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The Privatization of Human Research Ethics: An American Story

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Abstract

In recent decades, there has been a remarkable shift in the governance of human research ethics in the United States. A model once based on review by panels of local volunteers has given way to a system dominated by large, for-profit research ethics committees. America's reliance on for-profit ethics review is unique among wealthy industrialized countries. How can we account for this anomaly? In this article, I show that for-profit IRBs represent only the most visible aspect of the privatization of human research protections in the United States. I suggest that private institutions have emerged as “workaround” solutions to systemic problems, in the absence of comprehensive policy reforms.

Keywords

accreditation – biomedical research protections – Contract Research Organizations – commercial IRBs – independent IRBs – Institutional Review Boards (IRBs) – multi-site research – regulation

1 Introduction

About a half-century ago, the United States federal government first published official regulations for the protection of human participants in research studies. These rules were famously based on what medical sociologist Laura Stark calls an “ethics of place,” with judgments delegated to committees of local experts at universities and academic medical centers, which came to be

known as institutional review boards (IRBs).¹ Elements of this location-based, peer-review model were exported from the United States, shaping research ethics committees in other industrialized countries (see the other contributions in this special issue).

Since the 1990s, however, the models appear to have diverged. Whereas in Western Europe, governments have moved to play a more direct role in running research ethics committees,² the United States has gone in its own distinctive direction, with human research review of biomedical studies now dominated by large, for-profit companies known as “independent IRBs” or “commercial IRBs.” By 2016, these were reportedly reviewing around 70 per cent of U.S. clinical trials for drugs and medical devices.³ So profitable have these firms become that they have attracted the attention of private equity firms, leading to a wave of mergers and acquisitions.⁴

The American reliance on for-profit ethics review is unique among wealthy industrialized countries. How can we account for this anomaly? In this article, I argue that independent IRBs are the most visible dimension of an overall privatization of human research protections, and that privatization is a “workaround” adaptation to changes in the structure of biomedical research, to compensate for the lack of rationalizing policy reforms.⁵ The IRB case aligns well with social science literature on America’s unique political, ideological, and institutional barriers to investment in public institutions. As a result of

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- 1 Laura Jeanine Morris Stark, *Behind Closed Doors: IRBs and the Making of Ethical Research* (Chicago, IL, 2012).
 - 2 Adam Hedgecoe et al., “Research Ethics Committees in Europe: Implementing the Directive, Respecting Diversity,” *Journal of Medical Ethics*, 32 (2006): 483–486, <http://doi.org/10.1136/jme.2005.013888>.
 - 3 Sheila Kaplan, “In Clinical Trials, For-Profit Review Boards Are Taking over for Hospitals. Should They?” *STAT*, 6 July 2016, www.statnews.com/2016/07/06/institutional-review-boards-commercial-irbs, last accessed 17 July 2021.
 - 4 In 2008, Schulman IRB was sold to Imperial Capital Group. In 2013 Western was brought into the WIRB-Copernicus Group, along with several smaller boards, under Arsenal Capital Partners. In 2017, Chesapeake and Schulman IRB merged to form Advarra, which in 2019 acquired Quorum Review; see IRB Advisor, “Finding New Capital Partners” and “Central IRBs: Consistency Increases, but so Does Confusion,” *IRB Advisor*, 1 October 2014; Melissa Fassbender, “IRB Consolidation Continues as Chesapeake and Schulman Merge to Form Advarra,” 8 November 2017, www.outsourcing-pharma.com/Article/2017/11/08/Chesapeake-IRB-and-Schulman-IRB-merge-to-form-Advarra, last accessed 17 July 2021; eadem, “IRB Consolidation: Advarra Acquires Quorum Review and Kinetiq,” 5 March 2019, www.outsourcing-pharma.com/Article/2019/03/05/IRB-consolidation-Advarra-acquires-Quorum-Review-and-Kinetiq, last accessed 17 July 2021.
 - 5 See Sarah Babb, *Regulating Human Research: IRBs from Peer Review to Compliance Bureaucracy* (Redwood City, CA, 2020).

these obstacles, functions that in other countries are performed directly by governments are replaced by “an immensely complex tangle of indirect incentives, cross-cutting regulations, overlapping jurisdictions, delegated responsibility, and diffuse accountability.”⁶

I begin this article with a section describing the legal peculiarities of the American human research protection system, and an historical explanation of how the framework came to look this way. I then describe the turning point that occurred in the 1990s – when it became increasingly apparent that the American system was ill-suited to cope with the new realities of biomedical research. The section that follows shows how lawmakers’ failure to implement needed reforms led to the emergence of three privatized workarounds: large cadres of IRB staff, financed by research institutions and private sponsors; private accreditation and certification; and for-profit institutional review boards. America’s privatized approach ameliorates systemic dysfunctions, but at a considerable cost, and creates the potential for conflicts of interest.

2 The American System in Brief

Compared to many other national systems, the American legal framework for governing human research protections stands out as unusual in at least three respects. First, it is unusually fragmented. In reality, is two systems. Among academics, the better known of the two has jurisdiction over institutions that receive federal research funding, and is governed by the Code of Federal Regulations, Title 45, Part 46 (45 CFR 46), often referred to today as the Common Rule. Compliance with the Common Rule is currently overseen by the Office for Human Research Protections (OHRP), an office within the Department of Health and Human Services (DHHS), itself the parent organization of the National Institutes of Health (NIH). A second set of regulations has jurisdiction over privately-sponsored research, such as clinical trials financed by pharmaceutical companies (21 CFR 50, 56). It is overseen by the U.S. Food and Drug Administration (FDA), an agency also located within the DHHS that in practice behaves quite autonomously. The two sets of regulations corresponding to the different agencies are similar but not identical. Many IRBs

6 Elisabeth S. Clemens, “Lineages of the Rube Goldberg State: Building and Blurring Public Programs, 1900–1940,” in *Rethinking Political Institutions: The Art of the State*, ed. Ian Shapiro, Stephen Skowronek and Daniel Galvin (New York, 2006): 187–215, here 187.

