

MOVING BEYOND THE FEDERAL FUNDING HOOK: MANAGEMENT-BASED REGULATION IN BIOMEDICAL RESEARCH

Gabrielle Goldstein*

ABSTRACT

After World War II, the federal government established specific sets of regulations to oversee the conduct of biomedical research. These regulations tended to take the form of management-based regulations, and were generally imposed as conditions of federal funding. This Article identifies and describes the development of four areas of regulatory oversight: (1) human subjects research, (2) animal research, (3) scientific integrity and misconduct, and (4) financial conflicts of interest. Each is an example of management-based regulation: regulated entities have flexibility in designing policies and programs that meet generalized regulatory requirements. The Article highlights the policy stability of each regulatory set despite tremendous intervening changes in the institutional environment and identifies significant oversight gaps that have resulted from this policy drift. As research is increasingly conducted in corporate settings without federal funding, less research activity is regulated. These gaps create conditions under which regulations are unlikely to achieve their intended policy goals and may jeopardize public health and safety. Further, these case studies indicate that flexible regulation can also be susceptible to policy drift, as can more traditional regulatory tools, highlighting the need for attention to regulatory design and periodic review. The Article concludes with suggestions for mechanisms to improve research oversight by moving beyond the “federal funding hook,” including the suggestion that FDA product regulations be

* Gabrielle Goldstein is Counsel in Nixon Peabody LLP’s Health Services Practice Group in San Francisco, and is a Ph.D. Candidate in Health Policy at the University of California at Berkeley. The author acknowledges financial support from the National Science Foundation and the University of California at Berkeley School of Law. The author is grateful for feedback from Frances Miller, Robert Kagan, Christopher Ansell, Ann Keller, and David Vogel. An earlier version of the Article was delivered at the 2016 Annual Law and Society Association conference.

harmonized with the management-based regulations described herein that currently apply only as conditions of federal funding. Importantly, this Article includes an analysis of new legal developments including the HHS Final Rule regarding clinical research (Jan. 19, 2017) and the 21st Century Cures Act (Dec. 13, 2016).

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INTRODUCTION

Scholars have written extensively about the tectonic shifts in regulation and governance that have occurred over the past few decades across wide swaths of social and economic life. The

more recent concentration on “new governance” techniques emerged in response to the concern that a focus on traditional state-centered, top-down systems of regulation was both overly simplistic, given the range of mechanisms available to regulators,¹ and increasingly outmoded, given the progressively nodal nature of institutional reality. Such concern has, in turn, been situated within a broader context of the ascendancy of global capitalism and its frequent preference for less regulation when possible, and more flexible regulation when necessary.² A less normative (but not mutually exclusive) analysis would also note that, simply, it is hard to regulate certain activities; firms may be better equipped with the means and information to meet regulatory requirements in their own ways, and thus flexible regulation may be better suited to tackle complicated problems than more proscriptive approaches.

The interest in new governance reflected the realization that policy solutions would need to incorporate additional tools to more effectively produce socially valued behavior by regulated entities.³ Accordingly, a variety of more flexible, less state-centered regulatory instruments emerged. These include information disclosure requirements, tradable permits, industry self-regulation, third-party accreditation and certification programs, and management-based and principles-based regulation.⁴ These forms of regulation have been implemented in areas of environmental regulation, food safety, toxic chemical use and release, industrial safety, and renewable energy, among others. Although a few accounts of flexible regulation have described public policies that have been in place for more than a few decades, this scholarship has tended to take a historically

1. John Braithwaite et al., *Can Regulation and Governance Make a Difference?*, 1 REG. & GOVERNANCE 1, 1-7 (2007); Christopher Carrigan & Cary Coglianese, *The Politics of Regulation: From New Institutionalism to New Governance*, 14 ANN. REV. POL. SCI. 107, 114 (2011).

2. Scott Burris et al., *Changes in Governance: A Cross-Disciplinary Review of Current Scholarship*, 41 AKRON L. REV. 1, 37-38 (2008). Certainly, the corporate preference for deregulation is not universal. For instance, when stricter regulation is economically advantageous, firms may push to “trade up” regulatory standards. See, e.g., DAVID VOGEL, TRADING UP: CONSUMER AND ENVIRONMENTAL REGULATION IN A GLOBAL ECONOMY 6 (1995).

3. Carrigan & Coglianese, *supra* note 1, at 115.

4. *Id.* at 114.

narrow view of what constitutes “traditional” and “new” regulatory tools.

With these points in mind, this Article explores a particular policy domain in which flexible, management-based regulations have been in place for many decades: the oversight of biomedical research. Through this analysis, this Article offers empirical contributions to the new governance literature, as well as contributions to contemporary discussions about science and research regulation and the challenges posed by the increasing corporate funding and conduct of science.

First, this Article extends the work related to management-based regulation into the empirical domain of biomedical research regulation. Looking at four separate regulatory sets that govern the conduct of biomedical research in the United States, this Article describes how each uses management-based mechanisms to encourage regulated organizations to meet the socially valued regulatory goal of ethical and appropriate scientific research. Taking a longer view of the arc of regulation, the analysis shows that, in these policy areas, light-touch regulation has been in circulation long before the more recent interest in new governance—in some cases for as long as half a century or more.

After analyzing the design of these regulatory sets, this Article then describes the stability of this regulatory regime despite dramatic shifts in the institutional environment. Critically, when these regulatory sets were established, the federal government was the principal financier of medical research, and activities took place primarily in the academic medical setting. Thus, these regulatory sets were established principally as conditions of federal funding for academic physicians and researchers, rather than as business regulations. The institutional and funding environments, however, have changed dramatically, particularly since the 1980s. The pharmaceutical industry and corporate research have replaced the federal government as the principal funder of biomedical research, and clinical (and pre-clinical) research has largely moved from the academy into non-academic (industrial and other for-profit) settings.

These intervening changes in the institutional environment, however, have not coincided with an updating of policy, particularly and critically in terms of which firms and activities are regulated, and which are not—in other words, who is “in” and who is “out” as a regulated entity. Even though substantially less research now occurs in academic settings, in federally funded research environments, and with federal dollars, the main regulatory sets continue to apply principally as conditions of federal funding. In this way, much of the regulatory system has experienced “policy drift,” which occurs when the set of actors engaged in the activity originally targeted for regulation has changed significantly, but the regulatory regime has not adapted to subsume those new actors into the regulatory fold. The regulations, therefore, apply to an increasingly small subset of actors and activities over time.

The narrative advanced here is not one of simple capture, where regulation becomes colonized by the regulated subsystem, and regulators become “captured” by the firms and industries with which they interact. Rather, the observation is that, once established, the regulatory arena became subject to policy drift because of failures to update the applicable laws and regulations that undergird the system. As a result, the main stakeholders who now conduct the lion’s share of research fall largely outside of the regulatory regimes discussed herein. In this void, private industry may or may not decide to adopt its own standards for research, which may or may not align with the requirements or goals of the federal policies. The ultimate consequence of this policy drift is the creation of increasingly large swaths of unregulated space, which may expose the public to certain direct and indirect risks. While future empirical research will need to quantify the extent and magnitude of these risks in practice, this Article argues that we must revisit these public policies and identify alternative ways to regulate the relevant activities beyond the “federal funding hook.” One approach may be to bolster the existing management-based regulations described in this Article by expanding their juris-

dictional reach to non-federally funded research.⁵ This approach may prove challenging because of limitations in the underlying enabling legislation and in agency jurisdiction. Noting that the Food and Drug Administration (FDA) drug and device regulations do contain some relevant, if often cursory, provisions pertaining to research that are framed as *products* regulations, however, this Article suggests that harmonizing the FDA products regulations to align with policies governing federally funded research may provide an alternative regulatory pathway for more robust research oversight in an era of corporate funding.⁶

These observations about biomedical research oversight lead to a broader set of concerns: light-touch regulation and other new governance models can be flexible in some ways but not others. While they may have mechanisms to automatically capture newly emerging risks in the institutional environment, this is not necessarily so. One way in which they are likely to require updating over time is with regard to jurisdictional boundaries. Like any other form of law or regulation, flexible regulations have jurisdictional boundaries. If the boundaries of inclusion are not updated over time, flexible regulations may be subject to the same pathologies that arise in the context of more top-down regulatory regimes, including policy drift.⁷ If this occurs, it may be that the institutional landscape has “outgrown” the regulations, and alternatives must be sought in order to achieve the original public policy goals.⁸ To be sure, the claim is not that management-based regulations are more or less susceptible to policy drift than other forms of regulation, nor does this Article advance a causal link between management-based regulation and the observed outcome: policy drift. Rather, these empirical case studies indicate that flexible regulatory regimes that do not require revisiting under their enabling legislation and which become outdated are unlikely to achieve the goals and ideals of

5. See *infra* pp. 160–64.

6. See *infra* pp. 160–64.

7. See *infra* Part III.

8. See *infra* Section III.C.

a flexible and adaptable regulatory model as circumstances change in the institutional environment.

This Article proceeds as follows. Part I situates the new governance literature generally, and provides a description of management-based regulation in particular. Part II identifies and describes the historical development of management-based regulatory approaches in several long-standing sets of biomedical research oversight regulations in the United States. These are the regulatory oversight of: (1) human subjects research, (2) animal research, (3) research integrity and misconduct, and (4) financial conflicts of interest in research. Part III discusses the stability of this regulatory system, despite intervening changes in the institutional environment. This analysis demonstrates policy lock-in and drift, caused not by the *form* of regulation but by a failure to revise the jurisdictional framework over time to incorporate new risks and changing circumstances. Specifically regarding biomedical research, this Part also calls for review of the particular policies that are the subject of this case study, as the current policy drift may jeopardize public health and safety, and at a minimum fails to achieve intended policy goals.⁹ Finally, Part IV concludes with suggestions for potential strategies to address the policy gaps this Article identifies, particularly with regard to FDA regulatory authority and the possibility of harmonizing the FDA's product regulations to align with the management-based regulations described herein, as well as recommendations for future research.

I. "NEW GOVERNANCE" AND MANAGEMENT-BASED REGULATION

A. "New" *New Governance*

A few narratives often explain the rise of interest in new governance. First, scholars anchor their interest in the functional

9. See *infra* Part III.

fact that “traditional” approaches to regulation are often, and perhaps increasingly, ill-suited to deal with the complex and dynamic problems that regulations aim to address.¹⁰ Second, scholars point to dramatic changes in technology and the globalizing economy as catalysts to the fragmentation of traditional state-based modes of power.¹¹ Governments are no longer the only “regulators” in any given substantive space, and they now compete with other social actors for power and influence.¹² Non-governmental organizations, public-private partnerships, and corporations, among others, now form a regulatory matrix along with governments, in which each is a “node” in a distributed network of power.¹³

These empirical or external “push factors” in the broader political economy developed alongside important internal developments within legal and democratic theory.¹⁴ These include the decline of unified theories, a rejection of binary dichotomies, and dissatisfaction with fragmented schools of thought.¹⁵ Such legal scholars explore the limitations of traditional regulatory approaches and are critical of a dichotomy between regulation and deregulation, exploring instead a world of gradients and alternatives between those two poles,¹⁶ including experimentalist governance.¹⁷

Given these empirical phenomena and intellectual energy, regulatory scholars in the legal academy and political science and policy studies turned their analytical gaze beyond classical state-centered, highly prescriptive command-and-control regu-

10. See Burris et al., *supra* note 2, at 6.

11. See *id.* at 14.

12. See DAVID LEVI-FAUR, HANDBOOK ON THE POLITICS OF REGULATION 6 (2011), <http://levifaur.wiki.huji.ac.il/images/Chapter1hr.pdf>.

13. See Burris et al., *supra* note 2, at 26; see also LEVI-FAUR, *supra* note 12.

14. See Orly Lobel, *The Renew Deal: The Fall of Regulation and the Rise of Governance in Contemporary Legal Thought*, 89 MINN. L. REV. 342, 352 (2004).

15. *Id.*

16. Bradley C. Karkkainen, “New Governance” in *Legal Thought and in the World: Some Splitting as Antidote to Overzealous Lumping*, 89 MINN. L. REV. 471, 474 (2004).

17. Michael C. Dorf & Charles F. Sabel, *A Constitution of Democratic Experimentalism*, 98 COLUM. L. REV. 267, 340 (1998); see also Susan Sturm, *Second Generation Employment Discrimination: A Structural Approach*, 101 COLUM. L. REV. 458, 462–63 (2001).

lation, towards alternative methods of shaping the behavior of regulated entities to achieve social goals.¹⁸ Traditional tools took two main forms: means-based regulation, in which government mandates required all regulated entities to take the same actions or use the same technologies,¹⁹ and performance-based regulation, in which government mandates required regulated entities to hit certain targets or goals, without specifying how to meet the target.²⁰ Over time, command-and-control regulation came to be viewed as blunt, costly, and unnecessarily rigid.²¹ In addition, these tools required vigilant monitoring by government regulators, which became more difficult as many economies and agencies faced strident calls for smaller government and forced austerity.²²

Thus, the rise of new governance scholarship is situated within this confluence of energy around empirical and intellectual developments.²³ The scholarship acknowledges an awareness that policy solutions would need to incorporate additional tools to induce compliance with socially valued behavior, and a number of more flexible, less state-centered regulatory instruments were identified in theory and practice.²⁴ The identified instruments include self-regulation, information disclosure requirements, audit mandates, and as will be discussed in more detail shortly, management-based and principles-based regulatory regimes.²⁵ These tools differ in the particular mechanisms through which they aim to control the behavior of regulated targets. They share, however, a general perspective about a shift in the role of government from a one-stop shop for all aspects of regulatory control, including standard-setting, monitoring, and enforcement, to one node among many within a gover-

18. Karkkainen, *supra* note 16, at 490.

19. Carrigan & Coglianese, *supra* note 1.

20. *Id.* at 115.

