also* Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL'Y L. & ETHICS 717, 722-23 (2005) (describing drug patenting practices).

initial approval, companies may be reticent to ask the FDA to approve a product using a novel, untested manufacturing procedure for fear that it will delay approval (increasing the company's costs and eating into their patent-protected time on the market) or even lead to a rejection.[89] Pharmaceutical companies can point to specific historical examples of this practice.[90] Therefore, even if today's FDA is more willing to approve such processes (as it is suggesting publicly),[91] risk-averse companies may understandably err on the side of using older manufacturing techniques at first.

But companies will also find it difficult to update those manufacturing processes once their products are on the market.[92] The FDA requires companies seeking to make changes to approved products to notify the agency before doing so.[93] And for "major" changes—a category that includes any change in the "production process" with a "substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product"[94]—the company must obtain the FDA's permission before implementing the change.[95] The expense, time, and risk of this additional approval process may dissuade companies from seeking such changes.

The existing regulatory frameworks combine to lock in manufacturing processes at an intermediate stage of development and have essentially frozen our pharmaceutical manufacturing systems several decades in the past. Helpfully, the FDA recognizes that pharmaceutical companies will not adopt novel manufacturing processes until the FDA "create[s] a clear path toward their adoption, and provide[s] more regulatory certainty that changing over to a new manufacturing system won't be an obstacle."[96] To that end, the FDA and other actors have begun to take steps toward addressing the problem. For instance, in 2016, the 21st Century Cures Act gave the Secretary of Health and Human Services the authority to award grants "for the purpose of studying and recommending improvements to the process of continuous manufacturing of drugs and biological products."[97] If the structure of the patent system does not provide sufficient incentives for companies to develop new manufacturing technologies, as noted above, it may be that public investment in those

89. Price, *supra* note 71, at 512-14.

90. *Id*. at 513 (explaining the FDA's repeated rejections of companies who wanted to use high performance liquid chromatography techniques in their manufacturing processes).

91. *See, e.g*., Gottlieb, *supra* note 85.

92. Price, *supra* note 71, at 516-18.

93. 21 C.F.R. § 314.70 (2019).

94. *Id*. § 314.70(b)(1).

95. *Id*. § 314.70(b)(3).

96. Gottlieb, *supra* note 85.

97. 21st Century Cures Act, Pub. L. No. 114-255, § 3016, 130 Stat. 1033, 1095 (2016) (codified at 21 U.S.C. § 399h). The administration's proposed budget for FY 2019 requests $58 million to invest in advanced manufacturing techniques of this type. *See* Scott Gottlieb, *President's Fiscal Year 2019 Budget Request for FDA - House Testimony* (Apr. 17, 2018), https://www.fda.gov/news-events/congressional-testimony/presidents-fiscal-year-2019-budget-request-fda-house-testimony [https://perma.cc/AYP5-K4G6].

technologies is needed to modernize these processes.[98] However, the regulatory and legislative environment in this area has not yet changed,[99] so incentives for manufacturers to modernize their manufacturing processes remain weak at present.

The case of pharmaceutical manufacturing represents a different kind of intermediate technology than does diagnostic testing. In some ways, the end product itself of course remains constant—the pharmaceutical. This case of *process improvements into existing technologies* is nevertheless one of intermediacy, as the goal remains one of technological improvement in a particular field over time. Process improvements, rather than substantive improvements, should be thought of as no less subject to the qualities of intermediacy I focus on here, bringing this paper in agreement with Merges and Nelson's framing of them as "cumulative" technologies.[100]

3. Tissue as a Platform Technology

A third set of examples comes in the area of human tissues and their possible uses in the medical field. To choose a specific area within this broader category, in recent years, scientific interest in the microbiome, the community of microbes that lives within each of our bodies and exists in a symbiotic relationship with our own cells,[101] has exploded.[102] Scientists have linked the microbiome to a vast range of human diseases: autoimmune disorders like diabetes and arthritis; mental health conditions like schizophrenia and depression; and to a range of conditions affecting our intestinal systems, including Crohn's disease and antibiotic-resistant infections.[103] One day, scientists may be able to cure diseases not by administering typical medicines, which may achieve their goals while simultaneously imposing harmful side effects, but rather by altering the balance of our bodies' own internal flora.

As yet, however, only one effective microbiome-based treatment has been developed: fecal microbiota transplantation (FMT) for the treatment of recurrent *Clostridium difficile* infections. *C. difficile* is the most common

98. *See* Kapczynski & Syed, *supra* note 16.

99. The FDA has sought public comment on the topic of "best practices" regarding the development of continuous manufacturing technologies. *See* Submission of Proposed Recommendations for Industry on Developing Continuous Manufacturing of Solid Dosage Drug Products in Pharmaceutical Manufacturing; Establishment of a Public Docket, 82 Fed. Reg. 28664, 28665 (June 23, 2017).

100. Merges & Nelson, *supra* note 32, at 883, 898.

101. ED YONG, I CONTAIN MULTITUDES 5 (2016).

102. *See, e.g.*, *Innovations in the Microbiome*, SCI. AM. (Feb. 17, 2015), https://www.scientificamerican.com/report/innovations-in-the-microbiome [https://perma.cc/7E88-J8E3]; *Microbes Maketh Man*, ECONOMIST (Aug. 18, 2012), https://www.economist.com/leaders/2012/08/18/microbes-maketh-man [https://perma.cc/QGM8-WEHX].

103. Dirk Gevers et al., *The Treatment-Naïve Microbiome in New-Onset Crohn's Disease*, 15 CELL HOST & MICROBE 382 (2014). Some of these links have stronger scientific support than others, but it is clear that the microbiome plays a key role in maintaining human health.

hospital-acquired infection,[104] and it takes a large—and growing[105]—toll on our health care system and on the health of American patients.[106] To put it simply, FMT is the transfer of stool from a healthy donor into the bowel of a patient. The cure rate for those who experience two or more recurrences of *C. difficile* infection and receive a fecal transplant is 90%—far beyond the 30-to-40% chance they face with standard antibiotic medicines.[107]

Unfortunately, microbiome-based treatments have not demonstrated the same success in preliminary trials for other conditions. One recent randomized, placebo-controlled trial of FMT in ulcerative colitis showed moderate efficacy overall, but nearly all of that efficacy was traceable to patients receiving samples from a single donor.[108] Patients receiving samples from other donors did not experience as good clinical outcomes on average.[109] Scientists do not yet know why this donor's stool is particularly effective at treating patients with ulcerative colitis, but they are continuing to study the question.

Studies like these serve as important reminders of how much we have yet to learn about the microbiome—in other words, how the existing technologies are intermediate in nature. The use of stool is a bridge or platform technology.[110] Scientists and physicians do not hope that fecal transplants will still be the norm a decade from now. Instead, the hope is that scientists will learn more about which microbes, or even which genes, are most important for the healthy functioning of our gut microbiomes, allowing scientists to culture specific strains of bacteria, genetically engineer microbes, or isolate metabolites to fight and prevent disease. But we are not there yet.

A key concern at this time is that the two primary regulatory structures operating around the microbiome, FDA approval and patent protection, may

104. Shelley S. Magill et al., *Multistate Point-Prevalence Survey of Health Care-Associated Infections*, 370 N. ENG. J. MED. 1198, 1198 (2014).

105. The number of *C. difficile* infections doubled between 2000 and 2005, Marya D. Zilberberg, Andrew F. Shorr & Marin H. Kollef, *Increase in Adult* Clostridium Difficile*-Related Hospitalizations and Case-Fatality Rate, United States, 2000-2005*, 14 EMERGING INFECTIOUS DISEASE 929, 929 (2008), and hospitalizations due to these infections doubled between 2000 and 2010, Fernanda C. Lessa, et al., *Burden of* Clostridium Difficile *Infection in the United States*, 372 NEW ENGL. J. MED. 825, 826 (2015).

106. *C. difficile* causes more than twenty-nine thousand deaths in the U.S. each year, *National Action Plan for Combating Antibiotic-Resistant Bacteria*, WHITE HOUSE 60 (Mar. 2015), https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf [https://perma.cc/69VH-7R3E], and it is estimated to cost our health care system $4.8 billion annually, Erik R. Dubberke & Margaret A. Olsen, *Burden of* Clostridium Difficile *on the Health Care System*, 55 CLINICAL INFECTIOUS DISEASES S88, S88 (2012).

107. Gauree G. Konijeti et al., *Cost-Effectiveness of Competing Strategies for Management of Recurrent* Clostridium Difficile *Infection: A Decision Analysis*, 58 CLINICAL INFECTIOUS DISEASES 1507, 1511 (2014).

108. Paul Moayyedi et al., *Fecal Microbiota Transplantation Induces Remission in Patients with Active Ulcerative Colitis in a Randomized Controlled Trial*, 149 GASTROENTEROLOGY 102, 105 (2015).

109. *Id*.

110. Rachel E. Sachs & Carolyn A. Edelstein, *Ensuring the Safe and Effective FDA Regulation of Fecal Microbiota Transplantation*, 2 J.L. & BIOSCIENCES 396, 413 (2015).

make it difficult to develop the next generation of therapies, building on the foundation of evidence developed from FMT and related research. First, the FDA has chosen to regulate microbiome-based therapies as biologic drugs, rather than under its paradigms for regulating human tissues like blood.[111] That decision requires microbiome companies to traverse the lengthy, expensive clinical trial process before bringing microbiome-based therapies to market. It is true that the FDA review process generates critical information about new health care technologies and serves important public health purposes.[112] For pharmaceuticals that more closely resemble the Merges & Nelson ideal of a discrete innovation representing an end in itself,[113] the FDA approval process may not pose concerns for follow-on innovation.

However, in the microbiome context, there is reason to think that applying the standard FDA review process to these new therapies may slow or stifle the development of new information about the microbiome's relationship to different diseases. Under the standard FDA approval model, once a new drug is approved for a particular indication, doctors are typically free to prescribe that drug for *any* use, even ones not listed on the label or studied by the manufacturer.[114] Approving FMT or even a collection of cultured microbes for use in the treatment of recurrent *C. difficile* infections would permit physicians to prescribe that product for other, unproven indications, when it is the development of new information about those indications that society needs most intensely.

What company would do clinical trials on those new indications when there is a risk they might fail and when their product can be sold for these indications anyway?[115] This question—how to encourage pharmaceutical companies to invest in studying new uses for existing drugs[116]—is a broader one that has been studied in the literature, but typically in contexts where the biological basis for the drug in question was more well-understood than it is in the microbiome context and where the FDA did not have a choice about how to regulate the product in question.[117] In this case, the FDA made a choice to regulate microbiome-based technologies as biologic drugs. That choice has implications for innovation incentives in this field.

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111. Sachs & Edelstein, *supra* note 110, at 410-12. Importantly, this was not obviously required by existing statutes and regulations. *See* 21 U.S.C. § 321(g)(1) (2018) (defining "drug"); 42 U.S.C. § 262(i)(1) (2018) (defining "biological product"); 21 C.F.R. § 1271.3(d)(3) (2019) (defining human cells and tissues).

112. Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345 (2007).

113. *See supra* text accompanying notes 32-44 (explaining Merges & Nelson's taxonomy).

114. David C. Radley et al., *Off-label Prescribing Among Office-Based Physicians*, 166 ARCHIVES INTERNAL MED. 1021, 1021 (2006).

115. *See* Kapczynski & Syed, *supra* note 16, at 1926-27.

116. Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL'Y, L. & ETHICS 717, 720-21 (2005); Rachel E. Sachs, Paul B. Ginsburg, & Dana P. Goldman, *Encouraging New Uses for Old Drugs*, 24 J. AM. MED. ASS'N 2421 (2017).

117. *See* Sachs & Edelstein, *supra* note 110, at 413 n.109.

But the impact of the FDA approval process on innovation in the microbiome field cannot be understood alone. The interaction of the FDA approval process with a second regulatory structure—the patent system—has implications for innovation as well. Thus far, it has proven difficult for researchers to obtain patents on the current generation of microbiome therapies, chiefly those using FMT techniques or those studying cultures of specific bacterial strains.[118] If it were inexpensive to bring new microbiome-based therapies to market, perhaps the paucity of patent protection in this field would not be a warning sign for innovation. But the FDA's decision to impose the traditional pharmaceutical approval process on microbiome-based therapies renders the development process lengthy and expensive, and it is typically thought that patents are a critical incentive for encouraging companies to develop new pharmaceuticals and to transact in the informational goods necessary to complete that process.[119]

At present, some companies developing microbiome-based therapies are moving forward by relying on thin patent protection, combined with trade secrecy and the promise of FDA exclusivity periods that provide patent-like protection after a new drug is approved.[120] But others are likely opting out. At least some number of microbiome companies are looking at the regulatory landscape and choosing to develop products that will not be subject to FDA regulation. In short, it's possible that the existing regulatory structures are dissuading investors and companies from developing the current generation of microbiome-based therapies, raising questions about whether future generations will be developed.