manage compliance with both the Common Rule (for federally-funded studies) and FDA regulations (for privately-funded studies).⁷

Secondly, the federal offices in charge of overseeing IRBs are overstretched and underfunded. OHRP “provides clarification and guidance, develops educational programs and materials, maintains regulatory oversight, and provides advice on ethical and regulatory issues in biomedical and behavioral research” for more than 10,000 Common Rule signatories.⁸ This office has a mere 21 employees listed on its website, including secretarial staff. Resources for FDA oversight are more abundant, and unlike OHRP, the agency conducts routine inspections of ethics review boards. However, FDA is organized around the goal of consumer safety rather than research ethics; it has no office that is exclusively devoted to human research, instead distributing responsibility for IRB oversight across three separate offices in charge of regulating research with drugs, devices, and biologics, respectively.⁹

Thirdly, the system is characterized by diffuse authority. Neither OHRP nor FDA has the mandate to set ethical precedents or to accept appeals – in other words, to serve as a “Supreme Court of IRBs.” Instead, OHRP and its counterpart offices in FDA are charged with holding research institutions to rules around administrative procedures and paperwork – what characteristics of studies are considered, meetings minutes, and so on.¹⁰ Both OHRP and FDA issue guidance to clarify gray areas in the regulations. Yet clarification is often sparse and inadequate – a phenomenon that seems to stem both from regulators’ lack of resources, and their caution about pushing the boundaries of their limited authority. Regulators do not provide model policies, or even suggested policy templates. What this leads to, in practice, is a wholesale delegation of authority to local institutions and their IRBs – not only to decide on what is ethical, but also to navigate the meaning of regulatory compliance.

7 For an overview, see National Bioethics Advisory Commission (NBAC), *Ethical and Policy Issues in Research Involving Human Participants* (Bethesda, MD, 2001).

8 United States Department of Health and Human Services (DHHS), Office for Human Research Protections, www.hhs.gov/ohrp, last accessed 17 July 2021.

9 United States General Accounting Office, “Scientific Research: Continued Vigilance Critical to Protecting Human Subjects” (Washington, D.C., 1996).

10 Kristina Borrer et al., “A Review of OHRP Compliance Oversight Letters,” *IRB: Ethics and Human Research*, 25 (2003): 1–4; Scott Burris and Jen Welsh, “Regulatory Paradox: A Review of Enforcement Letters Issued by the Office for Human Research Protection,” *Northwestern University Law Review*, 101 (2007): 643–686.

3 The Birth of the IRB System

The IRB framework's mix of complexity, fragility, and diffuse authority were born out of the political dynamics present at its founding. In a series of Congressional hearings during the early 1970s, lawmakers heard testimony and debated how to prevent the recurrence of ethical abuses such as those of the infamous Tuskegee syphilis study. One bill introduced by Senator Hubert Humphrey (S. 934) proposed the creation of a powerful National Human Experimentation Board, empowered to pass regulations, set precedents, and "review all planned medical experiments that involve human beings which are funded in whole or in part with Federal funds." National board members would be "persons of demonstrated knowledge, education, and experience in the field of clinical investigations," paid federal salaries and appointed by the President.¹¹

Humphrey's National Human Experimentation Board would have set American human research regulations on a centralizing trajectory, similar to what emerged in European countries decades later. Yet this proposal quickly dropped out of Senate discussions. Subsequent debates focused on a second bill, proposed by Senator Edward Kennedy (S. 2072) that would have set up a permanent national commission with the power to promulgate and enforce regulations, as well as to certify local review boards. Unlike Humphrey's plan, the Kennedy option would have kept local IRBs in charge of reviewing research ethics. However, it would have provided them with strong leadership and direction: a permanent, expert commission with the authority to set the agenda for institutional review boards across the country, and to serve as a precedent-setting appeals body.¹²

Although Kennedy's plan influenced the National Research Act of 1974, it was significantly watered down in the process of political compromise. It established a national commission – but it was only a temporary one, with a purely advisory function. The act also authorized new regulations (45 CFR 46), but these essentially duplicated an existing NIH policy in which internal and

11 United States Congress Senate Committee on Labor and Public Welfare Subcommittee on Health, *Quality of Health Care—Human Experimentation, 1973. Hearings, Ninety-Third Congress, First Session, on S. 974* (Washington, D.C., 1973), 1659, <http://hdl.loc.gov/loc.law/lconghear.73601927>.

12 United States Congress House Committee on Interstate, Foreign Commerce Subcommittee on Public Health, and Environment, *Biomedical Research Ethics and the Protection of Human Research Subjects: Hearings before the Subcommittee on Public Health and Environment of the Committee on Interstate and Foreign Commerce, House of Representatives, Ninety-Third Congress, First Session ... September 27 and 28, 1973* (Washington, D.C., 1974), 272.

extramural researchers were required to submit proposed research for ethics review by a local panel of their colleagues.¹³ Not only did the 1974 regulations delegate the job of ethics review to the same local “institutional peer review committees” that had already been assessing NIH research for years, but it also gave the job of overseeing these committees to the same tiny office within the NIH.¹⁴

Two factors account for the failure to create a more robust framework for overseeing human research ethics in the United States. First, it was opposed by powerful actors: the biomedical research community (which resisted the potential intrusion on professional autonomy); and the NIH (which saw decentralization as a way of protecting itself from legal problems and public controversy).¹⁵ Secondly, there was limited appetite among lawmakers for expanding state capacity in this way – not only in Congress, but also in the Nixon administration, which explicitly sought “to stop the continued federal intrusion into matters that were not properly the concern of the government.”¹⁶

Thus, as it emerged in the mid-1970s, the American regime for regulating human research protections was founded on two bedrock premises: the delegation of decisions to local boards financed by research institutions; and the oversight of these boards by sub-agencies located deep within the federal health bureaucracy.¹⁷ These premises were preserved in subsequent revisions to the regulations, although they also brought important changes. The 1981 update to 45 CFR 46 incorporated recommendations from the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and other groups; some notable changes included a new requirement that boards include “non-scientist” members, and introduced more intensive procedural and recordkeeping requirements. This update was also accompanied by the first issuance of parallel FDA regulations (21 CFR 50, 56) with jurisdiction over privately-sponsored clinical trials. A decade later, in 1991, a long list of federal

13 Zachary M. Schrag, *Ethical Imperialism: Institutional Review Boards and the Social Sciences 1965–2009* (Baltimore, MD, 2010).

