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A Healthy Business: The evolution of the U.S. market for prescription drugs

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A Healthy Business: The evolution of the U.S. market for prescription drugs

By

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in

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of the

University of California, Berkeley

Committee in charge:
Professor Neil Fligstein, Chair
Professor Heather Haveman
Associate Professor Marion Fourcade
Professor Steven Shortell

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For Yi-Yi Chang Younkin, for, well for everything.
Acknowledgements

Nearly a decade ago I was sitting in an apartment on 150th St. and Broadway trying to decide where my life should go. I had applied to graduate school because of the allure of a professorial life but then, faced with the reality of sacrificing any chance at a good income to move away from my friends and family, all the way across the country to study... something (I was not yet sure then what that something would be). It would not be unreasonable to say that it sounded insane. And, like any good graduate student, there were moments, sometimes weeks or months, when I looked back at that 2001 me and thought: “What the hell was I thinking?” Graduate school is not a pleasurable or torturous process, it is better described as a limbo, a waiting for the world to decide whether or not you measure up, whether or not you’re worthy. The enjoyable parts come when you forget this and realize that you have few deadlines, no real responsibilities, it’s 80 degrees outside and you’re surrounded by some of the smartest people on the planet. The bad times, well, let’s just say they exist too.

But now, sitting just inches from the far side of it all, it is almost impossible for me to believe the consequences of a decision that I once considered almost arbitrary. Simply put: this dissertation would not have been possible if I had gone anywhere other than Berkeley. While not a perfect place, Berkeley provided two ingredients that were necessary and almost sufficient for a successful project: a unique set of institutional norms and a spectacular collection of people. The former has, and likely always will come under fire from administrators and external reviewers, so I feel obliged to recognize the role it played in my work.

The sociology department at Berkeley allows for a degree of autonomy in one’s research that is simply unavailable at almost any other school in the world. From the moment I got here I was encouraged to design a project of my own, to decide what interested me and then to explore it until I was done. No attempts were made to hasten this process of intellectual discovery, no attempts were made to confine my scope or to push me in any direction other than what I was most interested in. This is not to say that people did not help refine and develop the ideas, or that I was unsupported, but merely to say that I was encouraged to embrace a project of audacious scope and to attempt a large contribution to the literature rather than to merely offer a small extension of my advisor’s research stream.

Perhaps more important than this culture was the substantial support and guidance I received at every point along the way. I have been literally laughed at by faculty members at other schools who told me that my project was so ambitious it was practically inconceivable. But no one at Berkeley ever taught me that anything was inconceivable, instead they spent their hours trying to help me push myself beyond the pale of what was expected. I was fortunate to attend school with a number of exceptional scholars all of whom helped shape my thinking and reframe my arguments. In particular, I am indebted to Keyvan Kashkooli, Andrew Penner, Taek-Jin Shin, Kristel Acacio, Osagie Obasogie, Tom Medvetz, and Kelvin Black. It is
equally true that I was fortunate to have studied under such fine people and to have learned from Gil Eyal, Ann Swidler, Trond Peterson, Matt Rabin, and Henry Brady. However, as is true of nearly all students, I owe a particular debt of gratitude to my committee. Both Marion Fourcade and Steve Shortell offered valuable criticisms and helped me better recognize the way that the public health story and the economic sociology story intertwined. It is hard for me to imagine finishing this project at all without the help of Heather Haveman, whose reputation among her former students for her thorough critiques and seemingly endless insights is legendary. More than once I have been given a knowing look by a fellow alumni of Heather’s, one that implies our shared respect for her and appreciation for just how lucky we were to work with her. She may be the only advisor who will correct your spelling, but she is also the only person who can tell you in five minutes every single concern a reviewer will raise and how to correct them.

As valuable as these friends and faculty have proven, I am most obviously indebted to Neil Fligstein. I came to Neil years back with a vague idea about studying profitability in pharmaceuticals, nervous that he might just reject me on the spot, and I walk away a few years, and several dozen long conversations later with a deep understanding of A’s baseball, the Oakland public schools, what makes a job worth pursuing, and of course, the incredibly rich and complicated way in which the social world and the economic interact. A stranger once told me, after a talk, that I “sound like a student of Neil Fligstein.” I consider it the highest praise I’ve been awarded.

It would be a mistake of nearly equal stature to fail to thank my family: my parents, my grandparents, my sister, and my in-laws. All of whom stood by me unfailingly as I failed to graduate in anyone’s idea of a “quick” fashion. Your family is your greatest strength as a student, they are a sounding board and a support network, and mine were everything one could hope for. I thank them for allowing me to pursue my studies at my pace and for never pressuring me to leave even when they were sure it was well past time.

Finally, despite all the structural and personal support, I undoubtedly would have given all this up years ago and hit the “career default button” to send myself off to law school, consulting, or some other better paying and less fulfilling gig, if not for the constant support of my wife Yi-Yi. She is smarter, kinder, more interesting and more certain of my future than I am. I’m just lucky she hasn’t figured any of this out yet.
Preface: A Brief History of the Industry

In 1980, the pharmaceutical industry ranked first atop Fortune’s list of the world’s most profitable industries (Clifford 2000). The growth of pharmaceutical firms over the preceding forty years had been staggering, double-digit returns on assets were an industry standard, expansion and investment had occurred at a similarly daunting rate (Greener 2001). It was, depending upon the strength of your belief in the cyclical nature of markets, either easy or naïve to assume that these same firms could maintain their blistering pace. After all, no industry could continue to grow forever, eventually—it was reasoned—their returns would decline and their profits will sag, just as has happened in every other industry since the beginnings of time. Only that never happened. Thirty years later the pharmaceutical industry still sits atop Fortune’s rankings, returning nearly 20% on its assets in the last year alone. Sixty straight years as one of the most profitable industry in the world: How is this possible?

In 1980, the pharmaceutical industry was not alone in their incredible fortune. Other industries had also grown consistently and steadily over the preceding years, and were favored by the leading presses of the day, extolled as exemplars of business acumen. Unfortunately for their investors, twenty-five years affects industries just as it ages people and, for the industries like steel, textiles, or chemicals, their former abundance slowly abandoned them. For these firms, the passage of time meant watching their dominance become the province of their rivals. These declines result from divergent pressures, but the outcome for all is the same: a regression to the mean. Reading through past Fortune 500 lists is like watching the careers of professional athletes: they rise from obscurity, hit their peak, and then descend—often quickly and less than gracefully.

Often this fall comes on the heels of political change. Changes in anti-trust legislation can alter the corporate forms that are successful, bankrupting some firms and allowing others to rise (Fliigstein 1990). Other industries fall victim to technological changes that serve a similar need in a faster, cheaper, or more convincing fashion (Christensen and Bower 1996). Much as chemical companies and their improving plastics and synthetic fibers took over for the steel and cotton that had come before. While still others collapse from social change, as when permanent forms of pen, handkerchiefs, and diapers gave way to a preference for lower-quality, cheap and disposable alternatives.

That a firm, or even an industry, might collapse or merely slip from its previous heights hardly seems noteworthy. History has repeatedly shown that industries rise and fall over time, victims of changes in their environment. Which only makes the persistent success of the pharmaceutical industry all the more perplexing.

*How did they do it?* The pharmaceutical industry was subject to pressures not unlike those that brought an end to their former peers. Congress tried numerous times to place limits upon the profits these companies could earn. Legislators in the US called for the establishment of Canadian style systems of drug purchasing that might force the industry to accept lower profits. Others tried to establish a cap on the prices that
pharmaceutical companies could charge. Yet they never prevailed, each time the market shuddered and then resumed its march untroubled. Similarly, well-financed opposition arose to challenge the political prowess of pharmaceutical companies, as HMOs and insurance lobbyists bonded together to contest the classification of certain drugs and to alter the regulatory structure (Pringle 2003). Again, these adversaries were greeted with failure, the pharmaceutical profits unblemished. Even technological changes emerged to supplant their dominance, with biotech companies offering new ways of finding and producing medicines that traditional pharmaceuticals could not immediately replicate. Yet twenty some years after the birth of Genentech the pharmaceutical industry retains the highest profits in the world, while biotech sits idly on the margins. Over the last twenty-five years countless barriers have arisen to mitigate or even terminate the success of this industry, and yet unlike every other industry on earth, it appears unfazed: its profits unaffected, its future always brighter than the present.

The object of this dissertation is to offer both the casual reader an understanding of why the market for prescription drugs looks the way that it does—with the firms seemingly so profitable, the drugs so expensive and, the innovations so rare—and to offer the sociological reader a study of the relationship between environmental change and radical change within an industry. In order to meet both of those goals, the bulk of my chapters focus on specific moments in the history of the industry where events conspired to allow for radical change. To prevent this in-depth analysis of several key moments from coming at a cost to the larger story of the emergence and evolution of the industry, I bookend the three focused chapters with two chapters that take in a more comprehensive view of the history. In this chapter, I offer a brief history, explaining both the changes in the industry as well as the arrival of new regulatory efforts and new technologies. The intent is not to explore causal mechanisms or relationships, but rather to help create a context within which the reader can locate the subsequent in-depth discussions of specific events.¹ What is worth paying noticing in this brief history is both what has changed in the industry and what has remained the same. Most notably, while the organizational form of the individual companies and the structure of the industry changes, the success of those firms that come to be defined as pharmaceuticals remains fairly constant. It is this ability of the incumbent firms, once established, to mediate the more deleterious effects of the environmental changes that is worthy of additional scrutiny.

In 1790 the nascent federal government passed, “An Act to promote the progress of useful arts.” This elegant phrasing may be opaque to us today, but the law was the first attempt to create a patent system in the United States. This law established the interest of the federal government in encouraging innovation through the use of financial incentives, but it left open the question of what, exactly, should be patentable. Three years later Thomas Jefferson decided upon an answer and drafted a repeal of the original

¹ The seventh, and penultimate chapter, also adopts a broader perspective, expanding upon the previous chapters by comparing the effects of similar types of change at different points in time. The purpose of this chapter is to challenge the governing philosophy of pharmaceutical regulation and to estimate the degree to which similar kinds of political efforts yield comparable results. Together, these chapters work with the more detailed studies to create an accurate depiction of what transpired within this industry to produce the market we have today.
patent law that clarified both its purpose and its scope. Jefferson made an interesting choice, and one that would prove important to pharmaceutical companies, in rejecting the German model for a patent system in favor of a more open platform. The German system used high fees to discourage frivolous patents and set firm limits on what was a patentable object. For instance, they assumed that pharmaceutical innovation would not benefit from patents and therefore explicitly forbade the patenting of drugs or other products for “vital” industries. Jefferson opted for a different approach in both allowing patents for *everything* and in insisting that patent application fees be as low as feasible. This democratization of the process was intended to allow entrepreneurs, irrespective of their class origins, to benefit from their innovations.

However, it also helped structure the fledgling pharmaceutical industry. The low cost of patenting and the low threshold to achieve a patent, favored a pattern of behavior among drug companies where they patented every slight development and used patents to create artificial distinctions in otherwise identical products. For the next fifty years, the pharmaceutical industry was defined by its low cost of entry. This meant a crowded market of producers, the majority of whom only manufactured one or two products, with material costs and advertising costs occupying the largest portion of their investments. Research was non-existent, and profits were too low to allow any one set of firms to achieve the economies of scale that might have allowed greater growth. The industry, at this point, was not much of an industry at all, but was really just a scattered array of local compounders and the drugs they produced were equally unimpressive (Temin 1980b p 26).

This first attempt to improve this situation occurred in 1848 with the passage of the Drug Importation Act. This act addressed one of the obvious limitations of an unregulated drug industry: you never know what you are buying, by testing imported drugs for adulteration. It is interesting to note that customers and doctors remained confident in their ability to distinguish effective from ineffective medications, and did not therefore demand tests for safety or efficacy. Instead, they only wanted help ensuring that they actually received what they aimed to purchase or prescribe. At this point, the onus was upon the patient or the doctor to make determinations of safety and effectiveness, government operated only to prevent “cheating” in the form of adulteration. The assumption was that individuals and their physicians were capable of recognizing useless products, just as they could for other industries, and that market forces would drive ineffectual products out more quickly than regulation could.

Unfortunately, the market structure *encouraged* adulteration as firms, incapable of earning large profits in a market so crowded by indistinguishable goods, sought to increase their earnings by diluting their products. As a result of this structure, pharmaceutical profits were based on cutting manufacturing costs—not on the innovation of new medicines—and the easiest way to reduce those costs was to dilute their medicine with low cost “filler” products and thereby increase the volume of their supplies. This practice was so rampant that the Navy simply opted to compound its own drugs rather

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2 The Germans would amend their patent system in the 1890s to create a parallel “utility patent” for a wide range of products.
than risk placing their trust in the commercial markets. A reasonable decision given that, following the act, Massachusetts officials found that 37% of all imported drugs were adulterated (Hilts 2003) p 25).

For the next sixty years the products remained unreliable, the market remained unprofitable, and the firms continued to focus on developing manufacturing advantages. When innovations, like morphine or insulin, did occur they happened at universities that then licensed their ideas to neighboring manufacturers. The firms had few incentives to develop research capacities of their own, as the crowded market favored cheap production or good advertising over the therapeutic gains that would be difficult to demonstrate, let alone prove.

This began to change in 1883, when Dr. Harvey Wiley was appointed the chief chemist at the Bureau of Chemistry, that the campaign to remove all adulterated products (not just those manufactured abroad) began in earnest. At this point there was not yet a Food and Drug Administration, and the only federal laws governing the behavior of the drug companies were those listed here concerning patents and the importation of adulterated goods. As a result, Wiley’s team found that both food and drugs were routinely diluted: peas, beans, and soap were mixed in with chocolate, chalk and clay added to flour, lice carcasses included in brown sugar (Hilts 2003) p 22). These discoveries, aided by the publication of Upton Sinclair’s *The Jungle*, and exposes published in *Colliers* and *Ladies Home Journal* helped persuade 10 states to pass laws regulating food and drugs, and set the stage for the 1906 Food and Drug Act.

This law, the first to explicitly target the sale of American-made pharmaceuticals required that drug ingredients be published and established penalties for firms found to be selling misbranded products.3 Despite the seeming harmlessness of the act, it was not without opposition as manufacturers claimed that the actual cost of listing ingredients was too high and that the indirect cost to their business could be enormous. By indirect costs, the manufacturers explained that, while their products were harmless at worst and likely beneficial, listing the ingredients would confuse ignorant consumers and cause them to decline purchases they otherwise would make. In other words, they argued that this information was just enough information to prove dangerous, not helpful, to patients. Better then to keep them ignorant longer. Unsurprisingly, this argument won few fans in Congress and the bill passed quickly and to great publicity, with the New York Times declaring the new Food, Drug, and Insecticide’s first commissioner, Dr. Wiley, “…the man who has about the strongest hold on the American people today.” (1911a)

Despite the fanfare, the effect of the law on the pharmaceutical industry itself was more muted. Firms quickly learned that the way to maintain a profitable level of ignorance among their customers was simply to list incomprehensible ingredients.

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3 The law is, in many ways, an early attempt at regulation via a “deterrence effect” rather than through strict enforcement. This was partially because the law itself was fairly toothless: a $500 fee for any first offense, and $1000 for additional offenses. Second it was due to the fact that the Bureau of Chemistry was severely understaffed and underfunded to truly undertake such a large venture. The law therefore worked by creating a public uproar and the specter of enforcement, using their uncertainty to force firms to change.
Further, the law did not prevent unproven claims, it only required the proper labeling of ingredients. Therefore, when the new FDA agents seized “Johnson’s Mild Combination Treatment for Cancer” the Supreme Court ruled that the seizure was in violation of the law as there was no law prohibiting a manufacturer from claiming they had cured cancer or any other disease (1911b).

The most direct effort to change the behavior of the industry came in 1917 when the Alien Property Custodian, acting on behalf of Woodrow Wilson, sought to improve the state of innovation in the industry by eliminating competition from the Germans. As he wrote in his final report,

“In medicinals very little real American manufacture existed…The idea was accordingly conceived that if the German chemical patents could be placed in the hands of any American institution strong enough to protect them, a real obstacle might be opposed to German importation after the war, and at the same time the American industry might be freed from the prohibition enforced by the patents against the manufacture of the most valuable dyestuffs.”(Palmer 1920) p 38).

However, as will be discussed in the next chapter, this too proved unsuccessful in changing the character of the industry. By separating the American divisions from their German owners, it helped establish an American industry and helped to “Americanize” firms like Merck, Schering, Scherer and others, but the firms themselves resisted the opportunity to move towards greater innovation and continued to focus on manufacturing advantages.

These repeated failures and the frustration of the, renamed, Food and Drug Administration (FDA) officials lead to more public cries for reform. It was clear, by 1933 that the market for prescription drugs was not going to produce quality medicines of its own volition, some external aid was going to be necessary. With this in mind, Senator Copeland (D, NY) introduced the first revision to the 1906 Act, seeking to require additional tests beyond merely the proper labeling of ingredients. As is often the case, the bill was weighted down with amendments and stuck in committee for four years before it even reached a vote. By 1937, Senator Rees (D, KS) spoke out in frustration over the lengthy delay to pass a bill designed only to improve public health, “…this bill was amended and emasculated to a considerable extent by the Senate committee, as well as in the Senate. The bill passed the Senate, with amendments, more than a year ago. Since that time, it has been in the hands of the House Committee on Interstate and Foreign Commerce.” Rees continued to criticize the efforts of both parties to reduce the safety requirements, “…but I think I can say, without contradiction, that in nearly all cases where amendments and change have been made in this bill, that they have not been made in the interests of the consumer.” (1937)

But these efforts to delay and diminish the new drug bill came to an end when, in February of 1937, 107 people—the majority of whom were children—died because they consumed an unsafe medicine. The medicine in question was manufactured by Massengill & Co. of Tennessee and had been artificially sweetened in order to be more appealing to children. Unfortunately, in order to create a liquid version of this sweeter sulfa drug, the company used diethylene glycol, which per the law, they properly
included on the bottle’s list of ingredients. Unfortunately neither they, nor their consumers, realized that diethylene glycol was poisonous. The public outcry over the deaths of so many children grew even more fevered when it became clear that the unstructured regulatory environment would limit prosecution for this crime. In the end, the most severe penalty the FDA could pursue was “misbranding” which carried a penalty of $26,000 or, roughly $250 per child.

Driven by a tide of public outrage, the 1938 Amendment to the Food and Drug Act was resurrected and passed in quick succession. This law required, for the first time, that drugs be proven safe before they could be sold. Amazingly, and despite the public hostility, pharmaceutical interests succeeded in delaying the actual enactment of the legislation until 1940 because, they claimed, too many labels had already been printed (for drugs of unknown safety) and it wouldn’t serve the public interest to have them refashioned. So it is not until 1940 that American patients could be certain that the drugs they take to cure them would not actually kill them instead. A drug industry which was first regulated in the late 1700s, continued into the mid-20th century before there were any assurances that the medicines they offered were safe to consume.

The new laws have a remarkable effect on the industry, introducing a significant new cost to production—as all drugs now had to demonstrate evidence of safety—but they also transformed the relationship between patients and doctors. The law essentially told the public that neither they, nor their doctors, had been able to effectively determine the safety of drugs. As the Massengill tragedy demonstrated, the market had not succeeded in this regard, and therefore government was required to step in. While the regulatory efforts remained focused on the question of how to remove bad, or dangerous, drugs from the market the effect was to force pharmaceutical firms to begin to produce better drugs. Interestingly, the law also had a number of smaller clauses that less intentionally but more directly influenced the future behavior of firms.

First, the law required that drugs list both their potential dangers and their usage instructions, unless they were first prescribed by doctors. In other words the law assumed that despite the earlier problems, doctors were actually sufficiently aware of the dangers a drug may pose that there was no need to remind them. Firms quickly recognized that this meant that prescription drugs would face less scrutiny than non-prescribed drugs and would be less affected by any potentially damaging results of the safety studies. As a result, between 1936 and 1949 prescription drugs went from 25% of all pharmaceutical sales to 60%, rising to 83% by 1969 (Temin 1980a).

Second, the law provided the FDA with only 60 days in which to make a determination about the safety of the drug. It also assumed that the drug was safe, unless the FDA was able to demonstrate otherwise. This gave firms an incentive to delay, obfuscate, and harass the FDA until the deadline had passed rather than risk the uncertainty of a thorough investigation. Together these aspects of the new law had the cumulative effect of moving pharmaceutical firms towards the pursuit of more innovative drugs rather than merely pursuing manufacturing advantages, but it also taught them to focus their attentions on doctors rather than advertising to the public at large and it established a pattern of behavior where it was in the pharmaceutical firms interest to stifle the efforts of the FDA rather than to aid them. This helped establish the adversarial
relationship between the FDA and the pharmaceutical industry but it also gave the pharmaceutical industry the immediate advantage, and thus little reason to advocate for a different system.

While it may seem self-evident that a regulatory agency and the industry it scrutinized would adopt adversarial positions, this is not necessarily the case. If, instead, the law had been structured to place the burden of proof upon the pharmaceutical firms, and assumed that drugs were unsafe unless proven otherwise. Then, the firms would have been incentivized to work with the FDA to develop fast and efficient tests of safety. While some degree of evasion/corruption would certainly have remained, the firms would not have benefited from undermining the FDA, but would instead have needed to work in partnership with them to achieve greater sales. It is interesting to note that this initial contentious condition remained in place over time then, even as the laws themselves were changed in order to reduce the number of conflicts and to improve the degree of partnership.

The most radical changes in the industry, which helped concentrate the number of firms and moved the industry firmly away from process innovation (the pursuit of manufacturing gains) and towards product innovation (the pursuit of new products) would occur during the next decade. The causes of this development are explored in detail in the following chapter, but the effect was to produce, by 1950 a modern industry organized around a handful of large, innovative, and very profitable firms. Whereas in 1940 the firms remained regional, small, and manufacturing focused, by 1950 these scattered companies competing to find cheaper ways to produce similarly useless drugs had become the pharmaceutical industry we have today: large, profitable, and innovative.

The 1950s saw three developments that appear, at first glance, important in cementing this new industrial structure but, in reality, only had a limited influence over the development of pharmaceutical firms. First, in 1951, the Durham-Humphrey Act passed requiring prescriptions for drugs that cannot be safely used without medical supervision. This act, which formalized the increased authority of doctors, and helped push patients entirely out of the process of deciding which cure to take, was a major reversal from the 1930s in which patients were believed capable of deciding not just which drugs to take, but were considered the best way to determine drug were safe and effective. However the law only expedited a process begun with the 1938 act. Later, that same year, the Celler-Kefauver Act passed expanding the Clayton Anti-Trust Act and serving to curb monopolistic mergers and acquisitions. As both Davis and Fligstein have shown, this moved corporations to diversify and adopt a “holding corporation” mentality. However, as seen in chapter six, the effect was not as pronounced or as widespread within the pharmaceutical industry. In fact, while most firms did diversify, nearly all continued to acquire firms within the industry and to do so without penalty. Finally, the patent laws were amended to clarify the scope of discoveries that qualified for a patent, raising the bar for innovation in all fields, including pharmaceuticals.

In fact, the only significant change in the decade came at the very end when, in 1959, Estes Kefauver began his investigation of the price of drugs. Concerns over the high price of prescription drugs had begun again in 1952 when Congressional hearings debated the “fair trade laws” and examined the profits and prices of seven of the largest
drug companies. This was exacerbated in 1958 when a Senate subcommittee realized that all the manufacturers submitting bids to produce the polio vaccine had submitted identical bids that were nearly 2 ½ times the cost of production. Further study by the FTC revealed a similarly identical, and highly profitable, pricing scheme for the government contracts for tetracycline.

The tetracycline case was particularly interesting to the public as it showed that the prices had risen over time, and in identical increments, while the manufacturing costs had fallen. In fact, at every stage of the “blind” bidding process the various firms manufacturing tetracycline were within $0.004 of each other, even as they kept raising their prices, while a rival Italian firm offered a bid less than 1/3rd of the price of the identical US bids. Although the pharmaceutical companies claimed price-fixing was too difficult for them to manage, Congressman Holfield (D, CA), responded, “It has been suggested that a price-fixing conspiracy in polio vaccine is unlikely because voluntary price reductions were made. Actually, the fact that identical price reductions were made by all companies at the same time tends to prove rather than disprove the existence of a conspiracy.”

All of this helped set the stage for Sen. Estes Kefauver (D, TN) a one-time Vice Presidential candidate, to introduce an amendment that threatened to radically alter the structure of the industry. The specifics of Kefauver’s bill (S 1552) are discussed in a later chapter, but the consequence of the bill was to finally require drugs that all drugs first be proven effective before they could be sold. This further raised the cost of entry, firmly protecting the established firms from new challengers, as any new drugs would now require several rounds of costly tests to demonstrate both their safety and their effectiveness before they could be sold. This law also continued the previous pattern of focusing more on the removal of problematic drugs than on the ways to facilitate the creation of better ones. But the effect for the industry was quite clear: by removing the possibility of profiting of ineffective, but well-advertised drugs, the law helped usher in an era where the focus was firmly on the creation of “blockbuster” drugs.

This stage, where firms shifted their research entirely to the creation of new drugs and began developing an expertise in navigating the approval process, while simultaneously being protected by this process from the introduction of new competitors, persists through the present day. Following the enactment of Kefauver-Harris, the last vestiges of the old manner of production were gone and firms that existed on the fringes of the industry were absorbed by others, or reimagined themselves as consumer products companies rather than drug companies. However, this does not mean that the industry

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4 Abbott Laboratories; American Home Products; Merck; Parke, Davis & Co; Sharpe & Dohme; Squibb; Sterling Drug
5 Ironically, this issue became more salient after the pharmaceutical firms complained publically that soliciting bids from foreign manufacturers was “un-American.” Their attempt to capitalize on the jingoism of the day back-fired as the military returned the complaint, suggesting that the identical—and sky-high—prices the US firms were charging the armed forces for necessary medicine was itself perhaps not as patriotic an act as they might claim.
itself ceased to evolve, while these laws built the foundation, several final changes explain the specifics of the contemporary market.

The next of these environmental changes arose in the 1970s when pharmacists challenged the role of doctors in selecting drugs for patients. This decade-long contest, recounted in a later chapter, focused on the role of generic drugs and the professional authority of both doctors and pharmacists. The object was to redesign the process of drug-selection and to open the door for greater generic competition, and price savings. Although the debate raged for years, with PhRMA threatening an end to innovative practices and politicians promising savings in the hundreds of millions, the end result was a change in the environment but not in the market. And despite the shift in the role of doctors and pharmacists, going into the 1980s, the pharmaceutical industry was organized, and operated just as it had been for the past thirty years.

Two things caused this to change in the 1980s: the arrival of biotechnology and the arrival of generic drugs. Although the bulk of the press has focused on the former, there is no question among executives of the era about which was more relevant to the fortune of the industry: it was generics. While the Bayh-Dole Act, in 1979, facilitated the movement of University discoveries into the private sector, opening the door for firms like Genentech, Chiron, and Amgen. It was actually the later Hatch-Waxman Act, in 1984, that reshaped the industry by reducing the restrictions on generic drug introductions and fundamentally altering the role of product competition.

This counterintuitive claim requires some explanation. After all biotech firms received unprecedented attention from venture capitalists and the popular press, while generic firms won over few investors and fewer accolades. But both bills, along with the 1983 Orphan Drug Act and 1986 Technology Transfer Act, were part of the same fundamental shift in philosophy, and therefore had some similar features. Previously, as mentioned earlier, the focus of social pressure and the goal of political change was to reduce or eliminate dangerous/ineffective drugs. Little thought was given to the manner in which government might function to increase the number of innovative drugs. However, this began to change in the 1980s as patient-advocacy groups found ideological common ground with entrepreneurs and demanded a new role for government: support for better drugs. 6

In this fashion, Bayh-Dole operated by removing barriers to entry, in theory, allowing a host of dormant ideas to become viable products. Thus the object of the legislation was to help introduce new drugs that were being restrained by outdated regulatory structures. While this succeeded in facilitating the creation of hundreds of

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6 The Orphan Drug Act, in 1983, offered firms tax credits for research and direct aid for clinical trials on drugs that targeted diseases with populations under 200,000. There was a belief at this time, which later proved accurate, that firms possessed a number of potentially viable cures to rare (or “orphan”) diseases, where the potential sales did not outweigh the costs of approval, so the drugs sat idle. Faced with the evidence that drug companies simply did not produce cures for a host of “unprofitable” diseases, Congress acted to incentivize this research, again recasting the role of government as something more than a check on corruption, while still remaining committed to the notion that the market could yield answers, provided the imperfections were remedied.
biotech firms and technology ventures across the country, the impact on the pharmaceutical industry itself was more limited. First, most of these firms lacked the skills required to acquire approval, to market, or to manufacture their drugs. Those that attempted to act independently took years, even decades, to bring their drugs to the market. The firms that wanted faster approval, and more immediate returns, had few options but to seek out alliances with the industry titans: the incumbent pharmaceutical firms. In this way, pharmaceuticals were able to hold off biotechnology firms, to wait and assess their potential before investing and it explains why the earliest adopters, firms like Upjohn or Eli Lilly, were not significantly more successful in the short or long term than the firms that were more cautious in their approach. Second, in the initial stages (and by some accounts until the late 1990s) few biotech drugs threatened the viability of pharmaceutical products. For the most part, these were complementary goods, not substitutes, offering new cures for diseases without reducing the existing sales of the incumbent firms. Invariably, the incumbents opened biotech divisions and moved resources into these new arenas, but this occurred slowly and echoed the patterns found in earlier technological discoveries. Firms did not exit as a result of the arrival of biotechs, profits did not plummet, organizations were not recast, and the everyday operation of individual firms changed only slightly.

Hatch-Waxman however, sought to improve the quality of drugs by increasing competition. This law significantly lowered the barriers to entry for generic drugs, by allowing them to reach the market if they could demonstrate chemical equivalence to existing drugs. Previously the generic firms had to undergo the same rigorous tests of safety and efficacy that brand-name firms went through, but without the promise of great profits to entice them few firms accepted the challenge. Interestingly, several scholars have argued that the law did little to reduce the price of drugs (the original intent) but that it instead worked to increase product competition (Grabowski and Vernon 1992; Scherer 1993). In essence, they find that without generic competition firms had enjoyed extended, almost indefinite patent protection. Hatch-Waxman forced firms to recognize the actual patent limits and to introduce improvements as the patents were ending, rather than face competition from generics. In this way the Hatch-Waxman Act increased pressure on the incumbent firms to develop new ideas, rapidly escalating the pace of important new discoveries (as shown later in the dissertation) without actually reducing the overall cost structure. Either way, this law created changes both in firm behavior and in the number and frequency of new drug introductions.

The final significant change to the industry began in 1990 and, as had been the case previously, required nearly a decade of debate prior to enactment. The recession of the early 1990s reintroduced concerns over the cost of drugs, and their role in the rising costs of Medicaid. Congressmen found an easy villain in the form of the pharmaceutical companies, who continued to report record profits even as the rest of the country staggered. This lead to multiple bills in the early nineties trying to restructure the prices Medicaid paid for drugs, a practice that increased as Bill Clinton assumed the White House and promised a complete reform of health care. In response to this a number of firms, including Merck, introduced voluntary price reductions. The firms also responded to the accusations of high prices by claiming that FDA delays were forcing the high prices, but reducing the effective patent life of a drug. In 1992 these dueling claims lead
to the passage of the Prescription Drug User Fee Act (PDUFA) that introduced drug application fees that would be used to hire additional reviewers, thereby expediting the process. In essence, the law transformed the pharmaceutical firms from applicants to subsidizers of the approval process. This lead quickly to reductions in the review times for drugs, though not surprisingly, it did not lead to corresponding price reductions. While the subsequent political upheaval lead to the introduction of several bills attempting to eliminate the FDA (either in actuality or effectively), these bills were no more successful than their counterparts in the late 1970s. In the words of Senator Paul Wellstone (D, MN):

“I think there were some [pharmaceutical companies], this now goes back probably 2 years or so, who really looked at this as an opportunity to privatize FDA, roll back the really important consumer protection provisions. I think that is over.”

However, while it did not succeed in removing the FDA, PDUFA remains important because it was during the renewal process in 1997, that the FDA reversed course and allowed for the direct advertising of drugs to consumers. Concurrent with this was the introduction of a graphical interface for the web in 1995, allowing for the rise of the internet as it is presently known (as opposed to the internet used by academics and the military during the 1980s). These two most recent changes in the market have been the subject of much scrutiny and consternation. While the long-term effect is still being debated, it is clear that the short-term effect has been to reduce the authority of doctors and to reintroduce patients to the process of selecting their medicines, a process that regulation had effectively removed them from since 1938. Whether or not that will bring about the reorganization of firms or the introduction of specific types of medicine at the cost of others, is still to be decided.

**Selected References**


Abstract

A Healthy Business: The evolution of the U.S. market for prescription drugs

by

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Two central questions motivate my dissertation: First, how do variations in the political, social, or technological environment produce changes in the organization and orientation of pharmaceutical firms? Second, do these transformations alter either the kind or quality of new drugs that reach the market? To answer these, I study how the market originated in the 1940s and how the social, economic, and political pressures of the subsequent decades molded the firms and their orientation to produce both the market and medicine that we have today. The research combines interviews with pharmaceutical executives and archival research into corporate histories, along with previously unexamined accounts of the government’s role in establishing a more robust industry in the 1940s, to motivate a series of hypotheses. These hypotheses are tested using time series and event history methods on organizational and financial variables for the population of pharmaceutical firms between 1935 and 2005. The findings help explain the ability of pharmaceutical firms to mitigate the consequence of environmental changes and to reproduce their market, and their profits, despite the repeated intervention of powerful actors.
Chapter One: An Introduction

There are no new complaints about the pharmaceutical industry. In the 1840s people worried that drugs were too expensive, by 1900 newspapers warned that the era of innovation was over, by 1930 Congress felt compelled to hold hearings over the price of drugs, and by 1950 they thought mergers had left the industry too concentrated. Despite their fevered pitch and hints of impending doom, every single fear raised in 2010 about the plight or dangers of the pharmaceutical industry echoes verbatim the words of someone speaking as much as a century earlier. This unending litany of complaints can be distilled to one irrevocable fact: No one likes the market for prescription drugs in the United States, and no one ever has. This raises the question my dissertation seeks to answer: Why do we have the market for prescription drugs we have today?

The answer, I will show, is not the result of either a linear path of technological and scientific progress, or of mischievous and crooked politicians meddling with the proper function of a market. Instead, today’s market is the direct product of the erratic and occasionally irrational series of organizational responses to technological development, political change and, social pressure. To understand the emergence and evolution of this market is to examine the workings of a field: the relationship between actors from industry, politics, and medicine as they fought to advance their, ever-changing, notion of a more perfect market for health. The dissertation will focus on two particular aspects of this issue.