This third set of intermediate technologies can be conceived of as broader in nature: platform technologies that lay the foundation for *expansion of existing technologies*, indications, or uses. In some ways, this set of examples is different in kind from the previous two situations. The recognition of the platform nature of the technology may counsel in favor of different approaches that allow greater room for future experimentation and latitude than in the context of iterative improvements in a particular, existing technology.

One question raised by this diversity of examples is simple: isn't *everything* intermediate in some meaningful way? More specifically, if my examples of intermediate technologies display such different characteristics,

118. *See* Rachel E. Sachs, *The Uneasy Case for Patent Law*, 117 MICH. L. REV. 499, 528 (2018).

119. *See, e.g.*, Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1617 (2003); FED. TRADE COMM'N, TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW AND POLICY ch. 3, at 14 (2003).

120. Once a new drug is approved by the FDA, its sponsor will typically receive an FDA-administered exclusivity period for that drug. Depending on the type of drug involved, companies will receive either five, seven, or twelve years of exclusivity to market their drug, although these exclusivities differ by type and precise mechanics. *See, e.g.*, 21 U.S.C. § 355(j)(5)(F)(ii) (2018) (Hatch-Waxman Act, conferring a five-year period of exclusivity for small-molecule drugs); *Id*. § 360cc(a) (Orphan Drug Act, conferring seven years of market exclusivity); 42 U.S.C. § 262(k)(7)(A) (2018) (Biologics Price Competition and Innovation Act, conferring twelve years of data exclusivity).

don't the broader categories of regulated technologies that they represent cover the vast majority of technologies we might be concerned about? I have presented the above examples as discrete sets of inventions, but these examples might instead cover nearly the entire regulated field.

It is at least possible that this is the case. If so, however, it is important to consider what challenges, if any, this might pose to the overall inquiry. My core claim—that there is a set of technologies in need of this type of iterative improvement but where regulatory barriers exist to that improvement—would still hold even if the class of intermediate technologies is broader than I currently describe. With exceptions as described *infra* in Part II, existing regulations do not acknowledge the vast majority of technologies as intermediate, and they certainly do not acknowledge that technologies currently viewed as end stage (such as small-molecule drugs) are instead intermediate. This broader view would suggest that I have identified an even larger problem, in need of even more solutions, than I have otherwise articulated.

It is also possible that this question really reflects a clash between old and new forms of technological innovation, particularly in the life sciences and the pace at which those forms evolve. Small-molecule drugs, even if they eventually lead to new discoveries, do not approach the intermediacy displayed by medical algorithms or software on any reasonable timescale. The 1962 amendments to the Food, Drug, and Cosmetic Act giving the FDA new authority to regulate drugs[121] had in mind small-molecule drugs, as that was the particular type of technology the agency was faced with, not technologies that would come to prominence a half century or more later. A regulatory paradigm based around older technology is now in place to shape the development of very different kinds of technologies.

II. Existing Doctrinal Approaches to Temporal Regulation

Although the question of intermediacy has not been explicitly dealt with in the literature, different areas of law have dealt with related questions. First, patent law contains a set of doctrines designed to mediate between the interests of first inventors and subsequent improvers. Second, food and drug law has more specifically considered the problem of intermediacy in the context of health care software. Third, environmental law scholars and practitioners have developed a theory of adaptive management, in which agencies are able to alter their regulations in the face of new information or changing conditions. Fourth and finally, isolated doctrines within reimbursement policy can be understood within the intermediate-technology framework.

121. Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (codified as amended at 21 U.S.C. § 355).

A. Patent Law

As noted in Part I *supra*, there is a strong history of intellectual property scholarship examining the question of cumulative or sequential innovation.[122] The fundamental question is one of patent scope: how broadly or narrowly should initial innovators be granted protection over their invention? Some scholars (most notably Professor Edmund Kitch) have argued that granting broad, initial patents will best incentivize full development of a particular technological field,[123] while others have argued that broad patenting, particularly in fields characterized by "cumulative innovation" of the Merges and Nelson variety, is highly likely to stifle full development.[124] Many doctrines within patent law are tied explicitly or implicitly to this question of scope, but there are two doctrines in particular—blocking patents and the reverse doctrine of equivalents—which deal specifically with the rights of improvers.

The typical situation contemplated in the case of blocking patents has been expressed succinctly by Professor Arti Rai:

> [T]he second-generation inventor comes up with a patentable (that is, novel and nonobvious) improvement on the first-generation invention. Although the second-generation improvement is independently patentable, it nonetheless incorporates the first-generation invention and therefore infringes the first inventor's patent. In order to practice its improvement, the second-generation inventor must therefore seek a license from the first-generation inventor. (Conversely, if the first-generation inventor wants to practice the improvement, it must seek a license from the improver.)[125]

The first- and second-generation patents "block" each other in the sense that each patentee must seek a license from the other before being able to practice their invention.[126] Although ideally such licensing will occur, both

122. *See, e.g.*, Kevin Emerson Collins, *Getting into the "Spirit" of Innovative Things: Looking to Complementary and Substitute Properties to Shape Patent Protection for Improvements*, 26 BERKELEY TECH. L.J. 1217, 1271-72 (2011); Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEX. L. REV. 989, 991-92 (1997); Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. ECON. PERSP. 29, 33-35 (1991).

123. Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265, 275-80 (1977).

124. *See, e.g.*, Merges & Nelson, *supra* note 32, at 872-73; Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 BERKELEY TECH. L.J. 813, 831 (2001).

125. Rai, *supra* note 124, at 833. Professor Kevin Collins refers to the situation envisioned here as one involving "classic improvements," hypothesizing additional relationships between initial and subsequent patentees and their technologies. Collins, *supra* note 122, at 1272-73.

126. For examples of this phenomenon, see Robert Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75, 84 (1994).

theory and practice predict that in many cases the various rightsholders will be unable to reach an agreement.[127]

The reverse doctrine of equivalents goes further. In the case of moderate improvements to existing technologies, improvers may obtain blocking patents, even as they are also liable for infringement (in the event they attempt to practice the initial patent in question). But in the case of more radical improvements,[128] improvers may not only obtain a patent—they may be able to escape infringement entirely. An equitable doctrine, the purpose of the reverse doctrine of equivalents is to "prevent unwarranted extension of the claims beyond a fair scope of the patentee's invention."[129] Particularly in situations where "a device is so far changed in principle from a patented article that it performs the same or a similar function in a substantially different way, but nevertheless falls within the literal words of the claim,"[130] courts may limit the potential scope of a patentee's claims. Although the reverse doctrine of equivalents has lost favor with the Federal Circuit today,[131] some academics have called for the doctrine to be revitalized.[132]

Taken together, blocking patents and the reverse doctrine of equivalents encapsulate particular views about the relationship between initial and subsequent improvements in technology. Minor improvements may fall within the scope of an initial patent and may not receive any benefit for their efforts. Significant improvements may be able to be patented, even as they are subject to the constraint of an earlier patent. And radical improvements may be able to avoid infringement liability entirely.[133]

These scholarly debates also represent particular views about how many actors might be involved in the development of a particular technology. Kitch envisions a single initial innovator who is driven to develop (either on their own or through licensing) a particular technology, whereas Professor Suzanne Scotchmer, Rai, and others envision competing inventors driving progress forward.

In the intermediate-technologies context, it is not clear that one of these models will dominate. In the case of improvements to existing technologies (in the Myriad case), it might be more likely for a single innovator to focus on improving their technology,[134] whereas in the case of expansions of existing technologies, competing inventors may be more likely.

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127. Rai, *supra* note 124, at 833-35.

128. *See* Lemley, *supra* note 122, at 1010.

129. Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1581 (Fed. Cir. 1991).

130. Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 608-09 (1950).

131. *See* Samuel F. Ernst, *The Lost Precedent of the Reverse Doctrine of Equivalents*, 18 VAND. J. ENT. & TECH. L. 467, 472-73 (2016).

132. *See id*. at 496.

133. *See* Lemley, *supra* note 122, at 1007-10.

134. Even in this case, Kitch's argument in support of a broad patent scope would not necessarily apply, as the particular technology involved is not necessarily an expansive one.

B. Food and Drug Regulation

The FDA currently employs two regulatory strategies in the medical device context that could inform an updated regulatory approach to intermediate technologies. First, the FDA's procedure for evaluating new medical devices that make only incremental changes to existing devices is helpful in considering the relationship between existing technologies and potential improvements. Second, the FDA's newer approach to regulating software in the medical device context provides an example of a technology-specific accommodation that might have broader applications in the intermediate-technologies context.

1. Incremental Improvements and the 510(k) Pathway

In the context of medical devices, the FDA oversees a regulatory framework that explicitly distinguishes between devices that make only incremental changes to existing products and devices that make more significant advances. This oversight has given the FDA experience in thinking about the relationships between existing technologies and new, improved technologies, in a way that is helpful in enabling the agency to identify possible situations of intermediate technologies. But this program has also provided the FDA with an appreciation for the ways in which altered regulatory barriers may encourage companies to move forward with the development of new technologies—and the ways in which that encouragement can come with costs.

The FDA employs a risk-based framework for the evaluation and approval of new medical devices. High-risk, or Class III, devices (such as an artificial heart)[135] are subject to significant regulatory requirements, typically including a premarket approval (PMA) process resembling the set of clinical trials required in the pharmaceutical context, before they are permitted to come to market.[136] By contrast, low-risk, or Class I, devices (such as a tongue depressor)[137] are subject to relatively few requirements, such as adherence to good manufacturing practices, before they may be sold.[138] Intermediate, or Class II, devices (such as wheelchairs)[139] are those where the types of general controls governing Class I devices are insufficient, but the potential safety and efficacy concerns over the device's use do not rise to the level observed for Class III devices.[140]

135. Replacement Heart Valve, 21 C.F.R. § 870.3925 (2019).
136. 21 U.S.C. § 360c(a)(1)(C) (2018).
137. Tongue Depressor, 21 C.F.R. § 880.6230.
138. 21 U.S.C. § 360c(a)(1)(A).
139. Powered Wheelchair, 21 C.F.R. § 890.3860.
140. 21 U.S.C. § 360c(a)(1)(B).

Class II devices may be required to pursue the full PMA process. Yet in the vast majority of cases,[141] such devices are able to come to market through the 510(k) pathway.[142] This pathway requires companies to demonstrate that their device is "substantially equivalent" to another approved device.[143] Once they do so, companies are able to simply notify the FDA of their intention to market a new device, rather than wait for affirmative FDA approval.[144] Compared to the PMA process, the 510(k) pathway is significantly cheaper and quicker for companies.[145] Not only are the fees companies must pay to the FDA for review of their device far higher in the PMA context,[146] but the tens of millions of dollars needed to complete the clinical trial process for the PMA dwarf the costs associated with the 510(k) process.[147]

In many ways, it is helpful to think of the 510(k) process as mapping clearly onto the context of intermediate technologies. The initial justification for the 510(k) process was "to give manufacturers the opportunity to make small improvements on the devices already on the market,"[148] just as it is my hope in the intermediate technologies context that companies will be able to improve existing technologies. The 510(k) pathway thus presents one example of a situation in which the FDA (in collaboration with Congress) has lowered the regulatory barriers for companies to engage in incremental changes, and particularly incremental improvements. More generally, the idea of decreasing regulatory barriers to improvements in existing technologies is one strategy to address the problem of intermediate technologies.

But this strategy comes with a cost. In particular, we might be concerned that regulatory barriers may be lowered too far, resulting in the approval of unsafe or inefficacious medical devices, harming patient care in at

141. Jeffrey K. Shapiro, *Substantial Equivalence Premarket Review: The Right Approach for Most Medical Devices*, 69 FOOD & DRUG L.J. 365, 365 (2014) ("Of devices requiring premarket review, about 2% reach the market via premarket application (PMA) approval or the Humanitarian Device Exemption (HDE) variant, while the remaining 98% receive 510(k) clearance.").

142. Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, §§ 510(k), 513(f), 52 Stat. 1040 (codified as amended at 21 U.S.C. §§ 360(k), 360c(f) (2018)) (premarket notification process and substantial equivalence mechanism); *see also* Jonathan S. Kahan, *Premarket Approval Versus Premarket Notification: Different Routes to the Same Market*, 39 FOOD DRUG COSMETIC L.J. 510, 514-15 (1984) (describing advantages of the 510(k) pathway).

143. 21 U.S.C. § 360c(f)(1)(A)(ii) (2018).

144. *Premarket Notification 510(k)*, FOOD & DRUG ADMIN. (2018), https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/%20PremarketNotification510k/default.htm [https://perma.cc/V7S3-MQ9U].

145. U.S. GOV'T ACCOUNTABILITY OFF., FDA SHOULD TAKE STEPS TO ENSURE THAT HIGH-RISK DEVICE TYPES ARE APPROVED THROUGH THE MOST STRINGENT PREMARKET REVIEW PROCESS 15-16 (2009).