14 Charles R. McCarthy, “The Origins and Policies That Govern Institutional Review Boards,” in *The Oxford Handbook of Clinical Research Ethics*, ed. Ezekiel J. Emanuel et al. (Oxford, 2008), 50–75.

15 Sydney Halpern, “Hybrid Design, Systemic Rigidity: Institutional Dynamics in Human Research Oversight,” *Regulation & Governance*, 2 (2008): 85–102; Mark Steven Frankel, “Public Policymaking for Biomedical Research: The Case of Human Experimentation” (PhD diss., George Washington University, 1976); Stark, *Behind Closed Doors*.

16 Assistant Secretary of U.S. Department of Health, Education and Welfare, Merlin K. Duval interview in Frankel, “Public Policymaking for Biomedical Research,” 177.

17 Halpern, “Hybrid Design, Systemic Rigidity.”

funding agencies signed on to a revised version of the NIH regulations, which became known as the “Common Rule.”¹⁸

4 Turning Point in the 1990s

For about two decades, the system for regulating human research protections bumped along without major incident. By the mid-1990s, however, an eruption of well-publicized biomedical research scandals was putting pressure on regulators to act.¹⁹ This led to an unprecedented wave of federal enforcement that crested shortly after the beginning of the new century (see Fig. 1). In some egregious cases, regulators suspended research institutions’ federally-funded studies. “Across the country, university administrators and researchers are worried, even panicked, that the same thing could happen at their institutions,” observed the *Chronicle of Higher Education* in 2000.²⁰

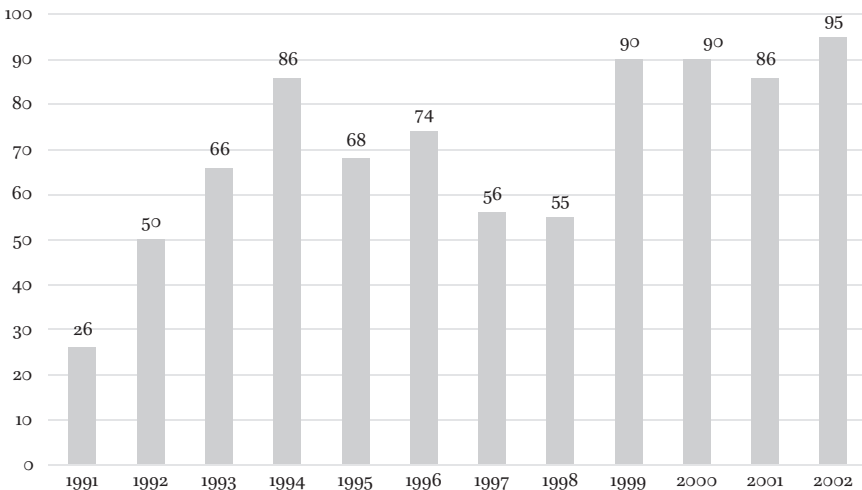


FIGURE 1 OPRR/OHRP Compliance Investigations Opened, 1991–2002.²¹

18 United States General Accounting Office, “Scientific Research: Continued Vigilance.”

19 Philip J. Hiltz, “Agency Faults a U.C.L.A. Study for Suffering of Mental Patients,” *New York Times*, 10 March 1994; Elisabeth Rosenthal, “New York Seeks to Tighten Rules on Medical Research,” *New York Times*, 27 September 1996; Sheryl Gay Stolberg, “Teenager’s Death Is Shaking Up Field of Human Gene-Therapy Experiments,” *New York Times*, 27 January 2000.

20 Jeffrey Brainard, “Spate of Suspensions of Academic Research Spurs Questions about Federal Strategy: A U.S. Agency, Its Own Future Uncertain, Unsettles College Officials with Its Crackdown,” *The Chronicle of Higher Education*, 96 (2000): A29–30, A32.

21 Source: OHRP internal database supplied to fulfill Freedom of Information Act request.

There was a growing sentiment amongst regulators, lawmakers, and advisory bodies that the IRB system was broken. As Connecticut Representative Christopher Shays told a Congressional subcommittee in 1998, “today’s research environment has changed dramatically. Institutional Review Boards have not.”²² Three of the leading problems were unsustainable IRB workloads; the incapacity of federal regulators; and the mismatch between review and multi-site research.

4.1 *Growing IRB Workloads*

In the decades since the birth of the original regulations, IRB’s workloads had become increasingly unmanageable. One reason was simply that there was more research to review, due to increased funding for sponsored biomedical research (see Fig. 2). This increased workload was not accompanied by increased resources: there were strict limitations on the administrative costs that could be charged to federal grants.²³ As a result, IRB’s were usually low-budget affairs, run by faculty volunteers with minimal staff assistance. “IRB members are usually physicians, scientists, university professors, and hospital department heads who are not paid for their IRB service,” explained the U.S. General Accounting Office in 1996. “In some cases, the sheer number of studies necessitates that IRB’s spend only 1 or 2 minutes of review per study.”²⁴

The workload was also enhanced by growing regulatory complexity, which took a growing amount of time and expertise to manage. After 1981, IRB’s needed to keep track of two sets of regulations – the NIH and FDA rules – which were similar but contained distinct terminology and definitions.²⁵ Over time, IRB’s were also expected to comprehend a growing list of additional regulatory mandates – such as the privacy provisions of the Health Insurance Portability and Accountability Act (HIPAA), conflict of interest, and institutional biosafety – under the jurisdiction of different federal offices.²⁶

22 United States Congress House Committee on Government Reform and Oversight Subcommittee on Human Resources, *Institutional Review Boards, a System in Jeopardy: Hearing before the Subcommittee on Human Resources of the Committee on Government Reform and Oversight, House of Representatives, One Hundred Fifth Congress, Second Session, June 11, 1998* (Washington, D.C., 1999), 2.