On a theoretical level, my interest is in the mechanisms that enabled some environmental change (e.g. technological development, political change, or social movements) to transform the industry, when others did not. This is a question that has received scant attention in the past, as the prevailing view of industrial behavior assumes firms are actors, responding as quickly as possible to the stimuli of their environment. Therefore, if you change the environment, by say threatening to enact price controls or require mass licensing of new drugs, firms will respond accordingly. This anthropomorphic vision of industry suffers from many limitations, but for the moment I will focus my attention on just one: it fails to explain why some changes are stimulating and others pass unnoticed. It is my intent to help remedy that through a careful study of both the environmental shocks that produce radical change in the industry and those that do not.

On a policy level, my interest is on the effect of these environmental changes on the kind or quality of new drugs developed. By offering a chronological account of the major environmental changes and the manner in which these did, or did not, render a change in the field, I hope to address both aspects of this issue and to answer the question of why we despite the best efforts of so many concerned people over so many decades we sit here today stuck with a market so despised even more.

Summary

Things were not always as they are today. In fact, as late as 1930, the U.S. pharmaceutical industry was so small a part of the U.S. economy that to even call it an industry required some imagination. Even Moody’s, which for over 100 years offered an
annual analysis of every major industry in the United States, did not include any mention of a U.S. pharmaceutical industry. Through the 1930s, pharmaceutical firms were peripheral businesses, a branch of the chemical industry, or the indulgence of a few cosmetic firms, but not an industry that anyone expected would amount to anything.

The American pharmaceutical companies of this era were regional, unprofitable, non-innovative firms that manufactured and distributed other people’s ideas. Few offered products of genuine therapeutic value and even fewer would still be in business in twenty years. But, by 1950, everything was different: out of a sea of hundreds, a handful of firms emerged to define a new American pharmaceutical industry. These firms were large, innovative, profitable, and so impervious to challengers that no new firms would ever surpass them. For half a century, this same collection of firms, that had only recently been an afterthought in the American economy, would survive every political, technological, and social challenge to become the most profitable industry in the world (Scherer 2001; Silverman and Lee 1974; Thomas 1990).

This dissertation examines the emergence and evolution of this, the U.S. pharmaceutical industry. The object is to clarify the mechanisms that allowed these firms to frequently mitigate the effect of dramatic technological breakthroughs, radical shifts in policy, and constantly shifting social norms to remain the most profitable industry of the last fifty years. Through this I aim to distinguish the characteristics of the changes they were able to mediate from those they were powerless to stop. Specifically, my dissertation proposes to answer two related questions. First, how did the political, technological, and social changes alter the organization and orientation of pharmaceutical firms? And second, what effect did this have on the kind and quality of medicine that is produced?

To answer these, I explore how the U.S. market for prescription medicine emerged during the 1940s and how it evolved with the passage of regulatory reform, the development of new technologies, and the changing social dynamics of the country. In particular, I am interested in whether these shifts altered who could compete, how they were organized, what they competed for, and what the result was for patients in the U.S. The chapters progress chronologically, tracing the impact of each decade’s environmental-level changes on firm and industry-level effects. As such, this research sits at the intersection of economics, sociology, public policy, and public health; and incorporates both organization theory and economic sociology to orient the approach. Methodologically, I combine archival research, interviews, and historical accounts with quantitative analysis of firm financial and organizational data, looking specifically at the population of publically traded firms between 1935-2005.

This work has three significant potential contributions. First, theoretically, this offers a rare opportunity to examine the mechanisms that translate an exogenous shock into a paradigm shift. Most studies offer historical snapshots and thus, focus exclusively on the environmental shocks that elicit changes at the organization or industry level (Greenwood and Hinings 1996; Meyer 1982; Meyer, Brooks, and Goes 1990). This both overstates the degree to which these shocks matter and limits our ability to discern what it is about a given shock that enables it to be transformative or not. By conducting a study of the evolution of the field, we see both how a variety of shocks erupt and are dealt with
by the actors within the field, occasionally reducing and occasionally increasing the anticipated effect of the shock (Davis and Marquis 2005). This type of work allows us to understand the relationship between the actors within the field and the political, technological, and social change that attempt to recast the field.

Second, politically, this work improves our ability to understand the effect of regulatory shifts on innovation. While the pharmaceutical industry has been subject to countless investigations by economists and public health scholars, these works have similarly focused on the effect of a single policy at a single point in time (Danzon and Chao 2000; Dranove and Meltzer 1994; Grabowski and Wang 2003; Olson 1994; Thomas 1990). Further, they focus almost exclusively on the question of whether a policy increases access to drugs or decreases the financial incentives to innovate (DiMasi, Hansen, and Grabowski 2003; Dranove and Meltzer 1994; Olson 1997; Scherer 2001; Wardell and DiRaddo 1980). The unquestioned embrace of the “access vs. innovation” frame distorts our understanding of the real trade-offs at work in pharmaceutical innovation by reducing the question of what stimulates innovation to solely the potential for profit. In so doing, we ignore the evidence that regulatory shifts operate to structure or direct innovative efforts as frequently as they act to reduce/expand the potential for profit (Misa 1985; Nemet 2009; Smith 1977; Smith 1985).

My dissertation offers a potential remedy for these oversights. Again, by examining the full historical context we can establish the range of policies available to and pursued by the federal government. This allows for a more robust examination of the relationship between regulatory shifts and innovative efforts than was available before. Further, by conducting a field-level analysis, we gain insight into the manner in which these regulatory shifts were adapted, mediated, and adopted by the various firms, allowing us to establish the full causal chain rather than just looking at outcomes and assuming they were policy-related. Finally, we are able to examine both the policy shifts that altered the direction of innovation for firms and those that had no effect to understand better the manner in which these regulatory changes alter innovation.

The third potential contribution is of a more practical bent. Prior histories of the pharmaceutical industry have been of two types: political and academic. While the political studies aimed at a popular audience and often railed at the presumed excesses of the industry, their analysis treated the pharmaceutical industry as an exceptional case from which little could be learned, except perhaps about the triumph of industry over public need (Avorn 2004; Greider 2003; Marsa 1997). The academic studies, acknowledge the value in using the pharmaceutical industry as a case, but then focused on either the effect of regulation (Temin 1979; Temin 1980a; Temin 1980b) or of industry-university relationships (Liebenau 1987; Liebenau 1985). Neither attempts to build on the work of Merrit Roe Smith (1977; 1985) and Alfred Chandler (2005) in using the pharmaceutical industry as a case through which to explore the emergence of high-tech industry within the United States. However, the pharmaceutical industry could serve as a valuable model for understanding the nascent green technology industry. Both, despite political support, economic demand, and rapid technological gains, struggled to establish themselves. Both serve vital public needs as well as offering tremendous economic opportunities and; the development of both industries has been buffeted by
political, social, and financial actors seeking to establish their own position as the dominant paradigm. For these reasons, I argue that a study of the emergence and evolution of the pharmaceutical industry can provide a necessary template to guide the emerging green technology industry, offering valuable examples of both what we should and what we should not do.

Relevance for Theory

The role of institutions and networks in framing individual and organizational definitions of the meaning of “efficiency” is well documented (Dobbin and Dowd 1997; Dobbin and Sutton 1998; Fligstein 2001; Granovetter 1985). A shift in the governing concept of “efficient behavior” is one of several ways in which the equilibrium of the market is punctured. This can lead to the creation of a new role within an organization (Zorn 2004), the development of a new division within an organization (Dobbin and Sutton 1998), or a wholesale change in how organizations operate (Davis, Diekmann, and Tinsley 1994; Fligstein 1990).

Studies of similarly radical environmental changes have called these moments: “paradigm shifts”, “discontinuities” and “second order changes.” (Frickel and Gross 2005; Kuhn 1970; Tushman and Anderson 1990). The sociological studies have focused largely on how a field adapts to the new rules and norms. This focus on the openings created by change is evident in Fligstein’s work on the shifting “conceptions of control” that emerged in response to environmental changes and lead to differing views of the purpose of a corporation over time (Fligstein 1990). More recently, Dobbin and Sutton (2008) describe the creation of human resource departments as a response to uncertainty following regulatory change that was later recast as a move to increase organizational efficiency. These studies describe processes involve multiple actors advancing competing claims on the appropriate adaptation in response to change, they rarely describe why change failed to occur.

This contrasts with the studies of science and technology, which contend that organizations almost universally resist potential paradigm shifts. So Kuhn (1970) found that new scientific discoveries were met with disdain and indifference, occasionally even failing to supplant existing dogmas despite their superior explanatory power. Later Tushman and Anderson (1986; 1990) found that firms in multiple industries rejected technological advances even if they offered gains in efficiency. Instead, they found that firms capitalized on the uncertainty that accompanied new developments to suggest that the technologies would be costly, have dangerous unintended consequences, or fail to meet expectations. Christensen and Bower (1996) reached similar conclusions in his analysis of innovation in the disk-drive industry, finding that because established firms are less capable of radical innovation, they will resist the entry of these technologies to the mainstream market. These competing claims create the theoretical tension that motivates my interest: what determines whether an environmental change is capable of overcoming resistance to transform an industry?
Studies of the response to a punctured equilibrium have shown that technological (Tushman and Anderson 1986), political (Fligstein 2001), and social (Lounsbury, Ventresca, and Hirsch 2003) changes can create these transformative moments, but why these effects are inconsistent remains unclear. In essence, we have been less successful in understanding why a given shock punctuates the equilibrium than we have in understanding how a new equilibrium is created after a puncture. The intent of my dissertation is to refine our knowledge of the causal mechanisms by which environmental change catalyzes new behaviors in actors that, in aggregate, produces the evolution of a field. Specifically, I am interested in examining the relationship between political change, technological advancement, and social shifts in influencing organizations to adopt a new strategy, a new organizational structure, or a new understanding of what constitutes efficient behavior. To understand the relationship between these factors requires, as Davis and Marquis (2005) call for, a study located at the field level that undertakes to explore how an entire field evolves in response to such diverse challenges.

Three Stages of Change

The relationship between institutional, organizational and, product change is understood to be a three-stage process. First, a dramatic environmental change punctuates the equilibrium of the field (Baum and Singh 1994; Chandler 1977; Pfeffer and Salancik 1978). These exogenous shocks can take on a variety of forms ranging from the introduction of a new political regime to the innovation of a new technology (Galambos 1970; Galambos 2005; Lamoreaux 1985; Piore and Sabel 1984; Roy 1997). In the second stage, the shock isolates/segregates one set of organizations from another and splits the population (Baum and Singh 1994; Freeman and Hannan 1989; Stinchcombe 1965). This act results in a population of organizations divided into (1) a group that benefits from the changed environment and will now succeed at a greater capacity and (2) a group harmed by the change that may soon dissolve. In the final stage, surviving and entering firms adopt organizational features similar to those of the now dominant organizations. These firms no longer receive the benefits earned by the early-adopters, but they gain a necessary patina of legitimacy (DiMaggio and Powell 1983). Together this creates a clear picture where shocks create opportunities that allow adaptive or well-situated firms to advance, and follower firms mimic this behavior to gain public approval, resulting in a reconstituted market.

Stage One: The Exogenous Shock

The most frequently examined shock is a change in the political environment. Change in the regulations surrounding the industry, a change in the philosophy of regulatory enforcement, and change in the political regime have all been found to cause dramatic transformations at the population-level (Dobbin and Dowd 2000; Fligstein 1990; Roy 1997). In particular, Dobbin and Dowd (1997), in their study of Massachusetts railroad companies, find that different policy regimes establish different rules of competition leading to the creation of new types of economic behavior. They demonstrated that changes in policy create openings in which different groups vie to establish a new organizational form. In this situation, the introduction of new policies transforms the market and affects which companies succeed and which fail by favoring certain organizational forms over others. The introduction of an exogenous shock, by favoring
one set of firms and disadvantaging others, is sufficient to alter the population and produce a dramatic change in the industry.

Fligstein (2001) reaches a similar conclusion in his study of the relationship between institutional structure and the type of competition that emerges. He argues that exogenous shocks can cause participants to question the norms that govern behavior and attempt to establish new rules of exchange. The institutional changes encourage new types of competition, and incumbents rarely adapt quickly enough to survive and take advantage of the new opportunities introduced by the exogenous shock. Thus, each exogenous shock permits the rise of newcomers and creates opportunities to rewrite the hierarchy of firms in an industry.

Technological change has also been found to alter the organization of firms within an industry (Tushman and Anderson 1986; Tushman and Anderson 1990). In their study of the cement, glass, and minicomputer industries, Tushman and Anderson (1990) define the developments that uproot the industry as “competence destroying” innovations. These breakthroughs offer such drastic performance or cost improvements that new firms, better able to incorporate the ideas, were able to supplant their more established predecessors. In the pharmaceutical industry, Galambos and Sturchio (1998) find that the introduction of both biotechnology and penicillin produced similar transformative opportunities. In these cases firms had to reorient themselves to capitalize on the new technologies or risk obsolescence. As with penicillin, genetic research elevated the value of a particular kind of knowledge, this time biologic, and the firms that were able to access that knowledge were the firms that succeeded (Powell, Koput, and Smith-Doerr 1996).

Stage Two: The Selection of New Organizations

Following the emergence of a shock there is a momentary opening in the polity, a potentially exploitable space that did not exist earlier. In theory, the desire to capitalize on this opportunity, to expand either the domain of a group of actors within an organization or the status of the entire organization drives some set of actors to capitalize. It is the movement of these actors that initiates the second stage, where a subset of organizations benefit from the new environment and a parallel set lose out. And, just as multiple types of exogenous shocks can produce opportunities for change, different theories predict that different types of firms will be able to capitalize. This produces a range of explanations for how a field will transform following an exogenous shock.

The broadest question concerns whether firms succeed because they adapt to the new environment or because the environment selects them to succeed. Pfeffer and Salancik (1978) favored adaptation, contending that it is the ability to adapt to a new environment that determines whether a firm will survive over time. Change would then result from firms being either too slow or too inert to adapt their organizations to the new surroundings, producing a new field with different players (Porter 1980).

This explanation is also preferred by the business historians and economists who have studied the pharmaceutical industry (Temin 1979; Liebenau 1987). They demonstrate that the industry transformed as competition selected the most efficient organizations and
removed the remainder, altering the composition of firms in the industry over time (Chandler 2005; Grabowski and Vernon 1992; Mahoney 1959; Scherer 1993; Temin 1979; Temin 1980b; Thomas 1990). In this story, exogenous shocks offer opportunities that only the most efficient organizations are able to take advantage of. Organizations without foresight or sufficient resources are merely selected out of the field.

Hannan and Freeman (1977; 1984) countered this to argue that adaptation is both too difficult to correctly predict and to execute. Therefore, fields change as environmental conditions render extant firms unfit and permit the arrival of new entrants. However they acknowledge that there may be multiple explanations for why an organization is selected by the new environment. For example, Chandler's (2005) explanation that pharmaceutical firms succeeded they had made the proper organizational changes prior to political changes.

Additionally, organizations may be selected because they have economies of scale, or the size necessary to insulate them from change. In his remarkable comparison of the record and pharmaceutical industries, Hirsch shows how new regulations raised both barriers to entry and the cost of putting products on the market. This redirected the pharmaceutical business towards a “hit” factory, where they had to finance hundreds of misses in order to find the one “big hit” that brought them profit. This is a substantial change from the previous structure of firms, in which marketing prowess enabled the sale of many goods of dubious effectiveness. Thus regulatory and technological change required both size and profitability to sustain a firm through the long dry spells that come between the infrequent successes. Past organizational research has reached similar conclusions, showing that the most profitable and the largest firms are the most insulated from regulatory and technological changes and therefore are best able to survive in new environments (Baum and Silverman 2004; Carroll and Swaminathan 2000; Freeman, Carroll, and Hannan 1983).

**Stage Three: Legitimacy and Diffusion**

While industrial economists suggest that the field now returns to a period of incremental, rather than exponential, change; sociologists have long been interested in understanding a last stage (Still and Strang 2009). They argue that a two-stage process fails to explain the puzzling similarity of organizations across different fields. Therefore, in the third and final, stage the remaining organizations, those that survived but did not benefit from the change or those that entered following it, adopt organizational features similar to the now dominant organizations. The critical difference between this stage and the second is that the returns to adapting have now diminished and may even be negative. The first-movers captured all of the benefits of the environmental shock, so any delayed adaptations cannot be explained as being efficiency-driven. Instead, sociologists have found that organizations persist in mimicking industry leaders as a means to gain external legitimacy, even if the firms themselves redefine the actions as being motivated by gains in efficiency (Dobbin and Sutton 2008; Zorn 2004).

Multiple studies document this phenomena, including Davis et al. (1994) analysis of why firms adopted and then abandoned the conglomerate model when they had long known the model to be suboptimal. Here the authors demonstrate that Fortune 500 firms felt compelled to diversify, even though they knew it was unprofitable, because they
wanted to be perceived as legitimate. Later, their decision to abandon this conglomerate model is similarly not explained by new knowledge as much as it is by their exposure to other firms that also abandoned the model. Subsequent work refined the mechanisms of isomorphism, explaining both how organizations that deviate from their expected role are penalized (Zuckerman 1999), and the process by which these isomorphic tendencies diffuse. In particular, Davis’ (1991) study of the adoption of poison pills showed that firms were more likely to adopt if they shared directors than if they were just in the same industry.

However, all of these studies confirm that these secondary organizations must, and do, follow the industry leaders in adopting organizational changes after an environmental shock. It is this final stage that then reconstitutes the field. The shock had created an opportunity, which a few firms seize or receive, but mimetic isomorphism drives the remainder to follow until the entire field now follows a new direction. In this manner these exogenous shocks act as triggers for a series of events that transform the field. In the case of the pharmaceutical industry, we would expect to see that each shift has dramatic consequences for which firms succeed, how they are organized, where they invest their research budget, and what kinds of drugs they produce.

Exceptions to the Model

However, before we embrace this three-stage model, we need to acknowledge that the progression of a field is not always so linear. In fact, environmental shocks frequently occur without any corresponding change to the field. Studies in science and technology have shown that rather than embrace and exploit new opportunities, incumbents resist new developments, even those that offer potential gains (Kuhn 1970; Tushman and Anderson 1990; Tushman and Rosenkopf 1992). These studies emphasize the fact that an environmental shock ushers in a period of uncertainty, and incumbents often prefer to cast doubt on any supposed advantages of new developments in order to maintain the existing order. When this fails, rival factions seek to use the opportunity to expand their own personal domain, resulting in the adoption of unpredictable and often less-efficient outcomes (Dobbin and Dowd 1997; Fligstein 1990; Fligstein 1996).

By focusing our attention exclusively on environmental changes that produced corresponding radical transformations in the market, we have selected on the dependent variable and failed to explore what it is about a given shock that results in the production of a new market. To remedy this and to better understand the way that a given shock catalyzes a change in an industry, I classify each environmental shock according to its features and the level at which the resulting radical change should manifest.

A Typology of Change

Environmental change that occurs because a coalition of actors has enough social or political capital to demand/force change in the market, is an example of “political change.” For instance, the changes in 1997 to the advertising restrictions on prescription drugs served no medical purpose, nor was it requested by either patients or doctors, but it came because pharmaceutical companies acted in concert during a period when they held a lot of political capital. They forced the market to change and no one was able to resist their efforts, resulting in our present inundation of pharmaceutical advertising.
Alternately, change can also occur voluntarily, for instance, in order to realize gains in efficiency. This “economic change” explains organizational changes made by firms trying to capitalize on new technological developments in the 1950s, 1970s and 1980s. No one forced the firms to invest in different types of research, but technological developments made it inefficient not to, so firms elected to change to minimize their comparative disadvantage.

A third type of change, “cultural change” occurs when actors in a given market no longer accept the prior conditions or system of behavior. For instance, the decision, in 1970, by the pharmacist’s trade organization began to question the validity of anti-substitution laws served to challenge the legitimacy of the acting model for prescribing and distributing drugs. The pharmacists lacked the capital necessary to simply force this change, nor were the economic gains obvious enough to entice states to change, but the process created sufficient doubt to invalidate the existing model and create an opening for a new system that allowed for generic substitution.

To understand the process by which a market evolves, we must pair these different causes of an environmental shock with the type of change they are liable to produce: political/regulatory, technological, organizational, population. While reductive, these dimensions serve to focus attention on both the forces that help produce/define a type of shock as well as to clarify what changed in the environment as a result of this process.

As stated, most past studies of focused on the environmental changes that elicited organizational adaptations. This mitigates our ability to determine what enables a given shock to be transformative. By adopting a broader perspective, my research shows how technological, social, and political changes combine to produce (or fail to produce) new organizational practices, structures, and strategies. And finally, to explain how this translates into the creation of new types of products and new forms of competition.

This dissertation provides an initial attempt to fill the hole Davis and Marquis (2005) identify and to offer a more detailed analysis of the features of an environmental change that enable it to influence an organization or that prevent it from being influential. Second, my dissertation offers concrete links to show how these higher-level changes produce both organizational and product level changes. This is especially important in the area of health-care where concerns about the impact of regulatory change on product innovation have crippled attempts to reorganize the structure of the industry.

Method

To answer these questions I employ a mixed-method approach. Qualitative data gathered from company and government archives help establish which events possessed the potential to transform the industry. Complementing this research with transcripts from Congressional hearings helps determine the players, positions, and arguments used for or against a given political shift. Similarly, relevant industry journals, and the journals of related fields (e.g. the Journal of the American Medical Association) help establish the social norms governing the role of patient as consumer began to shift. Therefore, to determine which events to examine, I examined discussions of the pharmaceutical industry in the Congressional Record from 1930-2005. I also consulted

I complemented these historical reports with twenty one-hour interviews of past and contemporary pharmaceutical executives, lobbyists, and politicians, to determine the recent and future challenges seen as threatening the stability of the industry. This qualitative research then serves two purposes: to help identify potentially transformative events, as well as to explain the anticipated consequences of these events and the arrangement of actors on either side of each issue.

The significance of these events is then estimated quantitatively using time series and event history methods. My sample is drawn from the entire population of publicly traded pharmaceutical companies that were in business for some portion of time between 1935-2005. Event-history methods allow for the analysis of exit & entry rates; organizational adaptations; the adoption of new corporate roles; and the introduction of new drugs before and after each event. Time-series methods allow for industry and firm-level studies of variations in the rates of innovation, profitability, or size across different periods of time. Specifically, in these instances I seek to estimate whether organizations made changes in anticipation or as a result of environmental changes and whether those changes were sufficient to prevent a loss in stature for the firm.

To control for variations across firm, I gathered data on each firm’s financials, organizational structure, the year in which they were founded, whether they were a dedicated pharmaceutical company or a conglomerate, the backgrounds of their CEOs, the number of scientists, the year they first hired scientists, as well as information on their research and development practices (e.g. resources allocated, staffing, number of PhDs, etc…). Data were gathered from a variety of sources including Compustat, Census of Manufacturing, as well as PhRMA and firm annual reports.

Simultaneously, I collected data on the type and quality of new drug introductions over time. To demonstrate a relationship between the environmental changes, organizational adaptations, and variations in the kind or quality of new drugs introduced. Although measuring the “quality” of a drug is, at best, a difficult proposition, several methods are available to minimize error. Most notably, the Food and Drug Administration (FDA) itself classifies drugs as they are being evaluated according to a seven-part system with “new molecular entities” representing the most innovative, if not the most therapeutically beneficial of drugs. This data was made available through the FDA’s office of history.

**Chapter Overview**

As a study in the evolution of an industry, the remainder of the dissertation progresses chronologically with each chapter focusing on emergence and aftermath of a particular challenge. The second chapter begins with the creation of the modern pharmaceutical industry, exploring the rise of an innovative, profitable industry during the 1940s. This chapter addresses the question: What happened to permit an overlooked
division of a few cosmetic companies to become the nation’s most profitable industry? I combine historical research done at the National Archives with time series analysis on the population of public pharmaceutical firms to demonstrate the critical role a top-secret military penicillin program played in selecting and organizing the firms that constitute the industry.

The third chapter moves ahead twenty years to examine the repeal of the “anti-substitution laws” that prevented pharmacists from offering a patient any alternatives to a doctor’s prescription. The question here is why the conclusion of a decade-long political and scientific battle resulted in major legislative and social change without any corresponding change in the industry. I find that PhRMA’s alliance with the AMA gave them control over drug information and enabled them to mitigate the effects of this legal change, creating a confusion that overrode any economic incentives for patients or pharmacists to pursue generics.

The fourth chapter examines the organizational evolution of the firms within the industry, beginning with their curious decision to purchase cosmetic companies in the 1950s. Here I examine the effect of institutional legacies on the pharmaceutical firms responses to changes in anti-trust policy and the effect that had on their organizational structure.

The fifth chapter complements the earlier chapters with two-stage least square regressions that measure the impact of the political, social, and technological shifts on the rate of both firm and industry level innovation. This chapter demonstrates that debates over the influence of regulation on innovation have been unduly influenced by a mistaken belief in a trade-off between incentives to innovate and access to new medicine.

The final chapter offers my concluding thoughts and brings these disparate chapters together to create a comprehensive portrait of the emergence and evolution of this industry, and the role of different environmental shocks in this process.

**Expected Significance**

The present-day pharmaceutical industry is the result of ceaseless alternating attempts to solve the same set of problems. However, although each policy and technological change has been, individually, subject to rigorous analysis by economists and public health scholars, without a more comprehensive picture it is difficult to understand the evolution of the industry. Simply put, the only way to make sense of the modern market is to uncover the choices and risks that brought it into being.

This type of historical, field-level analysis, quickly undoes any expectation of a linear, cause-effect, style story. The market is unlike a stream that can simply be diverted in a new direction by policy or technology and then later re-routed to serve the interests of society. The market is a raging river, and every attempt to redirect it is fraught with complications, a high probability of failure, and the understanding that the consequences of action will be hard to predict.

As such, the history of this industry is marked by numerous costly, lengthy debates over seemingly vital issues that end in legislation both hailed and decried, but
initiate no change. It is not that political, technological, or social changes have no impact on the market, but rather that their impact is highly variable and unpredictable. When we compile a history of the field, it becomes clear that actors frequently engage in resistance against change and that, not infrequently, they succeed. We see how coalitions of actors shift, how the perception of an appropriate response evolves, and how the preferred organizational form, activity, and role all fluctuate with the environment their in.

This raises a series of critical questions: How do we explain the evolution of a market? What distinguishes those times when an environmental change radically alters the market from those when it has a more marginal effect? How capable are actors of resisting these changes or in causing self-serving change? The only way to understand these, and to understand the modern pharmaceutical industry is to examine the success and failure of previous attempts to change the industry. I chose the case of the pharmaceutical industry in the US because for so many people it is particularly unclear how we ended up with the market for prescription drugs that we have, and whether there might be a better solution available to us.

A study of the evolution of the U.S. market for prescription drugs allows us to understand precisely this process by which markets are established and recreated by a host of different actors. How changing norms of physician-patient interactions, and altering the economic incentives for innovation, affect the efforts and interests of pharmaceutical companies. And, how and where organizations succeed in mediating environmental change. As such, this project has potential implications on three levels: theoretical, political, and practical.

Theoretically, the dissertation attempts to clarify the relationship between environmental, organizational, and product-level changes. While prior studies have repeatedly examined the effect of institutional and political change, the focus on environmental changes that elicited organizational responses may have caused us to overstate the degree to which organizations react and underestimate their ability to mitigate or resist change. What I propose is a systematic study of how different types of exogenous shocks (political, social, and technological) compare and via what mechanisms they produce their effects at both the organizational and product level.

This will contribute a clearer picture of the mechanisms by which environmental changes influence organizations as well as the methods by which these influences are mediated. Further, by comparing situations in which exogenous shocks yielded no effect with those instances when firms were forced to drastically reorganize, we better understand what features of a shock precipitate change. This has relevance both for economic sociologists interested in the formation of markets as well as for organizational theorists interested in the relationship between changes at different levels of organization.

Politically, this work will provide a valuable test of the influence of regulation and social change on innovation. Prior examinations of regulation and innovation in the pharmaceutical industry have focused exclusively on the question of whether regulation decreases or increases economic incentives. By adopting a historical perspective we can better analyze the actual effects of different regulatory regimes on the innovative efforts
of firms. Further, the question of “How did we get here?” can only be answered by first looking back to understand the decisions, controversies, and compromises that lead us to produce the market for prescription drugs we have today. Given the Obama administration’s ambitious health care agenda, and the ever-present concern over how best to “fairly” compensate pharmaceutical companies while ensuring access to medicine, a study of this kind is all the more necessary.

Finally, on a related note, this study has practical implications for how health care is distributed in America. By clarifying the relationship between technological developments, social changes, policy reforms and the kind and quality of drugs produced, we expand our understanding of the factors that motivate drug discovery. The current paradigm, that declares a zero-sum game between “access and innovation”, requires that greater rates of innovation must cost people access to drugs. Any attempt to add nuance to this debate has practical consequences for the additional people able to receive access as well as for the creation of more innovative medicines.
Chapter Two: Re-Making the Market

In 1940 the American pharmaceutical industry was composed of several hundred small, regional companies. Few of these companies were profitable, fewer offered products of genuine therapeutic value, and even fewer would still be in business in twenty years. By 1950, everything was different: out of a sea of hundreds, a handful of firms emerged to define the American pharmaceutical industry. These firms were large, innovative, profitable, and together they accounted for the majority of the entire industry’s sales and profits. Moreover, while the pre-1940 industry was marked by intense competition and turnover, with no one firm maintaining an advantage for any length of time, the firms that were the largest and most profitable in 1950 would remain the largest and most profitable in the industry for the next fifty years (Thomas 1990). Understanding what happened during this ten-year period to elicit such a dramatic change will be the object of this paper. Through this case I hope to address two questions: How does an industry transform from non-innovative to highly innovative? And, how does a diverse and competitive industry come to be dominated by a few large firms?

Similar dramatic transformations have been explained, by sociologists and organizational theorists, as the product of political, technological or, social changes (Dobbin and Dowd 1997; Dobbin and Dowd 2000; Fligstein 1996; Perrow 2002; Powell, Koput, Owen-Smith, and White 2005; Schneiberg 2005). These studies depict a field of actors creating a stable arrangement of relationships that are occasionally challenged by the introduction of an exogenous shock. The market transforms when the shock successfully alters the institutional environment, usually by: removing or adding regulations, introducing new technologies, or affecting the availability of resources. In the case of pharmaceuticals, there were multiple institutional changes that would be expected to account for the industry’s transformation: firms began investing in R&D for the first time, firms began building research laboratories, new regulations were introduced, and penicillin was discovered.

Industrial economists, however, have a different means of explaining similar dramatic changes in a field. While not dismissing the role of institutions, they demonstrate that transformations also occur as competition favors the most efficient organizations and removes the remainder, altering the composition of firms in an industry over time (Chandler 2005; Grabowski and Vernon 1992; Mahoney 1959; Scherer 1993; Temin 1979; Temin 1980b; Thomas 1990). This teleological description is favored by business histories, of the pharmaceutical industry in particular, that suggest that the emergence of a few large firms was both economically efficient and necessary in order to enable the innovation of the new drugs that allowed the industry to persist (Chandler 2005; Hirsch 1974; Temin 1979).

This produces two potentially conflicting accounts for what causes a market to transform, and specifically what explains the dramatic changes in the U.S. pharmaceutical industry. Either the industry was transformed by the introduction of an exogenous shock creating a new institutional environment that favored one set of firms, or it was merely a natural evolution where the bigger and more efficient firms gradually became too large to compete against. Alternately, these two disparate accounts may
combine to offer one answer, where the institutional changes served to expedite the success of the largest firms.

However there is also a third possibility: that the transformation of the industry was not the accidental result of institutional change or the inevitable march of economics, but rather the direct intent of governmental intervention. In 1941, the Office of Science and Research Development (OSRD), a bureau of the War Production Board for the US Military received permission to enlist a series of firms in a top-secret program to produce penicillin for the war effort. These firms received assistance in altering their manufacturing plants to produce penicillin and were given exclusive access to study and manufacture a drug that would soon be the most profitable in the world.

This process, in which the military or federal government work in partnership with private firms to develop a new industry has recurred throughout US history (Smith 1985). The most recent example can be found in the emergence of the internet out of the DARPA program, although similar efforts helped produce the modern semiconductor, gun, and energy industries (Mowery and Simcoe 2002; Sine, Haveman, and Tolbert 2005; Smith 1977). An ancillary goal of this study is to aid our understanding of the process by which these public projects are translated into the establishment of new markets and great private gains. In the case of the early pharmaceutical companies, for instance, it is possible that being selected for the penicillin project enabled firms to experience the exponential growth of the first dot-coms; and most importantly, that it enabled them to separate themselves from the hundreds of similar firms to become one of the handful that would dominate the industry for the next sixty years.

These competing explanations produce four hypotheses that I estimate using both logistic analysis and cross-sectional time series analysis on the forty-six publicly traded firms engaged in the production of pharmaceutical preparations, between 1935 and 1955. I find that the political, technological, and organizational changes alone were not sufficient to elicit any changes in the industry. No new products were developed, firms did not become more profitable or larger, and firms did not exit the industry as a direct result of these changes. Only after the government’s top-secret penicillin program developed an inexpensive way to produce penicillin and helped equip a select group of firms to produce this new drug, did the industry evolve.

Further, I find that firms were not selected to participate because they were the largest or perceived as the most qualified in the industry. Nonetheless, being selected for the penicillin program resulted in a statistically significant increase of a firm’s sales, profits, and likelihood of survival. This effect is unequaled by any organizational adaptation, regulatory change, or measures of incumbent advantage. This may explain why early size advantages were not beneficial or sustainable, with the large unselected firms being passed by smaller, less scientific firms that were selected. The relevance of industries being assembled and then protected by direct federal intervention is explored in the conclusion.

**Background**

For nearly one hundred years Moody’s has offered an annual analysis of every major industry in the United States. As late as 1925, this did not include any mention of a pharmaceutical industry. Through the mid-1920s, pharmaceutical firms were
considered peripheral, a branch of the chemical industry, or the indulgence of a few cosmetic firms, but not an independent industry worthy of a separate analysis. By 1928, change was under way and pharmaceuticals had risen to become the 16th most profitable industry in the country (Epstein 1934). Over the next twenty years they would become, indisputably, the single most profitable industry in the United States, a position they would retain for the next 50 years (Scherer 2001; Silverman and Lee 1974). Such a meteoric ascent begs the question: What happened to permit an overlooked division of a few cosmetic companies to become the nation’s most profitable industry?

Most examinations of the pharmaceutical industry’s historic rise begin in 1945, with the end of WWII (Chandler 2005). The consensus holds that the discovery of penicillin altered the possibilities of drug development and, through a process of “creative destruction,” transformed the industry to usher in a new era in drug manufacturing (Schumpeter 1947; Silverman and Lee 1974; Temin 1980b). However, the introduction of penicillin was not as immediately transformative as these accounts suggest, nor was penicillin the first event with the potential to catalyze the industry. Understanding the failure of prior attempts to transform the U.S. pharmaceutical industry is valuable in explaining what was unique about penicillin that enabled it to succeed.