146. *FY 2019 MDUFA User Fees,* FOOD & DRUG ADMIN., (2018), https://www.fda.gov/forindustry/userfees/medicaldeviceuserfee/ucm452519.htm [https://perma.cc/L744-XPRH] (setting the user fee for the 510(k) pathway at $10,953 and for the PMA process at $322,147).

147. Adam Lewin, *Medical Device Innovation in America: Tensions Between Food and Drug Law and Patent Law*, 26 HARV. J.L. & TECH. 403, 409 (2012).

148. Diana Zuckerman et al., *Medical Device Recalls and the FDA Approval Process*, 171 ARCHIVES INTERNAL MED. 1006, 1007 (2011).

least some cases. Indeed, the 510(k) process has been criticized along these lines (although the program has strong defenders as well[149]), leading the agency to propose reforms to the existing process.[150] This tradeoff between speed of innovation and quality of information developed about a particular product is one the FDA makes in many different contexts, and it must be managed each time. The problem of intermediate technologies will be no different.

2. Novel Approaches to Regulating Medical Software

The increasing development of digital health technologies over the last several years has created a number of challenges for the FDA and its traditional approval system for medical devices. The statutory definition of "device" is quite broad,[151] and it encompasses a wide range of medical software, whether that software establishes a simple electronic health care record or screens images to detect the presence of cancer. But the FDA has also recognized that software is often a poor fit with the classic medical device approval paradigm, in at least two senses. First, the risks posed by medical software are often different in kind from those posed by traditional medical devices, making it difficult to fit medical software within the risk-based medical device approval system. And second, it is beneficial for some technologies—such as medical software—to be iterated and updated on a far faster timescale than is typical of standard medical devices. As a result, the FDA (sometimes with the assistance of Congress) has made accommodations in its regulatory process to address both of these differences.

As noted *supra* in Section II.B.1, the FDA oversees a risk-based framework for the evaluation and approval of new medical devices. The difference in potential risks to the patient from the use of a Class I device like a tongue depressor versus a Class III device like an artificial heart may seem obvious. But it more difficult to translate this framework to the digital health or medical software context, where it is often not the software itself, but the decision made as a result of using the software, that poses risk to the patient.[152]

149. James M. Flaherty, Jr., *Defending Substantial Equivalence: An Argument for the Continuing Validity of the 510(k) Premarket Notification Process*, 63 FOOD & DRUG L.J. 901, 902-03 (2008); Shapiro, *supra* note 141, at 365-66.

150. *See, e.g.*, *Statement from FDA Commissioner Scott Gottlieb, M.D. and Jeff Shuren, M.D., Director of the Center for Devices and Radiological Health, on Transformative New Steps to Modernize FDA's 510(k) Program to Advance the Review of the Safety and Effectiveness of Medical Devices* (Nov. 26, 2018), FOOD & DRUG ADMIN., https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm626572.htm [https://perma.cc/8YZT-34LA].

151. 21 U.S.C. § 321(h) (2018) ("[A]n instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease").

152. The difficulty of applying the risk-based medical device framework has also carried over to the context of diagnostic tests, where the FDA has faced similar regulatory challenges. *See, e.g.*, Sachs, *supra* note 5, at 1896.

As a result, the FDA has endeavored to exempt entire categories of medical software from its regulatory oversight. The FDA initially announced its intention to exercise its enforcement discretion for mobile health technologies that performed tasks like assisting patients in organizing their health information, coaching patients on strategies for maintaining healthy diets, or assisting providers in the performance of basic calculations, most of which had been previously performed without the aid of mobile health technologies.[153] The FDA also offered an interpretation of the statute under which certain mobile health technologies would not be considered medical devices at all, such as those that provide access to electronic versions of hard-copy medical textbooks, help train health care providers, or automate health care office operations.[154] These interpretations were substantially codified in 2016's 21st Century Cures Act, which exempted these categories of software from the definition of "device,"[155] unless the agency makes a finding that a specific software program would be "reasonably likely to have serious adverse health consequences."[156]

Second, the FDA has recognized that it may be advantageous for patient care to permit medical software to update on a more rapid timescale than is standard for medical devices. Not only are product lifecycles in the software field typically much shorter than those in other contexts, including health care,[157] but it would likely be beneficial to permit companies to fix previously undiscovered glitches or adverse events in a piece of code without obtaining permission beforehand from the FDA.[158] The FDA has advanced a Digital Health Innovation Action Plan in the hopes of grappling with some of the challenges posed by medical software.[159] The Plan includes some of the strategies articulated above, carving out certain medical software systems from the FDA's jurisdiction. It also considers more novel regulatory approaches for this class of technologies.

153. *Mobile Medical Applications: Guidance for Industry and Food & Drug Administration Staff*, FOOD & DRUG ADMIN. 15-18 (Feb. 2015).

154. *Id*. at 20-22.

155. 21st Century Cures Act, Pub. L. No. 114-255, § 3060, 130 Stat. 1033, 1130 (2016) (codified at 21 U.S.C. § 360j (2018)).

156. 21 U.S.C. § 360j(o)(3)(A)(i) (2018).

157. Burk & Lemley, *supra* note 119, at 1622; Julie E. Cohen & Mark A. Lemley, *Patent Scope and Innovation in the Software Industry*, 89 CALIF. L. REV. 1, 39, 46 (2001).

158. *Digital Health Software Precertification Program*, FOOD & DRUG ADMIN. (2018), https://www.fda.gov/medicaldevices/digitalhealth/digitalhealthprecertprogram/default.htm [https://perma.cc/684T-WPM9] ("Because software products can be adapted to respond to glitches, adverse events, and other safety concerns quickly, the FDA is working to establish a regulatory framework that is equally responsive when issues arise to help ensure consumers continue to have access to safe and effective products.").

159. *Digital Health Innovation Action Plan*, FOOD & DRUG ADMIN. (2017), https://www.fda.gov/downloads/MedicalDevices/DigitalHealth/UCM568735.pdf [https://perma.cc/RS6N-V8B8].

Perhaps most notably, the FDA is now piloting the Digital Health Software Precertification Program,[160] which allows the agency to approve software *developers*, rather than software *technologies*, to speed the marketing and updating of a particular technology.[161] Pre-certified firms may be able to market a lower-risk device without FDA approval or with a streamlined review process, and would be able to support evolving product functions as well. In September 2017, the FDA selected nine companies for inclusion in the pilot program.[162] Although none have publicly been pre-certified yet, at least one—Apple—has recently won approval under a different FDA pathway for Apple Watch apps that monitor a user's heart rhythms to detect the presence of particular conditions.[163]

There are benefits and costs to both approaches. Perhaps most obviously, these programs make it easier for digital health companies to bring their products to market. To the extent that these technologies are beneficial for patient care, speeding their path to market enables those patients to reap the associated benefits sooner. These programs also assist the FDA in managing its scarce resources. Carving some technologies out of its jurisdiction or developing a policy of enforcement discretion enables the agency to focus on higher-risk technologies, while also providing companies with greater certainty about their regulatory obligations.

But there are potential costs to these approaches as well. First, because the point is for those technologies to iterate and improve with time, it is possible that earlier versions of the product might contain errors or fail to catch concerning symptoms, resulting in harm to patients. Second and relatedly, it is possible that consumers will not understand the difference between "FDA approval" and "FDA preclearance," meaning that they will not be appropriately informed about the risks involved.[164] Third, as Professor Nicolas Terry has

160. *Id*. at 5-6; *see also Digital Health Software Precertification Program*, *supra* note 158.

161. As of this writing, the Precertification Program applies only to software that is being used *as* a medical device, such as software that can analyze images to detect the presence or absence of a disease, rather than software *in* a medical device, such as software that is used to operate a pacemaker or infusion pump. *Examples of Software as a Medical Device*, FOOD & DRUG ADMIN. (2018), https://www.fda.gov/medicaldevices/digitalhealth/softwareasamedicaldevice/ucm587924.htm [https://perma.cc/C6DJ-WCFT].

162. *Digital Health Software Precertification Program*, *supra* note 158.

163. Letter from Angela Kruger, Food & Drug Admin. Ctr. for Devices & Radiological Health, to Donna-Bea Tillman, Biologics Consulting Grp. (Sept. 11, 2018), https://www.accessdata.fda.gov/cdrh_docs/pdf18/DEN180044.pdf [https://perma.cc/9QX4-QUYN] (noting that the request was for de novo review); *see also Statement from FDA Commissioner Scott Gottlieb, M.D., and Center for Devices and Radiological Health Director Jeff Shuren, M.D., J.D., on Agency Efforts to Work with Tech Industry to Spur Innovation in Digital Health*, FOOD & DRUG ADMIN. (Sept. 12, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/UCM620246.htm [https://perma.cc/UBM5-7F36] (describing the FDA's efforts to use "more modern, flexible, and risk-based approach[es] to regulation" for digital health products).

164. *See* DANIEL CARPENTER, REPUTATION AND POWER 10-11 (2010) (emphasizing the trust patients put in the FDA and its consumer protection function); Joy Victory, *What Did Journalists Overlook About the Apple Watch "Heart Monitor" Feature?*, HEALTHNEWSREVIEW.ORG (Sept. 18,

argued, companies may engage in "regulatory arbitrage."[165] That is, digital health companies, seeing that only some technologies will be subject to more costly FDA approval,[166] may design their technologies to avoid being subject to regulatory scrutiny.[167] Regulatory arbitrage of this kind has at least two kinds of costs. First, some patients may be harmed by a technology that arguably should have been subject to FDA review.[168] Second, some number of technologies will not be developed or will be developed with fewer features to avoid FDA scrutiny, and patients will miss out on the benefits of those undeveloped technologies.

There is an additional question about whether the precertification program is within the FDA's existing statutory authority. Recently, Senators Patty Murray, Tina Smith, and Elizabeth Warren sent a letter to the FDA asking what statutory and regulatory authority the agency seeks to rely on not only in conducting the precertification pilot program but also in granting "preliminary" approval in the way that precertification envisions.[169] Even if no company would be interested in or able to sue the FDA for what is essentially an exercise of enforcement discretion, congressional pressure might encourage the agency to slow or even abandon the program.

The FDA's regulatory accommodations in the medical software field provide insight into the problem of intermediate technologies. As I argued in Section I.B *supra*, the FDA's decision to exercise enforcement discretion over laboratory-developed tests may have enabled Myriad not only to launch but also to improve its genetic tests over time. But this enforcement discretion has come with costs for patients, suggesting that a system more akin to

2018), https://www.healthnewsreview.org/2018/09/what-did-journalists-overlook-about-the-apple-watch-heart-monitor-feature [https://perma.cc/7XGN-3NLV].

165. Nicolas P. Terry, *Regulatory Disruption and Arbitrage in Health care Data Protection*, 17 YALE J. HEALTH POL'Y L. & ETHICS 143 (2017); *see also* Victor Fleischer, *Regulatory Arbitrage*, 89 TEX. L. REV. 227, 230 (2010).

166. FDA approval is a costly process, even if the type of scrutiny Apple underwent for its apps does not rise to the level of clinical trials required for a more invasive medical device. One survey of medical device companies found that Class III devices are typically far more expensive to develop than Class II devices. Josh Makower et al., *FDA Impact on U.S. Medical Innovation* 28 (Nov. 2010), http://eucomed.org/uploads/Press%20Releases/FDA%20impact%20on%20U.S.%20Medical%20Technology%20Innovation.pdf (estimating the cost of developing a Class III device at $94 million, and a Class II device as $31 million). Other sources breaking these aggregate numbers down by stage of development confirm the survey's rough estimates. *See, e.g.*, Aaron V. Kaplan et al., *Medical Device Development: From Prototype to Regulatory Approval*, 109 Circulation 3068, 3069, 3072 (2004).

167. *See generally* Terry, *supra* note 165 (discussing regulatory arbitrage in the health care context).

168. *Cf. The Public Health Evidence for FDA Oversight of Laboratory Developed Tests: 20 Case Studies*, FOOD & DRUG ADMIN. (Nov. 2015), http://wayback.archive-it.org/7993/20171115144712/https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM472777.pdf [https://perma.cc/4FQC-Y29Z] (detailing consumer harms from laboratory-developed tests, which are essentially unregulated by the FDA).

169. Letter from Senators Murray, Smith, & Warren to Scott Gottlieb, FDA Comm'r (Oct. 10, 2018), https://www.warren.senate.gov/imo/media/doc/2018.10.10%20Letter%20to%20FDA%20on%20regulation%20of%20sofware%20as%20medical%20device.pdf [https://perma.cc/Z5WE-EH4E].

precertification—in which the manufacturer is identified and managed but rapid updates are permitted—might be appropriate as well. Similarly, a system of precertification might have relevance in the manufacturing context, as the idea of permitting a single company or manufacturer to undergo one oversight review for updating their manufacturing systems for multiple drugs could be considered.