23 NBAC, *Ethical and Policy Issues in Research Involving Human Participants*, 4.

24 United States General Accounting Office, “Scientific Research: Continued Vigilance,” 17.

25 NBAC, *Ethical and Policy Issues in Research Involving Human Participants*, 10.

26 Infectious Diseases Society of America, “Grinding to a Halt: The Effects of the Increasing Regulatory Burden on Research and Quality Improvement Efforts,” *Clinical Infectious Diseases*, 49 (2009): 328–335, <https://doi.org/10.1086/605454>; NBAC, *Ethical and Policy Issues in Research Involving Human Participants*.

Even within the original NIH rules there was greater complexity. With each subsequent update they became longer, layering new requirements atop the old, and resulting in an intricate, overlapping set of decision criteria, sub-criteria, and exceptions that could baffle even the most motivated faculty volunteer. To take just one example, there were six categories of research that qualified for exemption. One of these categories was research “involving survey or interview procedures” which could be exempt *unless* subjects could be identified, *and* such identification could put the subject at risk, *and* the study dealt with “sensitive topics” such as sexual behavior or drug use – *unless* the study subjects were “elected or appointed public officials or candidates for public office,” in which case they were exempted unconditionally.

IRB workloads were further amplified by enhanced regulatory expectations, revealed in federal enforcement actions. For decades, it had been common for faculty-run boards to overlook complex regulatory details, focusing their efforts instead on the ethical assessments at the heart of the review process. Since 1981, however, the regulations had contained substantial procedural requirements that were supposed not only to be followed but also meticulously recorded.²⁷ During the regulatory crackdown of the 1990s, a growing number of research institutions were sanctioned for failing to adhere to these technicalities. The mantra of regulators during the crackdown was, “if it wasn’t documented, it didn’t happen.”²⁸ When addressed more fastidiously, these rules absorbed a growing portion of IRB’s labor and attention, undoubtedly leaving less space for thoughtful ethical discussions.

4.2 *Regulatory Incapacity*

The regulators overseeing the American IRB system faced multiple constraints. Their role was not to second-guess IRB’s ethical judgments – they lacked the mandate to serve as a precedent-setting appeals body – but rather to uphold adherence to the various procedures and decision-criteria spelled out in the regulations.²⁹ In a federal audit, an IRB would be required to show comprehensive documentation demonstrating that rules had been followed – for example, to show that for each exemption determination a properly-authorized individual had determined that the study fell into one of the eligible categories.

Moreover, federal offices lacked the resources needed even to fully fulfill this circumscribed mandate. In 1999, fewer than 20 staff members, including

27 Burris and Welsh, “Regulatory Paradox.”

28 Daniel S. Greenberg, *Science for Sale: The Perils, Rewards, and Delusions of Campus Capitalism* (Chicago, IL, 2007), 132.

29 Burris and Welsh, “Regulatory Paradox.”

a single full-time investigator, were dedicated to the many thousands of IRB s under the jurisdiction of the NIH rules.³⁰ Stretched thin by enforcement actions, regulators were unable to always provide timely clarification of the regulations, which contained numerous ambiguities. “HHS [the Department of Health and Human Services] has not increased OHRP’s budget in proportion to the office’s increased scope of work,” reported the General Accounting Office in 2001, “and the office has not been able to hire the staff it planned to because of the federal hiring freeze.”³¹ As a result, IRB s had been waiting for years for important guidance on matters such as informed consent procedures.³²

A key side-effect of such incapacity was that regulators’ signals to research institutions could be sparse, inconsistent, and confusing. In the context of vigorous federal enforcement, IRB s experienced uncomfortable levels of uncertainty: failure to comply could have dire consequences, but what exactly did compliance entail? In the absence of a clear answer from the feds, it became common to engage in “hypercompliance” – that is to say, to go above and beyond the regulations as a buffer against uncertainty.³³ As former regulator Greg Koski noted in 2002, “a climate of fear [was] often resulting in inappropriately cautious interpretations and practices that have unnecessarily impeded research without enhancing protections for the participants.”³⁴ One of the many hypercompliant practices that became widespread during this era was putting low-risk research through time-consuming full board review.³⁵ For social and humanities researchers, this involved the subjection of unfunded studies to standard IRB review and the transformation from “exempting” low-risk research into a de facto IRB review process – neither technically required by the regulations.³⁶ For investigators, IRB hypercompliance was experienced as a notable increase in red tape and delays. For board members, it was experienced as a ratcheting-up of their already-crushing workloads, as

30 Greenberg, *Science for Sale*, 134.

31 Janet Heinrich, *Human Subjects Research: HHS Takes Steps to Strengthen Protections, But Concerns Remain*, US General Accounting Office (Washington, D.C., 2001), 12.

32 IRB Advisor, “Failures at Three Levels Equal a Loss of Momentum in Protection of Human Research Participants,” *IRB Advisor*, 1 July 2001.

33 Babb, *Regulating Human Research*.

34 Greg Koski, “Beyond Compliance... Is It Too Much to Ask?” *IRB: Ethics & Human Research*, 25 (2002): 5–6.

35 IRB Advisor, “Teaching IRB s to Be Flexible, Drop Bad Habits,” *IRB Advisor*, 1 June 2011.

36 IRB Advisor, “Fairness and Common Sense Can Ease Tensions,” *IRB Advisor*, 1 August 2006; Schrag, *Ethical Imperialism*.

they were asked to review more research more carefully, with more supporting documentation and lengthier application forms.³⁷