21. *Id.* at 114.

22. *Id.* at 115.

23. *Id.* at 118.

24. *Id.* at 114–15.

25. *Id.* at 116.

nance matrix—namely, the node that should “steer” the ship, letting the regulated entities do the “rowing.”²⁶

Some new governance literature is more functional or descriptive, often identifying instances of new governance empirically and considering the conditions under which such regimes may be more or less successful in producing social goods.²⁷ Other literature is animated by a more overtly normative concern that distributed governance is already or will be hijacked by better resourced actors, particularly those representing global capitalist enterprise,²⁸ and that by focusing on traditional state-centered forms of regulation, we are missing the opportunity to identify governance models that can lead to more effective results.²⁹ Another strand of scholarship, principally within legal scholarship, explores the theoretical limitations of top-down regulation and the potential (and sometimes realized) possibilities for experimentalist governance.³⁰ Overall, scholars frequently identify new governance approaches in public policy domains in the United States, including environmental protection,³¹ environmental health and safety systems,³²

26. Burris et al., *supra* note 2, at 45.

27. Lori Snyder Benneer, *Are Management-Based Regulations Effective? Evidence from State Pollution Prevention Programs*, 26 J. POL'Y ANALYSIS & MGMT. 327, 328–39 (2007) [hereinafter Benneer, *Are Management-Based Regulations Effective?*]; Lori Snyder Benneer, *Evaluating Management-Based Regulation: A Valuable Tool in the Regulatory Toolbox?*, in LEVERAGING THE PRIVATE SECTOR: MANAGEMENT-BASED STRATEGIES FOR IMPROVING ENVIRONMENTAL PERFORMANCE 51, 79–81 (Cary Coglianese & Jennifer Nash eds., 2006) [hereinafter Benneer, *Evaluating Management-Based Regulations*]; Lori S. Benneer & Cary Coglianese, *Flexible Approaches to Environmental Regulation*, in THE OXFORD HANDBOOK OF U.S. ENVIRONMENTAL POLICY 582 (Sheldon Kamieniecki & Michael E. Kraft eds., 2013); Sanya Carley, *State Renewable Energy Electricity Policies: An Empirical Evaluation of Effectiveness*, 37 ENERGY POL'Y 3071, 3073 (2009); Cary Coglianese & David Lazer, *Management-Based Regulation: Prescribing Private Management to Achieve Public Goals*, 37 LAW & SOC'Y REV. 691, 694–96 (2003); Neil Gunningham & Darren Sinclair, *Organizational Trust and the Limits of Management-Based Regulation*, 43 LAW & SOC'Y REV. 865, 867–68 (2009); Ruthanne Huising & Susan S. Silbey, *Constructing Consequences for Noncompliance: The Case of Academic Laboratories*, 649 ANNALS AM. ACAD. POL. & SOC. SCI. 157, 161–63 (2013).

28. John Braithwaite, *Responsive Regulation and Developing Economies*, 34 WORLD DEV. 884, 884–85 (2006); *see also* Burris et al., *supra* note 2, at 23.

29. Burris et al., *supra* note 2, at 12–19.

30. *See, e.g.*, Dorf & Sabel, *supra* note 17, at 465.

31. *See, e.g.*, Benneer & Coglianese, *supra* note 27, at 582–83.

32. *See, e.g.*, Huising & Silbey, *supra* note 27, at 160–62.

health care reform,³³ capital adequacy regulation,³⁴ and workplace discrimination.³⁵ Such approaches have also been identified in the European Union, particularly with regard to its “Open Method of Coordination,”³⁶ and in other transnational contexts.³⁷

B. “Old” New Governance

New governance scholarship tends to focus on the “newness” of flexible regulation. Scholars have described the shift towards new governance as a “seismic reorientation in both the public policymaking process and the tools employed in policy implementation,”³⁸ and it being an “entirely new regime”³⁹ or a “new kind of regulatory partnership” between private organizations and regulators.⁴⁰

When U.S. regulatory scholars describe command-and-control regulations, they tend to have in mind a regulatory style that was dominant in the New Deal era, although it perhaps reached its true apex during the 1960s and 1970s in the areas of health, the environment, and occupational safety.⁴¹ Thus new governance tools are often construed as coming later, principally as late twentieth-century and early twenty-first-century developments.⁴²

Taking a longer view of the arc of regulatory history, how-

33. See, e.g., Louise G. Trubek, *New Governance and Soft Law in Health Care Reform*, 3 IND. HEALTH L. REV. 139, 149–50 (2006).

34. See, e.g., Robert F. Weber, *New Governance, Financial Regulation, and Challenges to Legitimacy: The Example of the Internal Models Approach to Capital Adequacy Regulation*, 62 ADMIN. L. REV. 783, 784–88 (2010).

35. See, e.g., Sturm, *supra* note 17, at 459–65.

36. See Grainne de Búrca, *The Constitutional Challenge of New Governance in the European Union*, 28 EUR. L. REV. 814, 815 (2003).

37. See, e.g., Julia Black, *Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes*, 2 REG. & GOVERNANCE 137, 137–40 (2008) (explaining new governance’s role in international regulating bodies that have no official government involvement).

38. Karkkainen, *supra* note 16, at 473.

39. Lobel, *supra* note 14, at 354.

40. Huising & Silbey, *supra* note 27, at 160.

41. See Karkkainen, *supra* note 16, at 473–74, 474 n.10.

42. See *id.* at 473–74.

ever, it is clear that some of these “new” tools are not so new after all. Indeed, while not the only domain in which this is the case,⁴³ health care regulation is one area in which oft-described “innovative” regulatory mechanisms have been in place for a very long time, due in part to the legacy of self-regulation in medical practice.⁴⁴ This general fact has not been entirely lost on regulatory scholars.⁴⁵ For instance, Joseph F. Rees has traced the lineage of self-regulatory standard setting back to the establishment of national hospital standards by the American College of Surgeons around 1920.⁴⁶ Other scholars have noted that, although it has long been in practice, the institutional review board model of human subjects research oversight is an “audited self-regulation,”⁴⁷ “enforced self-regulation,” or hybrid regulatory tool.⁴⁸ Even in the area of health regulation, however, this attention to historical detail is the exception, not the rule, in new governance literature.

C. *A Specific Type of New Governance: Management-Based Regulation*

Management-based regulation is one of several alternatives to command-and-control regulation in the arsenal of new gov-

43. Another interesting early example of management-based regulation is the environmental impact statement requirements imposed under the National Environmental Policy Act. See Lobel, *supra* note 14, at 426 (citing 42 U.S.C. §§ 4321–4370f (2000)). This example is identified in Cary Coglianese & David Lazer, *Management-Based Regulation: Using Private-Sector Management to Achieve Public Goals* 42 n.4 (John F. Kennedy Sch. of Gov’t, Faculty Research Working Papers Series, RWP01-047, 2001), in which they cite the earlier study by SERGE TAYLOR, MAKING BUREAUCRACIES THINK: THE ENVIRONMENTAL IMPACT STATEMENT STRATEGY OF ADMINISTRATIVE REFORM (1984).

44. See Louise G. Trubek et al., *Health Care and New Governance: The Quest for Effective Regulation*, 2 REG. & GOVERNANCE 1, 5 (2008).

45. See *id.*

46. See Joseph V. Rees, *The Orderly Use of Experience: Pragmatism and the Development of Hospital Industry Self-Regulation*, 2 REG. & GOVERNANCE 9, 10–14 (2008).

47. Margaret Foster Riley, *Federal Funding and the Institutional Evolution of Federal Regulation of Biomedical Research*, 5 HARV. L. & POL’Y REV. 265, 276 (2011) (citing Douglas Michael, *Federal Agency Use of Audited Self-Regulation as a Regulatory Technique*, 47 ADMIN. L. REV. 171, 174–77 (1995)).

48. See Burris et al., *supra* note 2, at 49–50, 50 n.212; Sydney Halpern, *Hybrid Design, Systemic Rigidity: Institutional Dynamics in Human Research Oversight*, 2 REG. & GOVERNANCE 85, 85–88 (2008).

ernance tools available to policy makers. The central mechanism by which management-based regulations aim to achieve their goal of shaping behavior is by requiring regulated firms to engage in a process to plan how best to achieve public goals.⁴⁹ Unlike command-and-control regulations that either intervene at an organization's acting stage (namely through technology-based regulation) or output stage (through performance-based regulation), management-based regulation intervenes at the organization's *planning* stage.⁵⁰ Management-based regulations set broad framework goals leaving decisions about specific technology and outputs to the regulated entities.⁵¹

Instances of this regulatory approach vary in the level of specificity required of firms' plans. Some management-based regulations require that firms submit their plans to regulators for approval; others require that firms merely verify compliance publicly or to the government via a written assurance.⁵² Yet other variations require that regulated firms remain subject to government or third-party inspection and/or compliance audits.⁵³

Management-based regulations also vary regarding the specificity of criteria required of plans. For instance, some management-based regulations specify particular elements that each plan should or must have, including identification of risks, mitigation activities, procedures for monitoring and enforcement, and measures for updating the plan.⁵⁴ Other regulations may be more general. The commonality that all variations share is that firms are required to generate their own plans for how to

49. See Coglianese & Lazer, *supra* note 27, at 692; see also Christine Parker et al., *Regulating Law Firm Ethics Management: An Empirical Assessment of an Innovation in Regulation of the Legal Profession in New South Wales*, 37 J.L. & SOC'Y 466, 470 (2010); Ted Schneyer, *The Case for Proactive Management-Based Regulation to Improve Professional Self-Regulation for U.S. Lawyers*, 42 HOFSTRA L. REV. 233, 242 (2013).

50. See Coglianese & Lazer, *supra* note 27, at 691-92.

51. *Id.* at 692.

52. See *id.* at 699-700 (detailing the different compliance procedures of OSHA and the EPA aimed at ensuring compliance).

53. *Id.* at 699-700, 717-18.

54. See *id.* at 695-96.

comply with general criteria set by the government, with the purpose of achieving a specified social goal.⁵⁵ Often, regulators will provide regulated entities with soft-law guidance documents in order to assist firms in meeting management-based regulatory requirements.⁵⁶

New governance scholars have identified a number of management-based regulatory regimes in the United States, particularly in food safety, environmental and industrial safety, and pollution prevention. Some scholars have also evaluated the merits of this regulatory tool, noting that management-based approaches may be more effective than command-and-control regimes when: (1) regulated firms are heterogeneous, (2) regulating outputs is difficult, and (3) there is a high degree of uncertainty about the nature of the risk being regulated.⁵⁷ Others have tempered optimism with an acknowledgement of the limits of management-based regulation, particularly with regard to the role of organizational trust within a firm, and the fact that divided loyalties and mistrust within a firm can derail even the best-intentioned planning processes.⁵⁸

II. MANAGEMENT-BASED REGULATION OF BIOMEDICAL RESEARCH: WHEN "NEW GOVERNANCE" IS OLD

Interestingly, most of the main federal regulations pertaining to the conduct of biomedical research take the form of management-based regulations. Each regulatory set described below grants local institutions considerable autonomy and flexibility in designing policies and programs that meet generalized social goals set forth in federal regulations.⁵⁹ Further, each set of

55. *Id.*

56. *Id.* at 715. Citing an insight on this point by Robert Kagan and Eugene Bardach, the authors note that a risk of publishing soft law is that it will in practice come to be viewed as binding, thus limiting willingness of firms to take alternative approaches. *Id.* at 715 n.22. This is certainly a concern in the biomedical research context, though beyond the scope of the current analysis.

57. *Id.* at 691; see also Bennear, *Are Management-Based Regulations Effective?*, *supra* note 27, at 345; Bennear & Coglianese, *supra* note 27, at 591-92.

58. Gunningham & Sinclair, *supra* note 27, at 870.

59. Coglianese & Lazer, *supra* note 27, at 691.

regulations either requires a local committee as the mechanism for decision making and oversight, or the committee mechanism has been widely adopted in practice.⁶⁰ Each regulatory set has also been in force for decades, some for more than half a century, and generally long before more recent interest in the emergence of flexible regulatory instruments.⁶¹

It is relevant to note that the regulatory areas discussed below are not the only areas of biomedical research subject to regulation, nor are they the only ones that fit the management-based regulatory model.⁶² These four cases, however, were selected for in-depth analysis because they are the most significant components of domestic biomedical research compliance.⁶³ It also must be noted that the analysis below pertains to regulation at the federal level in the United States. There are several state-level policies and programs in these areas,⁶⁴ but they are few in number.⁶⁵ This is largely because, as discussed below, biomedical research regulation arose principally in the context of federal funding to research organizations. Therefore, the analysis below follows federal developments over time.⁶⁶

Each section below provides a brief description of the management-based regulatory approach to a particular issue in biomedical research. Briefly, each is governed by a set of federal

60. *Id.* at 692.