The first attempt to transform the U.S. pharmaceutical industry was the passage of the U.S. Pure Food and Drug Act in 1906. This law required manufacturers to list the ingredients of their products. After the law a firm could, for instance, continue to sell “Magical Elixir” and claim it cured cancer, but the firm had to acknowledge that the elixir was 80% whiskey and 20% soda. Several states had pre-existing laws with similar requirements, but the 1906 Act marked the first effort by the federal government to become involved in the structuring of the pharmaceutical market.

Unfortunately, faith in the ability of informed consumers to efficiently reward effective drugs and penalize ineffective ones did not produce a more profitable or a more innovative industry. And, by World War I, the U.S. government considered the state of the pharmaceutical industry to be a strategic disadvantage. At this point, the German firms were oriented towards product-innovations, while the U.S. firms focused on manufacturing and process-innovations. The federal government, hopeful that reduced competition would motivate more product-innovation, seized the American divisions of German firms under the Alien Property Custody Act and then auctioned them off to American investors. This created, for a brief period, a market in which only American firms competed to sell pharmaceutical products. But, restructuring the competition did not force firms to restructure their organizations and the industry remained no more innovative than before.

This meant that as late as the 1930s, most U.S. pharmaceutical companies maintained their marginal existence by selling nostrums and therapeutic combinations of limited value. There were occasional products, like insulin or morphine, of great therapeutic value, but these were notable exceptions to the rule. Moreover, these innovations were discovered by university professors, the pharmaceutical companies’ lone expertise was in determining how to manufacture and distribute the resulting products.
This may explain why the second major regulatory effort, the 1938 Amendment to the Food and Drug Act, also proved insufficient to transform the industry. This law, which required that firms demonstrate the safety of their products, followed a tragedy in which 107 people—many of whom were children—were killed after taking a toxic form of sulfanilamide. Theoretically, this introduced an additional barrier to entry for firms and should have helped narrow the field by eliminating small firms that were unable to absorb the greater cost of production. However, the legislation succeeded neither in dramatically reducing the number of firms nor in forcing firms to become significantly more innovative or to produce drugs that were more effective. After all, to return to an earlier example, a “Magical Elixir” of whiskey and soda is not technically “unsafe.” Further, the FDA was given only 60 days within which to review a drug before it was automatically approved. The law was so ineffective that it was estimated as much as two-thirds of approved drugs were not offering their advertised therapeutic benefit (Cannan 1968).

This brief history underscores how difficult it is to move an industry from non-innovative to innovative. Three successive rounds of legislative effort resulted in an industry that was not significantly different than the one that existed in the 1900s, with the noted exception that it no longer produced as many lethal “remedies.” It was not until after WWII that these companies began introducing products of their own design and of genuine therapeutic value. Previous historical accounts argue that this shift resulted from a combination of the introduction of new technological possibilities present in penicillin and the gradual move by some firms towards conducting independent chemical research (Chandler 2005; Hirsch 1974; Temin 1979).

However, the archives of the Office of Science and Research Development (OSRD) tell a more complicated story about penicillin and offer a competing view for how the pharmaceutical industry evolved. The OSRD was established during WWII to help the U.S. military achieve a number of scientific objectives deemed valuable for military success. Among these goals was the production of penicillin. Given the high post-injury mortality rate and the seemingly miraculous ability of penicillin to curtail precisely the infections that caused those deaths, ensuring a steady supply of penicillin was considered to be an issue of great military importance. Unfortunately, penicillin was very difficult to make in large quantities and the largest pharmaceutical firms expressed no interest in trying to remedy this situation. The process by which the government overcame these obstacles to produce penicillin and, the role of the OSRD’s Penicillin Program in shaping the modern pharmaceutical industry are the focus of the next section.

The Selection Process

Although penicillin was discovered in 1928 and used on patients in 1941, as late as early 1943 there was still no viable way to produce it in large quantities (Elder 1970). The Penicillin Program was established explicitly to solve this manufacturing quandary, however the selection of firms began well before the program itself. In 1939, Howard Florey and Ernst Chain, two of the three British scientists who would later earn the Nobel Prize in Medicine for their work on penicillin, were given a grant from the Rockefeller Foundation to develop better methods of manufacturing the drug. After some initial successes in increasing the yield, Florey realized that his principal limitation was in production. To remedy this he sought out the help of the British pharmaceutical industry.
While some of the companies expressed an interest, no one would commit any of their manufacturing capacity to study the production problem. Rejected by the British, Florey had few remaining options. As a last resort, he traveled to the United States to see if he could persuade any American pharmaceutical firms to manufacture penicillin.

This was in July, six months after the British medical journal *The Lancet* had first published an article extolling the miraculous abilities of penicillin, and the public interest in the possibilities of the drug was steadily growing. E.R. Squibb & Son, alone among American firms, had already seized upon the initial report to begin their own investigations into the drug. But they were the exception to the rule. The majority of U.S. firms were both skeptical of penicillin’s potential, and uninterested in joining Florey’s program. As Frank Hanson, of the Rockefeller Foundation, put it in a letter to Alfred N. Richards of the OSRD, “Though certain of the firms thought the matter worth attention, a number of them showed little interest, and some none at all.” Florey himself described his reception by U.S. pharmaceutical firms in these terms, “I felt like a carpet bag salesman, trying to promote a crazy idea for some ulterior motive.” (Lax 2004)

Belying the notion that firms with more scientific capabilities would be more able to recognize the potential value of the drug, nearly every firm Florey sought out—firms he selected based on their scientific prowess—turned him down. It was the received wisdom of the day that what Florey wanted to do, to mass-produce penicillin, was impossible to do in a cost-effective fashion (Elder 1970). Even the most technologically advanced firms failed to see the future therapeutic possibilities of antibiotic research. Instead, firms preferred to continue to operate in their traditional way. They did not want to investigate new manufacturing techniques nor did they want to study the design of the drug itself. They recognized it as effective and, therefore potentially profitable, but these firms did not often pursue pure research. And the arrival of a revolutionary therapeutic breakthrough was not itself sufficient to persuade them to change their ways.

Florey’s arrival in 1941 therefore offers a compelling historical counterfactual through which to understand the relevance of the Penicillin Program. After all, the unmitigated rejection of Florey’s proposal happened only a few years before penicillin became available commercially and, purportedly, transformed the pharmaceutical industry. Yet nothing happened to the structure of the industry during those years. No regulations were passed, no new organizational models emerged, no new drugs were discovered. Before the creation of a government program, all the pieces were in place for the industry to explode: firms had built labs, many had hired teams of chemists, the regulations were all in place and enforced. Penicillin was even discovered, proven effective, and literally carried to the firm’s doorstep by respected scientists and yet, nothing happened. Without the intervention of the government, firms were unwilling to pursue penicillin and the market remained as it always had: firms spent their time

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1 Letter from Frank Blair Hanson Assistant Director of Rockefeller Foundation to A.N. Richards, May 10, 1943
figuring out new ways to market similar products. Despite the existence of seemingly all relevant preconditions, the pharmaceutical market, both in the U.S. and the U.K., turned down penicillin and the risks it involved, preferring to remain unchanged.

Florey’s inability to persuade industry to participate in the project was counterbalanced by his good fortune in finding support in the government. Although the U.S. was wary of financing an explicitly research-oriented program, Dr. Alfred N. Richards was placed in charge of the Committee on Medical Research and given a virtual carte blanche. Richards, in turn, had run the laboratory in which Florey had conducted his post-doctoral research. He was therefore very receptive to Florey’s proposal and agreed to have the government fund and conduct penicillin research and to try, personally, to persuade firms to join their efforts.

Unfortunately, despite their efforts, most companies remained wary of joining in such a difficult project. The prospect of failure was so great that no one with the proper scientific credentials wanted anything to do with the project. The government was not, as is often assumed, able to simply place a call to the most esteemed scientists in the country and request their assistance in what was, undoubtedly, a project of tremendous urgency and value. Instead the first dozen requests were rejected precisely because the scientists understood how unlikely the venture was to succeed. As Albert Elder, the eventual coordinator of the project put it,

“I was ridiculed by some of my closest scientific friends for allowing myself to become associated with what obviously was to be a flop—namely, the commercial production of penicillin by a fermentation process.”(Elder 1970)

This reinforces the claim that, despite the expectation that the government was able to select the best and brightest firms to participate in the program, the government and Florey together could barely convince anyone to participate. In fact, at the first meeting A.N. Richards held in Washington in late 1941 to commence the penicillin program, only four pharmaceutical companies showed up: Lederle, Merck, Squibb, and Pfizer. And all four told Richards that they didn’t think they would be able to produce penicillin.

This was the state of the program at the end of 1941: four companies, only three of which were willing to actually commit resources (Lederle was more of an observer initially), under the coordination of a man with limited experience. None of the firms had any prior experience with penicillin or similar molds; several of them expressed reservations about their ability to commit resources to such a fruitless task. Meanwhile, the firms who were best able to judge the scientific potential, the first choice of both the British scientists and the U.S. federal government, opted not to participate.

All of this changed when government scientists, led by Robert Coghill at the Northern Regional Research Laboratory in Peoria, Illinois developed new methods that increased penicillin yields dramatically. Suddenly the mass production of penicillin was both feasible and profitable. Quickly, the firms that had previously expressed indifference, including, Eli Lilly, Sharpe & Dohme, Lederle, and Conaught Labs were clamoring to join the nascent project. Unsurprisingly, the early coalition of Merck, Pfizer, and Squibb tried to secure their unexpected advantage by arguing that no additional firms were necessary, writing that, since pure penicillin was so strong, “…a
relatively small amount of the product would be required to meet all foreseeable military and civilian requirements….It would, therefore, be uneconomical from the point of view of the war effort to construct many plants for this purpose…”

Whether these arguments betray the companies’ poor understanding of penicillin or their perfect understanding of their newfound fortune, these arguments did not persuade firms not to apply nor did they persuade the OSRD to limit the number of contracts. According to NRDC records, 175 firms submitted applications, and hundreds more were discouraged from sending applications, but only 21 were considered “legitimate contenders.”

Although few records were kept indicating what transpired during the selection committee’s meetings, correspondence between the members of the committee reveal a great deal about the ways in which firms were chosen. Contrary to the expectation that firms were selected based upon their known abilities, the correspondence conveys a picture of committee members grasping for rationales to reject firms they had already decided to reject, without knowing anything about their chemical or manufacturing capabilities. Moreover, other firms were selected despite acknowledged inadequacies while seemingly more appropriate, more capable firms were never considered at all. As Roger Adams, a member of the OSRD committee, explained in a letter to Hans Clark, the Chair of the selection committee,

“Personally, one excuse that we could make in the case of Reichel is that they do not have a substantial organic chemical research laboratory with adequate personnel (assuming that this is the case).”

Adams continues to discuss two other possible candidates, again offering seemingly post-hoc reasons for their dismissal,

“With Heyden and Commercial Solvents we could state that they are not manufacturers of pharmaceutical chemicals. It is true that Commercial Solvents does extract vitamin B2 from fermentation slop, but in my opinion this is far from putting them in the field as a pharmaceutical manufacturer.”

The language here is instructive, as Adams is not explicitly stating that these firms are incapable of participating or of doing quality work, instead he is offering his advice on rationales that could be used to exclude them. A few days later Robert Coghill responds to a similar letter from Hans Clark with the following,

“I feel that all the companies you mentioned, namely, Abbott, Merck, Squibb, Pfizer, Lilly, Parke Davis, Lederle, Winthrop, Upjohn, and Roche, should certainly receive the information. I furthermore agree that the other

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2 Letter from George Merck to A.N. Richards, September 19, 1943.
3 Resignation letter from Lee Elder to Dr. Morgan, February 24, 1944. Elder writes that these firms were discouraged from applying, “…because it appeared probable that he plants approved prior to my connection with this program should be completed before further expansion should be contemplated.”
4 Letter from Roger Adams, member NRDC, to Hans Clark, November 10, 1943.
listed companies, Allied Molasses, Cutter, Ben Venue, Cheplin, and Schenley, are probably not in a position to use it.”

What is most interesting about these two letters is that the seven firms the two committee members appear poised to reject, five of which Coghill explicitly considers incapable, are all invited to participate. Meanwhile, several of the firms that Florey had first approached in 1941, firms that were the scientific vanguard of the industry: Smith-Kline, Connaught Laboratories, Lambert Pharmacal and Mulford, all firms with extensive research laboratories and close ties to neighboring universities, were not selected. While this is never addressed explicitly in their correspondence, these firms were both initially considered capable by Florey and Chain and later applied to participate. But, for unknown reasons, they were passed over in favor of their clearly unqualified competitors. Hans Clark, the chairman of the committee offers his insight into why this was the case in his response to Coghill,

“…I feel that it would be unjust and certainly begging for trouble to exclude [the suggested firms]. As long as they have been included, rightly or wrongly, in the penicillin production picture and have the facilities for synthetic work, I do not see what the basis is for excluding them.” (emphasis added)

The process of selection and, in particular, the criteria used for evaluation was so opaque that three of the firms selected to participate never even attempted to produce penicillin because they never possessed the capability: Merrel & Co., Cherokee Biological, and Emerson & Dettleback. One firm, Ben Venue, even withdrew their application after they had been selected, stating that they lacked the facilities and expertise to continue, despite the committee’s confidence. So, out of the 175 firms to apply, 21 were selected and 1/5th of those firms were, by their own admission, unqualified. Despite the seemingly low bar, firms as established as Eastman Kodak or as scientifically inclined as Smith-Kline were not included. These facts suggest that Clark’s comment about firms being included “rightly or wrongly” accurately captures the degree to which the process focused on factors other than perceived ability.

To test the degree to which the committee selected the most talented firms, I develop three hypotheses. These hypotheses reflect the belief, contrary to what has been suggested in the correspondence presented here, that the OSRD selected the most capable firms. Given the urgency of the situation and the need for firms capable of developing more stable and effective versions of penicillin and to increase production of the drug, it is logical to assume that the OSRD would select proven firms with significant research investments and the capacity to manufacture large amounts of penicillin. Therefore, despite the individual accounts of the process, we should expect that the largest, most successful, and most research-oriented firms were the most likely to be selected. The null hypothesis would indicate that firms were selected irrespective of their prior success or scientific capabilities and, therefore, that any correlation between participation and

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5 Letter from Robert Coghill to Hans Clark, November 13, 1943.
6 Letter from Hans Clark to Robert Coghill November 15, 1943.
subsequent success resulted from benefits accrued through participation in the Penicillin Program rather than the pre-existing advantages of the selected firms.

*Hypothesis 1a:* Firms with past financial success were the most likely to be selected to participate in the penicillin program.

*Hypothesis 1b:* Firms with an existing research laboratory were the most likely to be selected to participate in the penicillin program.

*Hypothesis 1c:* Firms with experience in chemical-based research were the most likely to be selected to participate in the penicillin program

**Theory and Hypotheses**

Two nested questions motivate this paper. The first asks specifically: What happened, during the 1940s, to catalyze the U.S. pharmaceutical industry? The second seeks to expand upon this by asking: What generally causes the radical transformation of a market? Three theoretical traditions offer three different answers to these questions favoring the role of organizational fit, the value of economies of scale, and the influence of direct government intervention in a market respectively. I will discuss each of these approaches in sequence and use them as the basis for the next set of hypotheses.

**Exogenous Shocks and Organizational Fit**

Recent work in economic sociology and organizational theory suggests that to answer these questions requires us to incorporate both institutional and organizational perspectives. The former articulates how dramatic exogenous shocks can create the conditions for a change in the market. These political and technological developments may favor but they do not always instigate the organizational shifts that become pervasive in the new market. The latter theories explain how firm-level variations can predict the type of change that occurs and the type of firms that succeed in the new environment. Only by combining these approaches can we understand how an industry moves from non-innovative to innovative, from barely profitable to hugely profitable, and from dispersed to concentrated in just one decade.

In the organization literature, dramatic population-level changes are often precipitated by an environmental change (Baum and Singh 1994; Chandler 1977; Pfeffer and Salancik 1978). These exogenous shocks can take on a variety of forms ranging from the introduction of a new political regime to the innovation of a new technology (Galambos 1970; Galambos 2005; Lamoreaux 1985; Piore and Sabel 1984; Roy 1997). In each case, the shock isolates/segregates one set of organizations from another and splits the population (Baum and Singh 1994; Freeman and Hannan 1989; Stinchcombe 1965). This results in a population of firms divided into (1) a group that benefits from the changed environment and will now succeed at a greater capacity and (2) a group harmed by the change that may soon dissolve.

The most frequently examined shock is a change in the political environment. Change in the regulations surrounding the industry, a change in the philosophy of regulatory enforcement, and change in the political regime have all been found to cause dramatic transformations at the population-level (Dobbin and Dowd 2000; Fligstein
In particular, Dobbin and Dowd (1997), in their study of Massachusetts railroad companies, find that different policy regimes establish different rules of competition leading to the creation of new types of economic behavior. They demonstrated that changes in policy create openings in which different groups vie to establish a new organizational form. In this situation, the introduction of new policies transforms the market and affects which companies succeed and which fail by favoring certain organizational forms over others. The introduction of an exogenous shock, by favoring one set of firms and disadvantaging others, is sufficient to alter the population and produce a dramatic change in the industry.

Fligstein (Fligstein 2001) reaches a similar conclusion in his study of the relationship between institutional structure and the type of competition that emerges. He argues that exogenous shocks can cause participants to question the norms that govern behavior and attempt to establish new rules of exchange. The institutional changes encourage new types of competition, and incumbents rarely adapt quickly enough to survive and take advantage of the new opportunities introduced by the exogenous shock. Thus, each exogenous shock permits the rise of newcomers and rewrites the hierarchy of firms in an industry.

Technological change has also been found to alter the organization of firms within an industry (Tushman and Anderson 1986; Tushman and Anderson 1990). In their study of the cement, glass, and minicomputer industries, Tushman and Anderson define the developments that uproot the industry as “competence destroying” innovations. These breakthroughs offer such drastic performance or cost improvements that new firms, better able to incorporate the ideas, were able to supplant their more established predecessors. In the pharmaceutical industry, Galambos and Sturchio (Galambos and Sturchio 1998) find that the introduction of biotechnology paralleled the introduction of penicillin. In both cases firms had to reorient themselves to capitalize on the new technologies or risk obsolescence. As with penicillin, genetic research elevated the value of a particular kind of knowledge, this time biologic, and the firms that were able to access that knowledge were the firms that succeeded (Powell, Koput, and Smith-Doerr 1996).

These findings imply that industries evolve through a two-stage process in which an initial shock creates new openings in the market and then, in the second stage, the firms best situated to the new environment replace those more suited to the original. This suggests that the most adaptive firms are the most likely to persist through the series of successive shocks found here. Pfeffer and Salancik (1978) make this argument explicitly, contending that it is the ability to adapt to a new environment that determines whether a firm will survive over time. Change at the population level results from firms being either too slow or too inert to adapt their organizations to the new surroundings (Porter 1980).

Between 1935 and 1955, there were three organizational changes that a firm could have adopted in the pharmaceutical industry, each one of which may have produced an advantage over less adaptive firms. The first was the decision to incorporate. As late as the early 1930s, a majority of pharmaceutical firms remained family-owned and operated. However, the movement towards new technology required large investments in research and development and the ability to distribute products on a larger scale. Both of these changes require capital and a greater degree of insulation from failure, precisely the
benefits that come from incorporation. Therefore, just as Perrow (2002) found incorporation to be a significant factor in determining which firms became large corporations, we would expect to see a positive correlation between incorporating and the ability to succeed in a changing environment.

While raising capital helped insulate firms, the second and third changes derive from the claim that it is how a firm invested their capital that proved crucial in determining which firms succeeded (Chandler 2005; Temin 1979; Temin 1980b). MacGarvie and Furman (2005), in their study of organizational innovation in the pharmaceutical industry, highlight the importance of the second potential change: the establishment of an industrial research laboratory. Once penicillin became commercially available, it provided pharmaceutical firms with a new path toward discovering valuable, effective, new medicines: to modify and patent the existing antibiotics. To do this, firms first needed two things: first, they needed an industrial laboratory and second they needed to acquire an expertise in chemistry. The easiest way to do that was through the third organizational change, hiring employees trained in chemistry to staff the laboratories.

These are separate changes because they were undertaken at different points for different firms. Firms like Eli Lilly had a long history of working with chemically-trained staff, primarily to evaluate and extend the discoveries of other scientists, but lacked an industrial laboratory until much later. Other firms built laboratories but hired people who lacked the background in chemistry necessary to succeed later on, focusing instead on biologists and pharmacists (Liebenau 1987).

Even though these three shifts represent core changes of the kind that Hannan and Freeman (1984) argue can reintroduce liabilities of newness, studies of the pharmaceutical industry argue that firms that did not make these changes could not—to borrow Hirsch’s (1974) idea—finance or find the “hits” that enabled them to profit. Therefore, it is reasonable to assume that the firms who adapted to the new environment by incorporating, building laboratories, or hiring chemically-trained scientists would be more likely to succeed.

Hypothesis 2a: The firms that incorporated, created research laboratories, or hired scientists were more likely to show the greatest growth in the new environment.

One difficult distinction to parse is between the value of an organizational change that comes in response to environmental change and one that precedes it. Normally, in the organizations literature, the division between selection and adaptation assumes that firms adapt to the new environment and that those adaptations help the firm to survive (for review, see (Baum and Shipilov 2006). However, in this case there is an argument that firms did not adapt to the environment so much as their actions precipitated environmental changes. The firms lobbied for particular sets of regulations and worked hard to develop the technological breakthroughs that altered the market. These changes did not happen to them, they happened because of them.

Therefore, it is necessary to distinguish the effect of organizational changes made prior to rather than post the political and technological change. This helps us to offer a better test of whether organizational change promotes organizational success or not. Presumably, firms who adopted these organizational changes after the environment had changed did so in order to adapt, while those whose changes precede the environmental
change did so out of foresight. This additional time would then leave them more prepared for the changes and better able to cope. While their peers struggled to alter their routines to fit the new environment, these firms would be able to capitalize on the changes more quickly and therefore gain a valuable advantage.

*Hypothesis 2b: The earlier organizational changes were adopted, the more likely the firm was to benefit from the environmental change.*

**Size as Insulation**

Despite the intuitiveness of this argument, a review of studies on the benefits of adaptive organizational change shows, at best, inconsistent results (Baum and Shipilov 2006). Hannan and Freeman (1984) offer a cogent explanation for these mixed findings, arguing that while firm adaptations may matter, firms are unlikely to know which will be the most favorable beforehand. The success of an adaptation is less a sign of foresight than of fortune. Therefore when an environmental change occurs, the firms that succeed are likely to be the ones best situated for the change, not the ones best at adapting to the change.

Business historians and economists who have studied the pharmaceutical industry favor Hannan and Freeman’s argument (Temin 1979; Liebenau 1987). They contend that the firms that were in the best position before penicillin was commercialized were the ones most likely to benefit from the new environment. “Best position,” as Hirsch (1974) demonstrated, meant pharmaceutical firms able to capitalize upon economies of scale and to afford the research necessary to succeed. In other words, the biggest and most successful firms would be better equipped to develop the potential offered by penicillin.

In his remarkable comparison of the record and pharmaceutical industries, Hirsch shows how new regulations raised both barriers to entry and the cost of putting products on the market. This redirected the pharmaceutical business towards a “hit” factory, where they had to finance hundreds of misses in order to find the one “big hit” that brought them profit. This is a substantial change from the previous structure of firms, in which marketing prowess enabled the sale of many goods of dubious effectiveness. Thus regulatory and technological change required both size and profitability to sustain a firm through the long dry spells that come between the infrequent successes. Past organizational research has reached similar conclusions, showing that the most profitable and the largest firms are the most insulated from regulatory and technological changes and therefore are best able to survive in new environments (Baum and Silverman 2004; Carroll and Swaminathan 2000; Freeman, Carroll, and Hannan 1983).

Taken together, this would suggest that, although there were hundreds of similarly-sized firms in 1935, those that were larger or more profitable would be selected to survive in a changed environment, while the smaller, less profitable firms would be selected out, leaving the population with far fewer firms and explaining the rise of the oligopoly.

*Hypothesis 3a: The largest firms would benefit most from political and technological change and show the greatest growth.*

*Hypothesis 3b: The most profitable firms would benefit most from political and technological change and show the greatest growth.*
Direct Intervention

The final possibility is that the market was not transformed by environmental shock or any subsequent organizational change. Instead, it is possible that the market was deliberately transformed by governmental intervention and that the firms that succeeded were the firms chosen to do so. While several authors debate whether the most well-positioned firms benefited from fortunate environmental changes or not, no one has examined whether the government actively moved to transform the market (Silverman and Lee 1974; Temin 1980b).

An influential study of the US gun industry (Smith 1977) shows that the government is capable of radically transforming the organization of firms in an industry without introducing any regulations. Additional studies into the role of government in technological innovation has found that the value of governmental intervention is to serve as a customer for a product for which there is not an obvious initial commercial market (e.g. the internet) and to serve as a setter of standards, that then allows future progress to be more directed than dispersed (Smith 1985). It is possible that the federal government played the same role in creating the penicillin program that Smith and others describe in the creation of radar, the internet, synthetic rubber and other industries. However, what is unique in this instance is the mechanism by which government provided value.

In most cases, scholars have found that government initiated innovation by serving as a customer or standard-setter. However here, there was already a large commercial market for a penicillin-type product (evidenced by the widespread public demand once penicillin was introduced) and, second, government did not act to set any product or manufacturing standards with regards to penicillin. The mechanism by which the penicillin program altered the industry is therefore less clear and suggests an alternate way of understanding government’s role in shaping industry.

There are three different ways in which the government intervention may have operated to produce a transformed U.S. pharmaceutical industry. First, it may have been an issue of scale, i.e. previously the firms were too small to invest in the R&D that would enable them to experience greater profitability and innovations. However, the military helped increase the scale of the selected firms by building them manufacturing plants, giving their employees draft deferrals, and awarding them contracts.

The FTC subsequently determined that the military built six production plants at a cost of $7.6 million for members of the Penicillin Program, which the military later resold to the firms for $3.4 million. Several existing plants were also converted at government expense to facilitate penicillin production and then resold to the pharmaceutical firms at a fraction of their cost. For example, Pfizer paid $919,500 for a plant that the government spent $5.2 million converting and Lilly paid $2.5 million for a plant that cost $5.3 million (United States. Federal Trade Commission. 1958). Sixteen other plants were built by the participating firms themselves but were given special tax exceptions that significantly reduced their cost. The military spent an additional $2.8 million on federal research into penicillin production and purification, research that was then shared exclusively with the selected firms. If increasing the scale of firms was what
enabled their latter success then the firms for whom the military built plants should have experienced more rapid success.

Hypothesis 4a: The firms that the government built facilities for will be more likely to experience growth than those that received no facilities.

It is also possible that the advantage in being selected was primarily informational. The selected firms were shown how to create and modify a new product that would serve as the basis for the next decade’s most profitable innovations. The head-start these firms had in researching and manipulating the drug, and the requirement that each firm share information with the others, enabled them all to develop at a much more rapid pace than their peers who were excluded from these studies. In this case, it would not matter if a firm was small or large to begin with or at the end of the program, what was relevant was the time they spent researching the drug and the knowledge that came from that process.

Hypothesis 4b: The firms selected by the OSRD were more likely to experience growth as a result of their participation in the Penicillin Program.

As firms were selected both to conduct research on the drug itself and to develop manufacturing processes, it is possible to distinguish between the firms that were engaged in the product-research from those conducting process-research. If the product-information proved valuable, then we should see that those firms experienced greater subsequent returns.

Hypothesis 4c: The firms selected to conduct product-research will be more likely to experience growth than those selected to conduct process-research.

Finally, it is possible that the government selected the most talented firms and simply expedited their inevitable success. A selected firm that lacked prior organizational advantages would not experience any improvement, while firms that did grow would likely have succeeded irrespective of selection. This builds off the assumption that the greatest advantage of selection was in gaining knowledge for future research. However, it presumes that success is contingent upon the capacity to pursue future research. It is important to determine whether or not selection alone was a sufficient condition for success or whether selection provided a necessary but not sufficient advantage. This line of inquiry yields the final hypothesis:

Hypothesis 4d: Selection to join the penicillin program increased the value of past advantages and organizational changes.

Data

To estimate the hypotheses, I use the population of public companies engaged in the production of pharmaceutical products between 1935 and 1955. Information on the companies was drawn from Moody’s Industrial Reports, the National Research Council Industrial Surveys, and firm annual reports. There are three sample issues that merit discussion here. First, it is very difficult to determine the precise population of pharmaceutical firms in 1935. The industry had yet to coalesce around a single organizational form and therefore hundreds of companies engaged in manufacturing,
researching, marketing, or distributing medicines were all considered pharmaceutical companies despite the fact that some were dedicated pharmaceutical firms while others were single-owner pharmacies and others were large consumer products conglomerates with a line of medicinal goods. The second, and related issue in sampling from this population is that, as the majority of firms engaged in pharmaceutical production were both small and privately held, there are severe limitations on the availability of data.

To resolve these problems I draw a sample from the population of 46 pharmaceutical firms that were publicly traded between 1935 and 1955; this includes the entire population of pharmaceutical firms that had more than $1 million in sales in 1935. The sample includes 13 of the 17 firms that produced penicillin through the OSRD program, and 33 of their competitors. These firms represent the largest, most capable and most successful of the pharmaceutical companies at the beginning of the period. However, despite starting in similarly privileged positions, by 1955, they had divided into two distinct groups, as shown in figure 2.1.

INSERT FIGURE 2.1

This produced an unbalanced panel as 8 of these firms entered after the study began and 11 would exit the industry by 1955 (table 2.1), 5 as bankruptcies and 6 as the result of mergers. However, the panel captures the total population of publicly traded firms that engaged in some portion of the pharmaceutical business during the 20-year period, both the survivors and the failures. Table 1 also includes information on the number of firms Moody’s Industrial Reports classified as members of the “Drugs, Medicine, and Cosmetics Industry” in a given year, which offers an alternative measure for exit/entry into the industry.

INSERT TABLE 2.1: POPULATION EXIT/ENTRY DATA

There is a third sampling issue: the treatment I am studying is on a non-random selection of firms. However, as discussed earlier, the firms appear to have been selected for a number of reasons (geography, status, manufacturing capabilities, and research capabilities) not limited to their technological prowess or prior success. Because of this variety in the rationales for selection, it is unlikely that the selected firms shared any one characteristic that would have made them universally more liable to succeed post-penicillin. In that sense, the selected and non-selected firms represent similar populations of firms with few consistent differences that could account for any subsequent success.

Further, by using a sample of the 46 largest firms, I am able to determine which changes enabled successful firms to become more successful and which prevented future success irrespective of the firm’s past performance. Most notably, this ensures that when comparing firms selected for the OSRD program against those who were not selected, each sample reflects a similar population. Theoretically, this should bias the estimates downward, as a comparison between the OSRD firms and a random sample of all possible pharmaceutical firms of the era would include several that never demonstrated any financial growth.

Instead, I compare the selected firms to a group of equally profitable, equally large, equally successful firms. These are firms that should have continued to experience growth in their income, profit, and number of employees, even if they failed to win a
penicillin contract. Therefore, as all groups appeared poised to succeed, and as the OSRD firms were not chosen due to any greater scientific or organizational capacity, evidence of a significant correlation between participation and measures of success should be less likely to emerge than if I had compared the firms to a random sample of all possible pharmaceutical companies.

**Dependent Variables**

In order to operationalize the “success” of a firm during the period of study, data were collected on the firm’s annual sales, income, profits and, employee figures for every year available. While it is customary in studies of population-level change to focus largely upon the rates of founding and failure to measure change, in this situation the case does not readily lend itself to survival analyses. To conduct these studies requires the existence of well-defined boundaries dividing firms within and outside of the population. This condition is violated when studying a developing field where no dominant organizational model exists and the line separating members of the population from those outside is more porous. In the pharmaceutical industry, there were multiple competing organizational models: cosmetic companies with a division focused on pharmaceutical preparations, dedicated pharmaceutical companies, chemical manufacturers with a pharmaceutical division, medical device manufacturers, consumer products firms, etc… Eventually the industry coalesced around the model of a large, research-oriented, vertically-integrated firm. But determining a specific moment when firms without this model “exited” pharmaceuticals is an exercise in arbitrariness.

For instance, a company like Kendall Co. made and manufactured surgical bandages. These bandages were occasionally combined with a topical dressing. In 1940, they were clearly a pharmaceutical company as they made both ointments and bandages. Even in 1950, they would likely be called a pharmaceutical company, not a pharmaceutical. To declare Kendall to have “exited” the pharmaceutical industry at a particular moment, when the process appears to have taken several years, would be of questionable utility.\(^7\)

To remedy this, I measure two forms of survival. First, using a strict definition, I measure the rate of merger or bankruptcy for firms in the population. Second, I use the SIC classification for the pharmaceutical industry (2834) to see what factors determined whether a given firm was still considered a pharmaceutical company at the end of the period of study.\(^8\)

The most immediately evident finding, shown in table 2.1, is the success of firms selected to participate in the Penicillin Program. Of the 13 selected firms included in this study, only 1 could be said to “fail,” when E.R. Squibb & Sons agreed to merge with Olin-Mathieson, a merger that was dissolved in the 1960s. However, 10 of the 33 remaining unselected firms, or 30%, either were acquired or went bankrupt during the

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\(^7\) Market concentration measures, a possible alternative measure for population-level change, are also unavailable as too few firms separated their financial data to indicate sales by division.

\(^8\) Unfortunately, Dun & Bradstreet did not begin publishing their directory until 1959, preventing an earlier analysis of firms using SIC data. However, the data included in their 1959 survey is based on the classification of firms from 1954 and thus offers a snapshot of pharmaceutical firms at the end of my period of study.
period of study. Similarly, while all 13 firms were still considered “drug” companies by Moody’s in 1955, over 40% of the unselected firms (21 of 52) were no longer considered pharmaceuticals in 1955. Analysis of the firm’s SIC classification reinforces this picture as 12 of the 13 selected firms but only 10 of the remaining 33 firms were considered pharmaceutical companies at the close of the study.

Although none of these are perfect measures of survival, in combination with the financial measures of success I include, they offer a detailed portrait of how the population changed radically in one decade. While all of the firms began on equal footing, only the selected firms continued to succeed while their peers died and exited the industry. In fact, the overwhelming success of the selected firms made it impossible to evaluate the effect of selection using survival analysis, however the analysis of the remaining variables is available in table 2.6.

To prevent changes in the tax code from causing unexpected variance in the data (most notably the high tax rate imposed during WWII), I used pre-tax income. This produced five distinct dependent variables, each measuring a different performance-related outcome which is consistent with previous studies of growth at the firm level (Stuart 2000; Uzzi 1996).

Unfortunately, firms varied widely in both the data they reported and the consistency with which financial data was reported. Some firms offered annual employee data but no financial information, while others offered only data on profits but none on sales. These inconsistencies and omissions lead to slightly different samples for each of the dependent variables, complicating comparisons between them. However, running the same regressions on the more limited pool of firms that consistently reported all dependent variables produced comparable results (available from the author on request). Further, there is no reason to expect a correlation between the variables or frequency with which a firm reported its financials and the financial data itself. If anything, we would expect to see that firms did not report negative financial data, but several firms listed data at the end of a decade in categories they had previously ignored and which indicated robust growth in sales or profits. For these reasons, the regressions were run using the largest possible number of firms and observations.