C. Adaptive Regulation Models

Outside the context of health care regulation, regulatory structures that account for temporal technological development of the kind considered in this Article feature prominently in environmental law and legal scholarship.[170] Environmental law has made use of adaptive management and regulatory strategies to help enable environmental regulations to iterate in the face of new information or changing conditions. Although there are key differences between environmental regulation and the health care technologies context, the focus on administrative flexibility in the face of uncertainty about both factual situations and changing technology provides a helpful perspective from which to view the problem of intermediate technologies.

Adaptive management differs from the traditional model of administrative rulemaking, in which agencies devote resources on the front end to developing a particular regulatory structure and then observe how that structure plays out. In adaptive management, agencies instead "engage in a program of iterative decision-making following a structured, multistep protocol."[171] They may use a range of regulatory strategies to engage in this iterative process. For instance, they might provide for periodic opportunities to revisit existing rules,[172] include procedures for agency reconsideration as new information is developed,[173] or even provide for regulations to update automatically as events occur.[174] More generally, scholars have argued that adaptive regulation may be particularly useful where there is high uncertainty,

170. Adaptive management systems have been applied in other contexts, such as financial regulation. *See* Charles K. Whitehead, *The Goldilocks Approach: Financial Risk and Staged Regulation*, 97 CORNELL L. REV. 1267, 1302-04 (2012); *see also* Justin R. Pidot, *Governance and Uncertainty*, 37 CARDOZO L. REV. 113, 127-29 (2015) (describing financial regulation under conditions of uncertainty).

171. Robin Kundis Craig & J.B. Ruhl, *Designing Administrative Law for Adaptive Management*, 67 VAND. L. REV. 1, 7 (2014).

172. Pidot, *supra* note 170, at 142-45 (2015); *see also* Jacob E. Gersen, *Temporary Legislation*, 74 U. CHI. L. REV. 247, 247 (2007) (describing "temporary legislation" that limits its own duration); Zachary J. Gubler, *Experimental Rules*, 55 B.C. L. REV. 129, 130 (2014) (describing "reversible" rules that allow for reconsideration with additional information).

173. Pidot, *supra* note 170, at 151-56.

174. *Id*. at 164-65.

the agency has considerable control over its decisions, and the risk resulting from a potential regulatory error is low.[175]

In some ways, the ideas of adaptive regulation may seem to be a poor fit for the health care technologies context. First, adaptive management developed in the context of agencies engaging in notice-and-comment rulemaking, governed by the provisions of the Administrative Procedure Act, in an attempt to give agencies greater ability to oversee complex, evolving situations.[176] Although the FDA and CMS *can* and often do engage in substantive rulemaking,[177] their core functions at issue in this Article—the approval of and reimbursement for new health care technologies—take place at some removal from the formulation of those approval standards in the first instance. Second, a core goal of adaptive management is to enable *laws and regulations* to change, and only sometimes is that in response to changes in technologies (sometimes it is a response to the development of new information, which is a distinct concern). By contrast, my focus here is on appropriate regulatory structures to employ in the context of evolving *technology*, a question which may or may not involve legal structures that themselves change.

But in other ways, the FDA and CMS (if not the PTO)[178] have in fact developed regulatory strategies that differ for different technologies, depending on factors like the risks those technologies pose or the potential social value they provide. As noted in the previous Section, the FDA has chosen to develop novel regulatory approaches for digital health technologies. The FDA also employs a range of expedited approval programs, whose purpose is to abbreviate the regulatory review process for companies seeking approval for pharmaceuticals which treat serious conditions and which may represent a significant benefit relative to the current standard of care.[179] For instance, the

175. Craig R. Allen & Lance H. Gunderson, *Pathology and Failure in the Design and Implementation of Adaptive Management*, 92 J. ENVTL. MGMT. 1379, 1380, 1383 (2011); Craig & Ruhl, *supra* note 171, at 19-20.

176. Craig & Ruhl, *supra* note 171, at 4-5.

177. The PTO lacks substantive rulemaking authority. Michael J. Burstein, *Rules for Patents*, 52 WM. & MARY L. REV. 1747, 1755 (2011).

178. Patent law on its face is largely technology-neutral, but non-PTO actors, including both the Federal Circuit and other administrative agencies, may interpret patent statutes in ways that permit the law to be applied differently within different fields of technology. *See generally, e.g.*, Burk & Lemley, *supra* note 119; *see also* Tejas N. Narechania, *Patent Conflicts*, 103 GEO. L.J. 1483, 1488 (2015) (arguing that non-PTO administrative agencies can provide expertise with industry-specific patent tailoring); Arti K. Rai, *Building a Better Innovation System: Combining Facially Neutral Patent Standards with Therapeutics Regulation*, 45 HOUS. L. REV. 1037 (2008).

179. For an overview and comparison of the FDA's four programs in this area, see *Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics*, FOOD & DRUG ADMIN. 7-8 (May 2014), http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf [https://perma.cc/3HDS-WNGU] [hereinafter *Expedited Programs Guidance*]. The substance of the latter criterion is phrased slightly differently within each program. *See, e.g.*, 21 U.S.C. § 356(a)(1) (2018) (breakthrough therapy designation is triggered upon a showing of "substantial improvement over existing therapies"); *id*. § 356(b)(1) (fast track designation is triggered upon a showing of "potential to address unmet medical needs"); 21 C.F.R. § 314.500 (2019) (accelerated approval is triggered upon a showing of "meaningful therapeutic benefit . . . over available therapies"); *Expedited Programs Guidance*, *supra*, at 24 (priority review is triggered when a drug would

accelerated approval program permits the FDA to approve a new drug on the basis of a surrogate endpoint, rather than a true clinical endpoint,[180] shortening the clinical trial process.[181] For rare diseases, and especially for rare cancers, products are increasingly approved on the basis of a single-arm trial, in which the potential drug in question is not tested against any other intervention, whether placebo or active comparator.[182]

In theory, many of these new regulatory approaches come with a temporal aspect. The accelerated approval program typically requires companies to engage in confirmatory trials postapproval to ensure that the benefit observed in the context of a surrogate endpoint translates to the clinical context.[183] Such products also may be subject to expedited withdrawal protocols.[184] These additional requirements resemble the kinds of policy levers identified in the adaptive management literature, providing opportunities for reconsideration of an agency's initial decision.[185] However, it is common for companies to fail to complete these clinical trials,[186] depriving the public of information about the true clinical value of these expedited therapies. And even though failure to complete these trials may trigger the FDA's expedited withdrawal authority, the FDA essentially never uses that authority.[187] In

provide a "significant improvement in safety or effectiveness" relative to current therapies). However, they are phrased similarly enough that drugs will often qualify for multiple programs. *Breakthrough Therapy Designation: Exploring the Qualifying Criteria*, BROOKINGS CTR. FOR HEALTH POL'Y 3 (2015), https://www.brookings.edu/wp-content/uploads/2015/03/Breakthrough-Therapy-Designation_final.pdf [https://perma.cc/XJU4-9PUF].

180. 21 U.S.C. § 356(c)(1)(A). A surrogate endpoint is a "laboratory measurement or a physical sign used as a substitute for a clinically meaningful endpoint that measures directly how a patient feels, functions, or survives." Robert J. Temple, *A Regulatory Authority's Opinion About Surrogate Endpoints*, *in* CLINICAL MEASUREMENT IN DRUG EVALUATION 3, 4 (Walter Nimmo & Geoffrey Tucker eds., 1995); *see also* 21 C.F.R. § 314.500. A new drug may be evaluated based on its ability to lower a patient's level of cholesterol, a surrogate endpoint, rather than on its ability to decrease the patient's risk of death from heart disease, the relevant clinical endpoint. Katalin Bognar et al., *The Role of Imperfect Surrogate Endpoint Information in Drug Approval and Reimbursement Decisions*, 51 J. HEALTH ECON. 1, 2 (2017).

181. Thomas R. Fleming, *Surrogate Endpoints and FDA's Accelerated Approval Process*, 24 HEALTH AFF. 67, 67 (2005).

182. *See, e.g.*, Himabindu Gaddipati et al., *Rare Cancer Trial Design: Lessons from FDA Approvals*, 18 CLINICAL CANCER RES. 5172, 5176 (2012).

183. Huseyin Naci et al., *Characteristics of Preapproval and Postapproval Studies for Drugs Granted Accelerated Approval by the US Food and Drug Administration*, 318 J. AM. MED. ASS'N 626, 627 (2017); *Expedited Programs Guidance*, *supra* note 179, at 15.

184. *Expedited Programs Guidance*, *supra* note 179, at 8, 23-24.

185. *See* Craig & Ruhl, *supra* note 171, at 20-21 (noting that certain FDA approval questions fit the adaptive management paradigm well).

186. Naci et al., *supra* note 183, at 634 (noting that of twenty-four indications approved under the Accelerated Approval program, eight indications still had not fulfilled their postmarket requirements five years after approval).

187. The most cited case in which the FDA did use this authority is its revocation of accelerated approval of the drug Avastin for its use in patients with particular forms of breast cancer. *See* Andrew Pollack, *F.D.A. Revokes Approval of Avastin for Use as Breast Cancer Drug*, N.Y. TIMES (Nov. 18, 2011), https://www.nytimes.com/2011/11/19/business/fda-revokes-approval-of-avastin-as-breast-cancer-drug.html [https://perma.cc/74S5-JX9U]. FDA officials argued that Avastin not only was not helpful for these patients, but also that it came with a risk of potentially serious side effects. *See id*.

thinking about how adaptive management might be extended to the health care regulatory space, then, considering policy levers that will spring into being unless the FDA takes affirmative action in the opposite direction might be beneficial.

D. Reimbursement Policy

Each of the three previously discussed areas of law is explicitly, consciously focused on temporal regulation and technological improvement. The design of reimbursement policy, by contrast, has almost wholly ignored not only intermediate technologies but also innovation in general.[188] Yet CMS possesses a strong ability to influence the development of intermediate technologies in its capacity as the provider of health insurance for over 100 million Americans.[189] In that role, CMS makes choices about not only what health care products to purchase for those two programs but also how much it will pay for them.[190] These choices provide CMS with the ability to influence the types of technologies that are developed,[191] even if CMS is often not acting explicitly (and is definitely not acting only) as an innovation-promoting agency.

Even if CMS in general is focused on health care access rather than health care innovation, two particular aspects of CMS' reimbursement policy evince an awareness of temporal regulation and technological development. The first is the New Technology Add-on Payment (NTAP) system. The NTAP program arose when policymakers became concerned that Medicare's existing system for reimbursing hospital services was not adequately rewarding either the development of new technologies or their dissemination into standard medical practice. The program allows CMS to identify new medical technologies and

The contentious nature of this decision and the anger directed at the agency as a result is likely to be typical of any such decision. This is true even though the drug remained on the market due to its approval for other indications. Kurt R. Karst, *FDA Withdraws Avastin Breast Cancer Indication Approval*, FDA L. BLOG (Nov. 22, 2011), http://www.fdalawblog.net/2011/11/fda-withdraws-avastin-breast-cancer-indication-approval [https://perma.cc/G8UX-Q255].

188. *See* Sachs, *supra* note 14.

189. *See* Ctrs. for Medicare & Medicaid Servs., *Fiscal Year 2016: Justification of Estimates for Appropriations Committees*, DEP'T OF HEALTH & HUM. SERVS. 109-10 (2015) [hereinafter *FY 2016: Justification of Estimates*], https://www.cms.gov/About-CMS/Agency-Information/PerformanceBudget/Downloads/FY2016-CJ-Final.pdf.

190. *See* Sachs, *supra* note 8, at 2011.

191. *See* William Fisher, *Intellectual Property and Innovation: Theoretical, Empirical, and Historical Perspectives*, *in* 37 INDUSTRIAL PROPERTY, INNOVATION, AND THE KNOWLEDGE-BASED ECONOMY, BELEIDSSTUDIES TECHNOLOGIE ECONOMIE 12 (2001), https://cyber.law.harvard.edu/people/tfisher/Innovation.pdf [https://perma.cc/WVB7-3879]; Kevin Outterson, *The Legal Ecology of Resistance: The Role of Antibiotic Resistance in Pharmaceutical Innovation*, 31 CARDOZO L. REV. 613, 645-55 (2010); Arti K. Rai, *The Ends of Intellectual Property: Health as a Case Study*, 70 LAW & CONTEMP. PROBS. 125, 128-29 (2007); Roin, *supra* note 13, at 1013; Sachs, *supra* note 14, at 178, 193.

offer providers sufficient reimbursement for using them.[192] The program has notably been used where new technologies challenge the traditional reimbursement paradigm. CMS recently used the program for two new cancer immunotherapy products that presented reimbursement difficulties, pending development of new billing arrangements for those products.[193]

The second reimbursement lever which is tied to the developmental state of a technology is the Coverage with Evidence Development (CED) model. CED allows CMS to provide time-limited reimbursement for a health care technology while its manufacturer completes the relevant clinical trials to produce information that will be needed for a more fully informed coverage determination.[194] In some ways, it can be thought of as related to the FDA's accelerated approval system. Where existing data are not sufficient for regulators to determine whether and how much a new health care technology might benefit the Medicare population, but where there is a strong possibility of such benefit, the agency may make the new technology available to patients now and reserve a fuller judgment as information is gathered over time. Professor Becky Eisenberg and former NIH director Harold Varmus have recently argued for CED's use in the context of one intermediate technology: next-generation sequencing in oncology.[195]

Both the NTAP and CED models give due consideration to the developmental stage of a particular healthcare technology. However, neither focuses on technological development as its primary goal. Both models are largely aimed at providing patients with access to these new technologies, rather than providing researchers with incentives to develop them. As such, Part III considers ways in which these models might be reframed to place innovation at the forefront of CMS' agenda.