61. *Id.*

62. For instance, federal regulations require that institutions using radioactive materials in research establish an Institutional Radiation Safety Committee. 10 C.F.R. § 35.24(f) (2017). NIH guidelines require that institutions establish Institutional Biosafety Committees to oversee recombinant DNA research and other types of research with hazardous materials. See NAT'L INSTS. OF HEALTH, DEP'T OF HEALTH & HUMAN SERVS., NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES 15 (2016), https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf.

63. The only significant piece of such programs left out of this analysis is that of grant administration compliance. This is not addressed in this Article because it does not involve the conduct of research oversight, and is instead an administrative compliance matter.

64. For instance, several states have enacted legislation or promulgated regulations that add requirements to the federal regulatory baseline, particularly in the area of human subjects research. See, e.g., CAL. HEALTH & SAFETY CODE §§ 24170–179.5 (West 2017).

65. See, e.g., *id.*; N.Y. PUB. HEALTH LAW §§ 2440–46 (McKinney 2017); VA. CODE ANN. § 32.1-162.16 to .20 (2017).

66. The FDA has certain product safety regulations that intersect with research activities that are the subject of these management-based regulations. They are described where appropriate.

regulations that specify the planning and internal rulemaking efforts that regulated organizations must engage in to achieve the social goals of conducting ethical research. The regulations do not specify the technologies to be used, or the outputs to be achieved.⁶⁷ Instead, organizations have the flexibility to design their own research ethics programs, policies, and processes – all within broad framework criteria set forth in the regulations.⁶⁸ Decisions regarding particular projects or problems and the ongoing management of such are devolved to local, private sector actors (often committees), rather than through command-and-control style edicts or centralized, governmental decision making.⁶⁹ Further, each regime makes extensive use of non-binding guidance to provide additional detail for organizations in their efforts to devise local strategies and policies to achieve the overall goals of the regulations.⁷⁰

A. Oversight of Human Subjects Research

Federal regulations at 45 C.F.R. §§ 46.101–.505 set forth the requirements for conducting research involving human subjects that is supported by the federal government.⁷¹ Until recently, these regulations, which are often referred to as the Common Rule, also applied to all research, regardless of funding source, at institutions that had agreed to apply the standards to all research under the terms of the institutions' Federalwide Assurance contract with the government.⁷² On January 19, 2017, however, the last day of the Obama Administration, the Department of Health and Human Services (HHS) published a Final

67. Benneer, *Are Management-Based Regulations Effective?*, *supra* note 27, at 329.

68. *Id.*

69. Coglianese & Lazer, *supra* note 27, at 695–96.

70. *Id.* at 696.

71. The enabling statute for these regulations is the National Research Act, Pub. L. No. 93-348, 88 Stat. 342 (1974).

72. See Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149 (Jan. 19, 2017). The effective date of this provision was initially Jan. 19, 2018, *id.* at 7152, but has now been delayed to July 19, 2018. See Federal Policy for the Protection of Human Subjects: Delay of the Revisions to the Federal Policy for the Protection of Human Subjects, 83 Fed. Reg. 2885, 2885 (Jan. 22, 2018).

Rule in the Federal Register that will eliminate the option for institutions to “check the box” to voluntarily apply the Common Rule to all human subjects research.⁷³ As a consequence, the Common Rule will now only apply to federally funded research following the effective date of the Final Rule.⁷⁴ Further, a similar set of regulations in the Federal Food, Drug, and Cosmetic Act applies to clinical investigations of products regulated by the FDA.⁷⁵

The centerpiece of the Common Rule and FDA framework is the requirement that research investigators and institutions ensure that all applicable human subjects research protocols are overseen and approved by an institutional review board (IRB).⁷⁶ The regulations specify requirements for IRB membership, the functions and operations that IRBs must undertake, including the creation of and compliance with written procedures, and general criteria for IRBs to apply in reviewing research projects.⁷⁷ Institutions must also provide the federal government with an assurance of compliance and maintain and provide access to records upon request.⁷⁸

An extensive array of non-binding guidance issued by the Office for Human Research Protections (OHRP) at HHS and the FDA enrich the regime. For instance, the FDA’s website lists at least twenty-five guidance documents and “information sheets” specifically pertaining to clinical trials,⁷⁹ while OHRP’s

73. *Id.*

74. *Id.* at 7150.

75. See 21 C.F.R. §§ 56.101–.124 (2017). The HHS and FDA regulations do not, together or separately, cover *all* human subjects research. Research involving non-FDA regulated products, and certain research not sponsored by the federal government, falls outside of this regulatory regime. Unless covered by state law, such research is effectively unregulated by the government, but may be subject to institutional or other non-governmental policy. *Id.*; see also *supra* notes 71–74 and accompanying text.

76. See 21 C.F.R. § 56.101.

77. 45 C.F.R. §§ 46.107–.109, 46.111 (2017); 21 C.F.R. § 56.101.

78. 45 C.F.R. § 46.103; 21 C.F.R. § 56.115.

79. See *Information Sheet Guidance for Institutional Review Boards (IRBs), Clinical Investigators, and Sponsors*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/guidancesinformationsheetsandnotices/ucm113709.htm> (last updated Mar. 12, 2014).

online policy and guidance index lists at least sixty-five IRB guidance documents.⁸⁰ These materials, and the regulations overall, are informed by other soft-law documents, namely professional codes of research and international medical ethics statements tracing a lineage back to the Nuremberg Code.⁸¹

The IRB model was first instituted as internal National Institutes of Health (NIH) policy in the 1950s and was expanded in 1966 to be a requirement for extramural NIH grants.⁸² These grant requirements hardened into FDA regulations in 1971, as well as HHS regulations and federal law in 1974.⁸³ With various intervening expansions and revisions, including the recent Final Rule revisions, the basic regulatory regime has remained intact for the better part of half a century.⁸⁴

The Common Rule regulations were established as conditions of federal funding, because the federal government funded the lion's share of medical research in the postwar era and up until the 1980s.⁸⁵ This context is described in more detail later in this Article.⁸⁶ The model emerged as a settlement among the power-

80. See Office for Human Research Protections, U.S. DEP'T HEALTH & HUMAN SERVS., <https://www.hhs.gov/ohrp/regulations-and-policy/index.html> (last updated Feb. 16, 2016).

81. For soft law international codes of conduct pertaining to clinical research see THE INT'L COUNCIL FOR HARMONISATION OF TECH. REQUIREMENTS FOR PHARMS. FOR HUMAN USE, GUIDELINE FOR GOOD CLINICAL PRACTICE (2016), http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2_Step_4_2016_1109.pdf; World Medical Association Declaration of Helsinki: Ethical Problems for Research Involving Human Subjects, WORLD MED. ASS'N (Oct. 19, 2013), <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>.

82. See JILL A. FISHER, MEDICAL RESEARCH FOR HIRE: THE POLITICAL ECONOMY OF PHARMACEUTICAL CLINICAL TRIALS 25–26 (2008); LAURA STARK, BEHIND CLOSED DOORS: IRBS AND THE MAKING OF ETHICAL RESEARCH 106–10 (2012) (discussing the beginning uses of the IRB model).

83. Riley, *supra* note 47, at 270–74.

84. See Sandra V. Kotsis & Kevin C. Chung, *Institutional Review Boards: What's Old? What's New? What Needs to Change?*, 133 PLASTIC & RECONSTRUCTIVE SURGERY J. 439, 440 (2013). Note that this regulatory approach emerged as a result of professional efforts, without public input, and in any case many decades before public and patient groups engaged in activism around clinical research issues, such as the ACT UP coalition, which worked on advocacy related to HIV/AIDS clinical trials in the 1980s. Vanessa Heggie, *World Aids Day: How Aids Activists Changed Medical Research*, GUARDIAN (Dec. 1, 2013), <https://www.theguardian.com/science/2013/dec/01/world-aids-day-how-aids-activists-changed-medical-research>.

85. Riley, *supra* note 47, at 269; see also STARK, *supra* note 82, at 76.

86. See STARK, *supra* note 82, at 77 (explaining the NIH expanded rule to reduce the number of instances it was being sued by subjects of extramural studies that were not subject to same

ful medical and scientific community in the postwar era, and hardened into formal policy in response to egregious public scandals about federally funded research abuses including those at Willowbrook State School and Tuskegee.⁸⁷

The system was built upon two assumptions and one basic premise. The first assumption was that the vast majority of research would be covered by the regulations, since the federal government was the principal funder and compliance with the regulations was a condition of funding. Indeed, as described in more detail later in this Article, World War II and the postwar era marked an eruption in scientific enterprise, especially under the federal government's largesse. It was a time when the medical profession enjoyed broad public support and political power, and in which academic research capacities were greatly enlarged and network ties between the government and academia strengthened. Overall, federal investment in medical research more than doubled during the war, and continued to climb during the postwar period.⁸⁸

The second assumption undergirding the light-touch approach to human subjects research regulation was that the majority of research would occur in the academic medical setting, covered by the regulations, because that is where most medical research was taking place at the time.⁸⁹ This too began during the War. Since the federal government did not have the internal capacity to conduct the actual scientific work needed for the war effort, it entered into contracts with universities and medi-

stringent standards as NIH-run studies); *see also infra* Sections III.B.-C.

87. For an overview of these instances of research abuse, see David J. Rothman, *Were Tuskegee & Willowbrook 'Studies in Nature'?*, HASTINGS CTR. REP., Apr. 1982, at 5, 5-7, <http://www.jstor.org/stable/3561798>. For more extensive treatments, see JAMES H. JONES, *BAD BLOOD: THE TUSKEGEE SYPHILIS EXPERIMENT* (1993); Walter M. Robinson & Brandon T. Unruh, *The Hepatitis Experiments at the Willowbrook State School*, in *THE OXFORD TEXTBOOK OF CLINICAL RESEARCH ETHICS* 80, 80-85 (Ezekiel Emanuel et al. eds., 2008).

88. James A. Shannon & Charles V. Kidd, *Medical Research in Perspective*, 124 *SCIENCE* 1185, 1186 (1956) <http://www.jstor.org/stable/1752817>. It is worth noting that, while government funding of medical research increased during the war, so did industry's investment, constituting about \$31 million annually, or about 50% of total investment in medical research. *Id.* While the federal government was a rising player, it was not the only funder in town. *Id.*

89. *Id.* at 1185 (noting that this regulation began during World War II).

cal centers, both during and after the Second World War.⁹⁰

The public's widespread trust in the medical profession in the postwar era encouraged the government's collaboration with universities and medical centers.⁹¹ The public trusted the medical profession and the transformative power and possibilities of science, and did not have cause to demand prescriptive regulation.⁹² As a result of this trust, all major postwar health programs, including medical research, were designed to provide large levels of autonomy for medical professionals along with their universities and research institutions.⁹³

As with the other types of biomedical research oversight discussed in this Article, when self-regulation became politically unfeasible, management-based regulation of human subjects research was established as a ratchet up from total self-regulation by the medical and scientific community.⁹⁴ Unlike the Common Rule, however, the FDA regulations requiring IRB oversight apply to all clinical investigations involving FDA-regulated products and/or activities in support of a submission to the agency.⁹⁵ Thus these FDA regulations pertaining to human subjects research are aimed at research activity, but are couched within *product regulations*.⁹⁶ Nonetheless, the protections afforded to human subject participants are essentially equivalent for studies involving federal funding (regulated under the Common Rule) and studies testing FDA-regulated products (regulated under FDA regulations).⁹⁷ This is an important ex-

90. *Id.*

91. *Id.* at 1187.

92. *See id.* at 1188 (describing how National Advisory Councils act as a means to secure public consensus in the scientific sphere).

93. PAUL STARR, *THE SOCIAL TRANSFORMATION OF AMERICAN MEDICINE: THE RISE OF A SOVEREIGN PROFESSION AND THE MAKING OF A VAST INDUSTRY* 341, 351 (1982).

94. Carrigan & Coglianesse, *supra* note 1, at 118.

95. *See Institutional Review Boards Frequently Asked Questions - Information Sheet*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/RegulatoryInformation/Guidances/ucm126420.htm#IRBProcedures> (last visited Dec. 12, 2017) ("When research studies involving products regulated by the FDA are funded/supported by HHS, the research institution must comply with both the HHS and FDA regulations.").

96. *See* Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149 (Jan. 19, 2017).

97. *Id.* at 7149 (noting the need to update FDA regulations following the update to the

ception to the rest of the regulatory regimes described in this Article, and it suggests an alternative pathway for improved regulation of research activities, explored briefly in the Conclusion of this Article.