4.3 *Multi-Site Research*

By the mid-1990s, there was a painfully obvious structural discrepancy between a system designed around delegation to local decision-makers, on the one hand, and the new realities of biomedical research, on the other. “The current framework of IRB practices was shaped in the 1970s in an environment where research typically was carried out by a single investigator working under government funding with a small cohort of human subjects in a university teaching hospital,” observed the Health Department’s inspection office. “In recent years, that environment has been changing dramatically.”³⁸ By the 1990s, it was standard practice to conduct biomedical research across multiple locations. Because of the way that the system was set up, a study being conducted across seven medical centers was under the jurisdiction of seven separate IRBs, each with its own local precedents and standard operating procedures, and each potentially arriving at different decisions about how to conduct the same study ethically.³⁹ The need to reconcile these decisions led to long delays, and created increased administrative work for investigators and IRB members alike.⁴⁰

5 From Failed Reform to Private Workarounds

By the beginning of the twenty-first century, it was clear that the American system for protecting human research subjects was suffering from serious rigidities.⁴¹ The moment was ripe for comprehensive reform of the sort that was already occurring in other countries. In the United Kingdom, for example, a similarly outdated framework was in the process of being overhauled by the Health Department, and was eventually replaced by a centrally coordinated

37 Koski, “Beyond Compliance ... Is It Too Much to Ask?”

38 United States Department of Health and Human Services (DHHS), Office of the Inspector General, “Institutional Review Boards: A Time for Reform” (Washington, D.C., 1998), 11.

39 Thomas O. Stair et al., “Variation in Institutional Review Board Responses to a Standard Protocol for a Multicenter Clinical Trial,” *Academic Emergency Medicine*, 8 (2001): 636–641, <https://doi.org/10.1111/j.1553-2712.2001.tb00177.x>; Henry Silverman, Sara Chandros Hull and Jeremy Sugarman, “Variability among Institutional Review Boards’ Decisions within the Context of a Multicenter Trial,” *Critical Care Medicine*, 29 (2001): 235–241.

40 Infectious Diseases Society of America, “Grinding to a Halt”; National Science Foundation, “Reducing Investigators’ Administrative Workload for Federally Funded Research” (Arlington, VA, 2014).

41 Halpern, “Hybrid Design, Systemic Rigidity.”

system in which multi-site studies applied through a single nationwide portal.⁴² Other European countries were also moving in this direction.⁴³

In the United States, reform would require a major institutional overhaul. Once again, Senator Edward Kennedy took up the challenge – this time by sponsoring the Research Revitalization Act (S. 3060), which aimed at establishing an independent lead agency charged with overseeing the entire IRB structure, as well as promulgating, interpreting, and enforcing new regulations. Kennedy's bill also called for millions of dollars in new funding, both for the new agency and to improve local IRB function.⁴⁴ However, the bill died at the committee stage, and was never debated on the Senate floor.⁴⁵ Although there is no concrete evidence to account for the bill's early demise, it seems very likely that it faced the same insurmountable obstacles as had its predecessor back in 1973: opposition from vested biomedical research interests; and opposition from Republicans in both the White House and Congress.

Instead, with the acquiescence and encouragement of federal agencies, privatized adaptations to systemic failures began to emerge and flourish. To tackle the formidable labor of compliance, there was a rapid expansion in local IRB s' administrative staff, subsidized by research institutions and fees from private sponsors. To compensate for the lack of federal oversight and standards, research institutions and investigators sought licensing from private accreditors and certifiers. Most strikingly, the dilemma of multi-site research was addressed through the use of for-profit IRB s unencumbered by local institutional affiliations.

5.1 *Increased IRB Staffing*

For many years, regulators had recommended that research institutions devote more resources to IRB staffing. Research institutions resisted, pleading poverty and asking that the government defray the added costs by allowing them to be charged directly to federal grants.⁴⁶ By the early 2000s, however – with their resistance eroded by years of alarming federal enforcement – research institutions began to invest large sums of money in IRB offices, “in many cases

42 Rustam Al-Shahi Salman et al., “Increasing Value and Reducing Waste in Biomedical Research Regulation and Management,” *The Lancet*, 383 (2014): 176–185.

43 Hedgecoe et al., “Research Ethics Committees in Europe.”

44 Erin D. Williams, “Federal Protection for Human Research Subjects: An Analysis of the Common Rule and Its Interactions with FDA Regulations and the HIPAA Privacy Rule” (Washington, D.C., 2005).

45 A parallel bill (H.R. 4697) was introduced in the House of Representatives, and similarly died at the committee stage; see Williams, “Federal Protection for Human Research Subjects.”

46 Greenberg, *Science for Sale*, 132–133.

doubl[ing] and tripl[ing] their commitments of resources to their human subjects protection programs.⁴⁷ By 2007, more than half of respondents to a survey of the IRB world reported that they were working in offices with at least three full-time staff members, with some reporting numbers as high as fifteen or twenty. About half of the respondent had advanced postgraduate degrees.⁴⁸ These were no longer secretaries working under the supervision of faculty chairpersons, but rather skilled research administrators, embedded in a chain of command reaching up to the highest level of administration, and with a growing sense of professional identity.

For research institutions, the advantage of investing in staff was that it put regulatory compliance in the hands of people who had time to master complex regulations and evolving guidance, and to follow procedural and documentation requirements to the letter. It simultaneously lightened the workload of faculty volunteers, whose highly-compensated time was better spent attending to their academic obligations. The disadvantage, however, was that it was extremely costly. A 2007 study reported that the median cost to an academic medical center of maintaining an IRB was \$781,224, with staff salaries accounting for the biggest line item.⁴⁹

To help defray the expense, and in the absence of greater federal support, it became common for boards at biomedical institutions to charge review fees to commercial sponsors. "Is your IRB charging for reviews yet? If not, you are probably in the minority," proclaimed a trade journal in 2003.⁵⁰ A leading manual for IRB administrators advised that "charging [a] review fee for commercially sponsored research is a common way for an IRB to supplement the operating budget provided by the institution. Sponsors do not object to paying reasonable IRB review fees, and the additional revenue can be used by the IRB to improve the quality and efficiency of its service."⁵¹ Thus, the professionalization of IRB offices simultaneously fostered their growing dependence on private research sponsors.