III. Promoting Innovation in Intermediate Technologies

If existing regulations often threaten to ossify health care technologies at an earlier stage of development than might be socially valuable, how might agencies (perhaps with assistance from Congress) begin to address these concerns? As discussed in Part II *supra*, templates for possible solutions may be found in existing FDA regulations and in adaptive management techniques. But others may be imagined as well. This Part first attempts to articulate a

192. *See* 42 U.S.C. § 1395ww(d)(5)(K) (2018); *see also* Alexandra T. Clyde et al., *Experience with Medicare's New Technology Add-on Payment Program*, 27 HEALTH AFF. 1632, 1633 (2008) (detailing the history and mechanics of the New Technology Add-on Payment Program).

193. Alicia Gallegos, *CMS Finalizes CAR-T Cell Therapy Inpatient Payments*, MDEDGE (Aug. 21, 2018), https://www.mdedge.com/oncologypractice/article/173086/practice-management/cms-finalizes-car-t-cell-therapy-inpatient [https://perma.cc/D59Y-P2VY].

194. LIZ RICHARDSON, HEALTH AFFAIRS, HEALTH POLICY BRIEF: ALIGNING FDA AND CMS REVIEW 2-3 (2015).

195. Rebecca Eisenberg & Harold Varmus, *Insurance for Broad Genomic Tests in Oncology*, 358 SCI. 1133, 1134 (2017).

more generalized statement of the problem that informs my approach to identifying solutions and considers whether solutions can be identified at a high level of generality or must be envisioned in response to specific technological problems. It goes on to identify solutions that sound in both FDA regulation and in reimbursement policy, as those may better resolve the problems identified for intermediate technologies.

A. Generalizing Both the Problem and Potential Solutions

Attempting to articulate a general theory of when intermediate technologies can be expected to occur has at least two key benefits. First, as previously discussed, it is difficult, if not impossible, to forecast the paths that development may take in the life sciences, and identifying only a subset of potential intermediate technologies would leave other technologies without regulatory solutions. In other words, being able to predict rather than engage in somewhat post-hoc identification of intermediate technologies would be ideal. Second, for resource-limited administrative agencies, identifying specific problems (let alone specific solutions) requires time and capacity they may not readily possess. Being able to generalize the problem could address both of these concerns.

The problem of improving intermediate technologies in some ways[196] generalizes very easily to resemble other innovation-related problems in the life sciences. In the abstract, life-sciences technology companies must often invest significant resources (financially, in time, or otherwise) in developing new products and bringing them to market.[197] However, they are unlikely to make these investments unless they foresee that they will be able to earn sufficient returns on that investment to enable them to recoup their costs.[198] Legal tools operate on both sides of this equation—the investment of resources and the return on investment—to influence companies' decision-making.

For instance, sometimes companies would be required to invest a much larger amount than is typical on the front end to bring a product to market. Perhaps this is because the science is particularly difficult, as in the case of Alzheimer's disease, or perhaps it is because the regulatory approval process for a class of drugs is particularly long.[199] In these types of cases, scholars talk

196. In other ways, the problem generalizes quite poorly. It is not a matter of identifying particular legal levers (patents, FDA regulation, and health insurance reimbursement) and considering whether those levers are turned "on" or "off" in any particular case. The examples articulated here and others follow no clear pattern along these lines.

197. *See* MAKOWER, *supra* note 166, at 28 (estimating the cost of developing a Class III device at $94 million, and a Class II device as $31 million); Joseph A. DiMasi et al., *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20, 20 (2016) (estimating preapproval costs for new pharmaceuticals to be $2.558 billion).

198. I mean this in a broad sense. In the pharmaceutical industry, the cost of failures may be more salient than in the mobile health space, for instance.

199. Budish, Roin & Williams, *supra* note 10.

about "push" mechanisms to promote innovation.[200] They might consider grants,[201] R&D tax credits,[202] or lowering FDA barriers to approval.[203] More generally, these are investments that pay for inputs or otherwise reduce the cost of R&D.

Sometimes, though, the problem is on the other end. If companies can see that there is an insufficient paying market for a product, they may be reluctant to proceed through development. Exclusive rights (either patents or FDA-administered exclusivity periods) are the classic tool for encouraging companies who may question whether they can obtain a return on their investment. More broadly, scholars refer to more creative "pull" mechanisms.[204] Pull mechanisms include advance market commitments, where foundations or governments commit to purchase specified quantities of a particular product if it is developed;[205] prizes, where governments offer payouts for the development of new products;[206] or prescription drug reimbursement, which performs a similar function to a prize system.[207]

This generalized statement of potential innovation-related problems applies not only to the initial development of a particular product but also to subsequent, iterative decisions about the improvement of that product. If a pharmaceutical company predicts that it must invest more money to improve its manufacturing process than it will be able to earn as a result, it is unlikely to make those improvements. However, this might be true for multiple, overlapping reasons. On the front end, it could be that the science of continuous manufacturing is challenging *and* that FDA approval of the new manufacturing process is a risky proposition. On the back end, it could be that patents are likely unenforceable for these technologies *and* that reimbursement will not increase to account for the improvements. It may be all of the above. There is no single reason or set of regulatory structures that causes a technology to stagnate at an intermediate stage. Instead, the problem is similar in nature (although not in effect) to other types of innovation-related problems.

Stating the problem at this level of generality helps to appreciate potential solutions at this level as well. Where intermediate technologies face both front-end problems (like risky FDA approval processes) and back-end problems (like stagnating reimbursement levels), both push and pull mechanisms can be deployed as potential solutions. Relatedly, though, these "carrots"—whether in

200. Michael Kremer, *Pharmaceuticals and the Developing World*, 16 J. ECON. PERSP. 67, 82 (2002).

201. Price, *supra* note 11.

202. Hemel & Ouellette, *supra* note 12, at 306.

203. *Breakthrough Therapy Designation*, *supra* note 179, at 3.

204. Kremer, *supra* note 200, at 82. *See generally* MICHAEL KREMER & RACHEL GLENNERSTER, STRONG MEDICINE (2004).

205. Kremer, *supra* note 200, at 75.

206. *See* Roin, *supra* note 13.

207. Sachs, *supra* note 14, at 178 (arguing that "prescription drug insurance strongly resembles a prize system").

the form of mitigating regulatory hurdles on the front end[208] or providing additional incentives on the back end—ought to be considered alongside innovation "sticks," which penalize the failure to innovate.[209] For a number of the carrots I identify below, I identify accompanying sticks that might complement the carrot in a way that increases the likelihood of technological development while minimizing some of the costs of the proposal.[210]

One additional question is whether the solutions I identify here are specific to a particular technological example or are more general. Ideally, the solutions as well as the problem would be stated at a reasonably high level of generality because identifying specific solutions to specific problems requires work to identify those specific problems as well as work to identify and implement specific solutions. For resource-limited agencies, identifying common problems within a technological class and proposing solutions at that level will prove useful. However, this may not be achievable in all cases, and the level of generality may vary by example (as I consider *infra*).

At the same time, though, there may be reasons beyond agency resources to encourage more narrowly tailored solutions. These solutions have costs, as well as benefits. On balance, the benefits might be "worth" the costs in a situation of intermediate technologies, where otherwise the technology in question would not be developed fully. But an agency applying solutions broadly might reasonably be concerned about incurring the costs for technologies which do not face these same challenges of intermediacy.[211] As such, more risk-averse actors might prefer narrowly tailored solutions, even if they require more work to identify and implement on the front end.

Below, I consider one category of push mechanisms that might be implemented by the FDA and one category of pull mechanisms that might be implemented by actors within the reimbursement system. This is not because they are the only institutional actors with the ability to solve the problem in the sense of intervening on either side of the balance, but they may well have superior resources or capacities to do so.

For instance, even though patent law has developed several doctrines which fit closely with the problem of intermediate technologies,[212] in many ways the patent system and the PTO in particular are not well-suited for

208. Unlike much of the literature on innovation policy, which seeks to identify additional incentives (or bolster existing incentives) that might be used to promote innovation into health care technologies, my goal here is to mitigate the existing regulatory hurdles. Of course, it is highly likely that a mix of both strategies—addressing regulatory hurdles and providing innovation incentives—will be useful, but the existing literature on the latter is far more robust as compared to the former.

209. Ian Ayres & Amy Kapczynski, *Innovation Sticks: The Limited Case for Penalizing Failures to Innovate*, 82 U. CHI. L. REV. 1781, 1783 (2015).

210. *See id*. at 1811 ("[P]olicymakers can deploy carrots and sticks . . . together and may often wish to do so.").

211. *See supra* text accompanying notes 120-21 for a discussion about whether all technologies in this space are intermediate in some meaningful sense.

212. *See supra* Section II.A.

solving problems that are unique to particular subject matters. Chiefly, this is because of the facial uniformity of the patent statute.[213] Patent doctrine is formally one-size-fits-all,[214] even though pharmaceuticals and software may not be in need of the same length and breadth of patent protection, given the drastically different product lifecycles in the two fields.[215] Even within health care technologies, diagnostics, devices, and drugs may be in need of more finely tailored innovation incentives, given the very different paths each class of products takes to market. Policymakers have already created highly specific innovation incentives in the life sciences, including exclusivity periods, grants, tax credits, and reimbursement models—just not within the patent system.

Further, the PTO lacks the ability possessed by other administrative agencies to engage in substantive-rulemaking and to administer innovation-related programs like those I articulate below.[216] The PTO's lack of substantive rulemaking authority[217] means that it could not engage in tailoring of the kind that would be needed for intermediate technologies, even if it had the inclination to do so. At present, in part because of this lack of authority, the PTO also has little expertise in administering technology-specific incentives of this type. The creation of the PTO's Office of the Chief Economist[218] may help address this question. But as of now, the PTO is at a disadvantage when compared with other agencies that constantly make decisions about how to allocate scarce innovation resources.[219]

I am not claiming that patent law in principle is incapable of responding to these concerns, or that patents are not an important lever for health-related technologies (although they may be far less important, or even unimportant, in medical algorithmic technologies as compared to the pharmaceutical context). Instead, it may be that the institutional capacities currently possessed by the relevant actors within the patent system were simply not created to allow the agency to engage in this kind of problem-solving.

B. Leveraging the FDA to Encourage the Development of Information

As Professor Rebecca Eisenberg has argued, one of the central functions of the FDA is to shape the development of information about new

213. Sachs, *supra* note 8, at 1994-95. Of course, as scholars have argued, in practice the doctrine is often tailored to particular fields of technology. *See supra* note 178.

214. *See* Michael W. Carroll, *One Size Does Not Fit All: A Framework for Tailoring Intellectual Property Rights*, 70 OHIO ST. L.J. 1361, 1363-64 (2009) (questioning patent and copyright law's grants of "one-size-fits-all" bundles of rights).

215. Cohen & Lemley, *supra* note 157, at 39, 46.

216. Sachs, *supra* note 8, at 1995.

217. Michael J. Burstein, *Rules for Patents*, 52 WM. & MARY L. REV. 1747, 1755 (2011).

218. Robert P. Merges, *Kappos Legacy and PTO-Academia Relations*, IPWATCHDOG (July 28, 2014), https://www.ipwatchdog.com/2014/07/28/kappos-legacy-and-pto-academia-relations [https://perma.cc/FRH3-YXLS].

219. See Sachs, *supra* note 8, at 1994-96, for a fuller discussion of patent law's core competencies relative to those of other fields of law.

health care technologies.[220] The FDA's ability to require drug and device sponsors to produce information about the safety and efficacy of their products, information they would be unlikely to produce without the FDA's involvement,[221] is key to promoting innovation in the intermediate-technologies context. But the challenge is to make sure that information is not just *developed* but also *used and implemented* in a way that is beneficial for patient care and safety. Incentives to promote the development and use of such information are likely to differ across health care technologies. Here, I consider one potential taxonomy to distinguish between the types of intermediate technologies I identify in Part I, articulating ways in which regulatory burdens might be lessened while remaining attentive to safety and efficacy concerns.