The human subjects research regulations are a clear example of a management-based regime, which has been in place for many decades. The regulations delegate oversight and approval of clinical research projects to non-governmental, institutionally-based bodies, which must establish a “plan” to comply with the regulations in the form of policies and procedures.⁹⁸ Institutions provide the government with a compliance assurance, and the government retains the right to audit and inspect facilities and records on an ad hoc basis, or in response to complaints.⁹⁹ Extensive soft-law guidance assists regulated organizations with compliance activities.

Unlike the other regulatory regimes described in this Article, which have not yet been explored in the regulation and governance literature, the resemblance between the human subjects research regulations and new governance instruments has been noted in the literature.¹⁰⁰ Scholars have not identified the human subjects research regime as an instance of management-based regulation, instead describing the regime as enforced self-regulation or hybrid regulation.¹⁰¹ While the focus of prior studies has largely been to evaluate the failure of the human subjects regime to be as responsive (to the needs of researchers) as its more flexible regulatory structure or ideal type might allow, scholars have described how particular aspects of the regime appear similar to new governance techniques.¹⁰² In particular,

Common Rule).

98. *Id.* at 7149–50.

99. *Id.* at 7140.

100. Scott Burris, *Regulatory Innovation in the Governance of Human Subjects Research: A Cautionary Tale and Some Modest Proposals*, 2 REG. & GOVERNANCE 65, 65–67 (2008) [hereinafter Burris, *Regulatory Innovation*] (describing new governance as being “literature, where scholars look for legitimacy and effectiveness in regulatory strategies that listen, learn, particularize, and mobilize situated knowledge and capacity”); Halpern, *supra* note 48, at 85–86.

101. Halpern, *supra* note 48, at 98–99.

102. Burris, *Regulatory Innovation*, *supra* note 100, at 66–67.

Scott Burris notes that the regime looks, at least on paper, like a more “innovative” regulatory technique in that it substitutes local deliberation for state decision making. Consistent with new governance, this technique allows community stakeholders to create local norms under the “distant[] gaze” of the state.¹⁰³ Sydney Halpern has also described the human subjects research regime as a type of hybrid regulation, in which government and non-government controls are brought together.¹⁰⁴ Importantly, however, these scholars focus on academically situated IRBs, which, as this Article observes, is a quickly shrinking segment of IRBs and research locations.¹⁰⁵

B. Institutional Animal Care and Use Committees

Federal regulations setting forth criteria for the responsible use and treatment of animals in research are at 9 C.F.R. §§ 1.1-3.142. These regulations were promulgated pursuant to the Health Research Extension Act of 1985 and amendments to the Animal Welfare Act (the AWA regulations).¹⁰⁶ The cornerstone of the current regime is the requirement that covered institutions establish institutional animal care and use committees (IACUCs) to oversee the handling and care of certain research animals.¹⁰⁷ The AWA regulations set forth requirements for IACUC membership, functions, recordkeeping, and preparation of an annual report to be filed with regulators.¹⁰⁸ Research facilities are required to certify compliance, make facilities and records available for inspection, and develop and follow a plan for the provision of care of animals in the event of emergency

103. *Id.* at 67.

104. Halpern, *supra* note 48, at 86–87.

105. See FISHER, *supra* note 82, at 11 (finding auxiliary intermediary research organizations account for 64% of research worldwide).

106. Health Research Extension Act of 1985, Pub. L. No. 99-158, 99 Stat. 820; Food Security Act of 1985, Pub. L. No. 99-198, §§ 1751–59, 99 Stat. 1354, 1645–50.

107. 9 C.F.R. §§ 1.1, 2.31 (2017); see also Russell J. Borski & Ronald G. Hodson, *Fish Research and the Institutional Animal Care and Use Committee*, 44 INST. FOR LABORATORY ANIMAL RES. J. 286, 286–87 (2003).

108. 9 C.F.R. § 2.31.

or disaster.¹⁰⁹

The Public Health Service (PHS), NIH, and the U.S. Department of Agriculture (USDA) publish nonbinding yet official agency policies regarding animal facilities and care. The USDA has published at least ten guidance documents;¹¹⁰ and the NIH has published at least seventy-five relevant guidance documents and materials, each available on the applicable agency's public website.¹¹¹

Briefly, this regime's lineage stretches back to the PHS's first edition of the *Guide for Laboratory Animal Facilities and Care* (the Guide) in 1963.¹¹² Soft, intramural guidance hardened into federal law with the enactment of the Animal Welfare Act in 1966, which Congress charged the USDA with implementing.¹¹³ The NIH (and its parent agency, PHS) instituted its own policy in 1971, applicable to all facilities receiving federal funding for research (PHS Policy),¹¹⁴ which was hardened into law through passage of the Health Research Extension Act of 1985, and amendment of the Animal Welfare Act in the same year.¹¹⁵ Federal regulations were subsequently promulgated, setting forth various criteria for IACUCs.¹¹⁶ The Guide, PHS Policy, and the AWA regulations remain the three central documents that govern the conduct of animal care and use in research.¹¹⁷

109. *Id.* § 2.38.

110. See *Animal Welfare: Publications, Forms, and Guidance Documents*, U.S. DEP'T AGRIC., http://www.aphis.usda.gov/aphis/ourfocus/animalwelfare/sa_publications/ct_publications_and_guidance_documents (last updated Nov. 16, 2017).

111. See *Policy & Compliance, Office of Laboratory Animal Welfare*, NAT'L INSTS. HEALTH, <http://grants1.nih.gov/grants/olaw/olaw.htm> (last updated Feb. 6, 2017).

112. Helen S. Gordon, *The History of the Public Health Service Policy on the Humane Care and Use of Laboratory Animals*, in 50 YEARS OF LABORATORY ANIMAL SCIENCE 152, 152 (Charles W. McPherson & Steele F. Mattingly eds., 1999).

113. See Animal Welfare Act, 7 U.S.C. §§ 2131-59 (2016).

114. See OFFICE OF LAB. ANIMAL WELFARE, NAT'L INSTS. OF HEALTH, U.S. DEP'T OF HEALTH & HUMAN SERVS., PUBLIC HEALTH SERVICE POLICY ON HUMANE CARE AND USE OF LABORATORY ANIMALS 1-2 (2015), <https://grants.nih.gov/grants/olaw/references/phspolicylabanimals.pdf>.

115. Health Research Extension Act of 1985, Pub. L. No. 99-158, 99 Stat. 820; Food Security Act of 1985, Pub. L. No. 99-198, §§ 1751-59, 99 Stat. 1354, 1645-50.

116. See 9 C.F.R. §§ 2.31-.36 (2017).

117. Derrell J. Clark et al., *The 1996 Guide for the Care and Use of Laboratory Animals*, 38 INST.

In a nutshell, the antivivisectionist movement in the United States coalesced more slowly than in Europe.¹¹⁸ While highly organized Victorian-era antivivisectionists in Britain succeeded in pressuring Parliament to pass the Cruelty to Animals Act in 1876—creating a highly centralized system of animal research oversight¹¹⁹—the antivivisectionist movement in the United States came together more gradually. Animal rights activists did not mobilize until the end of the nineteenth century when medical schools became more formalized and used animals more methodically in teaching and research.¹²⁰ By the time animal rights groups organized, the profession and industry of medical science had itself become quite powerful, and had shown the public the undeniable benefits of animal experimentation for humans, through discoveries like the diphtheria toxin in 1894.¹²¹ If anything, the history of early American vivisectionist efforts worked to consolidate medical researchers' power. Medical researchers and scientists were forced to defend their work together, and were almost always successful in defeating policy proposals to limit their autonomy.¹²²

Over time, however, social norms around unfettered use of animals shifted, both among the public and scientists. In the early 1940s, the University of Chicago and other institutions began hiring veterinarians and other experts to develop centrally managed programs of lab animal care.¹²³ Professionals began meeting in Chicago to develop standards and protocols for humane and systematic treatment of experimental ani-

FOR LABORATORY ANIMAL RES. J. 1, 41-43 (1997).

118. See Rebecca Dresser, *Research on Animals: Values, Politics, and Regulatory Reform*, 58 S. CAL. L. REV. 1147, 1148-49 (1985); See also Jeri A. Sechzer, *Historical Issues Concerning Animal Experimentation in the United States*, 15 SOC. SCI. & MED. PART F: MED. & SOC. ETHICS 13, 13-15 (1981).

119. Sechzer, *supra* note 118, at 14.

120. *Id.* at 15.

121. Dresser, *supra* note 118, at 1149.

122. *Id.*; see also JAMES TURNER, RECKONING WITH THE BEAST: ANIMALS, PAIN, AND HUMANITY IN THE VICTORIAN MIND 108-09 (1980).

123. Harry Rozmiarek, *Origins of the IACUC*, in THE IACUC HANDBOOK 1, 2 (Jerald Silverman, Mark. A. Suckow & Sreekant Murthy eds., 2d ed. 2007).

imals.¹²⁴ This group became the Animal Care Panel in 1950.¹²⁵ In 1965, the American Association for Accreditation of Laboratory Animal Care (AAALAC) was established, which remains the foremost professional association devoted to laboratory animal care and use.¹²⁶ From the beginning, these groups recommended or required the use of an IACUC.¹²⁷ The model spread quickly, and by the time the federal government developed an interest in regulating animal research, there was already a non-governmentally centered, management-based approach in wide use.

The growth of biomedical research in the postwar period led to increased demand for research animals.¹²⁸ In the 1940s, the National Society for Medical Research began pushing for laws requiring that shelters release unclaimed cats and dogs to research institutions.¹²⁹ Minnesota enacted the first “pound release” law in 1949, and other states followed.¹³⁰ While alarming to some, these laws and ordinances largely passed public muster.¹³¹ After the local medical community in Los Angeles persuaded the city council to pass a pound release ordinance in 1949, the matter was put to a vote. Angelinos supported the measure, as did voters on similar measures in Baltimore and Illinois.¹³²

During the 1960s, however, a series of major news articles in *Life Magazine* and *Sports Illustrated* raised the issue of animal welfare in research onto the public agenda.¹³³ This culminated in the passage of the Laboratory Animal Welfare Act in 1966

124. *Id.* at 3.

125. *Id.*

126. *Id.* at 2–3.

127. *Id.* at 7–8.

128. BAYLOR UNIV., ANIMAL CARE AND USE TRAINING HANDBOOK, www.baylor.edu/content/services/document.php?id=22452.

129. *Id.*

130. *Id.*

131. *Id.*

132. ANDREW N. ROWAN, OF MICE, MODELS, AND MEN: A CRITICAL EVALUATION OF ANIMAL RESEARCH 52–53 (1984).

133. *Concentration Camp for Dogs*, *LIFE*, Feb. 4, 1966, at 22.

(LAWA; in 1970, renamed the Animal Welfare Act or AWA).¹³⁴ The medical research lobby successfully pushed for the law to be as limited as possible. The final bill regulated only the treatment of certain mammals while being held before or after experimentation, not during the testing itself.¹³⁵ In 1970, the AWA extended the law's protection to additional warm-blooded animals, although the law rather incredibly still does not cover a number of animals commonly involved in research, including rats and mice.¹³⁶

While the original LAWA did not mandate the use of an IACUC as the mechanism for animal research oversight, in fact many institutions had already established this committee. By 1971, the NIH's new *Policy, Care, and Treatment of Laboratory Animals* included the IACUC as a means of local assurance of good animal care and use in research; such committees were also already required at military facilities.¹³⁷ This committee structure was a means by which regulators could delegate oversight and enforcement to individual institutions, giving each institution the flexibility to tailor research and protection programs to individual needs and risk tolerances.

A vocal animal rights lobby continued to push for more regulation, particularly following public outcry over scandals involving cruel treatment of animals in research.¹³⁸ This eventually resulted in some reform in 1985, amending AWA to beef up enforcement a bit and to finally require regulated insti-

134. LAWA was later renamed the Animal Welfare Act in 1970, or AWA. Maurice B. Visscher, *The Animal Welfare Act of 1970*, 172 SCIENCE 916, 916-17 (1971), <http://www.jstor.org/stable/i299585>.

135. *Id.*

136. Rats and mice are the most commonly used animals in research laboratories, estimated to comprise 80%-90% of all animals used. Purpose-bred rats and mice used in federally funded research are regulated under PHS policy, although they are not covered under the AWA. Dresser, *supra* note 118, at 1153-54.

137. Rozmiarek, *supra* note 123, at 7.

138. These included the prosecution of Dr. Edward Taub at the Institution for Behavioral Research in DC (IBR), following publication of damning photos of grisly treatment of animals at the IBR taken by Alex Pacheco, then a student volunteer and later the co-founder of the People for the Ethical Treatment of Animals (PETA) organization. See Dresser, *supra* note 118, at 1164 n.94, 1166 n.121.

tutions to establish an IACUC.¹³⁹

Finally, two other points are worth noting. The first is that the FDA's product regulations include certain standards for non-clinical research studies involving "test system[s]," defined as an "animal, plant, microorganism, or subparts thereof."¹⁴⁰ Unlike the FDA regulations pertaining to human subjects research, which largely mirror the Common Rule standards for federally funded research, these good laboratory practice regulations do not mirror the standards for federally funded animal studies; they are in fact much more limited and they do not have the purpose of ensuring the care and welfare of animals in research.