47 Koski, "Beyond Compliance ... Is It Too Much to Ask?" 5.

48 Public Responsibility in Medicine and Research, "Workload and Salary Survey, 2007."

49 Jeanne L. Speckman et al., "Determining the Costs of Institutional Review Boards," *IRB: Ethics & Human Research*, 29 (2007): 7–13.

50 IRB Advisor, "Supply and Demand: IRB Fees Now Are the Norm," *IRB Advisor*, 1 October 2003.

51 Ernest Prentice, Sally L. Mann and Bruce G. Gordon, "Charging for Institutional Review Board Review," in *Institutional Review Board: Management and Function*, ed. Elizabeth A. Bankert and Robert J. Amdur, 2nd ed. (Boston, MA, 2006), 57.

5.2 *Accreditation and Certification*

To compensate for regulators' limited ability to oversee and set standards for IRBs, a private accreditation mechanism was established. The Association for the Accreditation of Human Research Protection Programs (AAHRPP, pronounced "ay-harp") was founded in 2001, with strong support from regulators, biomedical researchers and academic administrators.⁵²

Accreditation was understood as a way to achieve more intensive supervision without putting additional financial strain on meagerly-resourced federal offices.⁵³ The cost to research institutions, however, was substantial. In 2003, initial fees ranged from \$7,000 to more than \$23,000, depending on the number of reviews conducted annually, and to maintain accreditation, institutions needed to pay a significant annual fee and to renew their status every three to five years.⁵⁴ Moreover, the accreditor's demands were time-consuming, requiring extensive staff time and attention – for example, ongoing internal audits, tracking logs and performance metrics, and the regular updating and assessment of policies.⁵⁵

While research institutions were receiving the gold seal of private accreditation, investigators across the country were now expected to acquire private certification demonstrating their competence in human research protections. In 2000, the DHHS Secretary Donna Shalala directed research institutions to provide such training, but the agency failed to provide details on what the training should include or how it should be delivered. In response to this call, the Collaborative Institutional Training Initiative (CITI) online education platform was launched at the end of that same year. Research institutions paid substantial annual fees to the organization, and required that researchers present proof of CITI certification along with their IRB applications. By 2007, more than 600,000 individuals at over 700 institutions had acquired certification.⁵⁶

52 One of AAHRPP's two leading co-sponsors was the American Association of Medical Colleges – a lobbying organization representing medical school administrators. The second was Public Responsibility in Medicine and Research (PRIM&R). Other founding members included the Consortium of Social Science Associations, the Federation of American Societies for Experimental Biology, the National Association of State Universities and Land Grant Colleges, and the National Health Council; see Halpern, "Hybrid Design, Systemic Rigidity.

53 Ibid.

54 IRB Advisor, "Accreditation Requires Teamwork and Time," *IRB Advisor*, 1 February 2003.

55 IRB Advisor, "Data Driven: Accreditation Group Releases Metrics for IRB Performance," *IRB Advisor*, 1 September 2010.

56 Paul Braunschweiger and Kenneth W. Goodman, "The CITI Program: An International Online Resource for Education in Human Subjects Protection and the Responsible Conduct of Research," *Academic Medicine*, 82 (2007): 861–864.

The NIH subsequently created its own free online certification program. However, in 2018 the NIH course was phased out without explanation, leaving CITI with a de facto monopoly on the provision of human research protections training. The highly profitable certifier was acquired by a private firm specializing in biomedical research support services.⁵⁷

5.3 *For-Profit IRBs*

The most powerful actors to emerge in America's privatized human research protections ecosystem were for-profit independent IRBs. These free-standing committees were not precisely new; they had originally grown out of a sort of loophole in the 1981 FDA regulations. Unlike federally-funded studies, privately-sponsored research occurred mostly in places where there were no local review boards available. Recognizing this incompatibility, the preamble to the 1981 FDA rules recommended that in such cases, the review studies could either be given to an existing board at a research institution or to a board created outside a traditional research institution.⁵⁸

Independent IRBs grew out of this provision. They were not "institutional," technically speaking, but adhered to the same regulatory requirements as their traditional counterparts. Independent boards flourished along with the commercialization of biomedical research. By the mid-1990s, commercial investment in biomedical research had significantly surpassed NIH investment (see Fig. 2). Private firms typically outsourced the management of their clinical trials to Contract Research Organizations (CROs), which located sites, negotiated contracts, and monitored studies for data quality. CROs would hire independent IRBs to manage human research protections compliance.⁵⁹

Starting in the 2000s, the market for independent IRBs' services increased rapidly. At a time when federal enforcement actions were greatly increasing costs and red tape, independent boards were attractive for at least two reasons. First, they were not encumbered by local institutions. Board members could be selected from a list of providers, based on expertise and availability, rather than on geographical proximity, with all "scientist" members being paid for

57 Biomedical Research Alliance of New York, "BRANY Announces Acquisition of University of Miami's CITI Program," *BRANY*, 13 May 2016.

58 Erica Heath, "The History, Function, and Future of Independent Institutional Review Boards," in NBAC, *Ethical and Policy Issues in Research Involving Human Participants*, vol. 2, 9.

59 Jill Fisher, *Medical Research for Hire: The Political Economy of Pharmaceutical Clinical Trials* (Chicago, IL, 2008); Philip Mirowski and Robert Van Horn, "The Contract Research Organization and the Commercialization of Scientific Research," *Social Studies of Science*, 35 (2005): 503–548.