1. Improvement of Existing Technologies

The example of Myriad and laboratory-developed tests may be the cleanest example of an intermediate technology. At the time Myriad's test was marketed, it was beneficial to more than half of the women receiving the test. But for a large minority of women, Myriad's test failed to give them the information they needed about their breast cancer risk.[222] Ideally, all genetic testing companies would seek to both market their test at the time it provides meaningful clinical benefits for the majority of patients, and to strive to improve it over time to benefit a greater and greater percentage of patients. In short, we want diagnostic testing companies to engage in iterative improvement as Myriad did.

Myriad was able to carry out this business strategy due to the favorable regulatory climate. Myriad had patents to protect its monopoly position, and it did not need to obtain FDA approval for its test.[223] But the regulatory environment has changed. Myriad's key gene patents were invalidated in the Supreme Court on the grounds that they did not claim patent-eligible subject matter,[224] and cases in both the Supreme Court and Federal Circuit invalidating diagnostic-testing patents on these same grounds[225] suggest that it will be nearly impossible for companies to obtain patents on genetic tests going forward.[226] Reimbursement may also be threatened, given Congress's reform of

220. Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 348 (2007).

221. Kapczynski & Syed, *supra* note 16, at 1922.

222. Eggington, *supra* note 54.

223. Although Myriad was subject to regulation through both CMS and the State of New York, those regulatory structures are not as rigorous as the regulations the FDA had previously proposed through draft guidance. Sachs, *supra* note 5, at 1893-94.

224. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 591 (2013).

225. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66, 71-72 (2012); Ariosa Diagnostics, Inc. v. Sequenom, Inc., 809 F.3d 1282, 1288-89 (Fed. Cir. 2015).

226. *See, e.g.*, Rebecca S. Eisenberg, *Diagnostics Need Not Apply*, 21 B.U. J. SCI. & TECH. L. 256, 257 (2015); John M. Golden, *Flook Says One Thing, Diehr Says Another: A Need for Housecleaning in the Law of Patentable Subject Matter*, 82 GEO. WASH. L. REV. 1765, 1791-92 (2014).

diagnostic testing reimbursements in the Protecting Access to Medicare Act of 2014.[227] At the same time, the FDA may be moving toward increased agency scrutiny of laboratory-developed tests (LDTs).[228]

When these three legal developments are combined—removing patents, decreasing potential reimbursement, and increasing regulatory requirements—the incentive situation today for diagnostic tests companies wanting to enter the market may be far more difficult than it was for Myriad. As a result, the FDA might consider a temporally adjusted regulatory system, in which the burden of initial approval is somewhat less than is typical for a medical device of similar risk, but in which continuous improvement is not just expected but required.

The FDA might employ a number of strategies to carry out this regulatory goal. For example, the FDA might consider extending a program akin to the precertification pilot being used in the mobile-health context. That is, the FDA might certify testing companies, rather than the tests themselves. Alternatively, the FDA might adapt the temporal strategy used for drugs receiving an accelerated-approval designation and require additional reporting (perhaps on an annual basis) about the quality of the information being provided by the diagnostic-testing firm, as an accompanying stick. A failure to disclose publicly this information—or, more controversially, a failure to improve rapidly enough—would lead to label restrictions or a withdrawal from the market.[229]

Importantly, these proposals do not address one of the core difficulties with Myriad's business model: concerns over access and pricing, as noted in Part I. Now that patents have become unavailable for most of these technologies, it is possible that these access concerns will be unlikely to recur in the future. However, it is conceivable that companies will be able to obtain favorable market positions, if they are able to accrete sufficient amounts of data to establish an initial head start over potential competitors, or use proprietary algorithms that are protected through trade secrecy.[230]

A proposal that would both lower barriers to entry for these companies *and* address some of these access concerns would likely require institutions beyond the FDA. The use of a federal database of potentially pathogenic mutations for particular conditions—coupled with the requirement (enforced by

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Although this may change in light of some more recent cases and guidance from the PTO, *see* Vanda Pharm. Inc. v. W.-Ward Pharm. Int'l Ltd., 887 F.3d 1117, 1136 (Fed. Cir. 2018), it is too early to tell what impact those developments will have.

227. Sachs, *supra* note 5, at 1923.

228. The FDA has repeatedly attempted to regulate LDTs, and previous attempts have failed. See *supra* note 58 for an explanation of these attempts.

229. For a similar proposal conditioning a benefit upon fuller public disclosure of clinical trial information, although in the context of pharmaceuticals, see generally Daniel J. Gervais, *The Patent Option*, 20 N.C. J.L. & TECH. 357 (2019).

230. For instance, these algorithms are often held by companies exploring more complex genomic questions. *See, e.g.*, *Illumina Acquires Edico Genome to Accelerate Genomic Data Analysis*, ILLUMINA (May 15, 2018), http://investor.illumina.com/mobile.view?c=121127&v=203&d=1&id=2349147 [https://perma.cc/7584-6B65].

the FDA) that companies seeking to market genetic tests for these conditions contribute their knowledge to these databases—would democratize access to the relevant information by potential competitors. The FDA might expand its partnership with the NIH,[231] which already maintains several such databases,[232] to begin aggregating the relevant information.

2. Expansion of Existing Technologies

The example of the microbiome context presents somewhat different considerations than does the genetic testing example. Rather than focusing on a single technology and its improvement, the microbiome example focuses more closely on developing information about new uses for existing technologies. This problem has been discussed in the literature, with scholars advancing proposals that would encourage different actors to identify potential new uses for existing drugs.[233] The difference in the microbiome context is one of foreseeability.

The essential problem is as follows: approving a drug for one indication enables physicians to prescribe that drug off-label for other conditions for which it has not been approved. Companies will often not pursue FDA approval for those additional indications, in part because of the potential risk that the required clinical trials will fail to demonstrate efficacy for the new indications.[234] In some cases, these drugs will be safe and effective for their additional indications, but in others they will not, exposing patients to unnecessary risks and costs along the way. The FDA might *prefer* for these companies to proceed through the standard approval process for additional indications, but the FDA typically cannot require them to do so.[235] Further, the FDA usually does not have a choice about how to regulate standard prescription drugs, in the sense that the standard pharmaceutical-approval pathway permits this set of incentives to occur.

231. Sachs, *supra* note 8, at 2031; *FDA Takes New Action to Advance the Development of Reliable and Beneficial Genetic Tests that Can Improve Patient Care*, FOOD & DRUG ADMIN. (Dec. 4, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm627555.htm [https://perma.cc/MX8Z-MSVM].

232. *See, e.g.*, *ClinVar*, NAT'L CTR. FOR BIOTECHNOLOGY INFO. (2018), https://www.ncbi.nlm.nih.gov/clinvar [https://perma.cc/9LUT-EJMM] ("ClinVar aggregates information about genomic variation and its relationship to human health"); *Human Gene Mutation Database Professional*, NAT'L INSTS. OF HEALTH (2018), https://www.nihlibrary.nih.gov/resources/tools/human-gene-mutation-database-professional [https://perma.cc/QS5J-F5NF].

233. *See* Rebecca S. Eisenberg & W. Nicholson Price II, *Promoting Health care Innovation on the Demand Side*, 4 J.L. & BIOSCIENCES 3, 5-6 (2017); Sachs, Ginsburg, & Goldman, *supra* note 116, at 2421.

234. *See* Kapczynski & Syed, *supra* note 16, at 1923.

235. One class of exceptions would be in cases involving products subject to Risk Evaluation and Mitigation Strategies, where their prescription is constrained by law. *See, e.g.*, Jordan Paradise, *REMS as a Competitive Tactic: Is Big Pharma Hijacking Drug Access and Patient Safety?*, 15 HOUS. J. HEALTH L. & POL'Y 43, 57-62 (2015).

But in the microbiome context, the FDA had a choice. At the time it was deciding how to regulate microbiome-based technologies, the FDA was likely aware that scientists were investigating the microbiome's applications to a range of conditions. As a result, it should have understood that choosing to adopt the standard pharmaceutical-regulatory pathway for microbiome-based technologies would constrain its ability to regulate follow-on uses of these technologies. Instead, the FDA could have adopted a use-based regulatory paradigm, akin to the one employed in the context of human cellular products like cord blood. That paradigm would have allowed it to regulate each potential use of these microbiome-based technologies as they are raised, forcing companies to produce the relevant information about potential additional uses.[236]

It is possible that the FDA may reevaluate its choice of regulatory paradigm[237] and address this concern. But more generally, we can look to the literature on adaptive management for potential solutions to both this problem and the problem of new uses for old drugs. Out of concern for both patient safety and unnecessary medical spending on pharmaceuticals of questionable value, Congress might give the FDA additional authority to force pharmaceutical companies to conduct clinical trials on new uses for their existing drugs. This authority could be triggered under a range of imagined circumstances, and penalties might include imposing a risk-based prescription limitation on the drug in question[238] or significant fines.

In the context of the microbiome and other pharmaceuticals, the problem of intermediate technologies is primarily one of encouraging the production of information. Companies *can* but do not *have to* produce such information to enjoy sales of their products for off-label uses, so they often choose not to. To lower hurdles to information production, another strategy that could be adopted would be to lessen the regulatory burden on companies seeking approval for additional uses of their products, in the hope that lessening that burden encourages more of them to seek additional approvals. To some extent, Congress has approved this strategy, providing for the FDA to consider the use of "real-world evidence" in obtaining supplemental approvals in the 21st Century Cures Act.[239] But it may be that allowing companies to use such

236. Sachs & Edelstein, *supra* note 110, at 409-12.

237. The FDA has recently convened a meeting on this topic. *See Statement from FDA Commissioner Scott Gottlieb, M.D., on Advancing the Science and Regulation of Live Microbiome-Based Products Used to Prevent, Treat, or Cure Diseases in Humans*, FOOD & DRUG ADMIN. (Aug. 16, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm617168.htm [https://perma.cc/Z5JM-YQ5H].

238. The FDA might leverage its existing REMS authority for this purpose.

239. 21st Century Cures Act, Pub. L. No. 114-255, § 3022, 130 Stat. 1033, 1096 (2016) (codified at 21 U.S.C. § 355g); *Framework for FDA's Real-World Evidence Program*, FOOD & DRUG ADMIN. (2018), https://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RealWorldEvidence/UCM627769.pdf [https://perma.cc/UF9Q-DU3U].

evidence lowers the FDA's reviewing bar too much.[240] If so, solutions that increase and mandate, rather than lessen, the relevant regulatory burden may be necessary.

3. Process Improvements into Existing Technologies

The pharmaceutical-manufacturing context presents yet another set of considerations for the FDA. The goal is both to encourage companies to shift older products to a new manufacturing paradigm, and to introduce new products using that paradigm. The concern in this case seems to be a combination of hurdles in both innovation and regulation. Even though it might be advantageous for companies to shift from batch to continuous manufacturing, companies investing in such efforts may find it difficult to exclude competitors from free-riding on their investments, and the risk and time of FDA approval for the new manufacturing process render it unattractive to firms.

The FDA has already taken admirable steps to reduce each of these barriers. As noted above, the FDA is now authorized to award grants "for the purpose of studying and recommending improvements to the process of continuous manufacturing of drugs and biological products."[241] Further, the FDA's repeated public statements in support of shifting to novel manufacturing methods[242] and public praise of the few companies who have chosen to use these methods[243] may be an attempt to signal to companies that the risk (if not the time and expense) of the additional FDA-approval requirements is minimal.

But the FDA can do more. One option would be to employ a system of *manufacturer* process certification or even precertification, rather than certifying the process used for each product. Although the idea of manufacturer certification for safety and efficacy (as raised in the context of genetic tests) is a new idea to the digital health context, several questions about manufacturing processes are assessed at the facility level already.[244] Enabling companies to lower their per-product regulatory costs by spreading the review over the facility might provide a sufficient incentive for companies to do so.

240. *See, e.g.*, Rachel E. Sherman et al., *Real-World Evidence - What Is It and What Can it Tell Us?*, 375 NEW ENG. J. MED. 2293 (2016); *see also* FOOD & DRUG ADMIN., *supra* note 239, at 13.

241. 21st Century Cures Act § 3016, 130 Stat. at 1095 (codified at 21 U.S.C. § 399h).

242. *See, e.g.*, Scott Gottlieb, *FDA Budget Matters: Investing in Advanced Domestic Manufacturing*, FDA VOICE (July 13, 2018), https://blogs.fda.gov/fdavoice/index.php/2018/07/fda-budget-matters-investing-in-advanced-domestic-manufacturing [https://perma.cc/S82N-55KJ]; Michael Kopcha, *"Continuous Manufacturing" - Common Guiding Principles Can Help Ensure Progress*, FDA VOICE (Sept. 11, 2017), https://blogs.fda.gov/fdavoice/index.php/2017/09/continuous-manufacturing-common-guiding-principles-can-help-ensure-progress [https://perma.cc/5JFT-HH6D].