The second point is that the 21st Century Cures Act, signed by President Obama on December 13, 2016, contains certain provisions related to animal care in research.¹⁴¹ In particular, it requires the Director of the NIH, in collaboration with the Secretary of Agriculture and FDA Commissioner, to review all applicable regulations and policies for the care and use of laboratory animals and make revisions, as appropriate, to reduce "administrative burden" on investigators, while maintaining the "integrity and credibility of research findings and protection of research animals."¹⁴² More specifically, the Director of the NIH is required to take steps to eliminate any regulations and policies that are inconsistent, overlapping, or unnecessarily duplicative, including inspection and review requirements by federal agencies and accrediting associations.¹⁴³ These provisions are intended to promote harmonization between federal standards. Thus, it is possible that we may see some regulatory adjustments in this area in the future.

The regulatory regime that applies to federally funded research involving animals is also an early example of man-

139. The IACUC model has not been without its own critics. For a detailed analysis of the advantages and disadvantages of the IACUC system, see Lawrence Finsen, *Institutional Animal Care and Use Committees: A New Set of Clothes for the Emperor?*, 13 J. MED. & PHIL. 2, 145-58 (1988).

140. 21 C.F.R. § 58.3(i) (2017).

141. 21st Century Cures Act, Pub. L. No. 114-255, § 2034, 130 Stat. 1033, 1059-62 (2016).

142. *Id.* § 2034(d).

143. *See id.* § 2034(d)(1)-(3).

agement-based regulation. Regulated entities engage in planning and internal policy-making in order to achieve the social goal of ethical treatment of animals in research.¹⁴⁴ Individual institutions implement broad federal mandates, and decisions are made by local, non-governmental committees, which are charged with carrying out basic standards and principles. And an extensive set of soft-law guidance provides additional detail for regulated entities in their oversight and compliance efforts. As with human subjects research, the PHS regime is set up as a condition of federal funding.¹⁴⁵ While the AWA regulations have broader application, they exempt most animals in research and the PHS policy was intended to pick up the slack to cover those exempted animals.¹⁴⁶ As more research occurs in industry settings that do not accept federal funds, these policy decisions mean that the regulatory umbrella covers many fewer firms and actors now than in the past.

C. *Responsible Conduct of Research: Research Misconduct*

Federal regulations at 42 C.F.R. § 93.100 set forth the requirements for investigating and managing research misconduct at institutions conducting biomedical and behavioral research, training, and related activities supported by the federal government.¹⁴⁷ In describing the regulations, HHS states that such institutions “share responsibility for the integrity of the research process” with HHS.¹⁴⁸ The regulations set out key definitions and evidentiary standards for a finding of research misconduct.¹⁴⁹ Institutions must establish policies and procedures to address misconduct, including investigating allegations and reporting to the agency when research misconduct

144. See Food Security Act of 1985, Pub. L. No. 99-198, §§ 1751–54, 99 Stat. 1354, 1645-49.

145. See Gordon, *supra* note 112, at 154.

146. See *id.* at 153–54.

147. See 42 C.F.R. § 93.100 (2016).

148. *Id.* § 93.100(b).

149. *Id.* § 93.101.

is proven.¹⁵⁰ Institutions must also provide the federal government with assurance of compliance, maintain records, and allow the government to conduct audits and request records.¹⁵¹

The Office of Research Integrity (ORI) at HHS has primary enforcement powers in this area, including overseeing research misconduct investigations.¹⁵² ORI has published numerous guidance documents, including sample policies and procedures.¹⁵³ The sample policy includes provisions pertaining to the appointment and operation of inquiry and investigation committees, stating that the regulations do not require the appointment of a committee, “but many institutions have used such committees.”¹⁵⁴ An ORI-commissioned Final Report from 2000 analyzing 156 institutional scientific misconduct policies found that 96% of institutions use an ad hoc or standing committee to perform research misconduct investigations,¹⁵⁵ bolstering the conclusion that this committee-based approach has become a de facto requirement.

This regulatory regime dates to August 1989,¹⁵⁶ with its origins in the Health Research Extension Act of 1985.¹⁵⁷ Unlike regulations pertaining to human subjects research and animal welfare in research, which evolved from self-regulation to management-based regulation in the middle of the twentieth century, issues related to research misconduct and conflicts of interest remained in the shadows until the last few decades.

150. *Id.* § 93.300.

151. *Id.* § 93.300(c).

152. Chris B. Pascal, *The History and Future of the Office of Research Integrity: Scientific Misconduct and Beyond*, 5 SCI. & ENG. ETHICS 183, 183–98 (1999).

153. See, e.g., OFFICE OF RESEARCH INTEGRITY, DEP’T OF HEALTH & HUMAN SERVS., SAMPLE POLICY AND PROCEDURES FOR RESPONDING TO ALLEGATIONS OF RESEARCH MISCONDUCT [hereinafter SAMPLE POLICY AND PROCEDURES], <http://ori.hhs.gov/sites/default/files/SamplePolicyandProcedures-5-07.pdf>.

154. *Id.* at 10–14.

155. CHPS CONSULTING, FINAL REPORT: ANALYSIS OF INSTITUTIONAL POLICIES FOR RESPONDING TO ALLEGATIONS OF SCIENTIFIC MISCONDUCT 44 (2000), https://ori.hhs.gov/sites/default/files/institutional_policies.pdf.

156. Responsibilities of Awardee and Applicant Institutions for Dealing with and Reporting Possible Misconduct in Science, 54 Fed. Reg. 32,446, 32,449 (Aug. 8, 1989).

157. See *Historical Background*, OFF. RES. INTEGRITY, <http://ori.hhs.gov/historical-background> (last visited Nov. 18, 2017).

Until that point, these areas of research governance remained completely within the control of medical and research organizations, without any governmental requirements. As with all areas of biomedical research regulation, central assumptions undergirding the historical self-regulation of misconduct were the ideals of trust and accountability.¹⁵⁸ Universities and research institutions could be trusted to administer federal grants honestly, and medical researchers were trusted to carry out good science.

Research fraud first became an issue in the mid-1970s and early 1980s, when the discovery of a failure to investigate fraud at a number of large academic institutions, and other instances of academic research fraud, including William Summerlin's "painted" mice,¹⁵⁹ elevated what had been seen as the behavior of a few bad apples into a public issue. Congress held its first hearings on research misconduct in 1981, and later in a series of volatile hearings convened by Representative John Dingell (D-MI) in 1988 and 1989.¹⁶⁰

In the 1981 hearing, chaired by then-Representative Al Gore (D-TN), the President of the National Academy of Sciences (NAS) and NIH officials dismissed media coverage of research fraud as "grossly exaggerated."¹⁶¹ The President of NAS went further, suggesting that these rare instances of misconduct were the product of "psychopathic behavior" arising from certain sci-

158. Jennifer L. Gold, *Watching the Watchdogs: Negligence, Liability, and Research Ethics Boards*, 11 HEALTH L.J. 153, 173-74 (2003).

159. JOSEPH HIXSON, *THE PATCHWORK MOUSE*, 4-5 (1976). Summerlin, a dermatologist at Memorial Sloan-Kettering in New York, claimed in 1974 to have developed a skin transplantation process without immunosuppression, evidenced by a mouse born with white skin successfully surviving skin transplantation from a mouse born with black skin; it was discovered, however, that he had simply used a black pen to "paint" the white skin of experimental mice black, rather than having actually transplanted any skin. *Id.* Other examples of research misconduct that became news stories in the early 1980s were the exposure of Elias Alsabati's publication of over eighty plagiarized or fraudulent articles, and the Soman case, which raised questions about Yale University's internal investigatory processes. See Nicholas H. Steneck, *Research Universities and Scientific Misconduct: History, Policies, and the Future*, 63 J. HIGHER EDUC. 3, 310-11 (1994).

160. Marcel C. LaFollette, *The Politics of Research Misconduct: Congressional Oversight, Universities, and Science*, 65 J. HIGHER EDUC. 261, 270-71 (1994).

161. *Id.* at 272.

entists' "temporarily deranged" minds.¹⁶² The testimony, however, indicated that research organizations were not performing much internal oversight,¹⁶³ and the NIH was not doing much to sanction bad actors.¹⁶⁴ Coming out of the hearing, Congress had a clear message: fraud and misconduct should be dealt first and foremost within the professional community and within the institutions at which research takes place.¹⁶⁵ A few years later, the Health Research Extension Act of 1985 directed HHS to promulgate regulations for grantees of federal funding (principally academic institutions) that would require grantees to establish administrative processes for reviewing allegations of scientific fraud, and reporting substantial findings to HHS. Final regulations were published in 1989.

The hearings in 1988 and 1989, combined with the high-profile federal indictment of Dr. Stephen J. Breuning in 1988 for nearly a decade's worth of scientific fraud and the "Baltimore case" involving MIT professor Thereza Imanishi-Kari, revealed continuing problems with the scientific community's ability to "self-correct" fraud and misconduct.¹⁶⁶ As Congress took a closer look, the editors of the *New England Journal of Medicine* countered in a June 1988 editorial that "the biomedical-research community is willing and able to police itself and is taking steps to do so more effectively."¹⁶⁷ In the heated hearings, John Dingell criticized the NIH, research institutions, and the sci-

162. Drummond Rennie & C Kristina Gunsalus, *Regulations on Scientific Misconduct: Lessons from the US Experience*, in *FRAUD AND MISCONDUCT IN BIOMEDICAL RESEARCH* 13, 14-15 (Stephen Lock, Frank Wells, & Michael Farthing eds., 3d ed. 2001).

163. LaFollette, *supra* note 160, at 272.

164. *Id.*

165. *Id.*

166. See Philip Boffey, *U.S. Study Finds Fraud in Top Researcher's Work on Mentally Retarded*, N.Y. TIMES (May 24, 1987), <http://www.nytimes.com/1987/05/24/us/us-study-finds-fraud-in-top-researcher-s-work-onmentally-retarded.html?mcubz=1>. Dr. Breuning, a psychologist at a state psychiatric institution in Pennsylvania and a "major" scholar in the area of treating the mentally disabled, was found to have engaged in widespread fraud. *Id.* Dr. Imanishi-Kari's career proceeded under a cloud for a decade when she was accused of fraud. See *Imanishi-Keri Case Ends, but Debate on Scientific Conduct Continues*, MIT NEWS (July 24, 1996), <http://news.mit.edu/1996/imanishi-0724>. She was eventually cleared of wrongdoing by a federal appeals board in June 1996. *Id.*

167. LaFollette, *supra* note 160, at 275.

entific community, which Dingell remarked had been expected to “police itself,” and stated that Congress had been “severely disappointed” by its inability to do so.¹⁶⁸ Further ratcheting up of regulations, however, was not forthcoming. Instead, regulatory requirements remained largely institutional-level mandates, with grantees and researchers obligated to develop plans to identify, investigate, and resolve misconduct in-house.

The research misconduct regulations are another example of a relatively longstanding management-based approach. Regulations set forth broad ground rules, and delegate day-to-day management to local institutions. Soft law, guidance documents, and sample policies provide regulated entities with additional assistance with developing institutional-level plans and processes. As is true of several other policy areas described in this Article, these regulations only apply in the context of federally funded research, which is a shrinking segment of research overall.

D. Financial Conflicts of Interest in Research

Federal regulations at 42 C.F.R. § 50.601 and 45 C.F.R. § 94 set forth standards for managing financial conflicts of interest in federally funded research. These regulations provide a broad framework that applies at institutions where such research takes place, creating a “reasonable expectation” that the design, conduct, and reporting of federally funded research will be free from bias resulting from an investigator’s financial conflicts of interest.¹⁶⁹

The regulations set forth threshold financial interests deemed “significant,” definitions of who qualifies as an “investigator,” and what broadly constitutes a “financial conflict of interest.”¹⁷⁰ Each institution must develop a written policy on financial conflicts of interest, which must be made publicly available.¹⁷¹ Insti-

168. *Id.*

169. 42 C.F.R. § 50.601 (2016).

170. *Id.* § 50.603.

171. *Id.* § 50.604(a).

tutions are required to inform investigators of the policy, and create a system by which all investigators disclose their financial interests to the institution.¹⁷² Institutions are required to devise a system in which they review all disclosures, determine whether each disclosed interest constitutes a financial conflict and, if so, how to manage or eliminate the conflict.¹⁷³ Institutions must maintain and retain records and, in certain instances, report the existence of a conflict and the plan to manage it to the federal granting agency, which may review the organization's records at any time.¹⁷⁴ The basic standards are bolstered by extensive guidance from the NIH, including a thirty-page set of frequently asked questions and answers, and a checklist for institutional policy development.¹⁷⁵

Compared with the other regimes discussed in this Article, the federal financial conflicts-of-interest regulations were implemented most recently in 1995, with significant revisions in 2011, and promulgated under the general authority of 42 U.S.C. §§ 216, 299c-4.¹⁷⁶ Historically, regulators and the public did not pay attention to relationships between academic medical researchers and the for-profit medical and pharmaceutical industries because there weren't any relationship between them.¹⁷⁷ In the past, physicians in the community and medical researchers practicing within the academy did not have systematic or widespread connections with industry.¹⁷⁸ This, however, changed precipitously after the early 1980s. As

172. *Id.* § 50.604(b).