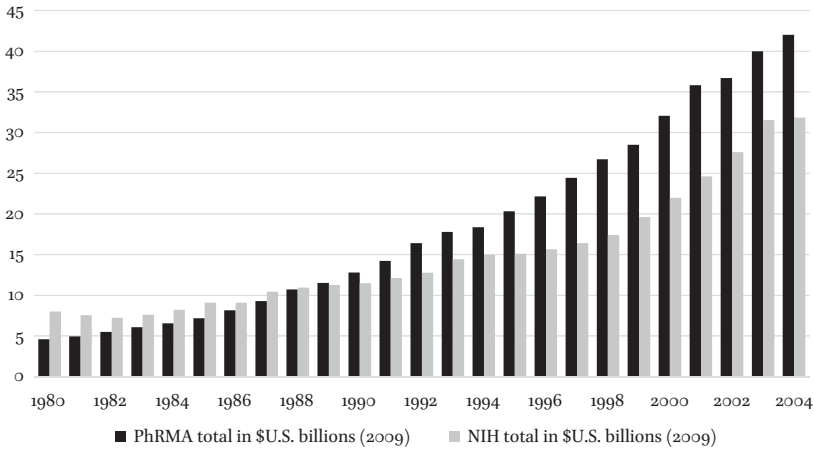


FIGURE 2 Research Financing, Commercial Pharmaceutical (PhRMA) vs. National Institutes of Health, 1980–2004.⁶⁰

their services.⁶¹ Because they were institutionally independent, these boards were immune to the malady of discrepant decisions in multi-site research. Indeed, they were extraordinarily adept at providing single review studies that could span dozens of research sites, long the dominant practice in commercial biomedical studies.⁶² Independent IRBs thus provided a solution to one of the IRB world’s most intractable problems.

Secondly, independent IRBs were famous for their efficiency – forged by years of operations in the world of private pharmaceutical research, where there was enormous pressure to get drugs and devices approved and to market as soon as possible. Independent boards conducted reviews quickly, offering protocol review times that could be two-thirds shorter than traditional IRBs.⁶³ They also benefited from economies of scale, which allowed them to maintain large cadres of administrative staff, using expensive “protocol management” software, and assisted by dedicated legal teams. The efficiency of independent

60 Sources: Pharmaceutical Research and Manufacturers of America (PhRMA), “2016 Industry Profile,” archived at <https://web.archive.org/web/20170517033057/http://phrma-docs.phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf>; United States National Institutes of Health (NIH), *NIH Almanac*, 7 (2016).

61 Heath, “The History, Function, and Future of Independent Institutional Review Boards.”

62 Fisher, *Medical Research for Hire*.

63 Ronald Rosenberg, “AMCs Vying to Better Compete for Industry Trials: Working to Conquer Study Start-up Delays, IRB Review Process,” *CenterWatch Monthly*, 2014.

IRBs became particularly attractive to sponsors and investigators during the era of enforcement-fueled hypercompliance, when traditional IRBs were notorious for red tape and delays.

Independent IRB review was expensive – the baseline fee of one of the leading IRBs in 2018 was just shy of \$1,900, with additional charges added depending on the number of sites, as well as for continuing review, extra consent documents, and protocol changes.⁶⁴ However, traditional boards were also charging commercial sponsors for review (as described above) to help defray the high cost of staffing IRB offices. Given independent boards' real and perceived advantages, commercial sponsors and their investigators tended to prefer them. Recognizing this preference, academic institutions, seeking to court commercial money, began to allow and even to encourage PIs to have their research reviewed by independent boards, rather than their own local IRBs. According to one industry source, by 2010 about half of academic medical centers were outsourcing industry-sponsored studies almost exclusively to independent boards.⁶⁵

As for-profit review gained prominence within the system, some observers began to worry that the profit motive would lead to the cutting of corners. These concerns were fueled by a 2009 federal sting operation that led to the closing of a small independent board in Colorado, after it approved a fake protocol that was obviously unethical and uncompliant.⁶⁶ To alleviate such worries, all the leading independent boards became accredited, thereby signaling to regulators, sponsors, and the public that they were both scrupulously compliant and ethically sound.⁶⁷ For a financially successful independent IRB, high accreditation fees and staff working-hours were a reasonable cost of doing business.

Meanwhile, government agencies began to give the green light to independent IRB review of federally-funded studies. Even though for-profit review of federal studies was permitted in theory, it was constrained in practice. Academic institutions worried that OHRP would hold them responsible if an independent board made a mistake, as was suggested by some of the office's regulatory decisions. Just as important, there were strict limitations on charging IRB expenses to federal grants, which prevented grant funds from being used exclusively to pay independent IRBs' substantial fees.

64 WIRB-Copernicus Group, "2018 Single Review Service Fee Schedule" (Princeton, NJ, 2018).

65 Rosenberg, "AMC's Vying to Better Compete for Industry Trials."

66 IRB Advisor, "IRB Seals Fate by Approving Fake Protocol in Federal Sting," *IRB Advisor*, 1 July 2009.

67 IRB Advisor, "OHRP Move Might Increase Trend of Research Sites Using Central IRBs," *IRB Advisor*, 1 August 2010.

Over time, however, federal authorities began to remove these barriers. Regulators were increasingly worried about systemic obstacles to getting studies up and running, and the biggest obstruction by far was divergent local IRB decisions in multi-site studies. “We recognize there can be inappropriate administrative burdens by having multiple reviews,” explained OHRP’s director in 2010, “and that can slow down research.” To solve the liability problem, the office made explicit that if it found deficiencies in outsourced review, it would hold the IRB responsible rather than the research institution.⁶⁸ In 2016, the NIH began to require “single IRB review” in multi-site studies – a requirement that would be echoed one year later in the updated Common Rule.⁶⁹

The single IRB requirement was widely interpreted as a boon to the for-profit IRB industry, bound to further augment the market for their services.⁷⁰ The possibility that the NIH could run its own centralized IRB to review its studies appears not to have been considered.⁷¹ There were non-profit single review models available – for example, sponsored by the U.S. Department of Veterans Affairs, or among academic institutions engaging in “IRB of record” agreements.⁷² However, for-profit boards – with their enormous cadres of staff, economies of scale, and decades of experience – remained the undisputed masters in handling specialized studies involving multiple sites. Under its single review policy, for the first time the NIH permitted investigators to charge review fees directly to their grants.⁷³ This provision untethered NIH-sponsored researchers from their local boards, and allowed them to act as consumers in a free marketplace of review services – a marketplace dominated by independent IRBs.

68 IRB Advisor.

69 IRB Advisor, “Single IRB NIH Guidance May Leave More Questions than Answers,” *IRB Advisor*, 1 March 2015; Melinda Young, “Beware of Good and Bad News About the New Common Rule,” *IRB Advisor*, 18 (2018).