243. *See* Kopcha, *supra* note 242 (praising Vertex and Janssen for their efforts in this area).

244. *See* 21 C.F.R. §§ 211.42-.58 (2019) (Buildings and Facilities).

C. Steering Innovation Through Reimbursement Policy

CMS' power to direct research and development resources has been shown empirically in a number of studies: when CMS decides to cover a new product or set of products, pharmaceutical companies react accordingly and invest more in those fields.[245] Using the taxonomy developed in Section III.A, I identify ways that CMS might use its existing legal authority or might be given new authority to steer innovation in a way that encourages improvement in intermediate technologies over time. In essence, I argue that we should pay more for technologies that work better or have greater health impacts—and we should pay less (or not at all) for technologies that do not work as well.

1. Improvement of Existing Technologies

In the context of LDTs or other algorithmic technologies, the goal is to encourage companies to invest in the continuous improvement of their products. Although it is certainly important to consider the regulatory barriers currently discouraging such improvements, as I have done in Section III.A above, it is also important to ensure that companies are being rewarded appropriately for their progress—and perhaps punished for their recalcitrance. A version of outcomes-based pricing that builds in principles of reimbursement based on cost-effectiveness may prove useful for striking this balance.

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245. Medicare Part D is one commonly cited example in the health-insurance context. Although the broader Medicare program was created in 1965, Medicare did not have a pharmacy-benefit component until 2006, when Medicare Part D went into effect. Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, § 1860D-1(2), 117 Stat. 2066, 2072 (codified in scattered sections of 26 and 42 U.S.C.). For enrollees who did not previously have access to prescription-drug coverage, Part D provided that benefit. *Prescription Drug Trends*, KAISER FAMILY FOUND. 5 (May 2010), https://kaiserfamilyfoundation.files.wordpress.com/2013/01/3057-08.pdf [https://perma.cc/3Q29-ZP6K] ("[A]bout one-quarter (27%) of seniors age 65 and older, and one-third of poor (34%) and near-poor (33%) seniors, had no drug coverage in 2003."). For seniors who had been able to access prescription drugs through Medicaid or other programs, Part D increased the prices pharmaceutical companies could expect for those drugs. Richard G. Frank & Joseph P. Newhouse, *Should Drug Prices Be Negotiated Under Part D of Medicare? And If so, How?*, 27 HEALTH AFF. 33, 34, 36-37 (2008). As a result, studies have shown that Part D is associated with increased investment in drug classes with higher market share among the Medicare population. Margaret E. Blume-Kohout & Neeraj Sood, *Market Size and Innovation: Effects of Medicare Part D on Pharmaceutical Research and Development*, 97 J. PUB. ECON. 327, 327 (2013); *see also* David Dranove et al., *Pharmaceutical Profits and the Social Value of Innovation* 2-3, 6-7 (Nat'l Bureau of Econ. Research, Working Paper No. 20212, 2014) (qualifying the findings of Blume-Kohout and Sood by noting that truly innovative activity takes longer to emerge). Other scholars have found similar results by studying individual-coverage mandates or population shifts. *See, e.g.*, Daron Acemoglu & Joshua Linn, *Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry*, 119 Q.J. ECON. 1049, 1084 (2004) ("[A] 1 percent increase in the potential market size for a drug category leads to approximately a 4 percent growth in the entry of new nongeneric drugs and new molecular entities."); Amy Finkelstein, *Static and Dynamic Effects of Health Policy: Evidence from the Vaccine Industry*, 119 Q.J. ECON. 527, 556-57 (2004) (finding that policies designed to increase the uptake of vaccines, including Medicare's 1993 decision to cover the flu vaccine, resulted in an increase in clinical trials for new vaccines).

An outcomes-based pricing system recognizes that health care technologies will not work for all patients and provides for a system of repayment if a drug or device fails to work for a particular patient.[246] This system can be implemented as a money-back rebate (a drug manufacturer might sell a drug for a particular price but owe some or all of that money back if the drug fails to work for its intended purpose) or as a bonus payment for meeting particular health-related milestones.[247] Pharmaceutical companies and health insurers have expressed interest in outcomes-based pricing systems, and although there are some regulatory obstacles to the practice, several outcomes-based deals between pharmaceutical companies and insurers have been publicly reported.[248]

However, it is important for outcomes-based systems to be supported by an underlying framework of cost-effectiveness or value-based reimbursement. Outcomes-based systems ask whether a product works for its intended purpose. They do not ask how *well* a product works; therefore it is possible for pharmaceutical companies to set outcomes-based prices that are still out of proportion to the health benefits provided by a product. Cost-effectiveness or value-based pricing, on the other hand, does incorporate these metrics of value[249] and can therefore allow a system to pay more for technologies that work better. In other words, cost-effectiveness pricing can enable a system to pay more for improved versions of existing technologies.

Although cost-effectiveness tools have been adopted by governmental insurers in other countries in their process for reimbursing new health care technologies,[250] they have not yet been adopted by governmental insurers in the United States.[251] Adopting these tools would encourage health care technology companies to improve existing technologies by enabling insurers to pay more for technologies that provide superior outcomes or health information. A woman who receives a VUS result from Myriad arguably should not be made to pay the same amount for the test as a woman who receives a clinically valuable result.[252] Relatedly, explicitly paying more for tests that return more

246. Anna Kaltenboeck & Peter B. Bach, *Value-Based Pricing for Drugs: Theme and Variations*, 319 J. AM. MED. ASS'N 2165, 2166 (2018).

247. Rachel E. Sachs, Nicholas Bagley & Darius N. Lakdawalla, *Innovative Contracting for Pharmaceuticals and Medicaid's Best-Price Rule*, 43 J. HEALTH POL., POL'Y, & L. 5, 10 (2018).

248. *Id*. at 10-11.

249. *See, e.g*., Kaltenboeck & Bach, *supra* note 246, at 2165.

250. *See, e.g*., *Technology Appraisal Guidance*, NAT'L INST. FOR HEALTH & CARE EXCELLENCE, https://www.nice.org.uk/About/What-we-do/Our-Programmes/NICE-guidance/NICE-technology-appraisal-guidance [https://perma.cc/TAN4-ZVQX].

251. One private company, CVS Health, has recently announced that it will be incorporating cost-effectiveness principles into its activities as a pharmacy benefit manager. Troyen Brennan & Surya Singh, *Why CVS is Giving Plans a New Tool to Target High Launch Prices*, HEALTH AFFS. BLOG (Sept. 17, 2018), https://www.healthaffairs.org/do/10.1377/hblog20180913.862850/full [https://perma.cc/FL5D-BF7S].

252. It is possible that adopting such strategies from the beginning of Myriad's development would have resulted in even more rapid improvement of the test, as a lower price initially could have mitigated some of the access concerns experienced by patients.

valuable information, on average, would encourage improvements in algorithmic technologies both in the LDT context and more broadly.

One strategy for implementing these ideas would be to repurpose the CED system discussed *supra* in Section II.D. As Eisenberg and Varmus note, one problem for many of these diagnostic tests at an early stage of development is that "[s]ubstantially more data are needed to evaluate clinical utility of such testing so that insurers can make rational decisions about coverage, but data collection on a large enough scale is impeded, in part, by uncertain reimbursement policies."[253] CED allows patients to access the technology today, perhaps providing its manufacturer with a reduced level of reimbursement, and enables the collection of the information needed for the technology's improvement tomorrow.

2. Expansion of Existing Technologies

Technologies that fit the model of the microbiome, where the inquiry in question is about the expansion of existing technological platforms, might seek to use a different model of innovative reimbursement: indication-based pricing. Indication-based pricing recognizes that new health care technologies are often used for different purposes. Some may be closely related to each other (as in the use of a cancer drug on tumors in different organs), while some may be far more distinct (as in the use of Colcrys to treat both gout and familial Mediterranean fever).[254] When the same drug is used to treat different diseases, it may have different health values to patients. That is, the drug may be far more effective in treating one condition than another, such that (again incorporating principles of cost-effectiveness in reimbursement) insurers and pharmaceutical firms would want to be able to price the drug differently for different conditions.[255]

Similarly to outcomes-based pricing, indication-based pricing that accounts for the cost-effectiveness of the technology for the particular disease in question would provide incentives for companies to develop and approve new indications for existing technologies. At present, the evidence shows that fecal transplants are highly effective for the treatment of recurrent *C. difficile* infections,[256] but the evidence is far more equivocal for its use in the treatment of other conditions, including ulcerative colitis or Crohn's disease. However, we do know that fecal transplants are being administered—albeit often in a do-

253. Eisenberg & Varmus, *supra* note 195, at 1133.

254. Aaron S. Kesselheim & Daniel H. Solomon, *Incentives for Drug Development - The Curious Case of Colchicine*, 362 NEW ENG. J. MED. 2045, 2045 (2010).

255. *See* Sachs et al., *supra* note 247, at 7-8.

256. *See* Moayyedi et al., *supra* note 108, at 105.

it-yourself context—for conditions like these.[257] If companies cannot be assured of reimbursement for a particular product unless the evidence supporting its use for the prescribed indication is strong, they may be more likely to invest in the development of such evidence and expand the relevant uses for the existing technology.

Although at least one private pharmacy benefit manager has begun to use indication-based pricing,[258] there has been little interest in the practice from governmental insurers. This disinterest is likely driven in large part by the same factors leading to the disinterest in outcomes-based pricing and cost-effectiveness analyses more generally. But it is also driven by more mundane factors, such as electronic health records. If insurers cannot discern which indication a drug is being prescribed for, they cannot assign differential payment amounts for the product.[259] The development of infrastructure which allows for tracking not only of prescriptions but also of indications may provide additional incentives for companies to expand their technologies in this way.

3. Process Improvements into Existing Technologies

In the pharmaceutical-manufacturing context, CMS might repurpose another lever it already possesses to drive improvements: the NTAP system, as discussed *supra* in Section II.D. The idea underlying the NTAP program could be repurposed to provide additional incentives for pharmaceutical companies to invest in manufacturing improvements. Upon receiving FDA approval for those improvements, companies might apply for and obtain a time-limited reimbursement bonus through Medicare and Medicaid. The NTAP program would in this case function much like a prize,[260] providing companies with the ability to recoup their investment into the improvements while also constraining the scope of that bonus payment. This promised incentive has the potential to encourage many companies to invest in new manufacturing technologies and make the switch on the front end.

Unfortunately, the NTAP program as it currently exists today could not easily be used for this purpose. The program's statutory scope—the hospital-

257. Emily Eakin, *The Excrement Experiment*, NEW YORKER (Nov. 24, 2014), https://www.newyorker.com/magazine/2014/12/01/excrement-experiment [https://perma.cc/N9F6-YMGP].

258. *See SafeGuardRx Improves Affordability and Access to Budget-Busting Drugs*, EXPRESS SCRIPTS (2015), http://lab.express-scripts.com/lab/insights/drug-options/safeguardrx-improves-affordability-and-access-to-budget-busting-drugs [https://perma.cc/SE3V-YJMW].

259. In some cases, this information may be backed out of the relevant documentation. For instance, Avastin is commonly used to treat both cancer and macular degeneration. Even if an electronic medical record does not disclose the indication for which it is being used, the identity of the prescribing doctor (and whether they are an ophthalmologist or an oncologist) may yield the necessary information.

260. Sachs, *supra* note 13, at 178.

based portions of Medicare[261]—is too narrow to take account of the full scope of pharmaceutical technologies for which it might be advantageous to use the program. And NTAP's current requirement of inadequate reimbursement is unlikely to be met in these manufacturing improvement cases.[262] But the basic structure of the program, its focus on new technologies, and CMS' experience administering the program lend itself to possible congressional expansion. As Congress has already proved willing to appropriate grant funding for further research into new manufacturing technologies, encouraging them to extend the NTAP program to account for these technological improvements may be possible as well.

IV. Generalizing Beyond Health Technologies

As noted in the Introduction, intermediate technologies are not limited to the health care context. This Part broadens the scope of the Article, considering whether the examples and ideas articulated in Parts II and III are generalizable to intermediate technologies in other sectors. In short, it argues that at least some technologies embedded within an existing regulatory framework (such as self-driving cars) may be susceptible to the same types of ossification- or stagnation-related concerns that exist in the health care context. However, for technologies that are not currently subject to meaningful regulation, even those that will improve and iterate over time, the "intermediate technologies" framing as presented in this Article is a poor fit for the kinds of challenges they face.