173. *Id.* § 50.605(a)(1).

174. *Id.* at § 50.605.

175. See NAT'L INSTS. OF HEALTH, DEP'T OF HEALTH & HUMAN SERVS., CHECKLIST FOR POLICY DEVELOPMENT RELATED TO THE 2011 REVISED FINANCIAL CONFLICT OF INTEREST (FCOI) REGULATION, PROMOTING OBJECTIVITY IN RESEARCH (42 C.F.R. §§ 50.601-50.607) [hereinafter CHECKLIST FOR POLICY DEVELOPMENT], http://grants.nih.gov/grants/policy/coi/checklist_policy_dev_20120412.pdf; *Frequently Asked Questions*, NAT'L INSTS. HEALTH, http://grants.nih.gov/grants/policy/coi/coi_faqs.htm (last updated Oct. 22, 2015) [hereinafter *National Institutes of Health FAQ*].

176. See 42 U.S.C. §§ 216, 299c-4 (2016).

177. See Robert Gatter, *Walking the Talk of Trust in Human Subjects Research: The Challenge of Regulating Financial Conflicts of Interest*, 52 EMORY L.J. 327, 335 (2003).

178. See *id.*

discussed later, the Bayh-Dole Act allowed universities and small business start-ups to take title to intellectual property created with support from extramural federal funds and to share royalties with researcher inventors.¹⁷⁹ Intended to spur commercialization of scientific innovations created in partnership between federal funders and academic sites, Bayh-Dole had profound effects on the development of biomedical inventions. It introduced commercial and financial incentives into academia, and created the market for “technology transfer.”¹⁸⁰ As industry eclipsed the federal government as the principal funder of research, scientists and physicians began having more relations with industry.¹⁸¹

The first rumblings about conflicts of interest occurred during the debate about the safety of recombinant DNA research in the 1970s, when questions were raised about potential conflicts due to faculty or academic contracts with industry.¹⁸² The issue then arose during the 1989 congressional hearings discussed earlier, in which several high profile cases of research misconduct involved scientists with financial interests in the outcomes of their research projects.¹⁸³ Shortly thereafter, the NIH proposed guidelines that would have prohibited researchers in NIH-funded clinical trials from owning any stock or options in a company that had an interest in the outcome of that trial.¹⁸⁴ The guidelines were the subject of wide criticism by the biomedical research community.¹⁸⁵ In 1995, the PHS pivoted from the NIH’s proposed guidelines and issued binding regulations applicable to all PHS-funded research (which includes the NIH).¹⁸⁶

The issue reemerged in the late 1990s, following the highly

179. See 35 U.S.C. §§ 200–212 (2016).

180. Gatter, *supra* note 177, at 336–37; see also Riley, *supra* note 47, at 279 (describing how the Bayh-Dole Act has changed parts of the research industry).

181. David Korn, *Conflicts of Interest in Biomedical Research*, 284 JAMA 2234, 2234–37 (2000).

182. LaFollette, *supra* note 160, at 264.

183. See Public Health Service Act Amendment, H.R. Res. 5661, 101st Cong. (1990); see also Gatter, *supra* note 177, at 348–49.

184. Gatter, *supra* note 177, at 348–49.

185. *Id.* at 348.

186. *Id.*

publicized death of Jesse Gelsinger, a young participant in a gene therapy clinical trial at University of Pennsylvania.¹⁸⁷ The study's principal investigator and the university each held equity in a company that owned the rights to commercialize the research results.¹⁸⁸ In addition, a scandal at the Fred Hutchinson Cancer Research Center around the same time revealed that researchers conducting clinical trials on graft-versus-host disease drugs held equity in, and were paid consulting fees by, the company sponsoring the trial.¹⁸⁹ In both cases, it was suggested that the financial relationships motivated the researchers and their institutions to conduct the studies despite unreasonable risks to patients.¹⁹⁰

It would be eleven more years, however, until the regulations were revised in 2011.¹⁹¹ Thus despite certain changes that went into effect in 2012, the basic regulatory structure remains intact: the regulations do not prohibit researchers from holding competing financial interests; instead, they require that researchers with interests meeting certain financial thresholds disclose them to their institutions.¹⁹² It is the obligation of institutions, not government, to devise systems to identify, eliminate, and manage financial conflicts of interest in federally funded research.¹⁹³

Finally, two more points are worth noting. First, FDA regulations at 21 C.F.R. § 54 require that manufacturers and other

187. *Id.* at 351.

188. *Id.* at 329–30.

189. *Id.* at 330.

190. *See id.* at 330–31.

191. *Financial Conflict of Interest*, NAT'L INSTS. HEALTH, <https://grants.nih.gov/grants/policy/coi/index.htm> (last updated Nov. 2, 2016); 42 C.F.R. § 50.604(e)(2) (2016). Also, the Physician Payments Sunshine Act, which was passed as part of the Affordable Care Act, is an information disclosure mechanism in which certain pharmaceutical and device manufacturers are required to disclose to the federal government the amounts of payments made in the preceding year to physicians and teaching hospitals. *See* Shantanu Agrawal, Niall Brennan, & Peter Budetti, *The Sunshine Act—Effects on Physicians*, 360 NEW ENG. J. OF MED. 2054 (2013). This law, and its regulations, constitutes a flexible alternative to more government-centered approaches to regulation, ripe for further exploration.

192. *See* 42 C.F.R. § 50.604(e)(2).

193. *See id.* § 50.604(c).

clinical research sponsors submit forms disclosing relevant interests of their investigators to the Agency.¹⁹⁴ These regulations are aimed at data integrity, not research oversight, and do not provide the same level or quality of research oversight as the federal financial conflict-of-interest regulations.

Second, it is also worth noting that 21st Century Cures Act's section on "Reducing Administrative Burdens for Researchers" includes a provision related to conflicts of interest.¹⁹⁵ In particular, it requires the Secretary of HHS to lead a review by federal research funding agencies of all regulations and policies related to financial conflicts of interest and to make revisions to harmonize existing policies.¹⁹⁶ This policy review process must occur, and revisions must be completed, by December 2018.¹⁹⁷ Thus, it is possible that these regulations may be adjusted in the near term.

In short, the federal financial conflict-of-interest regulations constitute a management-based approach—and are arguably the most flexible of all regulatory sets addressed in this analysis. Institutions conducting federally funded research are delegated responsibility and flexibility to create their own internal rule-making, monitoring, and enforcement mechanisms meeting general criteria, in order to ensure that research is reasonably free from the financial bias of researchers.¹⁹⁸ Decisions are devolved to local institutions, which generally use a committee to oversee and resolve conflicts, and regulated entities are provided with nonbinding guidance to assist in translating the general requirements into institutional policies.¹⁹⁹

III. POLICY STABILITY: LOCK-IN AND DRIFT

In each set of federal regulations described above, the original regulatory design emerged as the consequence of a bargain

194. 21 C.F.R. § 54.4 (2017).

195. 21st Century Cures Act, Pub. L. No. 114-255, § 2034(a), 130 Stat. 1033, 1059 (2016).

196. *Id.*

197. *Id.*

198. Bennear, *Are Management-Based Regulations Effective?*, *supra* note 27, at 329.

199. Coglianese & Lazer, *supra* note 27, 695-96.

struck at a particular time with a particular set of actors. These circumstances and actors, however, have changed substantially in intervening years. The federal government has been eclipsed in funding dominance by the pharmaceutical and biotechnology industries. And the research that industry sponsors is increasingly conducted in non-academic settings, coordinated by non-academic actors, and funded without any federal dollars. Thus, the historically contingent tapestry of players, incentives, and forces that came together to craft the initial policies in this domain has changed. Nonetheless, the policies themselves have not.

The result is the persistence of a system of oversight that does not track well to the empirical realities of the conduct and funding of biomedical research. While this point has been made by scholars in relation to the oversight of human subjects research by IRBs,²⁰⁰ the point has not been made more broadly in relation to the other areas of research oversight addressed in this Article. This section argues that the policies at issue have become subject to what political scientists term “drift.”²⁰¹ Briefly, drift occurs when public policies are not updated to reflect changing or changed social or institutional circumstances.²⁰² This has occurred in the context of biomedical research, and consequently, a great many biomedical research activities now fall outside of the regulations originally intended to oversee them. While these activities are often publicly invisible, the public consumes the final outputs of these activities in the form of health products and technologies. Further, the information that private science generates is often used to inform and guide public regulation.²⁰³ Thus this policy drift has the potential to jeopardize public health and safety, introduce biased and unreliable data into the public regulatory process, and at a bare minimum constitutes a failure to achieve intended policy

200. Riley, *supra* note 47, at 280.

201. See David Kamin, *Legislating for Good and Bad*, 54 HARV. J. ON LEGIS. 149, 150 (2017).

202. See *id.*

203. See Wendy Wagner & David Michaels, *Equal Treatment for Regulatory Science: Extending the Controls Governing the Quality of Public Research to Private Research*, 30 AM. J.L. & MED. 119, 120 (2004).

goals.

This section describes important intervening changes in the institutional environment since the establishment of the research regulations described above. The stability of each over time suggests policy lock-in and drift. This section also addresses consequences of that drift. These include an ever shrinking set of actors and activities subject to regulation, and a growing swath of unregulated or under-regulated space.

A. *Stability Despite Intervening Changes*

1. *Early developments: federal funding takes the spotlight*

To understand why the light-touch management based system of regulatory oversight emerged largely as conditions of federal funding in the United States, it is necessary to take a brief look at patterns of research and funding over time.

For the first few decades of the twentieth century, most medical research was financed privately—either by foundations and university endowments in an academic setting, or by the pharmaceutical industry in its own laboratories.²⁰⁴ Prior to World War II, the federal government did not have a particularly active role in medical research, either intramurally or extramurally.²⁰⁵ While prewar federal investment in medical research totaled around \$3 million annually (or 7% of total investment in research), its efforts were vastly eclipsed by industry, which invested about \$22 million annually (or 51% of total investment).²⁰⁶ There was simply little infrastructure for medical research outside of industry, either within the government or in academia.

The federal government, however, did take at least one significant step toward having a more active role in this sector during the prewar era. In 1937, Congress authorized establish-

204. STARR, *supra* note 93, at 339.

205. Shannon & Kidd, *supra* note 88, at 1185.

206. *Id.* at 1186.

ment of an extramural cancer grant and fellowship program.²⁰⁷ Before this development, essentially all federally funded medical research took place intramurally at government facilities.²⁰⁸ Thus, extending the possibility of federal funding to outside research sites allowed the federal government to begin to establish relationships with researchers beyond its own walls, especially within academia.

World War II marked an explosion in scientific inquiry, especially at the government's behest. The war effort was foundational in establishing the federal government's deep financial commitment to medicine and medical research.²⁰⁹ It was a time when the medical profession enjoyed broad public support and political power, and in which academic research capacities were greatly enlarged, along with a strengthening of network ties between the government and academia.²¹⁰ Indeed, the federal government simply did not have the internal capacity to handle the wartime research efforts it spearheaded, and so it entered into hundreds of contracts with universities, research institutes, hospitals, and other organizations to do the work.²¹¹

Overall, federal investment in medical research more than doubled during the war.²¹² Just as the federal government did not have the internal capacity to do the actual work, however, it also did not have the internal capacity to oversee the work.²¹³ And while it might have ramped up its regulatory capacity to oversee the work it funded, it did not.²¹⁴ As a result, there was little governmental control over the actual work of the con-

207. STARR, *supra* note 93, at 340.

208. Shannon & Kidd, *supra* note 88, at 1185.

209. *Id.*

210. *See id.*

211. *Id.*; *see also* COMM. ON FED. RESEARCH REGULATIONS & REPORTING REQUIREMENTS, NAT'L ACADS. OF SCIS. ENG'G MED., OPTIMIZING THE NATION'S INVESTMENT IN ACADEMIC RESEARCH, at ix (2016) [hereinafter OPTIMIZING].

212. Shannon & Kidd, *supra* note 88, at 1185-86 (noting that, while government funding of medical research increased during the war, so did industry's investment, constituting about \$31 million annually, or about 50% of total investment in medical research).

213. Riley, *supra* note 47, at 269.

214. STARR, *supra* note 93, at 340-341.

tracted scientists. The war effort thus established a precedent in which the federal government would supply the funds for biomedical research, but without extensive oversight.