As I compare the growth of firms of varying sizes, there is some reason to expect across-unit heteroskedasticity. It is possible that the larger firms will grow at a slower rate or will be more insulated, and therefore respond less dramatically to the changes in the market. This might produce greater variations in the small firms than in the large. To control for this, I elected to use fixed-effect regressions to estimate the coefficients, allowing the intercepts to vary for each unit and limiting any across-unit heteroskedasticity. A Breusch-Pagan test revealed no time-related heteroskedasticity.

Within-unit serial correlation is a more common problem in time-series data, especially when the variables display a time trend. Here, all three dependent variables show varying degrees of positive correlation with time. However, a Baltagi and Wu modification of the Dickey-Fuller test for panel data showed that none of the variables possessed a unit-root. To eliminate any serial-correlation in the variables or the error term, a first-order lag of the dependent variable was included and the coefficient of this term was less than 1 in each regression, further indicating the lack of a unit root. This lag
also produces a similar control for the influence of a random-walk pattern in the data. The inclusion of this variable makes theoretical sense as a firm’s annual sales (or employees, profits, income) are likely based on their previous year’s sales and some fluctuation due to the assembled variables. As the data are annual, it appeared unlikely that a second or third-order lag would be necessary and F-tests supported this assertion, proving that only a first-order lag was significant.

**Independent Variables**

To test hypotheses 1a-1c, and estimate the degree to which the OSRD merely selected the best firms, six variables are used. The sales and profit at each firm indicate the size of the firm at the time of selection. The data was collected from annual reports for each firm. Four organizational changes are included to estimate a firm’s capabilities: date of incorporation, date of investment in chemistry, the number of scientists employed by the firm, and a dummy variable for whether or not the firm established a research laboratory. The date of incorporation is determined by the year in which the firm first incorporated, taken from their annual reports. The date of the investment in chemistry is based on the first year the firm hired a scientist with a background in chemistry. This data and the data on the number of scientists employed by each firm were taken from the Bulletin of the National Resource Council and captures two dimensions of the scale of a firm’s investment in science. The date of laboratory founding was based upon the year in which the firm first established an internal research division staffed by people with a background in one of the natural sciences. Dates for the laboratory were found using a range of data sources including: annual reports, published corporate histories, and individual biographies.  

To test hypotheses 2a and 2b, and address the findings of organizational theorists, same measures of organizational change are used: incorporation, creation of a research laboratory, and the hiring of scientists. To these a dummy variable was added indicating the organizational structure of the company: whether they were a dedicated pharmaceutical firm, and whether they had an established research and development division.

To test hypotheses 3a and 3b, and evaluate the role that economies of scale played in selecting winners, three variables are used: profitability at time $t_0$, sales at $t_0$, and science employees at $t_0$. These three variables allow us to address the most obvious explanation for success: that the successful firms, post-1945, were also the largest, most successful firms before.

To test hypotheses 4a and 4b, a dummy variable that indicates whether a company was granted a government contract for the production of penicillin was added. The variable was coded as 0 for the period until a firm was selected for participation in the penicillin program and then 1 thereafter, assuming they were selected. These dates were taken from the OSRD records in the National Archives. This variable also served as the dependent variable in hypothesis 1, the modeling of the Penicillin Program selection process.

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9 I owe a special note of thanks to the Lehman Brothers Collection at the Baker Library at Harvard University for their collection of corporate histories.
In order to test 4b, and distinguish the mechanism by which selection conferred any advantages, the additional value by which prior advantages increased the impact of selection was estimated. For this, two interaction effects are included: (1) the number of employees*selection to join penicillin program and (2) creation of a lab*selection. The first of these estimates how the value of size changed with selection and the second estimates change in the value of organizational adaptations.

To further estimate the mechanism by which an OSRD contract conferred its advantage, the firms were divided into those that received contracts to conduct research on penicillin versus those that were contracted to manufacture the drug. This data was derived from distinctions made in the notes of the selection committee. FTC data is used to measure any scale advantages gained through the building of plants for the respective firms.

**Control Variables**

One plausible explanation for which firms succeeded is that firms are capable of growth once they reach a maturation point so that, during the 1940s, the oldest firms grow the fastest. This could be due to the fact that older firms had more time to experiment with different models or that they simply have more financial or scientific resources. To control for this, a variable for the age of the firm is included, taken from the year of its founding.

It is also possible that the improvement in the pharmaceutical industry is simply the product of war-related concerns driving up business in a fledgling industry. Historians have noted the impact of World War II on the revival of various American industries in several past studies. Therefore to control for the possible positive effect of war, a dummy variable was added to measure the effect of the period during which the U.S. was involved in WWII.

In response to the claim that the market changed not due to the Penicillin Program but as a result of separate political interventions, two additional variables were estimated. Both are dummy variables marking when new regulations governing the pharmaceutical industry were introduced. During this time period, there were two such regulations. The first came in 1938, but was not formally enacted (due to legal challenges) until 1939. This was the initial amendment to the Food and Drug Act stating that all medicines must first be proven safe before they could be sold. The second regulation arose from the 1951 Durham-Humphrey Act in which Congress formalized the distinction between over the counter and prescription medications, requiring prescriptions from licensed doctors for sale of the latter.

**INSERT TABLE 2.2**

Table 2.2 presents the descriptive statistics for these variables. The four financial variables, each measuring a different aspect of growth, displayed an expectedly high degree of correlation. This ranged from income and profit at .948 to employees and income at .674. However, none of the independent variables correlated strongly with each other, as shown in table 2, suggesting a lack of problems with multicollinearity.
Methods and Results

Table 2.3 evaluates the first hypotheses (1a, 1b, 1c), modeling the selection process for the Penicillin Program, and includes six models using a random effects logistic regression. I chose a random effects model over the preferred fixed effects because the observations were limited to the time when the firms were at risk of being selected and, for several firms, the independent variables were unchanged over that period. Unfortunately, as the smallest three selected firms were still private during this period, their data were unavailable and therefore the results will be skewed in favor of correlating increases in size to a stronger likelihood of selection.

The first model tests the effect of a firm’s past financial success on its likelihood of being selected. The second model adds a measure for how long the firm had been incorporated, the third model estimates the effect of having a research lab, the fourth estimates the effect of a longer investment in science, and the fifth estimates the effect of employing more scientists. The sixth model includes all seven variables. A seventh model that offers a population-averaged logistic regression and an eighth that offers a random effects probit regression are included in Appendix A, for the sake of comparison.

The first hypotheses predicted that selection to participate in the Penicillin Program was determined by either the size or the expertise of the firm. Hypothesis 1a, that past financial success predicted selection by the OSRD, is partially supported by models 1-5 of table 2.3. In each of the first five models, firms with greater profits are proven more likely to be selected. For example, in model 5, controlling for the effect of employing additional scientists, profitability is still positively and significantly correlated with selection (.337, .176). Although interpreting the coefficients of logistic regressions is often difficult, the findings can be understood using the exponentiated coefficients, which indicate that each additional million in profits translated into a roughly 40% increase in the likelihood of selection. However, in model 6, including all of the controls reduces the significance and the size of the profitability effect (.306, .184). This finding remains significant at the 90% level, but the effect of profitability is now closer to a 30% improvement in the likelihood of selection.

While this appears to be a substantial increase, it is important to include two caveats. First, as most firm’s profits were within $1 million of each other, less than 5 of the 46 firms had profits more than $1 million above the mean. This means that for the majority of firms their additional profitability was not sufficient to significantly alter the likelihood of selection. Second, a number of the smallest selected firms were private at the time and, as they did not release their financial data, they could not be included in the regressions. Including only the public firms skewed the data in favor of finding a

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10 Coefficients and standard errors are reported in parenthesis.
11 A reduced form of the equation was run with the most significant variables (lab, employed scientists, profit) and this produced a significant, though even more reduced, effect for profitability. Here the effect of an additional million in profits was closer to a 25% increase in the likelihood of selection. These can be found as models 9 and 10 of Appendix A.
relationship between success and selection, thus likely overstating the impact of this measure.

Size, as measured by the volume of sales, showed no comparable effect suggesting that it was not the largest but the most profitable firms who were favored by the committee. It is possible that the distinction here is between more innovative firms and larger firms, a distinction that is tested in hypotheses 1b and 1c.

Hypothesis 1b predicted that firms with an existing research laboratory were more likely to be selected. Models 3 and 6 of table 2.3 offer no evidence in support of this claim. In both cases, the effect of a research lab is positive but not statistically significant (.609, .815; .395, .917). This corroborates the individual accounts of the selection committee members, in which people attempted to create reasonable sounding justifications and then determine whether or not they were accurate. The evidence here affirms this recollection revealing that firms without a research laboratory were no less liable to be selected than firms with that capacity.

Models 4 and 5 of table 2.3 test the final selection hypothesis (1c): that firms with experience in chemistry-based research were the most likely to be selected. This is based on similar logic to the previous hypothesis and assumes that the selection committee made their decision based on the perceived technical abilities of a given company. However, again the results in models 4, 5, and 6 offer no evidence in support of this hypothesis. Model 6 shows firms that had employed scientists for years were at no advantage relative to their competitors with no scientists on staff (-.006, .023). Nor did hiring additional scientists increase the likelihood of being selected (.004, .007).

Together these results offer empirical confirmation of the qualitative evidence presented earlier in the paper: selection was not based strictly on size or technical capability. Firms with a longer history of experience or with the physical plants required to innovate were not favored over less technologically invested competitors. Further, the committee did not simply select the largest firms and ignore the hundreds of smaller firms. As figure 2.2 shows, while a cluster of the most profitable firms was selected, far less profitable firms were also chosen to participate. On the whole, among the firms profitable and successful enough to have gone public, the selected firms do not appear to be significantly different from those the committee turned down.

INSERT FIGURE 2.2 (graph of firms by pre-selection profit)

Tables 2.4, 2.5 and, 2.6 present the tests of the second, third, and fourth hypotheses. For each dependent variable, I estimated seven models using fixed effects regression (table 2.4) and three models with random effects regression (table 2.5). In table 2.6, I also include four models of survival, estimated with a cox proportional hazard regression.

The fixed effects model was chosen to prevent any unobserved variance between the units from affecting the estimators. The random effects model (models 7-10), though less preferred due to its additional assumptions about the lack of correlation between the error term and the variables, is included in order to measure the effect of time invariant variables and to estimate the effect of economies of scale. A Hausman test validated the use of the model for this purpose. However, fixed effects was preferred for the primary
models as random effects often leads to under-estimation of the error terms and a misspecification of the coefficient, although here it produced comparable results to the fixed effects.

Additional estimators, fixed and random effects including an AR (1) process and, a pooled OLS regression that includes both a time term and a first-order lag of the dependent variable, are included in Appendix B for sake of comparison. These models produce equivalent results to those presented in the body of the paper, with minor variance in the exact value of the coefficients but no change in their relationships or significance.

In table 2.4, the first model tested the effect of organizational changes on each dependent variable; the second model included measures for the political changes; the third model included a measure for whether a firm received a government contract, along with the previously tested variables. The fourth and fifth model include measures for the type of contract the firm signed and whether or not the government built them a manufacturing plant. The sixth and seventh models include interaction effects to estimate how receipt of an OSRD contract affected the value of other variables. The eighth through tenth models offered the random effects estimation of all the previously included variables along with measures of the firm’s size and organizational structure at the start of the period.

**INSERT TABLES 2.4 and 2.5**

The second hypotheses (2a, 2b) proposed that firm growth resulted from the adoption of organizational changes, and that the earlier these changes were adopted, the better the firm would do. Hypothesis 2a, specifically, predicted that the adoption of any of the three organizational changes would lead to greater growth. Models 1-5 in table 2.4 offer limited evidence in support of this hypothesis showing that the creation of a research laboratory corresponded to significant growth for only one of the four dependent variables. For income, profit, and sales, the effect of a lab was always positive, but only for sales was this effect statistically significant. Model 5 reports that creating a lab increased sales by over $8 million (8.37, 3.62), an effect that is replicated in the other models. These results suggest that adopting any of these organizational changes during the period of study was not the cause of future success of any firm.

Hypothesis 2b estimated this benefit of adopting organizational changes early. Although having incorporated sooner did not provide a significant effect on any of the dependent variables, hiring scientists did demonstrate a slight positive impact on profits and employee growth. Models 1-5 of Table 2.4 show that each additional year having a chemist on staff increased profits by $100,000 (.115, .047). Models 1 and 2 also indicate that each additional year with a chemist corresponded to a 50 employee increase in firm size (.053, .025). However both of these effects decreased and were rendered statistically insignificant in model 3, when a measure for selection was introduced. This suggests that the benefit was less a product of organizational change and more a result of selection.

However, the fact that in the random effect regressions, in table 2.5, possession of a lab does matter for income (2.09, .659), profit (.926, .288), sales (5.71, 1.95), and employees (.339, .144) could suggest that those firms that changed and added labs during the period of study did not earn a significant advantage, but the firms with pre-existing
labs (whose lab status did not change during the study) were at a significant advantage. This would indicate that the organizational changes only benefited firms that adopted them early. This lends support to the idea that firms cannot adapt to changes, so much as they need to be prepared for them.

While evidence for the benefit of early adaptations is inconsistent, firms that began the study as dedicated pharmaceutical firms, the organizational form that would become dominant in the 1950s, were more obviously unsuccessful. Model 8 of table 2.5 shows that dedicated pharmaceutical firms performed no better than firms in which pharmaceuticals were only one division among many. In fact, dedicated pharmaceutical firms had significantly lower profits (-.682, .283) and sales (-4.29, 1.91) than rival firms. Model 8 also reveals that firms that began the period of study with an established R&D division were no more likely to succeed on any of the four measures.

**INSERT TABLE 2.6**

Table 2.6 offers the results of tests of the independent variables on the likelihood of exit for the firms in the study. The first set of models use a cox proportional hazard regression to estimate variations in the rate of bankruptcy or acquisition. The second set estimate a logit regression of the likelihood that a firm would be classified as a pharmaceutical in 1954. Model 1 investigates the role of organizational change, model 2 includes test for economies of scale, model 3 includes measures of organizational structure, and model 4 incorporates all the variables.

The results in model 4 of table 2.6 suggest that some organizational adaptations were more important than others. As firms that were dedicated pharmaceutical firms were significantly more likely to fail than their peers (2.39, 1.04), but firms with a research division were significantly more likely to survive (-1.69, .859). This can be interpreted as meaning that dedicated pharmaceutical firms have a hazard rate nearly ten times that of more diversified firms, while firms with R&D investments had only 20% of the hazard of rival firms. In other words, while building labs may not have made one firm more successful than any other, you needed a research department if you even wanted to stay in business. Model 8 of table 2.6 reinforces this claim as dedicated pharmaceutical firms were no more likely to remain in the industry at the close of the period than their diversified peers, but firms with R&D divisions were significantly more likely to remain as pharmaceuticals (-3.51, 1.44).

Taken together, these are surprising findings, as they suggest that the intellectual capital gained through experience and the organizational advantage gained by years of fine-tuning how to operate as a dedicated, research-intensive pharmaceutical company, produced only a slight competitive advantage. What we may see here is that the earliest adopters of these ideas were not actually the best at implementing them; and despite early and intensive investment in science, firms continued to “get it wrong.” That is why firms slow to adopt the new organizational forms were still able to succeed. Alternately, this may imply that the real benefits to scientific research were still years away from being realized, and that investments in the 1930s simply were not able to produce any return, whereas later research endeavors returned multiples of their initial investment.
The third hypotheses (3a, 3b) assumed that economies of scale determined the success of firms in this period and that the largest and most profitable firms would therefore benefit the most from any changes. Hypothesis 3a, that the largest firms would experience the greatest growth, is estimated for each dependent variable by model 9 in table 5. This model does not support the hypothesis, showing that firms with more sales at \( t_0 \) did not experience greater subsequent growth. Models 2 and 4 of table 2.6 reinforce this finding, showing that the largest firms were no more likely to survive the period than smaller firms.

Even if size is measured solely by a firm’s investment in scientific research, the largest firms fail to outperform. In fact, employing more scientists actually decreased a firm’s income \((-0.044, 0.025)\), profit \((-0.025, 0.011)\), and sales \((-0.196, 0.077)\). These results suggest that larger firms were no more insulated from the changes in their environment than their smaller rivals. The environmental changes were sufficiently severe that size at the beginning of the period did not correspond to the size of the firm at the end. Again we find that 1935 was too early for investments in scientific research to pay off, and the opportunity costs of hiring additional science employees may have cost firms on multiple fronts.

However, hypothesis 3b, that the most profitable firms would experience the greatest growth, is supported by the data in model 8 of table 2.5. Profitability at the start of the period correlated with continued growth in profits, sales and employees throughout the period. In particular, an additional million in profits in 1935 corresponded to an increase in pre-tax income of nearly $400,000 \((0.386, 0.114)\), an $800,000 increase in sales \((0.799, 0.329)\), and $200,000 in profits \((0.209, 0.053)\). Model 8 of table 2.6 also shows that firms with an additional million in profits were nearly 40% less likely \((-0.653, 0.292)\) to exit the pharmaceutical industry. Although it is perhaps not surprising that a profitable firm would elect to remain in the industry that makes it profitable, it is surprising to see, as is evident in model 4 of table 2.6, that firms with early profitability were no less likely to fail during the period of study. Similarly, the largest and most scientific firms were also no more likely to survive or to remain members of the industry than rivals that began the study with fewer sales or scientific staff.

While these results indicate the most profitable firms possessed an advantage relative to their peers, it is worth noting that this was specifically restrained to profitability and that it was modest in scale. This may indicate that profitability, not size, serves as a buffer during periods of change. Small and profitable firms may actually have been in the best position, as they would have fewer obstacles to organizational change and the income necessary to finance the changes.

The final hypotheses (4a through 4d) proposed that more than these other factors, it was the selection to participate in the penicillin program that proved critical in determining which firms succeeded. Hypothesis 4a assumed that the value in selection lay in the scale increase that came from new manufacturing plants. Model 4 of table 2.4 offers limited support for this claim, as receipt of a new manufacturing plant only proved valuable in increasing firm sales \((8.95, 4.53)\) but had no corresponding effect on profit, income, or employees.
Hypothesis 4b presumed that the selected firms were more likely to experience growth as a result of their selection. The evidence, presented in model 3 of table 2.4, confirms this hypothesis and demonstrates the impact of the OSRD contracts. Each of the firms that received a contract to produce penicillin experienced unprecedented success relative to their peers. The effect of participation on income (3.25, 1.04) would have vaulted a mediocre firm past some of the most profitable. In terms of profit itself, the effect of participating in the OSRD program was worth a nearly two-decade head start in chemical research (2.09, .428). The effect on sales (7.82, 3.03) was greater than the effect of building a research laboratory or any other measure. These effects are all reproduced in table 2.5, where we see in model 9, that the effect of an OSRD contract was equivalent to a nearly $10 million advantage in initial profits, sales, or income. In other words, the smallest, least profitable firm in the study, if given an OSRD contract, was suddenly on par with the largest and most profitable firms. A graph of the firms, arrayed by their profits in 1946, offers evidence of just how radically the program altered the landscape. Only the number of employees failed to change as a result of participation in the program.

**INSERT FIGURE 2.3—PROFITS AFTER 1946**

Hypothesis 4c attempted to evaluate the mechanism by which these OSRD contracts operated to improve the performance of firms. Although the earlier results have shown that success was not a product of increased scale, the question remained whether the advantage was specific to firms conducting research or to those focused on manufacturing.

Model 5 of table 2.4 distinguished between firms that were hired to conduct research on penicillin from those hired to manufacture it. The overall favorability of both contracts suggests that neither was more advantageous than the other. Although firms hired to manufacture penicillin had slightly greater income (4.39, 1.36) and profit (2.28; .541) than those hired to research it (3.29, 1.33; 2.16, .575), they also had slightly lower sales (8.14, 3.95; 9.05, 3.96). Model 10, in table 5, reinforces the notion that both contracts were providential, as here the research contracts proved slightly more profitable (2.4, .429) than the manufacturing (1.58, .440). As none of the selected firms failed, it is impossible to use survival analysis to determine whether one contract had a greater effect than the other on the likelihood of failure. Clear in these results is the fact that participation in the penicillin project, irrespective of the manner in which the firm participated, proved valuable.

Hypothesis 4d also investigates the mechanism by which selection acted on firms, predicting that selection to join the penicillin program would increase the value of any prior advantages or organizational changes. To test this hypothesis I include, in models 6 and 7, interaction effects for the combined effect of selection and size, and selection and creation of a lab. These interactions model how the value of size or the creation of a research lab varied for firms that were granted an OSRD contract, and also how the value of the OSRD contract varied with the size of the recipient firm. This helps distinguish any changes in the benefits of being large and innovative before and after the market underwent its transformation.
In model 6 of table 2.4, I examine whether large firms benefited more than small firms from receipt of an OSRD contract. I find that an OSRD contract’s value had a slight variation for profitability (.229, .091) but had no effect on the other dependent variables. However, this effect is slight, as a firm with 1,000 additional employees would earn only $200,000 more in profits than a smaller firm. This, at a time when the majority of firms in the sample had fewer than 1,000 employees total. Model 7 of table 2.4 shows that the value of a research lab was similarly unchanged by selection into the penicillin program. The interaction of creating a lab and being selected proved statistically insignificant for all four of the dependent variables. This suggests that the value of a lab was not greater for firms who were selected nor was being selected more advantageous to firms that already had established research labs.12

Together these findings suggest that prior advantages were not enhanced by selection into the penicillin program. Instead, it indicates that the value of the program was external and new, not extending past capabilities so much as it succeeded in creating new ones. These findings show that the penicillin program created a new environment in which the selected firms were given a far greater likelihood of success and where success meant far more than it had before.

In the end, none of the control variables compete with the effect of the OSRD contracts in determining the within-panel variation. The changes experienced by individual firms were affected more by receipt of an OSRD contract than by any other set of variables. However, this does not explain all of the between panel variation. Clearly, pre-existing unobserved variations helped determine the initial conditions of the firms at the start of study and, moreover, these initial advantages perpetuated distinctions between firms. While this lends credence to the claim that what transpired here was really an issue of economies of scale, the OSRD results suggest that this initial advantage could be surmounted through receipt of a penicillin contract. This is precisely what occurred with Pfizer, which moved from under $5 million in sales in 1935 to $163 million by 1955. Moreover, as evidenced by the decline of Lambert Pharmacal—a firm that ended 1935 with $10 million in sales but by 1950 only had $21 million and was soon acquired—the failure to receive an OSRD contract helped to undermine whatever benefits accrued to even the largest firms.

Conclusion

This paper examines three accounts for how an industry undergoes a radical transformation. Specifically, was it (1) the inevitable progression of the largest firms, (2) a response to an exogenous shock, or (3) the intervention of the federal government that changed the U.S. pharmaceutical industry from a regional, non-innovative, barely profitable business into a national, highly innovative, highly profitable industry?

Past research focused on scientific advancement as the source of an exogenous shock. The discovery of penicillin providing a technological shock so great the industry was forced to evolve (Chandler 2005). But the ability of penicillin to transform an

12 Similarly, interactions of the OSRD with the number of scientifically trained staff employed at a firm did not prove significant (not reproduced here), suggesting that while having a lab was critical, the size of the lab was not as important.
industry should be the *explanandum* not the *explanans*. Studies of disruptive technological change have focused so heavily on successful transformations that we underestimate the effort required for even a spectacular technological breakthrough to produce the long-term change found in this case. The evidence gathered here offers a valuable counterpoint to these claims. It demonstrates that even a revolutionary discovery, like penicillin, does not transform a market by itself. Instead, the process by which a technology becomes a catalyst for evolution requires a network of actors, organizational and institutional changes, and not infrequently the ability to overcome the resistance of the most powerful members of a market.

Both the qualitative and quantitative evidence reinforce this finding as neither size nor exogenous shocks, even the discovery of penicillin, proved capable of transforming the industry individually. This is not for a lack of trying. The government made three successive legislative efforts to redirect the activities of U.S. pharmaceutical companies, each with only mild results. Penicillin was heralded as a transformative medical breakthrough by both academic and popular presses, but was greeted with indifference by the pharmaceutical firms. Only the threat of a second world war could motivate the government to directly intervene, pursuing their own research and then sharing the lucrative results with only a handful of selected firms. It was this intervention, and the subsequent creation of a Penicillin Program that required firms to collaborate that finally catalyzed the evolution of the industry. This program made penicillin valuable, it taught firms how to conduct research, and it limited the knowledge and the profits to only a handful of firms, the firms who would go on to dominate the industry for the next half century.

This disproved my other hypotheses, as the largest firms did not merely continue to expand and slowly drive the smaller firms away. In fact, the largest firms in 1935 were no more likely to remain in business or active in the pharmaceutical industry in 1950 than any of their smaller rivals. Nor did the market change in response to the prior exogenous shocks. Though each altered the environment, favoring one set of firms over another, they did not force the field to move to a new organizational form. Instead, firms were surprisingly averse to change, resisting multiple attempts to alter the industry, and only expressing an interest in penicillin when the risks were significantly reduced.

Eventually the firms did need to move towards a research-oriented model in order to survive, but moving early or quickly did not affect the degree to which firms succeeded. In this case, foresight, good fortune and, flexibility were all of equally slight importance. This is contrary to what theory proposed, as the shocks elicited few changes and the firms that made changes were at no great advantage to those that waited. While the most profitable firms experienced slightly greater success and an improved chance of survival, the only firms that experienced significant advantages were those firms that were selected to participate in the Penicillin Program.

Two limitations to these findings are important to note. First, although my questions address a population-level issue, the majority of my measures and hypotheses address firm-level variations. This can produce an apparent disconnect between what I propose to examine and what I actually am able to estimate. While this is a valid concern, I believe it is a mistake to assume that this apparent disconnect actually prevents an understanding of the process of market evolution.
By comparing the effect of size, organizational variables, and government intervention we are able to determine what factors enable firms to survive through and succeed after the market transforms. Further, by focusing on the effect of these variables on future success, we gain insight into the specific characteristics that mattered most in the new market. While these factors may not explain what caused the market to change, they do tell us how it changed, why the firms that dominated became dominant, and why so many firms fell away. They tell us why pharmaceuticals became an oligopoly in the 1940s as opposed to the 1930s, why the firms focused on antibiotics (e.g. the variants of penicillin), and why new firms did not emerge in the new market to challenge this hierarchy. In the end, focusing on the effect of firm-level variation allows us to determine which changes a firm had to make if they hoped to move from being mildly successful in 1935 to tremendously profitable in 1955. Equally important, we know which inactions or which delayed actions could injure a firm so severely that, despite prior success, they would no longer produce drugs by 1955.

A second concern is that the measure for selection remains a proxy for some unobserved characteristic that also explains the firm’s later success. The slight correlation between profitability and selection may indicate that firms were selected on the basis of some form of status. Alternately, selection or success may be explained by degree of political connectedness or some other network relationship. Unfortunately, the difficulty in measuring the number and quality of ties, during the 1940s, for a group of now defunct firms, has prevented any network analysis at this point.

However, it is possible that alternate measures exist that explain some degree of both selection and success. What I have been able to show here is that firms were not selected for the most likely reasons: size or technological ability. Instead, it appears that they were chosen for a variety of reasons, including manufacturing capacity, geographic diversity, political expediency, etc…. And, although possible, it is exceedingly unlikely that such a diverse group of firms shared one unobserved factor that also explained their subsequent success as pharmaceutical companies. Yet these selected firms did all go on to experience staggering levels of profitability previously unseen in the industry.

These findings are relevant for three distinct aspects of our understandings of markets, and the pharmaceutical industry in specific. First, they offer an alternative understanding of how high technology industries emerge in the United States, one that is more focused on the role of collaboration than competition. Conventional wisdom suggests that new industries, like the fledgling “green tech” industry, can best be supported by making capital cheap to as many innovators as possible. Thomas Friedman has characterized this by stating that innovation requires “thousands of inventors in thousands of garages” working on a solution. The hope is that competition between these engineers will eventually result in the rise of a dominant new design for the industry.

However the pharmaceutical industry was pointedly unable to evolve when competition was the sole driving force. Attempts to protect the market from foreign competition or to foster competition between the largest American firms did not succeed in altering the organization or orientation of U.S. firms. Instead, it was when the government required firms to collaborate on a given research project, to share their results and discoveries, that the industry was able to transform. Individually, the cost was too high and the time required too long for any firms to pursue, but collectively, they
were able to develop a method for researching and manufacturing new drugs that became the norm for the next half century.

Second, these findings improve our understanding of the role the state has played in the construction of American industry. In this case, we see that the state operates, more than firm managers, as the agent of change. Traditionally, the state acts to facilitate innovation, and to foster innovative industries, by serving as the primary and often the sole customer for unprofitable products. In this way, the nascent airline and computer industries were able to survive long enough to develop products for a larger audience. Less often, the state acts to stimulate innovation by attempting to force greater competition, as discussed above. This can occur through regulation that breaks up a monopoly, as in the telephone industry, or through more direct government efforts to create a better product than the market has offered, as in the Tennessee Valley Authority.

However the pharmaceutical industry presents a separate case where the government has stimulated innovation by first being the innovators themselves, and then turning over their ideas to private partners. A similar logic, that the state can be operate as an idea incubator, later served as the impetus for the Technology Transfer Act and the 1979 Bayh-Dole Act that helped initiate the biotechnology revolution, as well as the 1991 High Performance Computing Act that enabled the commercialization of the internet.

In each of these situations the established firms were uninterested in pursuing the government’s projects, so the government itself had to conduct the research. For instance, AT+T turned down overtures to help commercialize the internet, convinced that sending “packets” of data that way would never be of interest to consumers. Earlier, the large pharmaceutical companies, weighted down by heavy investments in chemical research, were slow to understand the possibilities of biological-based approaches to drug development. Just as during the penicillin era, the largest and most established firms had been convinced that antibiotics were a poor investment of their resources (as it was unlikely that they could ever be made profitably). Each time, the U.S. government chose to circumvent the reluctance of the existing market, and to coordinate research with a select few partner firms that were then given complete control when their ideas became profitable. And each time a new industry emerged, with these former collaborators becoming the initial players in an industry that would have been unlikely absent the government’s intervention.

Finally, just as this helps us better understand how some markets are transformed, it also helps us understand who succeeds in the new environment. Profit can serve as an insulator and survival requires that firms make some changes, but neither adaptation nor size predicts the success of the firms. While some prior studies have yielded similar results where “competence-destroying” innovations permit new challengers to usurp the dominant firms (Tushman and Rosenkopf 1992), this is not what we find here. In this case new players do not emerge to capitalize on this technology, but rather 175+ firms try to capitalize and only 17 are allowed. The success of these firms had less to do with their internal organizational structure or individual managerial decisions than it had to do with their access to the collaborative research that occurred during the Penicillin Program. Access to the information on penicillin and, more specifically, to how different firms conducted their research programs, proved critical in transforming those firms and separating them from their unselected rivals.
This produces a different understanding of how markets evolve, one in which exogenous shocks are resisted and require extraordinary circumstances to prove transformative. As well as a different account for the emergence of American industry, one in which the federal government played an instrumental role in first establishing the modern pharmaceutical industry.

For pharmaceutical companies, as later was the case with the internet, government researchers worked with private concerns to develop new technologies that these private firms then used to transform their industries. Both times these dramatic innovative shifts occurred despite the claims by the dominant firms in the industry that the new technologies were worthless. And in both cases the firms selected to participate in the government research were given enormous advantages over their peers.

In the pharmaceutical situation, this advantage was reinforced by both organizational changes and subsequent regulatory shifts to produce a class of companies that would dominate the industry unchallenged for half a century and counting. In the state’s attempt to incite innovation by encouraging a subset of firms to compete and collaborate they effectively elevated that subset into a new research-oriented, highly innovative industry that was as foreign to their former competitors as the internet was to telephone companies.
Chapter Three: The Anti-Substitution Laws

“Cheap drugs are not good medicine.”

“…the drug industry is fleecing the people by trying to convince them, through high-powered and expensive advertising, that drugs sold under a brand name at exorbitant prices are somehow or other more reliable than the same drugs sold under their official—generic—name from one-half to one-thirtieth as much.”
Senator Gaylord Nelson (D-WI), June 11, 1973

Every year, from 1950 to 1980, the twenty largest pharmaceutical companies have accounted for almost 80% of all drug sales. (Thomas 1983). New technologies were released, new discoveries made, new policies enacted, and dramatic changes made in insurance and health care delivery; yet the market remained in the hands of these few firms. Taken at a glance, this confirms what most people already believe about the pharmaceutical industry: it doesn’t change. To a more cynical pair of eyes, it might even suggest that the very structure of the market prevents these firms from failing. And indeed, numerous critics have challenged the nature of the industry, pointing to its persistent profitability as evidence of how corrupted and insulated it has become (Avorn 2004; Greider 2003; Hawthorne 2003). However this portrait strikes a dissonant chord for anyone who has worked in pharmaceuticals and recalls both the constant anxiety over omnipresent external threats and the level of activity and effort it took to maintain the stability we see at a distance. Like the metaphoric duck kicking wildly below the surface, the stability theory predicts and evidence reports is a much more delicate product than commonly recognized.

In that sense it is a mistake to equate perceived stability with inactivity, it is too simple and too misguided to assume that maintaining a market occurs easily or without contestation. As opposed to the other chapters in this dissertation, this chapter does not examine how environmental change influenced organizational or institutional change. Instead, this chapter focuses on the inverse; a case where a decade long battle resulted in an environmental change that had no effect on the organization of the firms or the field. The purpose is to explore a case where the dominant firms failed to prevent a change to their environment, and yet succeeded in maintaining their status, market-share, and profits. This unique case offers valuable insight into the mechanism by which the stability theory predicts and past research has found, is actually produced.

This chapter uses qualitative methods and archival data to examine the question of how stable markets are recreated. I use the repeal of anti-substitution laws in the 1970s in the United States as a case in which to study the varied efforts made by incumbents to maintain the structure of their field as it was first threatened with and then experienced dramatic regulatory changes. This case is of particular interest as it fails to conform to our standard expectations for how economic actors influence market structure. In this instance, lobbying efforts did not determine the outcome, and no regulatory agencies were “captured” by the interests they govern. Instead, this case demonstrates how firms employ both political and social means to stabilize their market, using their control over
access to information as a way to compensate for their political losses and to maintain a stable market through a turbulent time.

**How stability is created**

In earlier chapters I discussed the conventional three-stage description of market evolution. Where stable markets are (1) first ruptured by exogenous shocks, (2) leading to a period of debate and delegitimization followed by (3) the emergence and diffusion of a new understanding of how the market should be structured, that results in a new period of stability. In these cases stability is both a pre-existing condition and an end result; and evolution is what happens between stable periods. Recently, Ingram and Rao (2004) complicated this portrait, using the rise and repeal of anti-chain store legislation to document the potential for conflict in this presumably tranquil final period. Their research showed that diffusion is not inevitable because, as new norms diffuse, they engender resistance and contestation that can lead to their reversal.