A. Technologies Already Within an Existing Regulatory Framework

One technological area that bears similarities to the health care-technology context is self-driving or autonomous vehicles, which has been considered in a series of articles by Professor Tracy Pearl.[263] At present, most cars possess at least some basic autonomous features (such as cruise control), but increasingly many cars possess features that provide them with greater autonomy. A number of car manufacturers offer models with "Active Park Assist," which can help steer as drivers seek to parallel park.[264] Many manufacturers offer models that assist drivers in staying within their lane,

261. 42 U.S.C. § 1395ww(d)(5)(K) (2018), establishing the NTAP program, is contained within the section of the statute considering "Payment to Hospitals for Inpatient Hospital Services" and explicitly contemplates payment methodologies that are unique to that program. *See id*. § 1395ww(d)(5)(K)(ii)(I) (considering the diagnosis-related group (DRG) prospective payment rate).

262. *See id*. (setting forth the inadequacy requirement).

263. *See generally*, Pearl, *supra* note 4; Tracy Hresko Pearl, *Hands on the Wheel: A Call for Greater Regulation of Semi-Autonomous Cars*, 93 IND. L.J. 713 (2018).

264. Aaron Gold, *10 Cars with Active Park Assist*, AUTOBYTEL (2018), https://www.autobytel.com/car-buying-guides/features/10-cars-with-active-park-assist-131248 [https://perma.cc/BLD9-SLCE].

sometimes simply by notifying the driver that they have crossed over a line, but in more advanced cases by physically correcting the vehicle's path.[265] Tesla's "Autopilot" feature goes a step further, not only helping cars park and stay within their lane, but also instructing the car to actually brake when appropriate.[266] The goal, though, is full automation. Full automation (provided that consumers purchase these vehicles) could save tens of thousands of lives each year, reduce traffic accidents, lower insurance premiums,[267] and provide increased autonomy to older or disabled people.[268]

Self-driving cars therefore present a clear example of an intermediate technology in the sense that, although basic versions of some autonomous features are available to consumers today, the field has a vision for the future and where it hopes to go. The clear progression of autonomous features has allowed SAE International, a global professional association for engineers, to establish a taxonomy of six levels of automation, from Level 0 (no automation) to Level 5 (full automation).[269] This taxonomy has been adopted by the National Highway Traffic Safety Administration (NHTSA), the federal agency with regulatory jurisdiction over cars and motor-vehicle safety.[270]

Many of the features described above, such as lane assist and autopilot, are features of Level 2 (partial automation) cars, in which there is "automation of at least two primary control functions," but in which the driver "is still responsible for monitoring the roadway . . . and is expected to be available for control at all times."[271] NHTSA draws a regulatory line between Level 2 and Level 3 (conditional automation), in which the "major distinction" is that "the vehicle is designed so that the driver is not expected to constantly monitor the roadway while driving."[272] In other words, a Level 3 car's features allow the driver to relinquish control to the vehicle under certain situations, regaining it only as necessary. The norm is vehicular control, while the norm under Level 2 is human control.

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265. *10 Top Cars with Lane Departure Warning*, AUTOBYTEL (2018), https://www.autobytel.com/car-buying-guides/features/10-top-cars-with-lane-departure-warning-131158 [https://perma.cc/YB2D-BNFJ].

266. NAT'L HIGHWAY TRAFFIC SAFETY ADMIN., ODI RESUME: INVESTIGATION PE 16-007 4 (2016), https://static.nhtsa.gov/odi/inv/2016/INCLA-PE16007-7876.pdf [https://perma.cc/NW5C-8QBC].

267. Pearl, *supra* note 4, at 39.

268. U.S. DEP'T OF TRANSP., PREPARING FOR THE FUTURE OF TRANSPORTATION: AUTOMATED VEHICLES 3.0, at ii (2018).

269. *Id*. at vi.

270. NAT'L HIGHWAY TRAFFIC SAFETY ADMIN., FEDERAL AUTOMATED VEHICLE POLICY 9 (2016), https://www.transportation.gov/sites/dot.gov/files/docs/AV%20policy%20guidance%20PDF.pdf [https://perma.cc/6R57-M3FN].

271. NAT'L HIGHWAY TRAFFIC SAFETY ADMIN., PRELIMINARY STATEMENT OF POLICY CONCERNING AUTOMATED VEHICLES 5 (2013), https://www.nhtsa.gov/staticfiles/rulemaking/pdf/Automated_Vehicles_Policy.pdf [https://perma.cc/W32F-GEVN].

272. *Id*.

Autonomous vehicles are subject to a regulatory regime that may create some of the ossification-related concerns laid out in the health care context. Manufacturers must certify that their vehicles comply with detailed Federal Motor Vehicle Safety Standards,[273] and autonomous-vehicle manufacturers selling unsafe products would be subject to NHTSA's recall and enforcement authority.[274] NHTSA has also sought to distinguish vehicles from Levels 0 through 2 and vehicles from 3 through 5, given the shift in primary control from the human driver to the vehicle at that point. A guidance issued under the Obama administration envisioned a system in which manufacturers of cars Level 3 and above would need to submit mandatory Safety Assessments to the agency before marketing or even testing their new vehicles.[275] Taken together, these regulatory features resemble the types of potentially ossifying (yet well-meaning and material) regulations that appear in the health care context. If manufacturers of Level 3 vehicles would face significantly higher regulatory burdens than manufacturers of Level 2 vehicles, some may choose not to move forward under those circumstances.

However, there are at least two key differences between the autonomous vehicle context and the health care technologies context that may mitigate some of these concerns. First, NHTSA does not currently exercise any premarket approval authority over autonomous vehicles.[276] This allows companies to come to market earlier and mitigates some of the initial risk associated with the FDA approval process. Second and relatedly, the deregulatory focus of the Trump administration has impacted this area, with more recent statements from the administration emphasizing the currently voluntary nature of the mandatory safety assessments envisioned by the Obama administration.[277] A deregulatory FDA, on the other hand, mitigates (as through the precertification pilot) but does not eliminate premarket regulation of these technologies.

The autonomous-vehicle context in some ways resembles the Myriad example, in which vehicle manufacturers are seeking to improve existing technologies, and in some ways resembles the microbiome example, in which vehicle manufacturers are seeking to expand existing technologies. The change from a system in which your car *notifies* you that you are crossing lanes to a system in which it *corrects* that change may be more like the former. Other features may be more like the latter. In either case, the challenge is to adapt the regulatory framework that best balances innovation and safety.

Safety issues are particularly paramount in the autonomous-vehicle context, even more so than in the health care technologies context, because

273. *Id*. at 11.
274. *Id*.
275. *Id*. at 15, 70.
276. Pearl, *supra* note 263, at 739.
277. U.S. DEP'T OF TRANSPORTATION, *supra* note 268, at viii.

autonomous vehicles may jeopardize the safety of third parties.[278] In the FDA context, we may worry that patients will not understand that precertification does not produce the "gold standard" of evidence that the FDA has previously been known for and has touted.[279] But patients may be educated on this topic. However, mobile health apps are highly unlikely to jeopardize the safety of third parties. Professor Pearl argues that it will be difficult (though necessary) to educate drivers of semi-autonomous vehicles about the limits of their cars' capabilities,[280] but it is in some sense not even possible to educate third parties, who have not consented to the risks at issue. These third-party effects likely weigh in favor of more stringent NHTSA regulation for intermediate stages of autonomy, even where innovation might proceed more slowly as a result.

B. Technologies Lacking an Existing Regulatory Framework

There are certainly many other technological areas that are subject to constant iteration, where improvement over time is an explicit goal. But because these technologies are not subject to meaningful governmental regulation, the ossification-related concerns of the intermediate technologies identified above, in the health care context or otherwise, are not present. The oft-repeated Silicon Valley motto "move fast and break things"[281] comes to mind as an example here. Pharmaceutical companies needing FDA approval cannot, by definition, "move fast and break things," and the autonomous-vehicle firm who did would face extreme liability from both consumers and NHTSA. But Facebook, Google, and other tech companies can and have operated with relative immunity from regulation, even as they cause harms both large and small.[282]

To be sure, these companies have faced *threats* of regulation,[283] typically on topics including transparency and consent, data privacy, and related consumer protection issues.[284] Several technology companies have

278. Daisuke Wakabayashi, *Self-Driving Uber Car Kills Pedestrian in Arizona, Where Robots Roam*, N.Y. TIMES (Mar. 19, 2018), https://www.nytimes.com/2018/03/19/technology/uber-driverless-fatality.html [https://perma.cc/2Q2Z-6BVX].

279. *Statement by FDA Commissioner Scott Gottlieb on the Agency's Ongoing Work to Forcefully Address the Opioid Crisis*, FOOD & DRUG ADMIN. (Aug. 29, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm618831.htm [https://perma.cc/8B5S-2CNV].

280. Pearl, *Hands on the Wheel*, *supra* note 263, at 747-51.

281. Kevin Roose, *The Young and Brash of Tech Grow a Bit Older, and Wiser*, N.Y. TIMES (Mar. 14, 2018), https://www.nytimes.com/2018/03/14/technology/tech-leaders-growing-up.html [https://perma.cc/2PN2-U3BX].

282. *See, e.g.*, Alexandra Stevenson, *Facebook Admits It Was Used to Incite Violence in Myanmar*, N.Y. TIMES (Nov. 6, 2018), https://www.nytimes.com/2018/11/06/technology/myanmar-facebook.html [https://perma.cc/DF32-GSJN].

283. *See, e.g.*, Cecilia Kang & Kevin Roose, *Zuckerberg Faces Hostile Congress as Calls for Regulation Mount*, N.Y. TIMES (Apr. 11, 2018), https://www.nytimes.com/2018/04/11/business/zuckerberg-facebook-congress.html [https://perma.cc/649S-NAKN].

284. Questions have also been raised about Facebook's ability to influence an election, either through its own conduct or through the conduct of third parties. *See, e.g.*, Jonathan Zittrain, *Engineering*

argued that these threats of future regulation will stifle innovation and harm consumer choice.[285] This argument strains credulity when applied to certain proposals. For instance, the Honest Ads bill would "requir[e] those who purchase and publish [online political advertisements] to disclose information about the advertisements to the public."[286] It is not clear how requiring increased advertising transparency would prevent Facebook or other platforms from innovating. Indeed, Facebook has more recently implemented some of the bill's proposals,[287] perhaps in an attempt to forestall the passage of the remainder.

More concerning to companies like these are regulations around their use of data. Some data-privacy measures may, at heart, be transparency initiatives (as in the case of several provisions of the European Union's new General Data Protection Regulation (GDPR)),[288] but others aim for more substantive regulation with more severe penalties if violations or harms can be shown. Given that, at present, companies like Facebook seem to be unable or unwilling to prevent contractors from violating its existing stated policies (as in the Cambridge Analytica situation),[289] establishing harsher penalties for such violations may simply encourage companies to enforce their own rules more fully.

In general, though, the regulatory systems being proposed (seriously or not) for the tech giants are largely being conceived of as ex post remedies for violating more general consumer or data-privacy protections. These are fundamentally different from the overlapping regulatory structures we observe in the health care context, where preapproval of new products or of changes to existing products combines with governmental reimbursement and intellectual property systems to create conflicting incentives for companies. Even in the autonomous-vehicle context, which at present lacks a preapproval mechanism, the regulators in question are applying different levels of regulation to different levels of autonomy in a way that may bias innovation (appropriately or not). At present, there are no such barriers for tech firms.

The foregoing analysis suggests some general principles administrative agencies might choose to follow when considering whether the problem of intermediate technologies is relevant within their jurisdictional area. First,

an Election, 127 HARV. L. REV. F. 335, 335 (2014). Some of these questions relate to transparency concerns, as above. *See id*. at 337.

285. Tom Relihan, *Will Regulating Big Tech Stifle Innovation?*, MIT SLOAN (Sept. 27, 2018), http://mitsloan.mit.edu/newsroom/articles/will-regulating-big-tech-stifle-innovation [https://perma.cc/7GDC-94JP].

286. S. 1256, 116th Cong. (2019).

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agency leaders may identify technologies facing ossification concerns of the type articulated in this Article, part of which involves considering whether a technology sits within an existing regulatory framework or not. Second, in the process of identifying such technologies, regulators ought to identify barriers to their development on both the front and back end. Third and finally, regulators might articulate potential push and pull solutions to address those barriers.

These general solutions are likely to differ strongly by area of technology. Although several other technological areas may have a front-end regulator performing an FDA-like approval function, few if any other areas have an entity that replicates CMS' function, in which the government is also a primary purchaser of particular technologies. In those cases, other pull mechanisms like prizes or tax subsidies to lower prices for consumers may assume greater prominence.

V. Conclusion

Although scholars and policymakers are continuing to prioritize efforts to encourage companies in many different technological sectors to innovate, they have largely ignored the ways in which existing regulatory structures bear on technological development from a temporal perspective. This Article's recognition and description of the problem of intermediate technologies may assist scholars, agencies, and policymakers in advancing more flexible regulatory frameworks that reward companies for continued innovation and improvement, not only innovation in the first instance.