In a sense, this was no accident. While German models influenced early twentieth century efforts in American science and medical organization, Nazi centralization and extreme control of research was quickly seen as anything but a valuable template.²¹⁵ Sociologist Paul Starr has characterized American wartime funding of biomedical research with minimal government control as a moment of “structural choice,” in which the United States chose institutional designs favoring greater private control and local autonomy than had the European model.²¹⁶

By the conclusion of the war, the federal government had established itself as a formidable and hands-off patron of medical research, with extensive relationships with academic researchers and extramural institutions.²¹⁷ General postwar prosperity and optimism created an opportunity for the federal government to take stock of its long-term investments in domestic sectors. High on its list was the pursuit of science—which included medicine and medical research. Vannevar Bush’s 1945 report on the future of science, *The Endless Frontier*, called for a continuation and increase in extensive federal funding for medical research and training.²¹⁸ That call was answered with annual federal investment in medical research nearly tripling from \$10 million in 1944 to \$28 million in the immediate postwar period, essentially matching industry investment for the first time.²¹⁹ The federal government forged ahead with heavy investment in both its extramural and intramural medical research programs.²²⁰ Importantly, the postwar period saw a substantial deepening of the federal government’s network

215. *Id.* at 341.

216. *Id.*

217. Riley, *supra* note 47, at 269.

218. *Id.* at 268.

219. Shannon & Kidd, *supra* note 88, at 1185.

220. *Id.*

ties with academic researchers through its extramural funding program and partnerships.²²¹ Indeed, federal funding soon eclipsed annual industry investment in medical research, which continued in each year until the early 1990s.²²²

2. *Corporate funding surges ahead*

The tide began to turn back to corporate leadership in research investment in the early 1980s. In December 1980, Congress passed the Bayh-Dole Act, which allowed universities and small business spin-offs or start-ups to take title to intellectual property created using extramural federal funds and to share royalties with researcher inventors.²²³ Intended to spur commercialization of scientific innovations, Bayh-Dole had a forceful effect on the development of biomedical inventions. It introduced commercial and financial incentives into academia, which had clung staunchly to a purer vision of science as separate from corporate interests.²²⁴ In effect, Bayh-Dole created the market for “technology transfer,” allowing universities and academic researchers to forge deeper and different ties with industry.²²⁵ And they did. A decade later, academic medical centers received 80% of industry research and development funding.²²⁶

As the biomedical industry (and particularly the pharmaceutical industry) grew in size and power, its financial expenditures for medical research and development soon outpaced federal dollars.²²⁷ Up through the 1970s, federal funding had supported more than twice the costs of health product research and development provided by industry.²²⁸ This paradigm began to shift, however, and in each year since 1992, industry

221. Riley, *supra* note 47, at 268.

222. *Id.* at 279.

223. Gatter, *supra* note 177.

224. *Id.*

225. *Id.* at 336.

226. Riley, *supra* note 47, at 279.

227. *Id.*

228. *Id.*

has spent more in U.S. research and development than has the government.²²⁹ By 2004, total annual expenditures by industry for biomedical research and development were fully three times the amount spent by the NIH.²³⁰

Further, while the academy was the primary site for most industry-sponsored research from the postwar period through 1990s, this too has changed.²³¹ Seeking cheaper sites and lower compliance costs among other reasons, the pharmaceutical industry has increasingly moved medical research programs offshore – increasingly to Africa and Eastern Europe.²³² In addition, private companies in the form of contract research organizations and site-management organizations have emerged to manage clinical research for industry within the United States at sites other than universities, thus further displacing academic sites as the primary venue for biomedical research even domestically.²³³ Indeed, the pharmaceutical industry has significantly reorganized the clinical testing of its projects from predominantly occurring at academic medical centers to community settings in the past few decades.²³⁴ While 80% of industry funding for clinical research went to academic medical centers in 1991, by 1998 it had dropped to 40%,²³⁵ and by 2005, it was down to just 25%.²³⁶

B. *Lock-In and Drift*

Despite these dramatic shifts in the institutional environment, the regulatory policies applicable to biomedical research have not been modified. In particular, the main regulatory sets described in this Article have not been updated to move beyond

229. *Id.*

230. FISHER, *supra* note 82, at 5.

231. Adrianna Petryna, *Ethical Variability: Drug Development and Globalizing Clinical Trials*, 32 AM. ETHNOLOGIST 183, 185 (2005).

232. *See id.*

233. *Id.*

234. *Id.* at 186.

235. Gatter, *supra* note 177, at 338.

236. FISHER, *supra* note 82, at 2-5.

the federal funding hook so as to include non-federally funded research contexts. While some research activities are subject to the FDA's product regulations, these regulations focus on product safety, not the integrity of research and protection of (human and animal) participants.²³⁷ The exception is with regard to human subjects research, where FDA regulations largely mirror the federal Common Rule requirements.²³⁸ As described later in the Article, this suggests that pursuing FDA regulations for animal research, research misconduct, and conflicts of interest that harmonize with the regulations that apply to federally funded research may be an alternative avenue for more robust regulation of non-federally funded research. As it currently stands, however, research oversight generally remains subject to a light-touch system designed with academic freedom and medical professionalism in mind, despite the fact that most activities are now industrial and corporate in origin and execution.

The general failure to update policy in the face of significant shifts in the institutional environment has been described by political scientist Hugh Heclo,²³⁹ and later by Jacob Hacker and others as policy "drift."²⁴⁰ Drift occurs when policies are not updated to reflect changing or changed social or institutional circumstances.²⁴¹ By failing to update policies to match changed social risks or changes in the institutional environment, the policy itself transforms endogenously.²⁴² The main causes of drift are changes in the "social context of policies" – and the "hallmark" of drift is that it occurs largely outside the control of policymakers, "thus appearing natural or inadvertent."²⁴³

237. *See id.* at 28.

238. *See supra* Section II.A.

239. *See* HUGH HECLO, *MODERN SOCIAL POLITICS IN BRITAIN AND SWEDEN: FROM RELIEF TO INCOME MAINTENANCE* 63–64 (1974).

240. *Id.*

241. Jacob S. Hacker, *Privatizing Risk Without Privatizing the Welfare State: The Hidden Politics of Social Policy Retrenchment in the United States*, 98 *AM. POL. SCI. REV.* 243, 246 (2004).

242. *See id.*

243. *Id.*

Hacker notes that sometimes drift may indeed be inadvertent.²⁴⁴ However, he also emphasizes that drift is often a clearly political process, the result of intentional efforts by certain stakeholders to recalibrate public policies in their favor.²⁴⁵

It is important to note that policy drift does not necessarily imply that a certain public policy has simply become *ineffective* in achieving its goals over time. Instead, drift is a policy process by which the policy *itself* changes, often endogenously.²⁴⁶ Stated another way, drift is not a measure of the *output* or effectiveness of a public policy; rather, it is itself a policy *process*.²⁴⁷

While Hacker and other political scientists tend to use this concept in relation to larger scale social welfare programs (which often have large regulatory components),²⁴⁸ the concept is applicable to smaller scale regulatory programs and policies as well. The process is the same regardless of the policy domain: a slow trajectory towards retrenchment of protections afforded by public policies.

C. *Drift in Biomedical Research Oversight and Its Consequences*

As described above in detail, the key components of the domestic biomedical research regulatory oversight system were established during an era when the federal government funded most research, and academic scientists undertook it in limited settings.²⁴⁹ Much has changed in the institutional environment, but policy remains the same. Despite the intervening circumstances, these policies, and particularly their jurisdictional bases as conditions of federal funding, have locked-in and thus experienced drift.

Note that these observations do not advance normative claims about how these regimes are functioning in current prac-

244. *Id.*

245. *Id.*

246. *Id.*

247. *See id.* at 245.

248. *See id.* at 243 (applying drift theory to the American welfare state). *See generally* HECLC, *supra* note 239 (analyzing income maintenance policy in Britain and Sweden).

249. *See supra* Section II.A.

tice, or about the conditions under which similar types of light-touch regulatory regimes may or may not adequately serve the public interest. These are important questions that should be the focus of further empirical inquiry and analysis. Rather, this Article observes that this drift has certain structural consequences for biomedical research, which include both direct and indirect risks to the public, as well as conceptual consequences for how we think about the “flexibility” of new governance tools.

Structurally, the consequence of this drift is that much, if not most, biomedical research settings and activities fall outside of the regulatory regimes discussed in this article. Indeed, the pharmaceutical and for-profit research industries have, in many ways, inherited a regulatory structure created for the academy and third-sector, not them.²⁵⁰ Now that they have become dominant participants in this arena, their facilities and activities are often exempt from these rules.²⁵¹ The federal financial conflicts-of-interest regulations, research misconduct regulations, and the Common Rule human subjects research regulations apply only to federally funded projects; protections for almost all animals in research apply only at institutions that conduct research using federal funds.²⁵² It is likely that many if not most pharmaceutical, biotechnology and other corporate firms do not accept any federal research dollars, instead relying on corporate funding for in-house research projects.²⁵³ In such cases, the research falls outside of the regulatory regimes discussed in this Article.²⁵⁴ Further, industry-sponsored research

250. STARR, *supra* note 93, at 339.

251. FISHER, *supra* note 82, at 209–10.

252. See 45 C.F.R. §§ 46.101–.124 (2017); see also *supra* Section II.B.

253. See Barbara A. Noah, *Bioethical Malpractice: Risk and Responsibility in Human Research*, 7 J. HEALTH CARE L. & POL'Y 175, 199–200 (2004).

254. See 21 C.F.R. §§ 56.101–.114 (2017) (providing generally equivalent protections as the Common Rule). Injured research participants may be able to pursue damages under tort liability and general fraud statutes, even if these regulations do not apply to the underlying research. See, e.g., E. H. Morreim, *Litigation in Clinical Research: Malpractice Doctrine Versus Research Realities*, J. L. MED. & ETHICS 474, 479–80 (2004); see also Noah, *supra* note 253, at 199–200.

activities occurring even within settings that accept federal dollars are exempt from much required oversight, unless the particular institution has decided as a matter of policy to extend such regulations to all activities regardless of funding.²⁵⁵ The scant FDA regulations that address financial disclosures and non-clinical studies do not provide equivalent protections as do the regulations that apply to federally funded projects.²⁵⁶

Biomedical research activities are frequently invisible to the public, often shrouded behind trade secret or other corporate veils.²⁵⁷ These activities, however, when unregulated or under-regulated, presumably expose the public to a set of direct and indirect risks, which vary depending on the type of activity at issue.²⁵⁸

For instance, a research participant is exposed to certain risks when her physician has a financial interest in the outcome of the trial or a financial relationship with the company sponsoring the study, and participation occurs in settings or with funds not subject to the federal financial conflict of interest regulations. At a minimum, the participant may not receive this important information about her physician, because such disclosure is not required.²⁵⁹ This lack of knowledge might affect

255. See Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7189 (Jan. 19, 2017).

256. See 21 C.F.R. §§ 54.1-6 (2017). Note that many universities and nonprofit research organizations have adopted institutional policies that subject all research performed by its personnel to meet uniform standards that comply with federal requirements, but this is not universally so, and does not involve government oversight. For background on the relationship between the federal government and academia, see *OPTIMIZING*, *supra* note 211.

257. Wagner & Michaels, *supra* note 203.

258. See generally Burris, *Regulatory Innovation*, *supra* note 100, at 78. (“Yet the current regime seems to suffer from both over-punishment owing to the nodal character of the sanctions regime and under-deterrence owing to the etiology of the offense. Researchers conducting dangerous experiments on human beings seem able to convince themselves that what they are doing is right . . . ; the more or less realistic sense of insulation that comes with being part of the powerful biomedical industry may also play a role.”).

259. See 21 C.F.R. §§ 56.101-.124 (The FDA’s minimal financial disclosure requirements, assuming the study involves an FDA-regulated product, do not require disclosure to the research participant—only disclosure to the agency); see also Gatter, *supra* note 177, at 349 (“Current regulations are heavy on procedure and light on substance . . . [T]hey do not require that certain kinds of financial ties be prohibited, specify how other kinds of financial relationships must be managed, nor mandate that nonprohibited financial conflicts of interest

her decision to participate. At the extreme, when such conflicts are unmanaged, it may lead to biased research results or investigator conduct, which could expose the participant to physical risk. Similarly, people may be exposed to certain physical and emotional risks when participating in research that occurs in settings or in types of research not subject to regulatory oversight including IRB review. Such risks range from participating in studies that may simply be of low scientific or social value, all the way to risks that participants may be exposed to research activities that are altogether scientifically or ethically inappropriate.²⁶⁰

As another example, the public is exposed to certain risks in the context of research misconduct not subject to federal requirements and standards.²⁶¹ On the one hand, if research results are fabricated, falsified, or plagiarized in the context of regulated research, it will be handled through a process meeting a baseline set of federal regulatory standards, which as described earlier may include public disclosure.²⁶² Such misconduct, and its resulting publication and dissemination, is treated as a public policy issue.²⁶³ This is because such results can, upon dissemination, have serious and potentially long term consequences in terms of health and safety.²⁶⁴ On the other hand, if research misconduct occurs in the context of unregulated (purely industry-sponsored) research, it is treated largely as an internal business issue.²⁶⁵ It is up to the industry sponsor to set

be disclosed to prospective research subjects.”).

260. For a general discussion, see Gatter, *supra* note 177, at 346 (“When the individual to whom [human subject recruitment fees] are paid . . . is in a position to significantly affect the safety of human subjects, then such fees can undermine the institutional commitment to protecting human subject safety.”).