I hope to build upon this finding, and to use the case of the rise and repeal of anti-substitution laws to further explore how actors mediate changes to their environment. Just as Ingram and Rao focused on the final stage of evolution, to study the contested diffusion of new standards, I will focus on the first stage, to examine the process by which actors contest and mitigate the effects of the initial shocks to their environment. In contrast to Ingram and Rao, my analysis will include both the political and the social/scientific aspects of their approach to reveal the array of tactics employed. This will offer a valuable complement to their work and help illuminate the process by which stability is maintained in a field, a process we have previously treated as almost automatic.

**Economics, political science and organizational theory all offer competing accounts for why a market could remain so stable; but the easiest way to understand these disparate descriptions is to think in terms of constraint and choice. As we will see momentarily, these different traditions agree in principle that stability is achieved either by constraint: limited resources, limited network positions, normative pressure, or regulatory barriers. Or, stability arises out of choice: actors prefer the predictability of a stable arrangement to the potentially more profitable, but riskier, option of pursuing change.**

**Constraint**

Economic analyses reject the assumption of stability for an assumption of dynamism, where competition drives the rise and fall of individual firms. When stability does occur, it does so because external agents have succeeded in restricting competition by erecting high barriers to entry or by shoring up failing firms (Mueller 1986; Rumelt 1991). Although these conditions are rare, they do describe the case of the pharmaceutical industry in the 1960s where FDA required tests of safety and efficacy established the requisite barriers to entry for new firms.

In this reading, the stability of the market arises from excessive regulation limiting competition. It is an uncommon and unnatural state that exists as long as the barriers remain in place. However, this interpretation fails on two counts: it underestimates the degree of stability found in ordinary/less-regulated markets (e.g. the...
soft-drink market where Coke and Pepsi remain locked in a stable form of competition decade after decade) and it narrows our attention to only policy matters. As I will soon show, the regulatory impediments were only one of the tools actors employed to stabilize their market. To understand either the general tendency for markets to fluctuate between periods of stability and periods of change that is discussed in the first chapter of the dissertation, or the additional tactics available to economic actors, we need to use the insights of population ecology and institutional theory.

Population ecology explains the oscillation between stability and instability as part of the life-cycle of an industry (Freeman and Hannan 1977). When an industry first emerges there is instability as actors jockey for particular niches and access to scarce resources. As the field develops, more competitors enter and the density intensifies competition resulting in the exit of all but the hearty few survivors. These firms are then well entrenched in their positions and both disinclined towards and incapable of radical change (Freeman and Hannan 1984). The firms establish domains along geographic, technological, and consumer-oriented lines to reduce their degree of competition and to establish a symbiosis (Barnett and Carroll 1987; Baum and Haveman 1997). Stability then, is the result of the exit of the failed firms and the ossification of the survivors. Instability will arise again only if new technologies or new policies alter the value of the resources, allowing new firms to enter and setting off a second-wave of competition, that again will end in stability as the failing firms exit (Freeman and Hannan 1989).

In laymen’s terms, the firms behave like animals confined to a small space, they each carve out their own territory and guard it, but make only limited attempts to expand. Once all the territory is divided, any latecomers find themselves with nowhere to go, and either move on or die. Unless the weather changes drastically, moving food or water to new locations, the animals will remain in their territories, creating a stable distribution across the space.

Institutional theory explains similar patterns not in terms of an environmental equilibrium, but instead in terms of the establishment and enforcement of norms. Here, stability does not arise once the resources are divided, but rather once a legitimate method of operation is established. The classic pattern portrays stability as emerging after a legitimized innovation diffuses throughout a field causing actors to coalesce around a single model of action (DiMaggio and Powell 1983; Meyer and Rowan 1977). More recent research has shown that this normative pressure to appear legitimate is both actively pursued by the firms’ themselves and imposed upon them by external agencies (Hsu 2006; Zuckerman 1999). In both cases, the legitimized model forms a constraint on behavior, creating stability by penalizing actors who pursue boundary-spanning activities. While not formally required to behave in a given fashion, or organize in a particular way, transgressors experience negative repercussions that help maintain a stable, predictable field until an exogenous shock catalyzes the production of an alternative (Greenwood and Hinings 1996; Meyer, Brooks, and Goes 1990).

As illustrative as these theories are, they do suffer from a few limitations. Most notably, they underestimate the degree to which actors have agency. In each of these three theories, stability happens to the field not because of the actions of the participants. This implies an almost gravitational force, as if stability were a natural condition that we return to after momentary disruptions. To remedy this more recent work has looked at the role of individual actors in creating the conditions that produce the constraint. In this
case, stability is not a natural phenomenon but an artificial one, established through the concerted and repeated efforts of individual actors.

Choice

Just as regulation can create stability, savvy actors can seek to erect regulatory barriers to improve their fortunes. In other words, stability can be an intended or unintended consequence of legislative change. There is a rich literature in political science on the utility of lobbying officials or agencies to adopt a more favorable position (Austen-Smith and Wright 1996; Wright 1990). The emphasis of this work is to bridge the divide between economics and political science to explain the relationship between economic actors and the agencies that seek to regulate them. These theories favor two descriptions of regulatory action: it is intended to correct market imperfections, or it is intended to favor a group that has “captured” control of the agency (Lafrance and Tirole 1991).

The FDA has been accused of filling both roles in the past. In 1938, it sought to correct information asymmetries between producers and patients, by ensuring that all drugs be proven safe before they could be sold. In more recent years, it has been argued that the movement of staff from pharmaceutical companies to the FDA and back has compromised the integrity of the agency and reduced its effectiveness in protecting American patients. Therefore, it is logical to assume that pharmaceutical firms lobbied to erect additional barriers to stabilize their market and sought to coopt the FDA in order to ease their own path to profit.

However, the actual behavior of the pharmaceutical firms belies these expectations as the industry argued vociferously to both reduce regulatory hurdles by either limiting or even eliminating the FDA. Although these plans were never realized, Philip Hilts, in his encyclopedic history of the FDA, recounts just how close things came in the late 1970s, as pharmaceutical executives and government officials together argued that the FDA was no longer necessary and served mainly to impede medical progress (Hilts 2003). This indicates that the firms were electing the unstable path and seeking to remove the barriers that insulated them, in the hopes that lower costs would lead to greater profits.

Therefore, since it does not explain the stability found here, the lobbying behavior that has received justifiable attention in the past will not be my focus. Instead, I am interested here in the alternative methods employed by economic actors when their lobbying efforts failed. After all, we need some means to reconcile the inability of

13 The critics contend that regulators hoping to land a more lucrative job with a pharmaceutical company are loathe to alienate these companies by appearing “difficult” and therefore make extraordinary efforts to appease the companies and approve their products even if the scientific claims are dubious. This practice appeared especially prevalent during the 1980s when the external reviewers used by the FDA to test efficacy and safety were not required to report any financial ties they had to the pharmaceutical firms they were testing. Despite the face validity of these concerns, numerous investigations have not produced any damning evidence, suggesting that the degree to which the agency was “captured” may have been overstated.
pharmaceutical firms to succeed politically with their continued, and growing, financial success.

Dynamic Stability

To answer this we must think of stability as something constantly recreated and we must broaden our view of the tools that are available to these actors. The problem with the prior explanations is their rigid linearity and the unidirectional nature of the process. Institutional theory assumes that once a new organizational form is adopted, diffusion and conformity are inevitable. Ecology treats each domain as constrained and inviolable. In each case, the market trends towards stability and, once achieved, it remains stable until something arises that alters the balance of power, changes the scarcity of the resources, or causes the actors to question a given set of assumptions. Stability is an outcome, occurring between shocks and can only be undone by a shock. So we are again left with a three-stage process that smooths over any contestation that occurs after adoption, and makes it difficult to explain how conflict occurs prior to an exogenous shock, or how incumbents might act to mediate the shock.

Recent work has attempted to complicate this portrait by investigating the role of diffusion in eliciting contestation. Studies of the rise and repeal of anti-chain store legislation refute the linear narrative above and suggest that as a new practice, in this case the passing of anti-chain store legislation, becomes more common it also encourages greater resistance that can, in the end, result in a rejection of the norm and the establishment of a new practice (Ingram and Rao 2004). In studies of the evolution of inter-firm networks we see similar developments where established practices come under threat because they maintain the status quo and new firms seek to alter the governing “logic of attachment” in order to destabilize the field (Powell, Koput, Owen-Smith, and White 2005).

This suggests a more dynamic process of stability creation, one suggesting that the stable arrangements we encounter are more fraught and fragile than previously recognized. It demonstrates that incumbents must work to maintain a stable situation. It also suggests that there are multiple mechanisms, beyond those that are strictly political or economic, that can be used to perform this maintenance. To uncover some of these strategies I examined the rise and fall of anti-substitution laws in the United States.

Background

In 1848, there was a serious problem with the market for prescription drugs: no one knew what they were buying. While it could be argued that patients in 2009 still don’t know what they are buying, the earlier problem was more basic. If a patient today has a prescription for Zetia, they will get Zetia, even if they have no idea what Zetia is, how it works, or what it might do. A patient in 1848 faced a more substantial problem: when they took a prescription to a pharmacist, they could end up with anything. Literally.

This troubling predicament lead to the opening salvo in a battle between pharmacists and doctors over control of the dispensation of medicine. At the time, a doctor’s primary responsibility was to diagnose illness, while pharmacists held the
expertise in matching a diagnosis to a remedy. This meant that while doctors prescribed drugs, pharmacists enjoyed some latitude in deciding whether or not to fill a prescription as written. Depending upon the pharmacist’s interpretation of the situation, they were free to substitute the prescribed drug for a cheaper, or simply alternative, form of medication. As reports increased of patients receiving useless prescriptions doctors pointed their fingers at the pharmacists (Editorial 1877). The pharmacists meanwhile, blamed the pharmaceutical firms for manufacturing adulterated products.

In 1849, the New York Assembly decided to listen to the pharmacists and passed one of the first laws regulating the sale of drugs in the United States. The focus, as suggested by the pharmacists, was to limit the adulteration of drugs by foreign manufacturers. Specifically, the law required a customs officer to test all imported medicine for dilution, adulteration, or contamination. The first man to hold this position, MJ Bailey, was so proud of the work his team accomplished that, after his first year, he published an 18-page letter to the President of the New York Academy of Medicine. In this letter he enumerated the several thousand pounds of adulterated drugs customs agents had captured, writing, “Such, sir, are the fruits, thus far, at this port, of the wise and eminently beneficial sanitary measures, so heartily approved of by every friend of humanity.” Although wary of the evils of pharmacists themselves, he continued to thank the doctors for facing the nefarious pharmaceutical companies and passing a bill that, “…met from its inception, the open, determined and unremitting hostility of a God-forsaken portion of our trading community…who had long made the murderous traffic not only a source of profit, but of wealth” (Bailey 1849). The problem, as Bailey and others saw it, was quite simple: people had no information and no reason to trust the manufacturers. As Bailey explained, “…where is the man who can, by simply looking at the almost countless number of medicinal preparations, chemical and otherwise, say whether they are adulterated?”

By 1900, the early concerns over adulteration had transformed into a fear of substitution. Physicians, unconvinced that pharmacists were any less of a problem than the pharmaceutical companies, sought to convince the public that unprincipled actors were intervening in their medical care without their knowledge. They suggested that while physicians had no financial incentive in prescribing one brand over another, the pharmacists actually profited from selling false medicines at high prices. These fears lead, in 1903, to the Bostwick-Dowling bill, one of the country’s first attempts at a “substitution law.”

Bostwick-Dowling marked the second attempt by physicians to usurp the power of pharmacists. If passed, the bill would prevent pharmacists from offering a customer anything other than what a physician explicitly wrote down. The pharmacists responded in kind, accusing physicians of dangerous levels of professional incompetence. As the New York Times reported, “The doctors charged that the druggists make a practice of substitution to add to their income, and the druggists assert that they are obliged frequently to make changes in prescriptions brought to them from doctors in order to save the lives of patients” (1903). So the question in the 1900s became: which is more likely to kill you, an ignorant physician or an unethical pharmacist? The New York State
Assembly decided that they feared the pharmacists and passed the act. But the Governor, in vetoing the bill, acknowledged a need to maintain a balance of power in health care.

In 1904, the New York Times editorial board called on the state board of pharmacy to correct this predicament themselves, writing, “It is no exaggeration to say that, at the present time, the market is flooded with bogus preparations, dilutions, and imitations, and that the business is honeycombed with fraud.” They continued, “It would be easily possible to revolutionize the drug business…[to] offer the consumer substantial and satisfactory guarantees that what is sold him is exactly what he thinks he is buying” (1904). But there wasn’t much traction for this type of effort. In 1900, physicians were not significantly more powerful than pharmacists and each group was able to maintain their role in the health care system without ceding any ground to their opposition.

Helping to maintain this balance of power was the poor quality of the medicine. In 1900, the vast majority of drugs were ineffective or, at least, of questionable benefit to patients (1904). At that time there were no federal laws regulating the industry, no guarantees of quality, safety, or effectiveness, so the public had low expectations. In this environment, the cost of not receiving the proper medicine was relatively low. And, if you don’t expect the prescribed medicine to work very well, you aren’t liable to get upset that your pharmacist gave you a substitute.14

Finally the situation began to change when the discovery of antibiotics and the subsequent discovery of steroids established a wide gulf between the therapeutic effect of legitimate and fraudulent medicine. Frequent accounts of the “miraculous” qualities of these new drugs raised public expectations (Self 1942). Armed with such a genuine difference in effectiveness, doctors had no trouble persuading the states to finish the battle begun 100 years prior. Acting on reports that placed the rate of substitution at nearly 40%, in 1952, California passed the first law of this second wave. The California law required the Board of Pharmacy to revoke the license of any pharmacist who substituted another drug for the one prescribed (Report 1979).

Within a few years, nearly every state in the country had passed a similar measure, in most cases even requiring pharmacists to use the specific brand indicated by the physician. These initial “anti-substitution” laws were designed to compensate for the limitations of an instrumental mode of behavior. The market for prescription drugs was no longer seen as a market where economic incentives should dictate purchasing decisions. Instead, they reflect a shift away from the idea that an unencumbered market

14 As mentioned earlier, there were both federal and state attempts to ameliorate this situation. Most notably, in 1906, Congress passed the Pure Foods Act requiring firms to list the ingredients of all medical products. Then, in 1938, in the aftermath of the Sulfanilamide tragedy Congress required that all drugs be proven safe before they could be sold. But, as will be discussed later in this chapter, these changes were intended to change the market by influencing patient incentives. As such they had only a modest effect on the quality of new drug introductions or on the relationship between doctors and pharmacists.
produces optimal outcomes. Such a radical departure was rooted in three beliefs. First, patients were no longer considered capable of making an educated decision on the quality of different kinds of medicine. Second, pharmacists were no longer viewed as capable of helping patients make informed decisions. And further, the pharmacist’s economic incentives were believed to encourage them to capitalize on the ignorance of patients for their own benefit at the cost of the health of the patient. And third, the legislators felt that doctors were the only party capable of objectively selecting medicine and ought therefore to exercise total control over these decisions.

By 1957, the spread of anti-substitution laws caused the reported incidence of substitution to drop to 4.3% (United States. Congress. Senate. Select Committee on Small Business. Subcommittee on Monopoly. 1967). And, by 1960, pharmacists across the country had lost control over the dispensation of drugs, becoming retail employees who stocked and supplied the requested product, rather than professionals with an advanced degree (Report 1979). Attempts to redefine these roles were met with concerted resistance from both doctors and pharmaceutical manufacturers. Primarily, because they threatened the profitability of the market, but additionally, because they threatened the sanctity of the medical profession.

This chapter tells the story of the pharmacists’ attempt to reclaim this lost power. It is the story of a twenty-year battle to recast professional boundaries, to redefine how patients behave and, to reduce the overall costs of the U.S. health care system. But mostly, it is a story of why, despite the success of their efforts, none of these things happened. Instead, this is a chapter on the limitations of institutional change and the way in which motivated actors can delegitimize a set of options to mitigate the effect of any environmental changes. That the laws were eventually repealed is not, I will show, very surprising. That the repeal of these laws had such a minor effect was, however, completely unanticipated.

The Rise of Anti-Substitution

By 1960, nearly every state in the country had passed an “anti-substitution” law preventing a pharmacist from offering patients any drug other than the one that was specifically prescribed for them. This meant both that pharmacists could not offer a patient a different class of medicine and that they could not offer a generic version of the prescribed medicine. There were two public rationales behind the adoption of these laws: profit and safety.

Before the anti-substitution laws, if a prescription was written for a given brand, but the pharmacist didn’t carry it, the pharmacist just offered an alternative. Sometimes this alternative was a competitor’s brand; sometimes it was a generic brand. Either way, the ability of pharmacists to substitute required pharmaceutical companies to both convince doctors to prescribe their drugs and pharmacists to carry their drugs. Once the anti-substitution laws were passed, however, pharmaceutical companies only needed to focus their attention on the behavior of doctors. They could ignore pharmacists entirely,
both saving them money on detailing work and ensuring that they didn’t lose any money to substitutions (Commission 1956).  

By removing pharmacists from the equation, the pharmaceutical companies gave the power to select drugs to a class of people with neither knowledge of, nor interest in, the price of drugs. This produced a rare economic situation referred to as a “double-insulated” market. In double-insulated markets, the person selecting the product is not the same as the person paying for the product, nor are they given any economic incentives to reduce the eventual cost to consumers. Although both the pharmaceutical companies and the American Medical Association (AMA) challenged this characterization of doctors as indifferent to price, surveys conducted by the Federal Trade Commission (FTC) confirmed the claim.

In the FTC surveys, when asked to estimate the prices of drugs they commonly prescribed, doctors grossly underestimated the prices. And despite the claims of the AMA, the doctors themselves recognized their limitations, as 32% of them responded that they had “no idea” what their prescriptions cost. Similarly, 66% of the doctor’s surveyed ranked themselves as “very uninformed” on the cost of drugs (Report 1979). Without an incentive to learn the generic names of drugs or the cost of brand name ones, doctors routinely prescribed drugs by their, easier to remember, brand names. As a result, by the 1970s, 90% of prescriptions were written with the brand name (Report 1979).

This situation allowed pharmaceutical companies to restrict their marketing to only a few tens of thousands of people rather than the millions of potential patients. The laws also provided de facto barriers to competition from generics, thereby extending the exclusivity of a drug well beyond its’ patent. Further, they prevented the only people aware of the price of drugs from having any say over the dispensation of the drugs. All told, the anti-substitution laws created a market in which the people prescribing knew nothing of the cost, and the people paying had no alternative but to pay it or pass on the drug. In short, the economic incentives for the pharmaceutical firms to maintain this system were high.

The second motivation for the passage of anti-substitution laws arose from a territorial battle that was classified as a fear over drug safety. Starting in the 1800s there were concerns that either pharmacists or pharmaceutical companies were selling adulterated medicine. Unfortunately the difficulty in locating the faulty party, combined with the general public indifference, limited the AMA’s efforts to change things. But after penicillin was discovered, the public’s expectations increased. Suddenly, doctors

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15 “Detailing” is the term used for doctor-targeted pharmaceutical marketing activities. These practices include, but are not limited to: the hosting of free lunches for hospital staff, gifts given to doctors or their staff, trips and conferences were the doctors were paid to attend, and “seminars” in which the drug company representatives present the evidence of a drugs use. The drug companies claim that these practices help doctors become more aware of the details of a given drug and keep them up to date on the latest breakthroughs. Skeptics, including the AARP and Consumer Reports and the insurance industry, tend to believe that these are subtle or not-so-subtle ways of bribing physicians to prescribe a drug that they themselves don’t have to pay for.
were able to cure diseases they could only treat before. As a result, the market for prescription drugs grew exponentially. During the 1940s alone, sales of prescription drugs grew from $150 million to $1.1 billion (Facchinetti and Dickson 1982).

The promise of a miracle cure reduced public tolerance for adulterated products and stimulated demand for better protection (Goldberg, DeVito, and Raskin 1986). At this point, irrespective of their primary motivation, both pharmaceutical companies and doctors could make a legitimate claim that substitution laws were an issue of public safety. And, it was these public health claims that helped pass the anti-substitution bills of the 1950s.

**Anti-substitution Laws Evolve**

As the initial efforts focused on the public health concerns, they outlawed the substitution of one product for another, but often allowed generic substitution. Then, when the pace of innovation slowed, and no new drugs emerged to replace the drugs losing their patent protection, this arrangement became problematic for the pharmaceutical companies. Laws that allowed for generic substitution, combined with a lack of innovations, created an ideal opportunity for generic firms to take a larger portion of the prescription drug market. The economics of the issue, and the desire of the AMA to extend the physician’s domain, lead to a pursuit of more stringent measures.

In 1953, pharmacists moved proactively to retain their professional role and sought to have all prescriptions written using the generic name. This would then allow the pharmacist to decide which brands to stock, and would allow the patient to choose between a known brand or a generic (Giumarra 1964; Simmons 1973). The National Pharmaceutical Council (NPC) was formed by the Pharmaceutical Manufacturing Association (PMA) to counter these claims, prevent generic labeling and expand the anti-substitution laws. The NPC even attempted to pressure state pharmacy boards to penalize substituting pharmacists (1978).

Although the Food and Drug Administration (FDA) was the logical agency to rule on these issues, in 1957, they opted to pass. The FDA commissioner explained that substitution of a generic for a brand name was a patent, not medical, issue, as long as both used the proper ingredients. He explained, “The FDA cannot take the responsibility of protecting drug manufacturers’ patent rights” (Goldberg, DeVito, and Raskin 1986). The PMA seized upon this to argue to states that the FDA was abnegating their duties. Using the FDA’s own language they claimed that no one could know for sure if a generic was equal to brand product, transforming an economic issue again into a debate over public health.

Austin Smith, the President of PMA and former editor of the Journal of the American Medical Association (JAMA) wrote in JAMA, “A system allowing pharmacists to substitute generic equivalents for brand name prescriptions is tantamount to restricting the physician’s choice and authority and transferring some of his decisions to the pharmacist.” Continuing along the same line of argument he concluded, “Under
the American system of medical care, the physician alone arrives at the diagnosis, and he alone should decide precisely what drug is to be prescribed for his patient” (Smith 1960).

The PMA and AMA arguments worked and, by 1960, most states had passed laws outlawing generic substitution as well. In Facchinetti and Dickson’s review of the literature on anti-substitution they concluded that the actions of these lobbying groups had transformed the problem. Although there was never a true public health or medical concern, they had turned it into a social and political issues. They write, “…even though there was no objective evidence to establish brand substitution as a hazard to health brand name firms were able to create a social problem and convinced people that it required a legislative answer” (Facchinetti and Dickson 1982).

The Challenges Begin

The combined might of the AMA and the pharmaceutical manufacturers was far too great for the pharmacists, without any organized allies, to withstand. And so, after the last of the states passed their anti-substitution laws, the opposition quietly died out, and attempts to modify the laws ceased. Then, in 1965, with the passage of Medicaid, the federal government unwittingly issued a new challenge. To comply with Medicaid, states began to create formularies, or lists of drugs for which generics were preferred. To ensure that this did not pose a legal conflict with the anti-substitution laws, California amended their laws to establish a prescription pad that allowed physicians to permit or disallow substitution, by checking a box.

The argument here was fairly simple: just as the pharmaceutical companies sought to maximize their profits, the federal government wanted to minimize their costs. They recognized that preventing generic substitutions would cost them unnecessarily and therefore sought to prove their point and remedy the problem. The first step was, in 1967, to establish a Task Force on Prescription Drugs with the explicit purpose of examining the cost of prescription drugs to Medicare. Joseph Stetler, President of the PMA, responded to the task force before it had even issued a report, “The cost of prescription drugs only reflects costs of research, attendant and justifiable costs of promotion, distribution and quality control, and profits not out of line in high-risk enterprises” (1967).

In an attempt to reframe the issue around professional responsibility rather than cost, Stetler reiterated the PMA’s earlier argument, “I want to make it clear again that we do not oppose generic drugs per se, and that drug manufacturers are not unmindful of the costs faced by patients. But our position is that the interests of the patient will best be served only if the physician remains unrestricted in his judgment of the medicine to be administered in each case.” (1967)

When the Task Force concluded that no one had ever found generics to be of less value or utility than brand name drugs, Stetler and the PMA inverted the logic of their argument to warn the public. “The basic presumption of the proposal, rests on two undocumented claims: that inequivalency unproven is equivalency assured…”[emphasis added] (1967).
In one stroke the PMA returned the burden of proof to the FDA. They argued that, it is not sufficient to say that two products are not different, the government must *prove* that they are also the same. Government-funded studies emerged within months offering evidence that the PMA was mistaken and that generic quality was as high as any approved drug. First, the HEW Task Force said there was no evidence of differences in quality between branded and generic drugs. Then DHEW Sec. Robert Finch appointed an impartial committee chaired by John Dunlop of Harvard who concurred that substitution would not affect quality. Soon, a coalition began to form behind the government as the AARP began to actively promote substitution as a cost saving measure for seniors.

*Professional Boundaries: Beyond Cost/Benefit*

In 1970, twenty years after the anti-substitution laws were first enacted, the pharmacists rejoined the fray. At the American Pharmaceutical Association (APhA) Conference, the President of the APhA dedicated his entire presidential address to the question of why doctors, rather than pharmacists, should be entrusted to select among a number of suitable medicines. He sought to reclaim the lost ground that the anti-substitution laws had ceded to doctors, explicitly calling for anti-substitution laws to be amended to permit drug product selection by pharmacists (Dickson 1982; Facchinetti and Dickson 1982; Kolata 1979a).

His address focused on three core arguments. (1) Physicians don’t consciously choose brand-name drugs. So the fact that a doctor writes a brand name on their prescription pad should not be taken as evidence of their distrust of generics, but rather as evidence of their lack of incentives to learn generic names. (2) Pharmacists possess a professional expertise they should be allowed to exercise. Pharmacists, he argued, have graduate degrees and are trained to understand the subtle differences between various kinds of medication. Physicians are not trained in these practices, but instead are trained to diagnose an illness and treat it with a class of medicines. The expertise to select from this class more appropriately lies with the people who are trained in that art: the pharmacists. And (3), permitting substitution would lower total health care costs. Because physicians are largely insensitive to price, but pharmacists are both aware of and paid according to the price of the drug, it would better reduce the costs of health care to allow pharmacists to select the drugs. He also reiterated a call to have prescriptions written by generic names, rather than brand names, as a means to facilitate this process. He estimated the potential annual savings at $400-500 million for the U.S. as a whole. In the wake of this address, Massachusetts passed the first repeal of an anti-substitution law. Although their process was complicated, requiring physician signatures acknowledging consent, they now permitted the substitution of a generic drug for a brand name (Goldberg, DeVito, and Raskin 1986).

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16 The relationship between the price of the drug and the amount of money earned by a pharmacist is a complicated one that varies with state regulation, insurance policies, etc… But the argument used here is that pharmacists are at least aware of the price and the system can be structured so that they too favor low-priced drugs.
The American Medical Association did not require a lot of time before they too felt compelled to respond. In May of 1970, JAMA published an editorial on “Drug Substitution.” The editors wrote, “It is alarming that the APhA House of Delegates adopted the resolution of the Policy Committee on Public Affairs. Such ill-considered action by a segment of the pharmacy profession denigrates the profession itself and indicates a disrespect for the patients the profession serves.” They continued, “Without the anti-substitution laws, the physician would have no control over the drug product to be dispensed unless he remembered in each instance to insert a direction that substitution not be made.” In closing they moved away from professional responsibility and returned to the question of safety, and despite the FDA studies to the contrary they claimed, “It has been shown repeatedly, largely due to the efforts of scientists in schools of pharmacy, that there is no assurance of the therapeutic equivalency of chemically equivalent drug products.” (Editorial 1970)

At this point the battle over substitution laws returned to a dispute over professional boundaries, and the question of whether doctors or pharmacists should have the power to select among drugs. The PMA opined that this dispute had less to do with any potential health risks than it did with a question of basic professional rights. In a memorandum they wrote, “[The pharmacist] has no right… to substitute his own or anybody else’s preparation for the one specified, even if he is sure the substitute is as good, or as he may think, better” (PMA 1972). As other states began to follow California’s lead, the AMA and PMA reunited to prevent the spread of this epidemic. Using the Journal of the American Medical Association as their trumpet, they issued a joint statement in opposition not merely of substitution, but of the very idea of generic drugs (AMA 1973). They wrote:

The point has been made repeatedly that the anti-substitution laws were conceived to help restrain the unethical pharmacist and that they place no restriction on the ethical practice of pharmacy. The need for this restraint is no less real today than it was when the laws were first instituted… The APhA also contends that, of the health care team, the pharmacist is best suited by training to determine the most effective drug product containing the therapeutic entity desired by a physician and, furthermore, to determine which product would be therapeutically equivalent to a different product ordered by a physician. But what criteria would the pharmacist use? What information would be available to him that would not also be available to the physician?...Even the most talented pharmacist will not have examined the patient and will not possess first-hand knowledge of what the physician is trying to accomplish for his patient.”

They concluded their statement with this line, “The AMA and its Council on Drugs believe that the anti-substitution laws protect the patient, the pharmacist, and the physician. Accordingly, it is difficult to understand why a prominent branch of organized pharmacy would want the repeal of laws that in no way inhibit the pharmacist from practicing his profession or from having an intimate working relationship with any individual physician concerning the choice of drugs the physician may want to use…” (AMA 1973) Most interestingly, they directly challenge the pharmacist’s claims that this
is a professional, rather than a health, issue. "The anti-substitution laws have not
obstructed enhancement of the professional status of pharmacy any more than they have,
in and of themselves, guaranteed absolute protection from unsafe drugs or freed
physicians, dentists and pharmacists from their responsibilities to patients." In effect, the
PMA and AMA argue that any loss in status pharmacists may feel is due entirely to their
own inadequacies and in no way related to the reduction in their role as health care
professionals.

This is only the first of several editorials the AMA published on the subject. In an
effort to persuade physicians of the importance of this issue they gave each article a stern
title, such as, “Eroding Physician Control of Therapy” or “Cheap Drugs are Not Good
Medicine.” (Editorial 1973; Lasagna 1978) These articles make explicit that the issue
here is both one of health and also one retaining the professional stature of physicians.

They continue to argue that if the public trusts their physicians then they must
trust them to prescribe medicine and cannot allow a second cook into the kitchen:
“Without automatic and absolute control over the exact regimen of therapy, the physician
cannot possibly utilize all of his training and ability to help the patient”(Editorial 1973).
Later, in testimony before Congress, John Budd, the President-Elect of the AMA is even
more adamant about the potential harm that would befall the American public if
pharmacists were again entrusted to select between generics and brand name drugs.
“Enactment of this legislation would: (1) Adversely affect the quality of care rendered to
patients; (2) Interfere with the physician-patient relationship…”(United States. Congress.
House. Committee on Interstate and Foreign Commerce. Subcommittee on Consumer
Protection and Finance. 1977) Budd’s testimony increased in vitriol as he continued,
“As to provisions regarding substitution, this bill would adversely affect
quality patient care because it would allow for substitution of drugs which
could cause different therapeutic responses from that of the drug actually
prescribed by the physician…Apparently underlying the proposal
authorizing substitution is the premise—which is unestablished—that all
‘generically equivalent’ drugs—drugs having the same established
name—are equal in therapeutic response and bioavailability… To the
contrary, we are convinced that sufficient disparities do exist with respect
to equivalence of drugs that it is necessary to require strict adherence to
the prescribing requirements of the physician… In order to provide the
best patient care, physicians must be free to prescribe the drug of their
choice for any patient and to be assured that the patient will receive
exactly the drug prescribed when the prescription is filled by a
pharmacist.” (emphasis added)

To bolster the AMA’s cause, doctors like the famed Louis Lasagna, a former
professor at Johns Hopkins Medical School and a key figure in the earlier Kefauver-
Harris amendment, wrote in support of anti-substitution bills. “The debate has not been
helped by two flimflams perpetrated on the public—the notion that generic prescribing
invariably leads to savings for the consumer and the readiness with which everyone
ignores the importance of the pharmacist in determining prescription prices.” He
continued by arguing that the pharmacists were not the champions but the villains of the
poor, “It is a cruel hoax on the sick, rich or poor, to save money at the expense of good
treatment. It is thus appalling to find proponents of substitution bills and the maximum allowable cost plan so shamefully ready to give assurance to the public about interchangeability of generic and brand versions that no knowledgeable scientist in his right mind would give.” (Lasagna 1978) He concluded, and titled, his piece with the quote that started this chapter: “Cheap drugs are not good medicine.” (Lasagna 1978)

Despite these well-organized efforts, the political challenges had begun. While the American Medical Association and the PMA argued stridently that any such changes to the law would have catastrophic consequences for public health, the over-riding cost concerns and the reassurance of the FDA pushed both the federal government and the states themselves to act. In the summer of 1971, only a few months after the American Pharmaceutical Association address, the Department of Justice submitted a report to the Council of State Governments. This report, entitled the “Research Paper and Policy Statement of the US DOJ on the Advertising of Retail Prescription Drugs”, noted the federal concern about two developments, “State restrictions prohibiting the advertising or promotion of prescription drugs by name or price” and “state provisions restricting the type of drug price advertising which may be used.” The report urged state legislatures to reexamine and eliminate such anti-competitive restrictions. They concluded their report with this statement, “Competition is our basic national policy. It has proven to be the most effective spur to business efficiency, innovation, and low prices. Prohibitions on drug advertising represent departures from this national economic policy. Such inconsistencies should be countenanced only when clearly justified in terms of public need.” (1971)

Within a few months, the New York State Assembly, urged on by Robert Whalen, the State Commissioner of Health, passed a provision allowing for generic substitution. The state was immediately sued by, the freshly renamed Pharmaceutical Research and Manufacturing Association (PhRMA), citing due process violations. The plaintiffs argued that a generic drug law was not “rationally related” to the state’s goal to safely provide prescription drugs (Oradell 1978). They further challenged that generics are not as safe and effective as brand name. The court, noting the numerous hearings in the state legislatures, found it improper to hear evidence that the legislature was actually mistaken and rejected their claim. The State Court of Appeals later upheld the verdict, directing the Commissioner to establish a list of therapeutically equivalent drugs available for substitution.

The federal government was similarly aggressive in moving to challenge the laws. Democrats had been arguing, since the mid-1960s that the price of drugs was higher than necessary and that generics offered a viable alternative. However, their efforts to establish a formulary or to mandate generic labeling continually failed. Their opportunity for reform arrived when a second price-fixing scandal, involving several of the largest drug companies, combined with a growing frustration at the cost of prescription medicines gave their arguments greater traction. Senators from each state now felt that their individual states were being “over-charged” by pharmaceutical companies due to the restrictive anti-substitution laws.