70 Kaplan, “In Clinical Trials, For-Profit Review Boards Are Taking over for Hospitals.”

71 Decades earlier, according to medical sociologist Sidney Halpern, the NIH successfully lobbied against reviewing its own grant proposals when the system was formed in the 1970s. The two main reasons were that biomedical research leaders were more comfortable with review at the institutional level, and NIH lawyers felt that centralizing review would expose them to lawsuits; see Halpern, “Hybrid Design, Systemic Rigidity,” 91.

72 IRB Advisor, “Preparation, Communication Key to Establishing IRB of Record,” *IRB Advisor*, 1 April 2018.

73 National Institutes of Health, “Scenarios to Illustrate the Use of Direct and Indirect Costs for Single IRB Review under the NIH Policy on the Use of a Single IRB for Multi-Site Research (NOT-OD-16-109),” 21 June 2016, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-109.html>, last accessed 18 July 2021.

6 Conclusion

The outbreak of the COVID-19 pandemic has illustrated, perhaps as never before, the importance of balancing two goals: protecting human research participants; and getting life-saving research studies up and running with all due speed. To confront this challenge, distinct national frameworks were mobilized to review the ethics of human vaccine trials. In the United Kingdom, for example, the Oxford/AstraZeneca vaccine was reviewed and approved by the South Berkshire REC, a board under the authority of the Health Department.⁷⁴ In the United States, by contrast, COVID-19 vaccine trials were reviewed by WCG, one of the two largest for-profit IRB conglomerates.⁷⁵

Within the United States, there has been no shortage of critics of for-profit ethics review. For decades, governmental and non-governmental watchdogs and liberal lawmakers have expressed their unease.⁷⁶ Most recently, a group of Congressional Democrats have requested a Government Accountability Office (GAO) investigation into the industry, concerned that “this private, for-profit model creates an inherent conflict of interest for IRBs, which may incentivize them to approve as many studies as they can as rapidly as possible.”⁷⁷ A particularly acute worry concerns independent IRBs’ involvement in “pay-to-play” trials, in which patients pay large fees to participate in research studies.⁷⁸

What is seldom mentioned among the many critics of for-profit IRBs, however, is that independent boards play a critical role in a system of workaround fixes to systemic dysfunctions that the United States has been unwilling to fix

74 United Kingdom Health Research Authority, “Health Research Authority Reacts to Oxford/AstraZeneca Vaccine Being Authorised,” 30 December 2020, www.hra.nhs.uk/about-us/news-updates/health-research-authority-reacts-oxfordastrazeneca-vaccine-being-authorised, last accessed 18 July 2021.

75 Ed Miseta, “Post COVID-19: Clinical Trials Will Never Be The Same,” *Clinical Leader*, 23 April 2020, www.clinicalleader.com/doc/post-covid-clinical-trials-will-never-be-the-same-0001, last accessed 18 July 2021.

76 “Who Watches the Watchmen?” *Nature*, 476 (2011): 125; Heinrich, *Human Subjects Research*; United States DHHS, Office of the Inspector General, “Institutional Review Boards: A Time for Reform.”

77 Elizabeth Warren, Sherrod Brown and Bernard Sanders, “Letter to Gene L. Dodaro, U.S. Comptroller General, Government Accountability Office,” 16 June 2020, www.warren.senate.gov/imo/media/doc/2020.06.16%20Letter%20to%20GAO%20request%20on%20for-profit%20IRBs%20.pdf, last accessed 18 July 2021.

78 Rebecca Robbins, “Amid Rising Concern, Pay-to-Play Clinical Trials Are Drawing Federal Scrutiny,” *STAT*, 6 August 2019, www.statnews.com/2019/08/06/amid-rising-concern-pay-to-play-clinical-trials-are-drawing-federal-scrutiny, last accessed 17 July 2021.

through policy. For-profit IRBs have arguably been instrumental in patching over an expensive, labor-intensive, confusing regulatory system to ensure that clinical trials can be set up and running; thus far, they have done so without a recurrence of the types of research scandals last witnessed in the 1990s. We might ask ourselves whether the “warp-speed” development of COVID-19 vaccines by American companies would have been possible if independent boards had not been available to lubricate the gears of our outdated framework.

At the same time, we in the United States might also ask ourselves whether we can do better. Concerns about the conflict of interest in for-profit review cannot be dismissed, especially with the acquisition and merger of boards by private equity investors. Moreover, no matter how efficient independent boards are at setting clinical trials in motion, the system overall is complex and costly, involving multiple layers of paid private organizations and actors – including administrators, boards, certifiers, accreditors, consulting firms and software vendors. By contrast, in European-style, state-coordinated human research protection systems, the same functions – administration, monitoring, standard-setting, and investigator training – can be largely concentrated in a few government offices rather than delegated to a bevy of private offices. In addition to cost savings, the simplicity of this model makes it more transparent, and its public-sector location lends it greater accountability.

The American political system is famously resistant to invest in public institutions, preferring to outsource functions to subnational, non-governmental, and private entities.⁷⁹ Nevertheless, we can imagine some incremental steps toward strengthening American public oversight of human research protections. One obvious place to start would be the review of NIH research. Since 2016, the NIH – by far the largest federal sponsor of biomedical research in the United States – has allowed IRB fees, including those paid to for-profit IRBs, to be charged directly to grants. In effect, this means that taxpayer dollars are being used to pay private companies to manage compliance with federal regulations – a convoluted solution, even by American standards. There is no practical reason why a DHHS office could not efficiently administer a “public option” for multi-site NIH-funded studies, and incentivize the use of that option. The obstacles are not practical but political.

79 Andrea Louise Campbell and Kimberly J. Morgan, *The Delegated Welfare State: Medicare, Markets, and the Governance of Social Policy* (New York, 2011); Brian Balogh, *The Associational State: American Governance in the Twentieth Century* (Philadelphia, PA, 2015); Paul Starr, *Remedy and Reaction: The Peculiar American Struggle over Health Care Reform* (New Haven, CT, 2011).