261. For a discussion of the intersection between conflicts of interest and research misconduct, see Thomas Bodenheimer, *Conflict of Interest in Clinical Drug Trials: A Risk Factor for Scientific Misconduct* (Aug. 15, 2000) (transcript available in University of California San Francisco Library).

262. See 42 C.F.R. §§ 93.100–.523 (2016) (showing the process for handling regulated research misconduct).

263. See *id.* § 93.100.

264. See Noah, *supra* note 253, at 222–23.

265. 42 C.F.R. § 93.102(2)(d).

its own process, if any, for handling alleged misconduct, and the results of any investigation are generally kept secret.²⁶⁶ This secrecy and heterogeneity of process could expose the public to risks at two levels. First, there is no public accountability or disclosure required if these physicians or researchers engage in fraud, as there is in settings where public funds are used for research. Patients in purely private research contexts will likely never know that their physician engaged in fraud, and the only likely consequence for the physician will be the loss of future business with the industry sponsor. Second, the products that ultimately come to market based upon flawed science may expose the public to physical risks. If such activity had been subject to a baseline standard process, it might have been caught before being rolled into or towards a final consumer product.

The consequences of policy drift regarding animals in research are a bit different, because animal research does not expose the public to direct risk.²⁶⁷ Instead, it raises ethical concerns about the appropriate treatment of animals. As described earlier, these ethical debates have a long political and social history in the United States, which were meant to be resolved through the passage of laws and regulations pertaining to federally funded animal research to establish some basic protections for these vulnerable creatures.²⁶⁸ The fact that the regulatory net captures less activity involving animals over time constitutes a retrenchment of protection afforded to animals by the public policies enacted to safeguard them.

Beyond the direct risks to which (animal and human) research participants are exposed in privately funded research contexts, such research activities also form a critical base of data

266. *See id.* (showing absence of FDA regulations that would directly regulate such misconduct).

267. *See generally* Dresser, *supra* note 118, at 1181 (“Although the health interests of humans and other animals at times override the interests of laboratory animals, . . . less morally compelling interests do not.”).

268. Gordon, *supra* note 112 (“Thus, from its embryonic stages, NIH was addressing concerns about the use of laboratory animals.”).

upon which public regulation is based. Wendy Wagner and David Michaels have explored this issue at length, articulating the ways in which the quality of private research can be compromised, particularly compared to more scrutinized and regulated publicly funded research, and the potential impact of those compromised activities on the quality of regulatory science and decision making.²⁶⁹ For example, the long-term public health implications could be significant, if the FDA were to base its approval of a class of drugs, or even its approval for a single clinical trial, upon biased or compromised data generated by private entities not subject to the quality controls that apply to publicly funded research.²⁷⁰

Further, at a minimum, the policy drift described in this Article constitutes a failure to achieve the regulations' intended policy goals. Overall, the federal regulations described in this Article were established to set a floor of basic protections for humans and animals. They were meant to institute a baseline. As more activity moves into unregulated or underregulated space, however, these activities are not subject to this regulatory baseline. It may indeed be that industry ultimately sets its own standards that meet or even exceed the federal baseline. There is, however, no *a priori* reason to believe that this will be the case.²⁷¹ In the absence of a strong or applicable federal baseline, and in the increasingly secret realm of corporate research, there

269. Wagner & Michaels, *supra* note 203, at 119 (identifying scientific misconduct and human subjects protection among other areas in which federally funded research received higher scrutiny); *see also* Bodenhimer, *supra* note 261. *See generally* David Michaels & Celeste Monforton, *Manufactured Uncertainty, Contested Science and the Protection of the Public's Health and Environment*, 95 AM. J. PUB. HEALTH S39, S39-45 (2005) ("The public health system must ensure that scientific evidence is evaluated in a manner that assures the public's health and environment will be adequately protected.").

270. Donald S. Kornfeld, *Perspective: Research Misconduct: The Search for a Remedy*, 87 ACAD. MED. 877, 877-80 (2012); *See also* Patrick O'Leary, *Policing Research Misconduct*, 25 ALB. L.J. SCI. & TECH. 39, 42-43 (2015).

271. Interestingly, the Public Policy Research Manager and Research Management Lead at Facebook recently published a law review article describing the regulatory gap in which Facebook and other corporate research groups sit. Molly Jackman & Lauri Kanerva, *Evolving the IRB: Building Robust Review for Industry Research*, 72 WASH. & LEE L. REV. ONLINE 442, 445 (2016). That article also describes Facebook's process for devising its own internal research review process, specifically stating that the federal Common Rule policy was not adopted by the company because it did "not fully meet our research needs." *Id.*

is no reason to believe the public will have any significant or consistent transparency into what those alternative standards may be, if any. Thus, these instances of policy drift constitute a failure to achieve intended policy goals.

Finally, more conceptually, these case studies also offer a reminder that we must be careful to clearly articulate what we mean by a regulatory tool's "flexibility." The identification of drift in these regulatory sets is a reminder that even flexible regulatory instruments like management-based regulations have boundaries set by the enabling legislation and/or by the regulators implementing them. If not updated over time, "flexible" regulation, like any other kind of policy, may end up a poor match to the changed empirical landscape, and a casualty of policy drift.

CONCLUSION AND FUTURE RESEARCH: BEYOND THE FEDERAL FUNDING HOOK

This Article has offered a few contributions. The first is an extension of the empirical literature regarding management based regulation into the previously unexplored area of biomedical research oversight. By providing in-depth descriptions of four long-standing sets of regulations, this Article also challenges the frequent assertion of the "newness" of new governance approaches to regulation.

In looking at these mature regulatory systems, we can evaluate them with the benefit of temporal perspective. This leads to the second contribution, which is a discussion of policy stability despite tremendous intervening changes in the institutional environment, and the identification of policy drift. Importantly, policy drift is a policy process that unfolds over time. Because this Article describes the regulatory development of these case studies over the passage of many decades, we are able to make critical observations about policy drift over time.

Finally, this Article offers two observations about this policy drift. First, more conceptually, these case studies offer a tale of caution regarding the need to clearly define the mechanisms by which a governance approach may be "flexible." Flexible regu-

lation, just as more traditional forms of regulation, can be susceptible to lock-in and drift. One way this may be so is by failing to update the jurisdictional framework that undergirds the regulation. New governance and management-based regulations are certainly not alone or unique in the need for this attention to monitoring over time; however, despite optimism about their flexibility and adaptability, they are not self-updating, and may be subject to the same pathologies as other regulatory instruments without careful design and reappraisal.

The second observation is specific to biomedical research regulation itself: namely, the identification of significant regulatory gaps due to policy drift. At a minimum, these gaps create conditions under which the main sets of federal regulations are likely to fail to achieve their intended policy goals. More concretely, this Article has described a variety of ways in which these governance gaps may jeopardize public health and safety. These include direct physical risks to humans and animals, as well as indirect risks when lower-quality privately generated data is used in public policy decision making. It will be necessary for further empirical research efforts to measure the magnitude and frequency of such risks in practice.

A detailed analysis of possible policy solutions to address these regulatory gaps is beyond the scope of this Article. Looking forward, however, we must consider jurisdictional modifications to the regulatory sets that move beyond the federal funding hook, in order to capture important activities and actors not currently covered. One way to do so would be to simply extend the regulations pertaining to research oversight to apply to all research activities regardless of funding source. This approach may be infeasible because of the limitations of the underlying enabling legislation. Interestingly, HHS recently explored this approach. In the Notice of Proposed Rulemaking that preceded the Final Rule, HHS proposed extending the Common Rule to all clinical trials, regardless of funding source, as long as certain conditions were met.²⁷² This proposal was not

272. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7155 (Jan. 19, 2017).

adopted in the Final Rule. In the preamble, HHS noted that some commenters challenged whether the legal authority provided under the Common Rule's enabling legislation was sufficient to extend the rule to non-federally funded clinical trials.²⁷³ While HHS did not explicitly state that its decision not to finalize the proposal was due to these concerns, they were noted.²⁷⁴ It is possible that similar challenges would be posed regarding any proposal to extend the federal research oversight regulations to non-federally funded projects.

Another alternative is to look to the FDA to regulate these activities as part of the product lifecycle for regulated products. This would not require a complete reenvisioning of the FDA's role or its jurisdiction. Indeed, as noted at various points in this Article, the FDA already has some cursory regulations in place that intersect with the activities that are the subject of this Article. Most strongly, the FDA's regulations pertaining to research conducted on human subjects to test an FDA-regulated product or in support of an FDA marketing submission require essentially the same management-based process as is required of federally funded research.²⁷⁵ In this instance, the *research activity* (a research study of an FDA-regulated product) is regulated as part of the FDA's jurisdictional authority to regulate *products*.²⁷⁶

The FDA regulation for applicable clinical trials thus suggests an alternative: it may be possible to require all research activities undertaken as part of the research and development of FDA-regulated products to meet standards consistent with those applicable to publicly funded research. In other words, it is possible to imagine shifting the jurisdictional hook from *federal funding* to FDA-regulated *product development activities*.

As mentioned earlier, the FDA already has some minimal and cursory products regulations on point. It has the Part 50 regu-

273. *Id.* at 7156.

274. *Id.*

275. *Id.* at 7159–60.

276. See Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399 (2016).

lations, which govern human subjects research.²⁷⁷ These are process regulations that apply to products regulated by the FDA, and as noted above, they generally provide equivalent protections to human subjects as do the Common Rule regulations.²⁷⁸ The FDA also has good laboratory practices for non-clinical studies regulations.²⁷⁹ These cover “test systems” defined as “any animal, plant, microorganism, or subparts thereof.”²⁸⁰ These are decidedly not regulations aimed at the care and welfare of animals. They do not require an IACUC committee, nor do they mention discomfort, stress, pain, or other qualitative aspects of research that animals may feel, as do the policies that apply to federally funded animal research. Finally, the FDA regulations at 21 C.F.R. § 54 (Financial Disclosures by Clinical Investigators) require that clinical study sponsors provide the agency with a list of clinical investigators who conduct covered clinical studies, and some information.²⁸¹

In the case of pre-clinical good lab practice and financial disclosures, the FDA regulations do not provide the type or quality of protection to consumers and (animal and human) research participants afforded by the regulations that are structured as conditions of federal funding. They do, however, clearly indicate that the FDA has jurisdiction over these activities, at least with regard to research and development to support FDA-regulated products. The case of human subjects research, where its regulations are largely equivalent to those under the Common Rule, indicates that the FDA has jurisdiction over the conduct of research that goes beyond simply product safety matters and into ethical conduct of research and participant protection.

Therefore, it may well be possible for the FDA to modify its product regulations to harmonize with the requirements for

277. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. at 7155.

278. See National Research Act, Pub. L. No. 93-348, 88 Stat. 342.

279. 21 C.F.R. § 58.1(a) (2017).

280. *Id.* § 58.3(i).

281. *Id.* § 54.4.

federally funded projects. For instance, the Good Laboratory Practices for Non-Clinical Laboratory Studies regulations could be harmonized with the PHS policy standards so privately funded research efforts involving animals in support of the development of FDA-regulated products meet the same standards as federally funded studies.²⁸² This could be achieved through revisions to 21 C.F.R. § 58. Similarly, the FDA could require that physician-investigators conducting privately funded clinical investigations of FDA-regulated products meet the same conflict of interest requirements as investigators conducting federally funded research.²⁸³ This could be accomplished through revisions to 2 C.F.R. § 54.

Finally, the FDA could require that all privately funded research activities conducted in eventual support of FDA-regulated products be subject to the same research misconduct requirements and standards as federally funded research. This would likely require a new regulation.²⁸⁴ Importantly, the 21st Century Cures Act encourages, and in many instances requires, that federal agencies work to streamline and harmonize their regulations.²⁸⁵ There is nothing to prohibit the FDA from streamlining its regulations to the other policies in this space rather than vice versa. Future research should explore this alternative jurisdictional pathway in more detail.

As the conduct of biomedical research continues to move from academic settings and federal funding toward corporate environments utilizing private funds, it is imperative that regulatory standards are devised that meet the original policy goals of the regulations that apply to federally funded research: ethical and high quality research that adequately protects human and animal participants. The original sets of regulations, while flexible in terms of the means by which regulated organizations can meet broadly defined federal goals, are not designed to

282. *Id.* § 58.1(a). *See generally* Gordon, *supra* note 112 (outlining the history of regulation and protection of animal research subjects).

283. CHECKLIST FOR POLICY DEVELOPMENT, *supra* note 175. This could be accomplished through revisions to 21 C.F.R. § 54.

284. *See, e.g.*, SAMPLE POLICY AND PROCEDURES, *supra* note 153, at 1-29.

285. 21st Century Cures Act, Pub. L. No. 114-255, § 2042, 130 Stat. 1033, 1073 (2016).

incorporate new risks in terms of new actors in the institutional environment. The regulations were designed for a world that no longer exists. We must find alternative mechanisms to regulate these activities, so that we do not allow protections to drift away.