For instance, Senator Harris (D-OK) argued that his state lost hundreds of millions each year as a result of a lack of generic substitution. Senator Gaylord Nelson
(D-WI), made a pointed claim, “...the drug industry is fleecing the people by trying to convince them, through high-powered and expensive advertising, that drugs sold under a brand name at exorbitant prices are somehow or other more reliable than the same drugs sold under their official—generic—name from one-half to one-thirtieth as much.” Sen. Nelson went on to cite Dr. Henry Simmons, Director of the Bureau of Drugs within the FDA, who wrote, “Based on many years of experience with this program, we are confident there is no significant difference between so-called generic and brand name antibiotic products on the American market” (1973).

The following year, two more states moved against the anti-substitution laws. First, Kentucky passed a “formulary substitution law” that allowed pharmacists to substitute drugs explicitly listed for other approved drugs. Then Maryland introduced a law permitting generic substitution more broadly. Not surprisingly, this motion, received considerable support from the Maryland Pharmacists Association, “The pharmacists’ arguments in favor of the proposal, sponsored by Charles A Docter and Dr. Torrey C Brown, were that pharmacists in many instances know as much if not more about drugs than physicians, that physicians often prescribe drugs by their brand name because they don’t know the generic designation and that in most cases generic drugs are less expensive than brand name drugs with no significant difference in quality.”(Meyer 1972) Paul Freiman, chairman of the Maryland Pharmaceutical Association’s legislative committee pointed out that without substitution pharmacists must buy from several suppliers and cannot buy in bulk. The President of the Maryland Medical Society spoke out in opposition, using the same rally cry as before, “control of drugs should remain the physician’s hands,” but the measure passed (Meyer 1972).

While these nicks and scrapes bloodied the AMA-PMA coalition, the fatal blow to the anti-substitution laws came from an unlikely source: Caspar Weinberger. Seeking, once more, to reduce the costs of Medicaid, Weinberger issued a statement on Dec. 19, 1973, “...in absence of demonstrated differences in uniform quality and therapeutic equivalence, there is no reason why the Government should pay more for a drug than the lowest price at which it is widely available.” This statement was the beginning of the Maximum Allowable Cost plan, which required that pharmaceutical companies charge the federal government no more than the price of generics, irrespective of who prescribes the drug. Weinberger felt this could be done at no cost to the public as, “All the evidence to date indicates that clinically significant differences in bioavailability are not frequent” (Silverman and Lee 1974).

Emboldened by Weinberger’s statement, other agencies in the federal government joined the fight. The FDA, abandoning its position on the margins, begins to make assertive statements challenging the logic of PhRMA. “Some professionals seem to mistakenly equate ‘big manufacturer’ with good, and ‘smaller manufacturer’ or ‘generic’ with bad. This impression is not borne out by the facts.”(1973) The FDA went so far as to directly countermand the claims made by the pharmaceutical companies, and suggest that these laws discourage innovation and work against the public health, “Drug substitution laws serve mainly to preempt professional judgments and to discourage industry innovation. Drug firms that specialize in cheaper drugs and spend nothing on research may temporarily gain advantages here and there from a market artificially
restructured in their favor by Government. But ultimately consumers will lose the economic and health benefits of new drug therapies provided by research intensive firms” (Hecht 1978).

At the same time, the doctor-pharmaceutical coalition began to crumble as fellow doctors begin to react against the AMA, writing letters to JAMA arguing against the expansion of physician responsibilities. Dr, David Duhme captured this position in a letter he published in JAMA, “No physician’s clinical experience is adequate to make valid distinctions between different brands of the same drug!” He concluded his missive, “It is unclear to me why the AMA takes such a stand. The PMA endorses the joint statement out of obvious financial self-interest. There seems to me no advantage to the medical profession (except falsely inflating the ego) to claim skills and responsibilities that no one could reasonably ascribe to a busy practicing physician.” [emphasis added] (Duhme 1973)

In 1974, PhRMA lost the first stage of the battle four years after it had begun. After twenty years of anti-substitution laws, the U.S. government instituted a policy to require, when possible, the use of generic rather than brand names for all drugs bought with federal funds. By 1975, six more states had followed the federal government’s lead, increasing the number of states allowing substitution to nine (Hunt 1976). Although forty-one states still restricted substitution, the tide was turning against the pharmaceutical companies and doctors. As seen in figure 3.1, 1976 would prove to be the year in which the trend became irreversible and the anti-substitution laws started falling with frequency.

**INSERT FIGURE 3.1: GRAPH OF STATE REPEALS**

The year began when the Virginia legislature passed two separate bills on generic drugs. The first, which the governor signed, repealed their substitution law and allowed pharmacists to substitute drugs that were on a formulary created by the state board of pharmacy. The second, which the governor vetoed, went considerably farther, to entice patients to request substitution by requiring that pharmacists post the prices to brand name and generic drugs in their stores. Wisconsin, after six years analyzing the issue, decided that they too felt the savings were greater than any possible risk and passed a similar measure, allowing substitution for drugs on a formulary list.

In June, Florida demonstrating the range of potential solutions, inched the line even further away from the interests of the pharmaceuticals. Unlike the laws allowing substitution, the Florida legislature passed a law that required the druggist to offer to fill the prescription with the least expensive medication in stock. PhRMA countered that the drug bill will not save patients very much money, but it will place them at risk. As one PhRMA officer put it, “If Florida consumers save $40 million in the first year, I’ll eat my hat.” (Clarke 1976)

By November 1976, nearly twenty states had repealed their laws, and the debate was central enough to be the focus of the *New York Times* op-ed page. In a two-page editorial debate, the arguments for each side were clear. Those in favor of the current
anti-substitution laws pointed out that other states had yet to demonstrate the promised savings and that the potential health risks were high. They presented the issue as a possibility of eventual savings at the cost of a guaranteed decrease in the quality of medicine. They closed by again returning to warn of health risks, “In fact, then, the Federal Government cannot and does not guarantee the quality and equivalence of drug products. Differences between so-called duplicate products have been demonstrated again and again.” (Hunt 1976)

The contrasting editorial, arguing for the repeal of the laws, took issue with every claim presented. They begin by challenging the suggestion that the laws would not produce savings, “According to the FTC of the $11 billion annually spent by Americans for prescription medicine, more than $130 million could be saved if those Americans were given the opportunity to comparison shop and buy generic drugs.” (Bauer 1976) And, they continued, to reject the suggestion that generics were any less safe or effective than their brand-name counterparts: “A case history of the brand-generic conflict proves that while examples of inferior generic products are well-documented, they are rare.” They remind the reader of the HEW Task Force that looked into the issue and was composed of industry people, medical school people and government people, and yet found no evidence of increased risk in generic drugs. Reserving their strongest language for the boldest claim of the pharmaceutical companies, they concluded with the statement: “...on the basis of available evidence, lack of clinical equivalency among chemical equivalents meeting all official standards has been grossly exaggerated as a major hazard to public health.”

PhRMA’s Final Shot: Create Confusion

By the late 1970s, PhRMA and the AMA had lost the legislative battle. The majority of states had repealed their laws and several had adopted provisions to encourage, and in some cases require, substitution. Unable to prevent substitution through legislative fiat, the coalition pressed harder on an issue that resonated with the public: uncertainty. As consumers lacked information or the ability to self-determine quality, the pharmaceutical companies continued to imply that generics were less safe and/or effective. Simultaneously, capitalizing on the uncertainty that attends any legislative shift, they began to suggest that these legal changes placed any liability for adverse reactions squarely upon the shoulders of the pharmacists.

Of course, this did not prevent PhRMA from continuing to sue each state to delay the implementation of their laws, but it served as a valuable safety net in the case that their legal efforts failed. Either way the lawsuits, at the very least, allowed them time to build their case before the public. Their argument had two main components: (1) challenge the claim that generics are equally safe and effective and (2) place the burden of proof on the generic companies.

This began very simply with the claim that generics are not chemically equivalent. First, PhRMA released a “Biography on Biopharmaceutics” in which they claimed 221 different studies had all found generics were not equivalent to brand name drugs. When
the HEW Task Force on Prescription Drugs reexamined these same studies, they found that only 12 were legitimate studies and even those compared non-identical drugs (e.g. different dosages, forms, etc…) rendering the comparisons useless (HEW 1969).

Later, Pfizer created an advertisement saying that 10 of 17 generic lots it tested were below standards (Leeson 1977). But, in reality, they tested 65 samples, only 10 of which were bad, and the lab had no experience conducting these tests and may have botched it (Kolata 1979a). The implication of the Pfizer advertisement and the chemical equivalency argument was that generic drugs were more prone to impurities or inexact concentrations of active ingredients. Therefore, if a patient used a generic medication they could not be sure whether they were getting too much or too little of the actual medication. The claim focused on the manufacturing capacity of the generic companies, and argued that their processes were inexact. This argument curiously ignored the fact that many generic medications were produced by large manufacturers using the same plants that produced their brand name versions.

The FDA responded, by sending Pfizer a warning letter and requiring them to remove the advertisement. They publically admonished the company writing, “In addition, it appears that Pfizer very selectively used these data to discredit the quality of competitive generic products.” (Kolata 1979a) Further, as shown earlier, the FDA itself conducted a number of studies demonstrating that generics were no less impure, no more liable to defect, than any brand name drugs (Report 1979). But concerns were so widespread, that in 1974, the Office of Technology Assessment felt compelled to conduct another round of studies. In this they again found that 90% of brand-name drugs had equivalents and that the concerns of safety and efficacy were overblown. However, to appease the public, they suggested creating a formulary of approved exchangeable products demonstrated to be equivalent (United States. Congress. House. Committee on Interstate and Foreign Commerce. Subcommittee on Consumer Protection and Finance. 1977).

The pharmaceutical industry accepted this setback and then launched a new campaign, against the lack of bioequivalency in generic drugs. The argument, again, was simple: while it may be true that generic drugs are chemically indistinguishable from brand names, they do not act the same way once delivered. In other words, once inside the body, these drugs break down and behave differently. Given the immense variability of the American people, PhRMA argued, only a person’s doctor is capable of understanding how a given drug will behave in their body.

Dr. Howard Binkley, PhRMA VP for Research and Planning, articulated this clearly in Congressional hearings on Prescription Drug Labeling and Price Advertising,

“The bill as we read it would authorize a pharmacist to literally override a doctor’s request for a prescription drug product made by a particular manufacturer.”

Mr. Murphy: “Override’ is a pretty strong word around this vicinity. I think it is pretty clear that it wouldn’t be an overriding, but it would be a substituting unless the doctor felt there was a reason not to substitute.”
Dr. Binkley: “Vital to our position is the fact that neither manufacturers, physicians, pharmacists, or the FDA can guarantee that prescription drug products with identical generic names will perform in the same fashion.”

He went on to raise the specter of liability, “When a pharmacist is authorized to substitute a drug brand without conferring with the prescriber, the professional liability we think becomes complicated and subject to considerable speculation.”

PhRMA continued to push the question of bioequivalence, even using it as the basis for a class-action lawsuit brought against the government’s MAC program by the AMA, PhRMA, Lilly and Hoffman-LaRoche. In *AMA v Matthews*, the plaintiffs argued that the FDA is incapable of determining bioequivalence based on present studies. They argued that only doctors, with their intimate knowledge of each patient could correctly predict how each drug will behave in each person. The court disagreed, striking down the claim that bioequivalence was relevant, “(1) FDA programs, despite some inadequacies, are functioning well enough to assure drug quality and (2) that bioinequivalence is neither a major problem nor an insurmountable obstacle to the MAC program.”

Again, undeterred by their failure, or perhaps even encouraged by the delay it caused, the pharmaceutical companies issued a new complaint. While the drugs may indeed be chemically equivalent, and even break down the same way within each body, they were not yet proven to be *therapeutically equivalent*. By which they meant, only by conducting a double-blind test could we be absolutely certain that these generic drugs produced the same level of therapeutic benefit that the brand names produced.

To further this claim Pfizer published, “Generic Drugs: Safety and Effectiveness.” In this, they wrote,

> “Advocates of generics take the position that their opponents’ motivation is exclusively a matter of money, that the effectiveness of generics in lowering drug costs is not in doubt, and that its side effects (such as unpredictability of drug quality) are relatively minor. Analysis of the evidence at hand, however, shows that the opposite is true.”

> “Drug products containing the same amount of active ingredient (generic equivalents) may vary greatly in their rate of absorption and in their therapeutic activity, and have often been reported to do so. Official chemical tests are of little value in predicting such irregularities.” (emphasis added)

They go on to write, despite numerous objective reports to the contrary, “Clinical nonequivalence between generically equivalent drugs has been found virtually whenever it has been looked for.” This publication concludes, “The public health issue in the generic controversy is whether drugs produced by little-known inexperienced manufacturers are consistently interchangeable with drugs produced by reputable, competent firms; they are not.” (emphasis added). When asked about their efforts, executives at Pfizer offered these quotes, “To condone and promote substitution of
‘generic drugs’ that are, in fact, qualitatively different from the clinically tested product is really a rejection of our whole system of regulatory preapproval of prescription drug products.” (Kolata 1979b)

Finally, as even this argument begin to fade (though it never fades entirely, and reappeared as late as 2000), they return to the old standby, claiming that repeal of the substitution laws will cause an inevitable decline in the rate of innovation. Although this Cassandra cry is heard each time changes in the market are suggested, the companies have no trouble rounding up a bevy of experts to bolster their claims.

For instance, in 1980, Laubach published, “Federal Regulation and Pharmaceutical Innovation”, in which he noted a puzzling trend: even as we increased research expenditures, innovative output declined. He concluded that the fault lies in, “the social and political environment as expressed by federal drug regulations.” This, he argued, was the only way to make sense of a situation in which the preconditions for innovation were in place (demonstrated need, technological capability and, resource commitment) but innovation was not occurring. Even Joseph A. Califano, the former Secretary of Health, Education, & Welfare worried that each time the laws change we decrease the incentives to innovate, “While the 1962 amendments contained some progressive provisions, they also set in motion a process of regulatory proliferation that has increasingly hampered drug research and development.” The amendments that concern him, are the same amendments that required drugs be proven effective before they can be sold.

In the end, none of these three claims were able to prevent the demise of anti-substitution laws. The final states to repeal their substitution laws were Louisiana (1980), Texas (1982) and, Indiana (1984) almost 15 years after the APhA address that helped ignite the issue. Although every objective source argued, almost from the beginning, that this was a safe, practical way for consumers and the government to save millions of dollars, the pharmaceutical industry and the American Medical Association succeeded in creating enough confusion and fear that it took more than a decade to finish.

After the Repeal: Waiting for Change

As the final states repealed their laws, once more permitting pharmacists to exercise some control over the selection of drugs, it seemed obvious that the market would soon change. Clearly, at the very least, the pharmaceutical firms and AMA feared that patients or their pharmacists would begin to exercise their new power to select cheaper versions of the prescribed drugs. Similarly, it would be logical to assume that the pharmacists themselves, after lobbying for over a decade to repeal the laws would respond positively to the new environment and would act upon the responsibilities they had fought to earn. The mere fact that so many powerful groups spent so much money and so many years fighting for or against these bills suggested that, on all sides, there was an expectation that their passage would herald a new age. Finally, for the first time since the 1920s, patients would be allowed to exercise a degree of choice over their treatment.

Academic studies reinforce this anecdotal expectation, showing how fundamental environmental change produces organizational and individual change. That secondary
change may take one of four forms, it may be (1) immediate and temporary, (2) immediate and permanent, (3) delayed and temporary, or (4) delayed and permanent. But, the possibility of a fifth outcome, one in which the redefining of professional boundaries and rewriting of regulations sparks no change, has no effect, is hard to imagine. In this situation, we may not expect physicians to change their behavior, but we do expect pharmacists and patients to change. Moreover, to ensure this transition, several states gave pharmacists financial incentives to dispense a generic rather than a leading brand, “because typically the retail dollar gross margin on the generic is higher” (Masson, Steiner, and United States. Federal Trade Commission. Bureau of Economics. 1985).

So what happened? In a word: nothing. While few studies attempted to predict the likely rate of substitution after the laws were changed, the expectation was that it would occur regularly. Instead, it occurred rarely. In 1980, when over 40 states had passed laws, substitutions occurred in only 9.5% of possible cases (Masson, Steiner, and United States. Federal Trade Commission. Bureau of Economics. 1985). While this figure increased as people became more comfortable with the new laws, as late as 1987 it happened only 22% of the time (Simpson and Neff 1992).17

While differences in the state’s laws lead to some variations in the substitution rates by state, no state experienced a dramatic rise in substitutions. For instance, in Illinois, substitutions occurred in 12.6% of eligible cases (Stewart, Grussing, and Purohit 1982). Meanwhile in Michigan it only occurred in 1.5% of cases. Wisconsin, at 2.7%, and Florida, at 6.2%, were not far ahead (Masson, Steiner, and United States. Federal Trade Commission. Bureau of Economics. 1985). Most surprisingly, these results remained consistently low, even a few years after the laws passed, ranging from 1.1% of cases in Maryland to 10.6% in Michigan (Carroll, Fincham, and Cox 1987).

Despite the expected radical shifts in pharmacist and patient behavior, few substitutions occurred and therefore few pharmaceutical companies felt obligated to remedy their practices. As seen in figures 3.2 and 3.3, in the years following the repeal of substitution laws the profits, innovation rates, and market concentration of the top pharmaceutical firms remained surprisingly constant.

**INSERT FIGURES 3.2 & 3.3: INNOVATION & PROFIT RATE**

After a protracted multi-decade debate over the potentially disastrous consequences of allowing generic substitution, there were no consequences. At the public health level, there was no increase in reports of adverse reactions, the FDA did not recall more drugs than it had previously, nor did death from drug complications increase. At the organizational level, firms did not enter or exit as a result of the new environment, incumbent firms did not slip in their status vis-à-vis challengers, and the industry as a whole remained robust and profitable. Even if we focus our attention, as in figure 3.4, on

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17 As will be discussed in the Chapter 6, subsequent changes to the law, most notably the passage of the Hatch-Waxman Act, greatly increased both the availability of generic drugs and the rate of substitution in more recent years.
just the ten years during which the states began to repeal their anti-substitution laws, we find there is no great change in the behavior of the firms.

**INSERT FIGURE 3.4**

A Federal Trade Commission report investigating the issue described the lack of change this way, “this is puzzling in light of the incentives both consumers and pharmacists have to substitute.” (Masson, Steiner, and United States. Federal Trade Commission. Bureau of Economics. 1985). Despite expectations that the change would save hundreds of millions of dollars each year at both the federal and state levels, the FTC estimated that the total savings in the first few years was between $44-80 million. An initial examination of the effect of these laws concluded, “It may be a bit of an exaggeration, but it seems fair to conclude that consumers generally do not request substitution, physicians generally do not prohibit substitution, and pharmacists generally do not substitute. It seems apparent that relative apathy has prevailed on all sides.” (Goldberg, DeVito, Smith, Stano, and Vidis 1979)

This raises one question: why wasn’t there a change? How is it possible to institute such a fundamental change in the environment without causing any corresponding change at the industry or organization level?

*Explaining a Non-Response*

The initial analyses favored three different explanations. First, the state laws were too complicated for anyone to understand. Because the laws were instituted and then repealed at the state level there was no federal standard for how to allow substitution. The FDA and FTC both attempted to offer guidelines, which did help establish the elements that each plan relied upon, but there was still a great deal of variation. For instance, some states assumed substitution was allowed unless a doctor specifically disallowed it, in other states they assumed it was not allowed unless specifically permitted by the doctor. Similarly, some states created a list of drugs that could be substituted, while others assumed all drugs could be substituted, and others assumed that all drugs except those on a list could be.

If doctors and pharmacists were frequently traveling between states this could clearly have lead to some confusion. However, as most practiced only within a given state, the variations in state laws are unlikely to explain any confusion on the part of the prescribers. Further, these differences only explain why some states had 10% substitution and others had 1%, they do not explain why no states saw substitutions reach even 30% of allowable instances.

Skepticism over the role of differences in the law lead to the second claim: physicians must not have allowed substitution. However, that was both easily analyzed and refuted. A 1985 FTC study gathered prescriptions and found that, in 80% of the cases, physicians allowed generic drugs to be substituted for brand names. This is interesting on two fronts: (1) it proves that the lack of substitutions was not the result of recalcitrant physicians, and (2) it suggests that individual physicians were less concerned
about the loss of their professional control than the AMA had implied. Whereas the AMA had long claimed that substitutions represented a dangerous usurpation of physician rights, and would invariably reduce the quality of care. Individual physicians displayed no hesitation in allowing pharmacists to substitute a prescribed drug for a generic alternative.

The failure of these explanations lead to a final claim: it must be that patients and pharmacists were wary of challenging physicians. This is best summed up in the conclusion of an FTC study: “In particular, it may be that consumers and pharmacists read into the fact that physicians specify a brand a strong preference on the physician’s part for that particular brand, even when the physician does not choose to exercise the legal option to prohibit substitution explicitly.” (Masson, Steiner, and United States. Federal Trade Commission. Bureau of Economics. 1985). This explanation hinged on information. Patients lack the information to comfortably question a doctor’s advice and therefore preferred not to deviate from the recommendation. But this thesis did not explain the reluctance of pharmacists, who should both be aware of the trade-offs in choosing a generic, and should also know whether a physician required or suggested a given brand.

The limitations of these three initial explanations suggested the need for alternatives. One argument is that it is possible that the behavior of both individuals and organizations did not change because the structure of the market did not change. Although the laws theoretically increased competition, by allowing for substitution, they did not make it any easier for generic drugs to reach the market. Until 1984, for generics to reach the market, they needed to pass the same series of tests required of brand name drugs. In other words, manufacturers could not merely demonstrate that the drugs were chemically identical to an already approved drug and then assume they were equally safe. The FDA instead required them to go through the same approval process it required for the identical, brand name, drugs that preceded them.

As a result of this law and the preceding anti-substitution laws, there were not many generic drugs available and there were even fewer generic companies pursuing them. The change in the anti-substitution laws made it more attractive to form generic companies and to pursue generic work, but it did not alter the cost and difficulty of having a generic drug approved. Therefore, after the law was passed, there was no gap for challenger firms to rush into. The difficulty in bringing a generic to market remained a substantial enough barrier to protect the incumbent pharmaceuticals and prevent change at any level.

Second, just as there were redundant rules in effect to mitigate change, individuals resisted the offer to change their behavior. While initial analyses assumed that this was due to a reluctance on the individuals part to challenge their doctors, it may have arisen more out of their doubt over the alternatives than their fear of, or confidence in, their physicians.

Pharmacist and patient doubt was largely due to a lack of available information and the success of the pharmaceutical companies in creating the appearance of controversy. Despite the constant reassurance of the FDA, popular press, and elected
officials, people remained skeptical that generics were as safe and as effective as brand-name drugs (Lambert, Doering, Goldstein, and McCormick 1980). In fact, the Lambert et al. study argued that substitution had little to do with an aversion to challenging physicians or towards remaining in a traditional “patient” role. Instead, the patients were behaving instrumentally; they acted rationally based on the assumption that generics were less effective. Therefore, as people became persuaded that no difference existed, they slowly did begin to request substitutes.

The reluctance of the public to change is a credit to the efforts of the AMA and PhRMA at maintaining a specter of doubt. Even as late as 1987, leading nursing journals published articles asking, “How Safe Are Generic Drugs?” (Birdsall and Uretsky 1987). These articles, published years after the last states had repealed their laws, sought to convince nurses of the value of generics. The articles reminded nurses, “There are, however, no well-documented reports of clinical problems due to generic substitution.” They even went so far as to offer mock discussions along the lines of: “What do you tell patients?” Suggesting that the nurses, “...explain that it is made by a different company but that it is equal to his customary product.” It did not matter that the FDA had long considered this a decided issue, with the Commissioner himself stating, back in 1979: “The differences are largely semantic.” (Library of Congress. Congressional Research Service., Lemke, and United States. Congress. Senate. Select Committee on Small Business. 1979) These health care professionals remained wary of generics into the late 1980s.

In similar situations, where the cost of adopting a new pattern of behavior is ambiguous, individuals frequently adopt the risk-averse position (Kahneman and Tversky 2000; Thaler 1992). This strong preference for the status quo and reluctance to take risks with possible negative consequences is referred to by economists as “loss aversion.” The term refers to situations in which choices that may change the status quo for the worse weigh more heavily on people than the corresponding potential for gain. A classic experiment illustrates this principal more clearly.

In a study by Viscusi, Magat and Huber they asked people in a shopping mall about their willingness to buy a can of imaginary insecticide. The customers were told that insecticide cost $10 and that it could cause minor injuries if misused, but that it only harmed about 15 out of every 10,000 users. The customers were then asked how much they might be willing to pay extra to eliminate the risk entirely. People without children, on average, said they would only pay $3.78 more to completely eliminate the risk. But when asked how much of a discount they would want if the risk increased just slightly to 16 out of 10,000 people, 77% of the people said they wouldn’t buy it at any price. What economists focus on here is the discrepancy between what people will pay to reduce risks versus add risks. However, what is relevant for our case is that although the risk was minimal, once they had established the status quo as 15 injuries per 10,000, most people were unwilling to accept any additional risks in order to save money (WK, Magat, and Huber 1987).

The lessons of loss aversion suggest that people are hypersensitive to damage and far less sensitive to the perceived reward. So, while switching to generics does result in financial savings, they believed it might also cause harm. Unless the rewards were
exceptional, people will not accept the increased risks associated with that change. This explains the failure of the laws as a consequence of their focus on patients and pharmacists as instrumentally motivated actors. The law offered them economic enticements that, it was presumed, would be sufficient to motivate rational actors to change their behavior. If, however, actors in the face of uncertainty prefer traditional roles, then the law would have no effect unless it succeeded in making the costs of change more transparent.

The patients and pharmacists were therefore not unlike the pharmaceutical companies. They did not immediately change to exploit the openings presented to them, instead all three actors adopted a “wait and see” attitude, preferring the obvious costs of the status quo to the uncertain risks of change. The norm, the traditional mode of behavior, was for a pharmacist to fill, not question, a prescription. Patients, wary that low cost and low quality must be correlated, were unable to accept a new framework where two equal goods can have different prices without a decrease in quality. And the rewards were insufficient to stimulate the experimentation that would eventually produce change.

This tells us something interesting about patients through the 1990s: they abnegated choice. The structure of the market had taught them not to decide. Even when given a cheaper alternative with a government seal ensuring its quality, they deferred to the physician or pharmacist. Studies conducted as late as 2000 found that patients continue not to even ask about substitutes. They will accept them if the pharmacist or physician offers, but the majority prefer not to make decisions on their own health care (Mott and Cline 2002). Obviously, this behavior has changed radically in the past decade. The causes and consequences of that shift will be explored in later chapters, but it easy to anticipate how increased access to information renders the risks less ambiguous and enables people to move away from the status quo.

As a result of these factors, the pharmaceutical companies did not face any pressure to adapt. Although the market was technically different, the changes were not of the right kind to force a response. There was no loss in profit, no shift in behavior, and therefore no need to change. This suggests, in keeping with Prechel (2000) and Zorn (2004) that organizational changes happen not when the environment changes, but when organizations reach a point of crisis.

The law didn’t require a change in individual or organizational behavior, but it sought to create one indirectly by altering the incentives for pharmacists and patients. The expectation was that individual-level shifts would create the crisis that would change the firms. Even the firms expected this to happen, although none of them began to prepare for it by, for instance, investing in generic companies. This lack of proactive behavior is worth pointing out, as it was not merely patients or pharmacists who preferred the status quo. Organizations, when faced with potentially negative outcomes, proved equally averse to change. This explains why, even though the firms spent a decade and tens of millions in resources fighting the law, once it passed, they did nothing. They just waited. No firms sought to attain an advantage, instead each firm waited to see if the environment was going to force them to change or not.
Conclusion

For an exogenous shock to cause change, it needs to alter the degree or type of competition in the market. As Tushman and Anderson have shown, transformative changes are either competence-enhancing or competence-destroying (Tushman and Anderson 1986; Tushman and Anderson 1990). They either reinforce the strength of the dominant firms or they allow challengers to supplant incumbents. Here, although the battle was hard fought and the changes appeared imminent, there remained enough structural barriers to prevent these types of transformations. Although the laws allowed for the possibility of greater competition, the structural and behavioral impediments were too large to overcome with minor financial incentives. As a result, the legal reforms did not allow new firms to enter or cause old firms to die, and the market remained unchanged.

There were two main reasons for the stability of the market: structure and information. Structurally, these changes had the effect of turning one key in a door with multiple locks. The laws allowed pharmacists to substitute, and patients to request cheaper drugs, but it did not facilitate the creation or approval of generics. On a 10 point scale, the incentives to produce generic drugs moved from 0 to 1. A market was now possible that was not before, but with the structural barriers still so high, investors moved slowly and cautiously to enter.

In terms of information, both patients and pharmacists were faced with a situation clouded in ambiguity. Even if the legislatures had not, in the end, believed the claims of the pharmaceutical companies, a decade of debate was sufficient to create serious doubts in the minds of these newly empowered patients. So, while they had more space in which to act, this only matters when they feel confident/capable. And, over the past several decades both pharmacists and patients had been conditioned to believe they were not capable and should not feel confident.

Pharmacists, in particular, were uncertain of their position in this new health care scheme. Would modifying prescriptions be seen as a “challenge” to doctors? Would it open the pharmacist to potential liability? Would it cause doctors to direct patients to other pharmacists? Their behavior did not resemble the opening of a metaphorical dam hoped for by legislators, but instead was like the opening of a door into a dark room. Pharmacists were wary to enter. They moved slowly and cautiously, more afraid of the consequences of a misstep than the rewards that came with any first-mover advantage. This helps clarify why institutions are so slow to change, even if the status quo is suboptimal from their standpoint, it is known.

Finally, this chapter reveals the glaring flaws in our understanding of the market for prescription drugs. The laws that preceded these, and those that would follow, emphasize the role that economic motivation can have in reshaping the market. In so doing, they underestimate the ability of rational actors to prefer the status quo to the uncertainty of change, irrespective of what they may gain professionally or financially from the change. Therefore, to modify the market, requires more than a manipulation of financial incentives.
This establishes a pattern that will recur throughout the dissertation where changes in the timing or quantity of information available to consumers are met with greater resistance than all other changes. In the end, the roles didn’t change because that the pharmaceutical industry and AMA succeeded in creating uncertainty. They strove to create a medical controversy, and while that failed they did manage to create uncertainty. And uncertainty in this arena favors traditional modes of operation. Thus, even though the pharmaceutical industry lost on every possible ground, they lost nothing in the end. Because very few people are willing to take risks with their health. And they had convincingly made change look like a risk. They convinced people that they should not attempt to choose their own drugs.
Chapter Four: From Drugs to Candy and Back

“I wonder if any member of the subcommittee knows how much it costs to die?”

Austin Smith, President of the Pharmaceutical Manufacturer’s Association

What happens if the drug companies get out of the business of making drugs? Despite the hyperbolic claims of the PMA (since rechristened PhRMA) that regulation would drive firms out of the industry, it has long been unfathomable that a drug company would do anything other than sell drugs. Simply put, drugs are, and have long been, phenomenally profitable. The high costs Austin Smith is defending in the quote above, translate into spectacular profits that are actually protected by the regulatory structures the firms claim to disdain. By all accounts, including those of the firms themselves, it is a remarkable industry that firms are fortunate to be part of. Which makes what happened in the 1960s that much harder to explain.

By the late 1950s the twenty largest pharmaceutical firms accounted for nearly 80% of all pharmaceutical sales, the profits of nearly every firm were at record levels, and the industry was in the middle of what many later called its “golden age” (Grabowski 1976). After decades of floundering, being a pharmaceutical company was not just a good thing, if your goal was to make money, it was the best place you could be. So what, in the middle of this unparalleled prosperity, drove Merck to buy a poultry farm, Pfizer to buy perfume companies, Smith Kline to make ski goggles, and Squibb to try and run LifeSavers candy? And, perhaps equally important, why by the mid-1980s had nearly all of these firms reverted back to concentrating on their pharmaceutical interests?

It would be easy to scoff at these decisions and simply chalk them up as part of the diversification movement of the mid-20th Century. But that ignores some important aspects of this particular situation that make it worth investigating. First, past research points to the Celler-Kefauver Act (1950) as the jolt that forced firms to diversify (Fligstein 1990), and yet (as seen in Figure 4.1) the bulk of pharmaceutical acquisitions remained within the medical industry until the mid-1960s.

INSERT FIGURE 4.1—MERGER COUNT (with external mergers separated)

Second, research by Davis et al. (1994) argued that the decline of the diversification movement occurred as one side in a debate over the boundaries of a firm gained government support in pursuing their cause. As a result leveraged-buyouts helped remove diversified firms from the market while the new firms that entered were careful to steer clear of diversification. Before long, the American firms that had been remarkable for the degree of diversification were equally remarkable for their concentration within a particular industry. But this also fails to explain how the same changes occurred in an

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18 Administered Price Hearings, Part 19, February 23, 1957. Smith continued to warn of the dangers of restricting the drug industry by saying, “In fact, statistically in this room this morning, which seems filled, there probably are 11 or 12 people presently alive who would have been dead if our death rate of 1935 still existed. And I cannot help but wonder which of us might have been included in the 11 or 12.”
industry, like pharmaceuticals, where no new firms entered and few old firms left. The firms weren’t replaced; they simply changed what they were doing.

Finally, writing this off as a simply part of a momentary shift in industry practice fails to account for the particularities about the ways in which these firms diversified. Why did firms diversify out of a highly profitable industry, in which they possessed a very specific expertise, and try to enter industries with little to no relation to their business and whose practices offered no opportunities for economies of scale?

For these reasons, this chapter focuses on what motivated this curious decision to radically alter the organizational structure of these profitable, scientifically advanced firms by purchasing a series of candy and cosmetic companies. In keeping with the foci of the dissertation, this case offers an ideal opportunity to test assumptions about the role of environmental change in catalyzing both the adoption of new organizational practices and in their subsequent retreat to traditional modes of operation. Unlike the previous chapters, in which I focused on a particular environmental change to understand the role it played in influencing the evolution of the industry, in this chapter I reverse the direction of my lens, to study the embrace and rejection of a new organizational practice and to determine the role that environmental changes may have played in both decisions.

**Introduction**

Historically, research has separated studies of the process by which new organizational practices are instituted and the process by which they are dismissed. As a result, we lack a comprehensive study of the life cycle of new organizational routines: a holistic view of the process by which new practices emerge, are adopted and then abandoned. In its place, we have studies of: the creation of new organizational routines (Dobbin and Sutton 1998; Fligstein 1990), the diffusion of new practices (Davis 1991), the factors that explain first adoption (Zorn 2004), and those that explain abandonment (Davis, Diekmann, and Tinsley 1994). But the studies continue to focus on one process at a time, examining each action independently rather than as a relationship. This disaggregation makes comparisons of the processes more difficult and obscures the degree to which these are separate or related events.

In this chapter, I offer an attempt to unify these two types of studies by charting both the diffusion of a new organizational practice and its later collapse. Prior research suggests four hypotheses that may explain either, or both, processes. These can be separated into two classes, according to the manner in which they elicit action: direct and indirect. By an “indirect” action, I mean that organizational change may occur without any specific formal change in the environment, but rather via a more diffuse process through which ideas about the best practices gradually change.

There are two forms of “indirect” pressures that may explain both adoption and rejection. Normative pressure (mimicry), where similar strategic decisions by related firms creates an internal and external pressure for a given firm to follow suit. Or, efficiency (demonstrated success of others), where rival firms become more profitable after adopting a strategy, so the remaining firms follow to keep pace.
A “direct” cause, conversely, is one for which there is a unique event that can be claimed as inciting the change. This works by either requiring the change, through regulatory reform, or by creating an environment of uncertainty that requires firms to make a calculated gamble on the appropriate response/need for change. For this reason the direct threat can come either via an action or merely the promise of action. For instance, both the passage of regulatory reform and the prospect of regulatory reform can produce a belief that change is necessary. Prosecution of firms for violating the new regulations works, on a deterrence principal, to reinforce these beliefs and can therefore act as an additional cause for change. Finally, in this specific case, as Davis et al. (1994) discussed, the threat of leveraged buyouts created a complementary incentive for firms to reform, as the failure to do so might result in the loss of control of their firm.

The question is: for a given practice, do the same forces that drive adoption later drive abandonment? I use survival analysis and fixed-effect logistic regressions on the population of public pharmaceutical firms over a forty-year period to demonstrate that the decision to adopt and abandon a new strategy follows different logic. And, the social cost of this specific strategy arose from the movement of resources away from new drug development and the reduction of pharmaceutical innovation.

**Background: The Interest in Diversification**

The first mention, in the *New York Times*, of the principal of diversification occurred in 1889 and referred specifically to problems in agricultural production. However, by 1926 the same principals that helped increase crop yields were now being cited as a valued investment strategy (1926). What is interesting to note here is the timing, more than three years before the October crash that precipitated the Great Depression and far removed from any changes in anti-trust law, we see the strategy of diversification moving through the financial community. What began as a method for farming was reinvented as a tool for individual investors and would soon become recognized as an equally effective method for corporations.

**INSERT FIGURE 4.2 –Diversification Articles**

In 1927 two more articles extolled the virtues of this strategy for individual investors, as a way of increasing the “safety” of their investments (see Chart 5.2). And, by the spring of 1929, journalists were suggesting diversification as a means to create stability in a firm. The focus of these first articles was on the most successful firms of the day: DuPont, General Motors, and Standard Oil. Standard Oil, in particular, had experienced unprecedented success during the 1920s. And, as the *Times* explained: “It is the diversification of its interests which is the outstanding feature of the Standard of New Jersey’s developments, as Wall St. sees it.”(1929a)

As the year progressed the number of articles favoring diversification continued to grow and, in the immediate aftermath of the crash, the concept was embraced as a way to prevent a recurrence.

“Impetus is being given to the movement towards greater diversification in industry as a result of the strides made in that direction by some of the
country’s largest corporations… The trend has been gathering momentum for two to three years, but lately it has spread to such an extent that it is being discussed in Wall Street much the same way that crop diversification was being emphasized six to eight years ago as the solution of the problems of agriculture.” (1929b)

This marked the beginning of the first wave of diversification for American firms. The Great Depression provided a financial rationale for firms to imitate the actions of individual investors, spreading their assets among multiple industries. It led gun manufacturers like Colt and Remington to produce vending machines, cash registers, and dish washing equipment (1929b). However, without much excess capital to invest and absent state intervention mandating it, the practice of diversification spread slowly and primarily among the largest firms.

The second wave arose in the 1950s, after the passage of the Cellar-Kefauver Act, which required firms to diversify if they sought to expand (by outlawing within-industry mergers). The combination of a thriving economy and the restrictions on within-industry mergers lead to a more widespread adoption of diversification, and one that was trumpeted by the press. By 1955 the Times could declare diversification, “a way of life” as part of a two-part series on the necessity of diversification for all industries and all types of business. Interestingly, these popular accounts cited neither the depression nor regulatory change as the source of interest in diversification. Instead, they framed it as a rational strategy to hedge against the uncertainties of any one industry. These journalistic depictions unconsciously embraced the notion that the goal of a firm is not tied to any one product, but only to the creation of profit. A notion well captured in this quote from William O’Neill, then President of General Tire, “People invest in our company not to make tires, but to make money” (Rutter 1955). This is how O’Neill explained the decisions that lead an Akron-based tire company to acquire chemical companies, radio stations, television stations, a movie studio, and finally a rocket manufacturer.

What emerged was a pattern where the largest firms diversified in the 1930s and a second wave, of smaller firms, followed them in the 1950s. In his thorough discussion of the evolution of corporate strategies Fligstein (1990) described the rise of diversification as the result of a change in how people conceived of the purpose of a firm, a claim that resonates with the quote from William O’Neill. When people stopped thinking that the goal was to protect the firm from the predatory behavior of their competitors and began to think of the goal as the creation of new markets, they moved from pursuing vertical integration to pursuing diversification. This cognitive shift was then sanctioned by regulatory reforms, both by Roosevelt’s decision to more actively pursue antitrust violators during the 1940s, and with the passage, in 1950, of the Celler-Kefauver Act, leaving diversification as the only possible means for growth.

This second round of diversification came to an end for both financial and political reasons. Financially, as with any market, the more firms moved to diversify, the fewer “bargains” existed; eventually firms were buying unprofitable or unmanageable firms just to continue the practice of diversification. Analysts grew wise to this and began to chastise firms for wasting their proceeds rather than distributing them to shareholders (Bedingfield 1970; Bender 1975; Freeman 1957). Penn Railroads in particular was
strongly criticized for diversifying, its eventual collapse seen as a product of a misguided attempt to move from railroads into real estate.

The political pressure came originally from changes in the Kennedy Administration that were expanded by Nixon. Both decided to evaluate all mergers, even those aimed at diversification, with greater rigor than their predecessors. As a result, Proctor & Gamble’s merger with Clorox was delayed, the proposed Warner-Lambert merger with 3M fell apart and greater scrutiny was promised for all mergers. As the *Wall Street Journal* reported, “Nothing in the law prevents federal authorities from reaching back several years to challenge mergers already consummated” (Beecher 1961).

This raised the specter of greater federal scrutiny and served as a further disincentive to continue diversification. But the final, and by most accounts decisive blow, arrived with the election of Ronald Reagan. His decision to reduce regulatory oversight enough to create a *de facto* unregulated market offered an alternative strategy for growth. Less regulation immediately opened up the possibility for firms to return to their previous patterns and focus on monopolization of a single industry rather than attempt growth through the acquisition of unrelated interests.

But is this general story the same story we see within a particular industry? When it came to the drug companies, the answer is an unequivocal: “no.” Instead, the majority of pharmaceutical firms actually continued to concentrate on pharmaceutical matters throughout both periods and, as they began to expand, they moved into closely related industries. For instance, after realizing that many of their medicines were being repackaged and sold, without modification, as animal medicines, firms began to establish or to acquire veterinary medicine divisions. Similarly, realizing that their distribution channels and advertising goals were the same as medical instrument and device manufacturers, firms began purchasing or creating medical instrument divisions.

The firms appear to be prime candidates for the standard diversification story: they were immensely profitable and therefore had money to spend; regulation, stock analysts, and conventional wisdom all advocated that firms create a diversified portfolio of interests to hedge against downward cycles in any one industry; they were unable to acquire enough firms within their industry to create a monopoly and; the industry was already highly concentrated (less 20 firms accounted for over 80% of sales). On top of all of this, many of the dedicated pharmaceutical firms of the 1950s had actually been divisions within diversified companies in the 1920s and 1930s; their pharmaceutical focus was a recent development. If any industry should have witnessed greater diversification it was pharmaceuticals, they had excess capital and few places to put it and they had experience with diversification. And yet, for the most part, they moved cautiously and into closely-related fields.

The conventional history implies a dance in which industry and the state move in step with each other, constantly trying to remain close without stepping on each other’s toes. However, the specifics of the pharmaceutical case suggest that, where the state is concerned, there may be multiple potential partners to watch. Leaving the metaphor behind, the pharmaceutical industry’s behavior is almost independent of the larger
national trends in diversification, but it does reflect attentiveness to the threat of regulatory reform within the industry.

To the extent that the pharmaceutical industry “diversified” after Cellar-Kefauver, they acquired foreign pharmaceutical firms, and moved cautiously into the related fields of veterinary medicine and medical devices. Their growth was entirely within the health industry and reflected more of a defensive strategy that held off potential competitors, rather than an offensive one that saw them trying to expand into new markets.

Instead, diversification was a strategy they adopted later, in the 1960s, when—in their telling—they feared the introduction of the Kefauver-Harris Act might reduce pharmaceutical profits. In the words of Henry Gasden, President of Merck, “I think it is no coincidence that since the attacks on our industry began a decade ago, every one of the dozen ‘drug houses’ in this country has moved toward diversification…” (Cray 1968). Speaking at the start of the decade about the potential passage of Kefauver-Harris, an act whose main consequence was to require tests of drug effectiveness, Abbott Labs wrote in their annual report, “The major cloud on the horizon is legislative in origin…Bill S 1522 poses a punitive threat not only to the industry but medical progress.” (1961) Eight years later Abbott wrote that the situation had not changed, “Heavy federal regulation continues to be a problem for Abbott and all companies in our industry.” Despite the onerous nature of this new regulation and the great fear it inspired it should be noted that Abbott, like nearly all pharmaceutical firms, reported record profits in its pharmaceutical division throughout this difficult period.

And so, in the firm’s own accounting, diversification was not undertaken to imitate the success of others or to dodge antitrust regulators; instead it was a strategy they imported in order to deal with the threat of declining profitability in their primary industry. These dalliances with the non-medical world were not undertaken lightly or done to improve overall efficiency, they were done because the firms were uncertain about the future of the industry. Of course, this does not explain why their forays into non-health related fields were largely limited to cosmetic and candy companies. Why would such careful firms, placing such enormous weight on diversification, all make such poor decisions?

What qualifies as a poor decision? In 1970 Squibb, one of the largest and most storied pharmaceutical companies in the United States, bought the rights to make Yves St Laurent perfume. Eight years earlier, Warner-Lambert branched out of pharmaceuticals to buy American Chicle, the makers of Dentyne and Trident gum. And four years before that Schering-Plough, who would go on to invent the most profitable allergy medicine of all time—Claritin—bought Clairol, a shampoo company. And these companies were far from alone, as they completed these acquisitions their rivals moved into golf balls, cosmetics, suntan lotion, and movie production (see Table 4.1). All interests that would be divested in the 1980s as the firms acknowledged their forays into unrelated industries had not proven profitable.

INSERT Table 4.1- Pharmaceutical Diversifications
Theory and Hypotheses

Scholars who are skeptical of the degree to which organizations are capable of change favor the saying: no church suddenly started to sell shoes. Reminding us that, as much as any organization (non-profit or for-profit) may evolve, there are certain immutable aspects of their character. And, although this sentiment may capture a general truth, it is also true that, in the specific case of the U.S. pharmaceutical industry, some of the most profitable and technologically advanced firms in the world, did one day start raising chickens, selling gum, and making golf balls. This is a change worth understanding.

What causes dramatic change?

The literature on organizational change distinguishes between first order, or incremental, and second order, or disruptive change (Greenwood and Hinings 1996; Meyer, Brooks, and Goes 1990). These can be characterized as change within a type (incremental) and change between types (disruptive). If we imagine firms as having “core” components (e.g. what they produce; the technology they use; who their customers are) then a disruptive change involves a reconfiguration of one of these basic aspects. As happened when pharmaceutical firms began to research, manufacture, and distribute products like perfume, lipstick, and candy. While most organizations are engaged in a constant process of incremental change, disruptive change occurs more infrequently and often requires an external stimulus to overcome the internal and external pressure organizations face to remain committed to a given practice (Gersick 1991).

This may explain why second order change often begins when an exogenous or environmental shock, i.e. an economic crisis or regulatory change, destabilizes the market (Carroll 1987). During the uncertain aftermath of those shocks questions about how an organization should be structured, and what ends it should pursue, gain legitimacy (Greenwood and Hinings 1996; Tushman and Anderson 1986; van de Ven and Poole 1995). Legal challenges and pressure from banks, investors, or third party associations all help clarify the viability of these new directions, as the field comes to a new understanding of what might constitute “proper” behavior for a given organization in the new environment.

These punctuations in the equilibrium of the field lead to the creation of new organizational practices or structures. The focus of the prior studies into these processes has been on two questions: which firms survive the period of foment, and what determines the rate of diffusion of the new organizational forms (Haveman 1992; Haveman 1993a; Haveman 1993b)?

There has been a curious lack of interest in examining the longevity of these forms and the process of deinstitutionalization, in which these new organizational forms are later abandoned. In effect, rather than studying the birth and death of a given organizational practice, we begin with the death of an old practice and examine the birth of a new one. However, without understanding what promotes the longevity or decline of these forms after their adoption, we are left with only a partial understanding of the relationship between the external environment and the rise and fall of organizational routines.
In this chapter I use the case of the spread of diversification strategies and subsequent re-consolidation of the pharmaceutical industry to explore the process by which new organizational practices arise and are abandoned. My interest lies in comparing the processes that first lead to the dispersion of a new strategy with those that lead to its eventual abandonment. It is my contention that a study of this type will enrich our understanding of how organizations, despite their known proclivity for maintaining the status quo, manage to remain nimble enough to adopt and discard new forms.

Why do organizations adopt new routines?

Studies of the adoption of new practices describe a process in which an exogenous shock creates the perceived need, or opportunity, for change followed by two waves of adoption (Tolbert and Zucker 1983). In the first, a subset of firms move to capitalize on the opportunities present in the changed environment. In the clearest cases, these firms are driven by gains to efficiency. The shock—whether it was political or technological—allows them to pursue a line of inquiry that had been blocked prior. For instance, the passage of the Orphan Drug Act persuaded firms to both research and manufacture drugs for smaller populations. For several firms this meant taking old discoveries “off the shelf”, as the new environment made distribution of these long-known, but unreleased, cures suddenly profitable.

However, it is perhaps more common that firms are driven by uncertainty. In the aftermath of a shock it can be unclear what constitutes legal behavior, what actions the market will praise or penalize, and what rival organizations will do in response (Dobbin and Sutton 1998). To mitigate the potential for failure, organizations examine neighboring fields, and look to government or rival firms for cues on how to proceed. In either situation, the organizational changes are perceived as necessary and, irrespective of their short or long-term benefit, often clothed in the language of efficiency.

Although this suggests that firms respond quickly to changes in their environment, multiple authors describe change as a very difficult process. They point out that often even when an organization knows that a strategy is failing they find themselves unable to stop doing it and to move towards a more profitable tack (Greenwood and Hinings 1996; Tushman and Anderson 1990). However, as these new practices become legitimized by a lack of regulatory action against them or by profit gains to the firms that made them, change does become easier and the strategies diffuse across the field to similar organizations and become institutionalized. The entire field is now reoriented around a different mode of organization, practice, or philosophy.

Why do these new practices collapse?

The question of how these new practices dissolve has received significantly less attention than the spread of new forms (Oliver 1992). Partially this arises from a belief that old processes do not disappear, they are simply replaced. However, a study by Davis et al. offers one perspective on the complicated process that enables replacement (Davis, Diekmann, and Tinsley 1994). The authors use the collapse of conglomerates to show that institutions fail as a result of two related processes.
First, the organizations that adopt them exit the field, either by choice or through failure, they are selected out of the system (Freeman and Hannan 1977). Simultaneously, the new organizations that enter do not adopt the new practice. Gradually, the organizations that adopted the new strategy are replaced by those employing an alternative approach. This study uses a popular case, the end of diversification, to argue that the use of a practice declines when conflict emerges between the environment and the practice. In the case of diversification, they find that diversification began when actors accepted the notion that a firm could be considered as nothing more than a portfolio of investments. However, this same view of the firm helped produce greater pressure on firms to produce returns for investors, which not all diversified firms did very well. Underperformance, or even the perception that diversification reduced performance, led analysts in the 1980s to downgrade their stocks. This, in turn, left diversified firms vulnerable to leveraged-buyouts from “corporate raiders” eager to disassemble these undervalued firms. When the Reagan administration moved away from enforcing antitrust regulations, it validated these practices, helping to delegitimize the diversified model.

In essence, a contrary logic emerged and became actionable. Existing firms were left with only two choices: either change their model or be replaced by firms with a more concentrated portfolio. The only limit to this explanation is that it requires turnover in the industry. This raises the question of whether it is only possible to witness the decline of a strategy or a practice through the exit of the adopting firms?

One purpose of this chapter is to combine the work of Davis et al. in exploring the causes of deinstitutionalization with the work of Haveman (1992; 1993a; 1993b) in specifying the factors that influence the adoption of a new practice. The pharmaceutical industry of the mid-20th century offers an interesting case in which new organizational practices were both adopted and discarded without any corresponding turnover in the industry, no fall of dominant firms nor any ascendant new firms. This suggests that there may be multiple processes by which a given practice is first adopted and then discarded, of which the replacement process explained by Davis et al. is but one.

**Hypotheses**

As Greve explained there are two problems that must be overcome to study strategy abandonment. First, you must be able to link the organizational decision-making process to the multiple potential environmental influences. Second, you must be able to distinguish between the abandonment of one practice and the adoption of a replacement (Greve 1995). The second problem is resolved here by the structure of the enterprise, charting the life of a practice enables us to understand both its adoption and its replacement. The first problem however, requires a more specific method to resolve. Fortunately, prior research gives us some guidance in laying out the factors that lead to diversification (Fligstein 1985) and on the factors that may make this practice vulnerable to collapse (Oliver 1992). So, to determine what processes might explain both the initial embrace and the eventual demise of diversification within this industry; I test four hypotheses.
Contagion

Institutional theory has long relied on the forces of normative pressure to explain other cases of isomorphism (DiMaggio and Powell 1983). This began with the observation of a puzzling amount of similarity among organizations that should, theoretically, be engaged in differentiation. Once it became clear that isomorphism was not the result of competitive forces in a market selecting the most efficient method, the question became why organizations would feel pressure to resemble each other. Recent work on organizational identity has helped to solve this puzzle and clarify the mechanisms that enforce and reproduce these structural similarities (Hsu 2006; Zuckerman 1999).

These studies explain the role of external actors in reinforcing organizational boundaries by penalizing violators, lowering their stock price or rejecting their product if it fails to conform to the norm. This pressure to conform has been used to explain both the limits of organizational change (i.e. it is difficult to change when change is penalized) and why there is convergence, over time, to a given organizational form (Starr 1982). However, by expanding the claim that organizations are encouraged to imitate their peers to include a desire to “follow the leader”, institutional pressure can also explain the initial adoption of a new practice by established firms (Haveman 1993a).

In fact, studies on diversification have specifically cited imitation of industry leaders as a driver for the expansion of firms into new fields. Haveman found that both small and large firms imitate the behavior of profitable firms in moving into new fields in banking. This suggests that both adoption and abandonment could occur as small firms try to mimic the behavior of the more established pharmaceutical firms.

_Hypothesis 1a_: Smaller pharmaceutical firms were more likely to diversify after the largest and most profitable pharmaceutical firms diversified.

_Hypothesis 1b_: Smaller pharmaceutical firms were more likely to abandon diversification after the largest and most profitable pharmaceutical firms abandoned diversification.

Of course, just as firms follow the leader, they have also been known to follow the pack. Fligstein demonstrates this principal by showing that diversification is poorly explained by efficiency claims and more properly explained as a result of firms looking to each other for cues on how to handle uncertainty (Fligstein 1985).

In one of the few studies of de-institutionalization, Greve (1995) finds further evidence of this practice. His research, on the abandonment of an easy listening format by radio stations, found that the _act of abandonment_ was not driven by competitive forces but rather by managers responding to future uncertainty by taking stock of what others were doing—what he refers to as contagion. In these cases, the organizational change was less a response to cues from industry leaders and more a response to uncertainty with the cues being taken from peer organizations. This leads to two related explanations for the cause of diversification and its abandonment by pharmaceutical firms.

_Hypothesis 1c_: A given pharmaceutical firm was more likely to diversify after other pharmaceutical firms diversified.
Hypothesis 1d: A given pharmaceutical firm was more likely to abandon diversification after other pharmaceutical firms stopped.

Efficiency

Alternately, the decision to both adopt and abandon a strategy may arise out of certainty, rather than uncertainty. It may be a means of mediating the effect of increasing competition between firms, to explore new markets or to copy a strategy that has proven successful. Abandonment, in turn, occurs after the strategy became unprofitable or increases the likelihood of exit by acquisition or bankruptcy.

This claim resonates with some of the earliest and most comprehensive studies of diversification, in which Rumelt found that diversification improved performance, provided that firms moved into areas “that drew on some common core skill or resource.” (Rumelt 1982) Similarly, in her study of the California Savings & Loan industry, Haveman (1993b) showed that banks expanding into new areas did not induce liabilities automatically, but, depending upon the context actually benefited from the action. In particular, she found that for large firms, expanding into new markets improved firm performance without increasing their likelihood of failure.

Chandler (2005) argues that the evolution of the pharmaceutical industry was similarly deliberate and beneficial. He finds that the largest firms were able to benefit from the economies of scale attending the practice of “related diversification.” These firms were not blindly selecting partners, but were after integrated learning bases, and their successful pursuit of this explains why no firms founded after 1920 ever became dominant in the industry. He suggests that this may explain why a firm like Eastman-Kodak, an established firm with lots of technical knowledge, couldn’t break in to the industry; they were diversifying into an inadequately related field.

These findings suggest that both the adoption and abandonment of a new practice may not be an unconscious response to the vagaries of a changed environment, but may be a refined attempt to improve firm performance by moving into or out of carefully selected fields. Adoption was a means of improving performance and increasing profitability, and therefore evidence that diversification produced these goals would entice undiversified firms to follow suit. In this story, the decline of a practice comes as firms recognize the failure of the new practice and revert to their old strategies.

Hypothesis 2a: Firms were more likely to diversify if the profits of diversified firms increased.

Hypothesis 2b: Firms were more likely to abandon the strategy if the profits of diversified firms decreased.

Internal Politics

While the prior studies of de-institutionalization focus exclusively on the external factors that drive abandonment, there are processes internal to the firm that may also explain the practice. In particular, studies of the conflicts between groups inside a firm
suggest that strategies are abandoned and adopted as one group seizes control of the organization from another (Staw 1981).

Charles Perrow (1970) uses similar logic to explain how sales and marketing executives were able to claim control over the strategic direction of firms in the 1960s. As manufacturing practices were routinized, the sales executives argued that future growth lay in expanding to new markets (as opposed to greater manufacturing efficiencies) and, as their view took hold, they assumed positions of greater power and redirected firm activities.

Fliedstein (1990) expanded on this to show that similar processes occurred later in the 20th Century as the managers in finance wrested the mantel of control from marketing and again redirected firm activities and resources in a novel direction. In these cases, new leadership is less committed to the strategies of the old and change in the political climate within an organization can produce strategy abandonment as a feature of political turnover.

**Hypothesis 3: Firms that experienced executive turnover will be more likely to adopt a new strategy.**

**Threat Response**

Finally, it is also possible that firms behave both instrumentally and by imitation. Firms may prefer, and be encouraged, to do nothing unless the environment requires a change. At which point, they look to imitate either peers or industry leaders. In particular, Davis discusses how one of the factors driving the decline of the conglomerate model was that corporate raiders started buying up the assets of diversified firms. Stock analysts penalized diversified firms, lowering their stock value below their book value and increasing their vulnerability. Similarly, Tolbert and Zucker (1983) examined the adoption of civil service reforms and found that the first wave of adoption was driven by attempts to solve a specific problem, it was only the second wave of adoption that was driven by legitimacy-based pressure.

In this sense, firms behave instrumentally, altering their practice in response to a perceived threat. And, the actions of peers and neighboring organizations serve to help actors construct viable alternatives. Abandonment of an old practice and adoption of a new one both result from the perception that the old practice opens the firm to greater risk. This is distinct from a change made to improve performance, as the old strategy may well be very profitable or successful by most measures, but still increase the likelihood of a threat, such as an E.P.A. investigation or an F.T.C. antitrust claim. Therefore it is not the performance aspect of the strategy that leads to its decline, but rather the perception that continuing the practice entails too great of a risk.

Research in the legal sphere, on “deterrence effects” has found that high-profile prosecution of regulatory violators has a ripple effect throughout an industry, causing firms to change their behavior without additional prosecution. This line of reasoning builds off the notion that firms are attentive to each other’s actions and to the consequences of these actions. For instance, in a study of Equal Employment
Opportunity programs, Beth Hirsh (2009) found that organizations desegregate after enforcement efforts reach their area, not simply in response to the passage of a law. Similarly, Thornton et al. (2005) found that even small-scale chemical companies were aware of environmental prosecution of related firms and used it to justify their own moves towards compliance.

Given the role of antitrust legislation in spurring diversification in the first place and the presumed role of corporate raiders in reducing interest in continuing the practice, there were two viable threats that may explain either adoption or abandonment of diversification. This suggests two final hypotheses:

*Hypothesis 4a: A given pharmaceutical firm was more likely to adopt diversification after other pharmaceutical firms were subject to antitrust suits.*

*Hypothesis 4b: A given pharmaceutical firm was more likely to abandon diversification after other diversified pharmaceutical firms were acquired.*

**Data and Methods**

To test these four sets of hypotheses, I gathered forty years of data (1950-1990) on the diversification decisions of twenty-five firms, the population of publicly traded pharmaceutical companies. I examined both their initial pattern of acquisitions and their later pattern of divestments. To properly model this I used two dependent variables and two methods that work together to capture the complicated process of first adopting and then abandoning a strategy.

**INSERT Figure 4.3: Distribution of Actions**

For my dependent variables, I used an indicator for whether or not a pharmaceutical firm acquired or divested a non-medical company in a given year. This provided the most basic measure for adoption and abandonment and allowed me to measure the influence of covariates on a firm’s likelihood to adopt or abandon a given practice. The distribution of diversification and divestment activities by firm is presented in figure 4.3. This shows a fairly normal distribution of events, with most firms acquiring a few non-medical businesses and only three firms acquiring more than ten, during the forty year period. The line tracing firm divestments reveals that most firms rid themselves of all their acquired businesses at some point in the study, although the fact that new acquisitions were often combined into single entities produced a slightly lower number of divestments than acquisitions. These individual actions of diversifying and divesting combined to document the rise and fall of a new organizational practice, shown in figure 4.4, with popularity peaking in the early 1960s before it collapsing during the 1970s.

**INSERT: Figure 4.4: Percentage of Industry Diversified**

I estimate these using a Cox proportional hazard model to model the instantaneous likelihood of a firm acquiring or divesting companies outside of the pharmaceutical industry. The Cox model is a commonly used form of semi-parametric analysis for the modeling of event histories. Although it is less robust than a parametric...
model, it does not require an *a priori* assumption about the distribution of events over time. Without a theory of time dependence it is preferable to use a semi-parametric model of a type like the Cox model. The Cox model follows the form:

\[ h(t \mid x_j) = h_0(t) \exp(x_j \beta) \]

Where the dependent variable is the hazard rate for the *j*th subject at time *t*. This model accounts for unobserved differences between firms while requiring that all firm share hazard rates of parallel shape (even if the specific values may vary).

This model allows for two forms of analysis. First, it enables the estimation of the likelihood of a firm’s first act to diversify or divest their holdings. Second, by allowing for the estimation of repeated events, it allows me to assess the overall influence of the covariates on the degree to which a given firm pursued the strategy of diversification or divestment.\(^{19}\)

To estimate both the rise and fall of the practice I rely on two separate dependent variables, tested in independent regressions. The first is an indicator variable for whether or not a firm had diversified at a given time (0 indicates that the firm had not yet diversified). The second dependent variable is an indicator for whether or not a firm had divested their diversified holdings (0 indicates that the firm had begun the act of divesting). These two variables were also coded as count data in subsequent regressions, with each acquisition or divestment being treated as a one unit increase for a firm. Data on both acquisitions and divestments were gathered from the annual reports of the firms.

To test my specific hypotheses, my independent variables include a range of firm and industry-level measures. Specifically, data was gathered on firm size, sales, profitability; and executive turnover. To estimate the effect of specific environmental pressures on the actions of individual firms I collected data on whether a sample firm was acquired and, whether an antitrust suit was brought against a sample firm. I also explored the effect of having a product recalled by the FDA, but this occurred so rarely and had such a limited effect, that it did not appear to motivate firm decisions to diversify or divest.

To test my hypotheses on the effect of large firms on small firms, the firms were separated into two categories, large and small, with the large firms being the five firms that accounted for the largest percentage of prescription sales during the period. The

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\(^{19}\) I have also estimated several other dependent variables, including the percent of firms in the sample that diversified or divested in relation to the covariates. This captures the industry-level phenomena, to see if the overall rate of adoption/abandonment changed in relation to the independent variables. This was estimated using fixed effect regressions to control for unobserved variations between firms and produced comparable results.
remaining twenty firms together accounted for over 40% of all sales and were grouped together as “small.”

In addition, I controlled for ownership structure (family run, external CEO), organizational history (was the firm always a dedicated pharmaceutical or had it begun as part of a conglomerate) and whether Congress had voted on price-control legislation in a given year. This last variable may seem too far removed to consider, but both the accounts of executives at the time and of economic analyses conducted later suggest that diversification may have been an attempt to protect against federal threats to the profitability of the pharmaceutical market.

Finally, I include controls for the popularity of diversification, measured by the number of articles discussing “diversification” that appear in the New York Times in a calendar year. This captures the degree to which diversification actions were motivated by a public consensus around the value of diversifying. All data were gathered directly from the annual reports of the firms in the sample, with the exception of data on price-control legislation, which came instead from the Congressional Record.

Although the data were both right and left-censored, the Cox model uses the probability of failure at a given time rather than assessing the distribution of events over time, reducing the influence of right-censoring on the analysis. To control for events and situations that occurred prior to the start of the study, I include variables capturing organizational history in the model.

**INSERT TABLE 4.2—Summary Statistics**

**Results**

For each hypothesis I test two models. The first model examines the effect of the variables on the initial likelihood of adopting or abandoning a new strategy. The second model examines the effect of covariates on the degree to which a firm pursued the strategy.

**INSERT TABLE 4.3—Hypothesis 1**

The first pair of hypotheses (H1a, H1b) proposed that small firms would follow the lead of larger firms in both adopting and abandoning a strategy. To test this I used a stratified survival analysis separating the behavior of the larger and smaller pharmaceutical firms. I then used the behavior of the larger pharmaceutical firms as an independent variable in the regressions to see whether or not the smaller firms were responding to the actions of the larger.

Unfortunately, stratifying the sample to determine the effect of the limited pool of larger firms on the actions of the smaller lessened the utility of survival analysis.

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20 The two groups here together accounted for less than 100% of pharmaceutical sales, but the remaining sales were distributed across dozens of small privately-held firms for which there was no data available. These firms were not of the same type as the larger firms included here (in that they were not research-driven) and would therefore not be expected to behave the same way.
Therefore the likelihood of adoption was modeled using fixed-effect logistic regressions, controlling for unobserved differences between firms. This produced robust results confirming the hypotheses and demonstrating that the decision to diversify by large firms significantly raised the odds that small firms would also diversify (1.24, .241). Moreover, each time the five largest firms acquired non-medical businesses, it raised the likelihood that small firms would also acquire an additional non-medical business (.057, .022). In other words, both the large firm’s initial act of diversification and every subsequent move to greater diversify were influential for small firms. They did not simply diversify after the large firms did so, but they continued to diversify and to invest their resources in the acquisition of unrelated firms each time they saw the larger firms do so.

Most interestingly, this same effect was true in reverse, when large firms divested their businesses the small firms were almost twice as likely to divest theirs as well (1.95, .809). Again, this proved true both in the initial abandonment decision and for subsequent actions, as each divestment by large firms raised the likelihood that small firms would divest more of their own non-medical businesses (.122, .038).

The next pair of hypotheses (1c, 1d) tested the related position that firms follow the crowd as much as they follow industry leaders. The results here found no support for this proposition, as the increasing diversification of the industry did not exert any influence on the remaining firms to diversify. This was also true of the decision to abandon the strategy, as a larger percent of the industry returned to its “core competencies” the remaining firms became no more likely to abandon their position as well. Together, these results indicate that both adoption and abandonment were strategic choices, attempts to emulate market leaders, and not the result of external or internal pressure to conform to a developing norm.

The second hypotheses expanded upon this, proposing that both adoption (2a) and abandonment (2b) were performance-related decisions. Specifically, I hypothesized that if the performance of diversified firms rose, more firms would adopt the strategy; and as the returns declined, firms would abandon the strategy.

**INSERT TABLE 4.4—Hypotheses 2-4**

The results presented in table 4.4 offer mixed support for this hypothesis. While it is evident that positive returns to diversification increased the likelihood that additional firms would adopt the strategy (.134, .032), there is no evidence that that the subsequent performance of diversified firms—either positive or negative—had any influence over either the decision to continue pursuing the strategy or the decision to abandon it and return to a more pure pharmaceutical model.21

This implies an important distinction between the factors that lead to the adoption of a new strategy and those that lead to its dismissal, and one that is consistent with related findings in institutional theory. Firms watch peers to mediate the gains

21 Although the relationship is presented as linear here, more complicated relationships were also tested and found not to be statistically significant.
competitors might experience from moving into new fields. So the adoption of a strategy is very much related to a given firms perception of the economic benefits of the strategy. But, once they adopt the strategy as well, the firms are less sensitive to changes in their rival’s performance and therefore less liable to abandon the strategy even if their competitor’s profits decline.

This may be because changing strategies comes at a high cost and firms are loathe to quickly abandon an expensive new enterprise, or it may result from internal friction, as a group of employees now has a vested interest in continuing the new program. The results in this chapter are not capable of specifying the mechanism that prevents abandonment. They are however useful in pointing out the change in how a strategy is evaluated before and after adoption.

Additional fixed effect logit regressions modeling the decision to abandon the strategy reinforces this claim, showing that even as the firms themselves experienced profitability declines in the wake of a new strategy, they were no more likely to abandon it. The annual reports of the individual firms offers rich qualitative evidence of this as multiple firms explained away the losses that followed diversification as “short-term” problems or even as evidence of the past management’s inadequacies that their own managers would quickly correct.

For instance, Eli Lilly lost money nearly every year that it owned Elizabeth Arden and yet they held on to this unrelated cosmetic firm for seventeen years, rationalizing the losses using a mutable logic: a way to offset taxes, a problem that would end with new products, or as carry-over costs from pre-merger actions by Arden managers. Not once did they acknowledge that an Indiana-based pharmaceutical company had simply no idea how to make money running an international cosmetic company.

The third hypotheses presumed that the adoption or abandonment of a strategy would be more likely to arise in the wake of executive turnover. The results shown here offer no support for this hypothesis. There is also no support found for the fourth hypothesis, that the decision to adopt or abandon diversification would arise as a response to specific threats, either the threat of antitrust action or the threat of a hostile takeover. Although firms in the sample were both acquired and subject to FTC inquiries during the period of study, these events had no bearing on the diversification of other firms in the industry.

This last finding is perhaps less surprising than it seems, as the exiting firms were acquired after the majority of firms had already abandoned diversification. It is worth mentioning that, consistent with hypothesis, though not all the still-diversified firms were acquired, the only firms acquired were those that remained committed to diversification.

Conclusion

I began this chapter by posing the question of what would happen if the drug companies stopped making drugs. While this question was posed rhetorically, we have evidence here of what happens when the firms tried to broaden their interests. And what we find is that a multi-decade dalliance with unrelated interests had a minimal effect on
their fortunes, but produced a noticeable effect on the quality of new drugs produced (see figure 4.3). Despite the claims of multiple scholars that the Kefauver-Harris Act resulted in a permanent decline in productivity, it is apparent that the production of high-quality new drugs rebounded quickly to exceed the pre 1962 Act performance. However, the decline in innovation does perfectly coincide with an interest in diversification.

During the 1960s and 1970s, pharmaceutical firms moved capital away from research and towards the acquisition of suntan lotion companies, perfume manufacturers, and cosmetic companies, significantly reducing their output of creative new drugs. As these firms abandoned the strategy and returned their focus to pharmaceuticals, the number of high-quality new drugs approved each year regained and then surpassed their earlier records. This is even more impressive given the higher standards the drugs were held to following the 1962 Act.

Interestingly, critics of regulation point to this act, which required only that drugs be proven safe, as an example of the deleterious effect of regulation. However, what we see here is not that regulation limited firms abilities, nor that regulations drove them to diversify, but rather that as pharmaceutical firms got caught in a nationwide wave of diversification they stopped innovating. While their annual R&D budget continued to climb it is clear that these flirtations with candy and cosmetic companies had a high social cost. What we see here is both that pharmaceutical firms, as an industry, follow the lead of a few central players and that if those actors choose, like Bristol-Myers, to make movies instead of drugs then everyone else will do the same.

Yet the nature of the market is such that the firms were able to pursue these ventures without any cost. For, despite their multiple forays into unrelated areas, the relative market position of the firms remained almost constant throughout this period. Although there were some fluctuations between, say, the fifth and seventh most profitable firm, the top twenty companies remained in their lofty position atop all other manufacturers. Their diversification phase passed almost without incidence as no new firms upset their ranks and few old firms exited throughout the experiment. Those firms that were acquired, for the most part, had suffered unrelated financial losses—often due to liability issues concerning their pharmaceutical products (not their diversified interests). While a few of these firms were initially purchased by external firms trying to enter the industry, they were all quickly resold to “native” pharmaceutical firms as even large chemical companies like DuPont, Eastman-Kodak, or Proctor & Gamble found themselves incapable of competing in that rarified air. This is the quintessential nature of the industry: the firms are so protected by the regulations they claim to abhor, that while they can lose millions making candy, perfume, and lipstick before they returned to drugs, some of the largest and most scientifically advanced firms in the world cannot reciprocate and enter their industry.

Given then, that the firms adopted a radical organizational shift, abandoned it, and ended up none the poorer for it, what lessons can be drawn from this chapter? First, on the theoretical level, it is clear here that this practice did not decline as the firms that practiced it died out, as found by Davis et al. Instead, in keeping with Haveman’s findings, adoption occurred as lead firms embraced a new strategy and the remainder of the industry simply followed. The decline of the practice occurred as these same lead
firms became enticed by new possibilities, not as they became concerned about declining performance or as environmental pressures required them to change. No, the decline occurred as new scientific opportunities emerged in biotech and prescription benefit management firms offered a new means to control the market. To raise the capital to pursue these interests the firms had to sell off some of the underperforming assets they had been content to carry until then.

There is therefore an important distinction to be made between the appraisal of a strategy before and after adoption. While the initial adoption is a largely instrumental decision, based on recognition of the gains made by rivals and a desire to remain spatially proximate to leading firms. The eventual abandonment of a strategy is not a performance-related decision. Instead, all of the pharmaceuticals proved adept at rationalizing why a company dedicated to the pursuit of new medicine should also pursue cheap golf balls, develop movies, and make candy. The practice was not detrimental only because the continually high returns from their pharmaceutical units provided sufficient insulation to protect both management and the firm’s status from the worse effects of these diversions. Abandonment finally occurred when industry opinion leaders needed additional capital to pursue a new strategy during the 1980s. This means that while the process of abandonment and adoption are linked temporally and influence each other, they are evaluated and acted upon according to distinct logical frames.

Extending the Analysis

What is, perhaps, even more interesting than the question of why a firm adopted or abandoned a strategy, is to examine which firms were leaders and which were laggards. Although we may expect the most recognizable firms to be well represented among the first set of movers, it is surprising how many of the major pharmaceutical companies: Upjohn, Abbott Laboratories, and Squibb, were among the final firms to diversify. In fact, what table 4.5 makes clear is that the largest firms fell into two groups either moving very quickly or very slowly to diversify, while the smaller firms (by 1950 sales) fell in-between. The pattern recurs in terms of divestments, where again the smaller firms are neither the fastest nor the slowest to abandon the strategy, but instead fall between two groups of larger firms

**INSERT TABLE 4.5—TIMING OF ACTIONS**

This suggests that there are two processes at work: the largest firms have the ability to move at their own speed, independent of the pressure to conform, while smaller firms are caught continually following their lead. This raises a second related question: what were the consequences of pursuing diversification? While these questions might normally merit their own chapter, I will offer a brief analysis of who lead and who lagged, and whether or not being in the leading or lagging group had serious repercussions for the firm’s performance.

To model these I used survival analysis to estimate the influence of covariates on the likelihood a firm would diversify or divest. In essence, testing the relationship between firm characteristics and the speed with which a given firm adopted and then abandoned the strategy.
To estimate the influence of the timing of adoption and abandonment on firm performance I used survival analysis and random effect regressions. The survival analysis modeled the influence of the timing of adoption and abandonment (divided into equally spaced periods of five years) on the likelihood of exit via bankruptcy or hostile takeover. I then used random effects to estimate the influence of the timing of the diversification decisions on a firm’s profitability and sales growth. Random effects were used rather than the preferred fixed effects because many of the variables were time-invariant. To correct for time trending in the data, the first difference was used for each variable, so the model is more accurately described as estimating the influence of adoption/abandonment decisions on the change in profit or sales. The variables themselves are the same ones used in the first set of analyses, although here I break down the diversification and divestment actions into discrete time periods to compare the experience of firms that diversified between 1950-55 with those that waited until 1965-70.

Although I am not testing specifically enumerated hypotheses, it follows from the findings in the first part of this chapter that small firms should lag in adopting new strategies and should, therefore, suffer the penalties of being a late arrival, while larger firms should be both the leaders and the ultimate laggards. However, the question of which firms will be the first to adopt or abandon the strategy and what they gain by doing so is an open question that these analyses will seek to explain.

**INSERT Table 4.6—TIMING EFFECT REGRESSIONS**

**Extended Results**

It is clear from model 1, in table 4.6, that the firm-level variables had no consistent influence over the timing of diversification. In keeping with what was found earlier in the chapter, we see that the uncertainty surrounding executive change and FDA actions did not motivate the firms to move any more quickly than their peers, nor were firms that continued to be family-run or lead by former pharmacists display any greater resistance to the strategy. The decision to diversify was therefore not hastened by specific or inchoate concerns about the state of the market nor was it delayed by greater ties to older models of management. Instead, similar firms adopted very different strategies when it came to diversification—some moving quickly to embrace it, while others adopted a “wait and see” attitude before they too succumbed.

The same is not true of the time to divestment, as family run firms were significantly slower to abandon the strategy, once adopted (-.752, .394). This suggests a greater degree of insulation, these firms were more confident or more committed to a course of action once adopted than their rivals. It is also interesting that, while not statistically significant at the .9 level, it appears that firms run by people with a pharmaceutical background were slightly slower to abandon diversification than other firms. Together, this implies that these “less modern” firms, were more cautious in their decisions and took longer to declare a strategy as failed. Whether this arose from their inability to judge or a greater degree of security in their position is impossible to determine, but it is clear that they were less impulsive than their modernized rivals with financial CEOs and greater separation between ownership and management.
The timing of divestment and diversification decisions also had no effect on the likelihood of firm survival. The earlier firms gained no significant advantage and later firms were no more likely to fail, strangely the only statistically significant effect was felt for the middle firms (2.25, 1.22). In combination with the results presented above, this suggests that there were three classes of firms: Leaders, Followers, and Laggards. While the leaders and laggards seemed to draw equally from the population of large firms and—as we’ll see in a moment—garnered the lion’s share of rewards, the followers were those firms that waited until someone else acted to act themselves, but were never the last to act. These firms were smaller and suffered the penalties of acting in the wake of the industry leaders. As shown here, only those firms that divested in 1972-76 were at a higher risk of exit, those that were the last to divest and the first to do so were equally protected.

The pattern of leaders, followers, and laggards recurs when we examine the results in table 4.7 the analysis of diversification’s influence on firm performance.

**INSERT TABLE 4.7**

The pattern for profitability gains was more in keeping with what was expected, the first firms to diversify experienced a gain in profitability (45.5, 23.5) that was not found for any of the later adopters. This suggests that there were some values to be found, or some advantage to be gained from diversifying that quickly disappeared. The same pattern appears in tests of sales growth, where the early firms had sizeable gains (80.4, 27.8) that were not experienced by the later firms. However, it is worth noting that even the last firms to adopt the strategy did not experience a decline in their fortunes despite their lengthy (in some cases two-decade long) delay in action.

The returns to abandoning diversification were more complicated. The first firms to abandon experienced robust positive effects, gaining millions in profits from being among the first firms to switch strategies (46.5, 23.3). However the first firms to abandon the strategy proved no more successful than firms that remained diversified for an additional several decades. These results suggest that there was no true “first-mover advantage” here where the most nimble firms were better able to garner the rewards inherent in switching strategies. Instead, the early adopters neither benefited nor were harmed for their actions and late arrivals were at no disadvantage for having been slow to adjust.

This is especially surprising given the robust positive effect that acquisitions and divestments had on performance. The overwhelming and consistent positive returns to the acquisitions and divestments suggests that the firms knew what they were doing and were not acting irresponsibly or blindly due to pressure, but were instead making careful strategic decisions. It may also indicate that their market was so extraordinarily profitable that the yearly gains were not noticeably reduced by even the disastrous acquisitions that never proved profitable. In fact, as mentioned before, many pharmaceutical companies touted the tax advantages that these money-losing acquisitions provided them in the short term while simultaneously claiming that, in the long-term and with their management team in charge, even these failing divisions would soon be profitable.
Extending the Conclusion

This brief analysis complements the research presented earlier in the chapter by clarifying both which firms moved when, and how much did the timing of their decision influence their eventual performance. What we see is that there were three classes of firms: leaders, followers, and laggards. While both the leaders and laggards had recognizable firms, it is evident that the larger firms moved first, the medium sized firms moved second, and the smallest firms moved last (see table 5.4). What is interesting, and evident in the regressions, is that this delayed reaction did not harm the smaller firms. Although the earliest movers remained the largest, they did not extend their lead, as both the medium and small firms continued to grow at a rapid pace, especially during the 1960s. Their core business in pharmaceuticals was just too strong, and too profitable, for these dalliances to register or cause any change in the market position of the firms.

The pattern is not the same for divestment, again paralleling the claim made earlier in the chapter that these are separate, if related, practices. Here the firms that begin as large but unprofitable are quick to abandon the practice, while their smaller more profitable rivals remain committed. This appears to be a mistake, as the firms that move most quickly to return to their core business of pharmaceuticals experience rapid gains in both sales and profit, while the firms that are slower to divest continue to grow at the previous rate. It is clear then, that while the market is sufficiently protected to allow firms to experiment without cost, the opportunity cost of diverting attention to these unrelated interests is extraordinarily high. The drug companies were like the owners of a gold mine that, periodically, decided to stop mining and start building and selling carved stone figurines. If you own an active gold mine, you can probably get away with this without much cost, but the quicker you return to mining gold the more profitable you are going to be. What remains extraordinary in this story, is just how completely an entire industry of gold miners could become persuaded to turn their attention away from the gold and towards golf balls, candy, and perfume.
Chapter Five: The Politics of Innovation

The question that arises in these chapters is whether or not one can separate the consequences of an environmental shock from its context. The last three chapters have offered a detailed study of specific attempts to transform the industry. While this has allowed for greater clarity in understanding the mechanisms by which different types of environmental change yield, or fail to yield, changes in the market, the lack of comparisons across time can reduce the utility of these lessons. To balance the depth of those chapters with some greater breadth, this penultimate chapter offers a comparative study of similar political efforts attempted at different points in time.

Up until now I have examined these transformative moments independently, but what happens if we adopt a broader perspective and compare repeated attempts? If we seek to understand the manner in which environmental change acts to transform an industry, it makes sense to look across time at multiple similar attempts at change. This enables us to determine whether repeated efforts yield consistent results or, if not, then what prevents them from being effective in one instance and allows them to be relevant in another?

In this chapter I explore the relationship between regulatory change and patterns of pharmaceutical innovation as a means of comparing the value of multiple attempts at change over time on this, the most significant, of dimensions. This allows me to test the validity of the “access vs. innovation” paradigm that has governed pharmaceutical regulation since the 1950s and continues to serve as the framework for regulatory efforts today. It also allows me to investigate the ability of regulatory change to influence industrial innovation, a question that has profound implications for public health outcomes and as a study of how government can mediate the direction of innovation within an industry.

Theories of Innovation

There exists a disconnect between the popular conception of innovation as the province of a lone genius, driven by necessity, and the policies aimed to catalyze innovation by increasing the financial incentives. While not mutually exclusive, if the popular conception were true, reducing the cost of development, or increasing the potential for profit would not alter the number of inventors or the quality of their efforts. Yet even as we replace the myth of the lone genius with an appreciation for the value in collaboration and access to diverse ideas our policies remain tied to the claim that innovation is a function of profitability (Hargadon and Douglas 2001; Powell, Koput, and Smith-Doerr 1996; Tushman and Anderson 1990). Therefore, despite our increasing knowledge of the complex array of factors motivating and limiting innovation, our policy options remain tethered to the simple notion that government can only “push” or “pull” new ideas by adjusting a firm’s costs or potential profits (Nemet 2009).

This has lead to the adoption of policies with high social and economic costs. For example, regulation of the US pharmaceutical industry has, for over seventy years, rested upon one central assumption: government can either increase public access to new drugs by lowering their price or it can increase the flow of new drugs (innovation) by allowing
the price to rise (Pakes and Temin 1991; Scherer 1993; Temin 1980b), but *it cannot do both*. This “access vs. innovation” framework produced an alternating series of policies: attempts to foster innovation followed by attempts to increase access. Recent economic analyses have measured the effect of the individual policies on rates of both access and innovation (Danzon and Chao 2000; DiMasi, Hansen, and Grabowski 2003; Grabowski 2002; Grabowski and Vernon 1986). However we have not studied whether similar policies consistently altered the kind or quality of innovation. The object of this paper will be to test the assumed historical relationship between the quality of innovation and policies aimed at altering market incentives. Specifically, I will investigate the evidence for an “access vs. innovation” binary by examining whether different regulatory efforts have altered either the kind or quality of new medicine.

This study looks at the effect of four different policy types on the kind and quality of medicine that is produced, using distributed lag two-stage least squares regressions on industry-level data from 1950-2005. I find that, despite popular concerns, the pharmaceutical industry become more innovative over time, devoting a greater effort to produce breakthrough medications. Further, I find that while regulation has reduced the total number of drugs approved each year, it has not altered the quality of pharmaceutical research nor has it reduced the number of innovative new drugs. This challenges the basic assumption behind the “access vs. innovation” rubric and suggests that reductions in potential profitability have not yet been great enough to alter the incentive to innovate. The broader significance of this with relation to innovation policy is explored in the conclusion.

**Theory and Hypotheses: Innovation and the Potential for Profit**

The degree to which government can influence either the rate or quality of innovation remains an unsettled question. Claims that government acts as a catalyst center upon the notion that innovation responds to the “attractiveness” of the market. Further, government can alter how “attractive” a market is to innovators by either subsidizing their research and reducing costs (what Nemet calls “technology-push”), or by raising/lowering the potential profitability of the product (“demand-pull”). Studies of these effects have found that legislation does alter the rate of new drugs approved by the FDA (Grabowski and Vernon 1990; Kane 1997), the profitability of the prescription drug market (Finkelstein 2004; Thomas 1990), and the R&D investments of firms (Acemoglu and Linn 2004; Cockburn 2004; Vernon 2005). These studies combine to tell a convincing story: regulation reduces profitability, the anticipation of lost profitability discourages R&D investment, less investment results in less innovation (Grabowski 2006; Lichtenberg and Waldfogel 2003).

However, it is possible that while these fluctuations in potential profitability affect the total number, they have a very limited bearing on the number of quality innovations (what Tushman calls “competence destroying/enhancing” innovations). For instance, Nemet has shown that developments in alternative energy technology became *less* innovative over time, despite legislative efforts to increase the potential profitability (Nemet 2009). Similarly, demand by the military for U.S. transistors increased the
profitability of American firms, but also prevented them from developing the technologies necessary to make transistors for a commercial audience, ultimately allowing Japanese firms to surpass them (Misa 1985). In both of these cases technology became locked-in as firms opted to enjoy the profits that came from minor adjustments rather than to pursue high-risk innovations.

It is also possible that innovations are driven by developments in science and technology that are unrelated to fluctuations in the markets. These “technological discontinuities” do not occur in response to the market but emerge of their own accord following long periods of incremental change (Tushman and Anderson 1986; Tushman and Anderson 1990). MacKenzie (1996) contends that this pattern results from a firm’s limited ability to gauge which technologies will maximize their profits, causing them to pursue conservative innovations irrespective of market fluctuation. Breakthroughs occur because scientific knowledge reaches a critical juncture, allowing for new possibilities, not because inventors redouble their efforts to exploit new potentials for profit. Therefore, attempts by the government to alter the potential profitability of an innovation will not result in changes in the kind or quality of new drugs.

Despite this uncertainty over the role of market incentives on the quality of innovation, the philosophy of the U.S. government has been to assume a zero-sum trade-off between regulation and innovation. In this section, I develop four hypotheses to test this relationship in the context of the pharmaceutical industry and to examine the logic of adopting an “access vs. innovation” paradigm.

From the origin of the modern pharmaceutical industry in 1950 through 2005, Congress introduced six legislative reforms directed at the creation and distribution of pharmaceutical products in the U.S. These policies reflect four distinct regulatory strategies (see table 5.1): increase competition within the industry, decrease the cost of regulation, increase the amount of innovation and, increase the quality of innovations. The intended effects of these policies form the basis for the four hypotheses developed below.

**INSERT TABLE 5.1**

To clarify: the null hypothesis is not that innovation occurs without any potential for profit; it is that the relationship between innovative output and funding is non-linear. While a basic expectation of profit is essential, increasing the potential profitability will have a rapidly diminishing effect on the quality of innovations. If true, this suggests that federal attempts to alter innovation by increasing the potential for profit will have limited efficacy and attempts to increase access by reducing costs will have less dire costs to future innovation than feared. The hypotheses featured below test the contrary claim that legislative efforts can directly alter the degree of innovation within an industry.

**How Regulation Limits Innovation**

The first type of legislation sought to increase the quality of new medicine by creating additional forms of regulation requiring tests of safety and effectiveness prior to
sale. The most well-documented of these efforts was the 1962 Kefauver-Harris Amendment to the Food and Drug Act, which, for the first time, required that drugs be proven effective before they could be sold to the public. This act established the three phase clinical trial system in practice today, introducing a massive new cost to producing drugs and increasing the risk that a drug would fail to be approved. As such the act was met with concerted resistance, with even the American Medical Association declaring that these tests were unnecessary and liable to retard the pace of new medical innovation.

Although few people today would hope to revert to a market in which untested drugs were sold, there is evidence that these regulations cost the public more in decreased innovation than was gained through the assurance of efficacy. The first analyses of the Kefauver-Harris Act found that the act had a negative impact on the rate of new drug innovation, concluding that the higher cost and lower probability of success forced manufacturers to pursue safer, less innovative, strategies (Peltzman 1973). Subsequent studies offered further evidence that pharmaceutical firms responded to all new regulations by slowing their pace of innovation (Grabowski, Vernon, and Thomas 1978). Simply put, regulations increased both the cost of development and the possibility that a drug would fail to reach the market. Pharmaceutical firms balanced this greater uncertainty by pursuing less-risky options, which decreased the total number of innovations (Birnbaum 1984).

These findings are reinforced by research conducted in other industries. For instance, environmental regulations forced chemical firms to reallocate R&D resources towards compliance programs, reducing the innovative output of the firms (Chakrabati 1990). More recently, efforts lead by the Recording Industry Association of America to regulate online file-sharing has reduced innovation in new media (Ku 2008). While in the latter case the regulations were aimed at protecting the producer rather than the consumer, in each the introduction of additional forms of regulation resulted in less innovation across the industry.

Even in the rare case where a firm developed a promising compound, changes in the expected profitability of the drug affected the firm’s willingness to initiate clinical trials (Finkelstein 2004). In fact, some firms stopped testing on seemingly effective drugs as the costs of additional testing increased (Reed, Califf, and Schulman 2006).22

This link between the costs of regulation and a firm’s willingness to invest in research has been well-documented both in the pharmaceutical industry (Acemoglu and Linn 2004; Cockburn and Henderson 1994) and in other industries (Damanpour 1992). These results conclude that, requiring additional tests reduced the potential for profit, which encouraged firms to pursue more product-extensions and to pursue drugs in fields with proven sales records as opposed to riskier, more innovative, directions. This leads to the first hypothesis:

22 The FDA requires three phases, or stages, of drug testing prior to approval. Each phase requires a larger sample and more comprehensive efficacy tests, correspondingly, the costs rise with each phase.
Hypothesis 1: The introduction of new regulatory requirements will decrease the number of innovative new drugs produced.

How Reduced Regulations Increase Innovation

The second type of regulation represents the inverse philosophy of hypothesis one: if more regulation reduces innovation, then less regulation will increase innovation. This could occur through multiple different mechanisms. First, just as increased regulations handicap small firms, decreasing regulations should produce a more competitive market and give firms more incentive to innovate (Danzon and Chao 2000; Thomas 1990). Second, as it is often difficult to assess the value of drugs early in the research process, reducing regulatory costs would permit firms to pursue multiple lines of research and prevent them from inadvertently stopping research on promising new drugs (Wardell and DiRaddo 1980).

Congress, fearful that their prior regulatory efforts unduly curbed innovation, used this logic as the basis for bills that expedited the movement of drugs to market and lessened the regulatory burden on pharmaceutical manufacturers. These reform efforts began in the late 1970s and culminated in the Prescription Drug User Fee Act of 1992 (PDUFA). PDUFA expedited the FDA review process by requiring that all drugs be reviewed within set time limits. The cost of the additional personnel required to meet these goals was then distributed among all the participating pharmaceutical agencies. Although this represented a slight annual cost to the firms, the expedited review process more than offset the costs.23 These laws were renewed and modified again in 1997 and 2002, to ensure that the review process remained efficient and objective.

Although the two PDUFA renewals had different component elements, the 1997 act included provisions for the legalization of direct-to-consumer (DTC) advertisements, the intent of each was to lessen the regulatory costs to industry. The initial legislation and its renewals sought to decrease the uncertainty associated with product development. Therefore, by reducing the cost of bringing products to market the laws should allow companies to make greater investments in innovation. This leads to the second hypothesis:

Hypothesis 2: Legislation intended to decrease the regulatory costs for pharmaceutical companies will increase the number of innovative new drugs produced.

23 Some critics of the industry, and the PDFUA legislation, have claimed that the need for expedited review coupled with the fact that the people reviewing the drugs are now paid by the pharmaceutical companies has produced a less rigorous regulatory environment. They contend that more drugs are granted approval than are warranted and that these undeserving approvals produce a large economic benefit for the individual firms.
How Increased Competition Sparks Innovation

The third type of policy was also the most frequently debated in Congress and the media: whether or not to increase competition in the pharmaceutical industry. At multiple points in the last half-century, legislators claimed that the pharmaceutical industry was tending towards an oligopoly. Despite the best efforts of economists to demonstrate that this was not true, indeed, that the market share of the leading firms had actually declined over time (Grabowski 2002), the comments resonated with the public. Popular frustration with high prescription-drug prices and repeated calls for price controls lead legislators to conclude that increasing product competition would create price competition and reduce the costs without significantly altering the incentives to innovate. Starting in 1970, this led a number of states to repeal their anti-substitution laws, which had prevented pharmacists from offering to substitute cheaper generic drugs for brand-name drugs. In 1984, the federal government complemented these state acts with the passage of the Hatch-Waxman Act. Hatch-Waxman increased competition by allowing generics to prove that they were chemically equivalent to approved medicines, rather than having to run their own clinical safety trials. Prior to its passage, the clinical trials required of generics essentially prevented them from reaching the market and sheltered brand-name drugs from competition, even after the patents expired.

In theory, while this additional competition should decrease the profit margin of the large pharmaceutical firms, reducing a drug’s period of exclusivity to that warranted by its’ patents could also provide additional incentives to innovate. This is contrary to the received wisdom which, as stated earlier, has repeatedly found that reducing prices decreases R&D investment (Giacotto, R, and Vernon 2005). However, by increasing competition for off-patent drugs, the legislation allows for the maintenance of some profitability combined with a greater need to improve a drug when the patent expires. Therefore, this type of legislation offers a potential to combine increased innovation with increased access and leads to the third hypothesis:

*Hypothesis 3: Legislation intended to increase competition will increase the number of innovative new drugs produced.*

How Regulation Structures Innovation

Congress’ regulatory efforts have not been limited to increasing and decreasing the number of requirements that separate a product from the market. And, it is this second set of regulations that deserves attention, precisely because their intent is not to increase innovation but to alter the very type of innovation that occurs. For instance, in the pharmaceutical industry, regulations sought to facilitate networking across professional boundaries, which can increase the degree of collaboration and increase the quality and quantity of innovation (Powell and Brantley 1992; Powell, Koput, and Smith-Doerr 1996). Therefore it is also important to consider legislation that was not aimed specifically at the pharmaceutical industry, but nonetheless helped restructure innovative activity.
Michael Porter adopted this rationale in arguing that environmental regulation could produce more innovative industries in the United States by forcing them to alter their practices (Porter 1991). Subsequent tests did not find that American firms produced more innovations as a result but they did suggest that regulation reoriented research activities (Jaffe, Peterson, Portney, and Stavins 1995). Similarly, studies of the effect of environmental regulation on the automobile industry in California found that by increasing regulations California forced automakers, and their suppliers, to develop new technologies that proved critical in allowing them to remain globally competitive. Absent the increased regulations, the automakers would have preferred not to develop the costly technologies, which would have been profitable in the short-term but a poor long-term strategy. Environmental regulations yielded similar results in the nonferrous metals industry, where compliance forced firms to develop production practices that were both more efficient and less polluting (Barbera and McConnell 1990). In these cases, regulations worked to structure innovative activities as opposed to reducing them.

Congress introduced two bills to either initiate a change in the direction of innovation or to increase the quantity of innovations in the pharmaceutical industry. First, in 1979, the Bayh-Dole Act enabled universities to license their innovations to private companies, even if a portion of the research was paid for by the federal government (e.g. NIH, NCI). Owen-Smith and Powell (2003a; 2003b) have shown how this legislative change altered the relationship between university and industry, leading to new commercial innovations. Hicks et al. (2001) corroborated this to show that, after the Bayh-Dole Act, academic research has become a critical part of the commercial innovation process. While more recent work by Mowery et al. (Mowery, Nelson, Sampat, and Ziedonis 2001; Mowery and Simcoe 2002) challenges the degree of Bayh-Dole’s effect, their results still reinforce the claim that legislative change altered the path of innovative activities.

In 1984, Congress passed a related piece of legislation: The Orphan Drug Act. This act sought to redirect pharmaceutical research towards diseases that affected smaller populations of patients. The act offered substantial tax rebates to firms that developed orphan drugs, essentially amounting to federal subsidies for orphan drug research. While this act adopted the framework from above: innovation will not occur without profit. The object here was not simply to increase or decrease the profitability of a given product, it was to ensure a base level of profitability that did not yet exist. Further the act did not affect the entire industry, but merely offered incentives for a particular line of research.

These pieces of legislation aim not simply to increase the rate of innovation, but to alter the very process by which drugs reach the market. The object was to enable greater collaborations across disciplinary boundaries and to facilitate the production of new innovations. Further, these changes encouraged universities to reorient their research towards ideas with more commercial potential. For both of these reasons we would expect to see that:

Hypothesis 4: Legislation intended to increase innovations will increase the number of innovative new drugs produced.
I began by assembling a list of the federal legislation passed between 1950 and 2000 that intended to alter some aspect of the production or distribution of new medicine.\textsuperscript{24} This enabled me to document the entire legislative history of the modern industry from the moment historians mark its origin, post-Penicillin, through the present day (Chandler 2005). I classified these six efforts according to whether they sought to: increase innovation, increase competition, increase regulation, or decrease regulation. Obviously, some policies pursued multiple objectives. For instance, the Hatch-Waxman Act increased the ease of entry for generic drugs, both reducing regulation and increasing competition. For this reason, each policy was both evaluated independently in the regressions, then listed in groups according to their intended effect. Table 5.1 includes an annotated timeline of these legislative efforts; a graph of the mean number of innovations within each policy period, presented in Figure 5.1, depicts the effects of each policy.

**INSERT TABLE 5.1**

**Dependent Variables**

In order to operationalize the effect of policy shifts on the quality of medicine, I collected data on each new drug application approved by the FDA during this period. While past studies have relied upon the use of new drug applications or patents, the goal here was to measure the innovative effort rather than the total number of new drug approvals (NDAs). Therefore, I used three different dependent variables to capture quality: the number of new molecular entities (NME), the number of priority new molecular entities (NME-P) and, the percentage of NDAs that qualified as a new molecular entity.\textsuperscript{25} The difference between estimating the total number of new drugs and the number of innovative new drugs is clear in the graph of approvals over time presented in Figure 5.1. For instance, while the total number of NDAs dropped radically in the wake of Kefauver-Harris, the decline in NMEs was both smaller and less sustained, while there was no evidence of any decline in NME-Ps. Later, a similar trend occurred in reverse, where the number of NDAs jumped following the passage of PDUFA but there was no corresponding increase in either form of NME.

**INSERT FIGURE 5.1**

The FDA classifies drug applications NME if it represents a novel chemical compound and NME-P if it represents a significant advance over prior medications or if it is aimed at a predetermined, high-priority illness. This contrasts with NDAs which can be granted for any of seven conditions including: a new combination of existing drugs, a new manufacturer of an existing drug, a new formulation of an existing drug, or a new

\textsuperscript{24} Although there were more regulations post-2000, notably the revised PDUFA in 2002, I used 2000 as a cut-off in order to have a minimum of 5 years of post-passage data to analyze for all bills.

\textsuperscript{25} Recent work by Gambardella makes a compelling case for the use of a patent citation index as the primary means to measure innovation, while Grabowski et al. suggest a “Global NCE” which is an NME introduced in four of the eight largest markets. While a patent citation index is an excellent measure here I use the more conventional NME because of the transparency of its definition.
indications for existing drugs. The inclusion of a variable measuring the percent of NDAs that are classified NME captures how the resource allocation of firms shifted with each policy.

Unfortunately, while it is logical to assume that the most innovative and most valued drugs were the ones classified by the FDA as an NME, this is not always the case. Frequently NMEs prove, over the long run, to offer no great therapeutic advantage over existing medicines. Similarly, sometimes a new formulation, for example the ability to give a medication as a single weekly rather than twice-daily pill can improve or reduce noncompliance, and drastically reduce complications and side-effects. But, this does not render the use of NME or NME-Priority categories ineffective. Instead, it changes the interpretation of the data. By using either NME or NME-P as a dependent variable I cannot accurately capture the degree of therapeutic advance offered by a particular drug. The NME classifications are rendered in pre-clinical trials and therefore do not reflect the degree of therapeutic advance, which may only emerge after years of use. However, I follow the logic of the FDA in arguing that they reflect the perceived degree of innovation and as such, they indicate the individual company’s willingness to innovate. In other words, a company that produces a NME and submits it for review by the FDA is deliberately pursuing a more innovative, and riskier, path than a company that merely offers a modification of an existing drug. While I cannot determine whether the NME will prove more valuable than the modification, we do know that it represents a new chemical or biological approach to the problem. As the object of the study is to determine what influenced the willingness or ability of companies to innovate, this measure offers valuable leverage.26

Because policy shifts do not produce instantaneous changes in the number of drugs approved the dependent variables were first lagged three years before analysis and the results were estimated using a Koyck lag model. This is based on estimates that, during the period of study, drugs required an average of three years to gain approval from the FDA. This means that any present-day changes in firm behavior will alter the number of drugs approved three years later.27

Additionally, it is possible that firms respond to new policies not instantaneously but over the course of years. This will not alter the drugs they already intended to submit for approval, but will change the drugs they produce four, five, and six years in the future. The delayed effect is captured through the use of a distributed lag model that estimates the rate at which a policy gradually produces a permanent change.

26 Further complicating the matter is the difficulty in determining therapeutic quality. The pharmaceutical companies were so convinced that scientists could not determine effectiveness that they took the FDA to court in *Upjohn v. Finch* to force the Supreme Court to decide the matter. The Supreme Court did decide in favor of the government, but acknowledged that proving the quality of a new drug is not without its problems.

27 I am less interested in whether the policy changed the overall number of drugs approved and more interested if it changed the number of quality drugs submitted. However the FDA has been reluctant thus far to release information on when drugs were submitted, therefore I have been forced to use this as a proxy to measure firm behavior.
Control Variables

In order to control for the possibility that variances in either the kind or quality of new medicines are produced by fluctuations in the availability of financing for research, I include a number of variables that address the prevailing economic conditions, federal support for research, and the FDA. To measure the economic condition of the industry I use both the average return on capital for the past twelve months, for the members of Pharmaceutical Research and Manufacturing Association (PhRMA), and the total size of the U.S. prescription drug market. Data on the annual research and development expenditures of the pharmaceutical industry were also reported by PhRMA. These were included to address the concern that decline in total innovative output resulted from a decline in the economic fortunes of the industry. Data on federal funding to NIH, NCI, and the FDA came from annual editions of the Federal Budget. Although the NCI is considered to be a division of NIH, I separated these two sources because the NCI itself has been frequently cited as the source of a number of innovative medicines and the NIH includes, as of 2001, 24 separate research institutes while NCI is a single entity. As a result, I subtracted the NCI funding from the NIH annual totals. These data were included to help distinguish between the effect of policy implementation and corresponding changes in federal funding for R&D research which Mowery et al. (Mowery, Nelson, Sampat, and Ziedonis 2001; Mowery and Ziedonis 2002) suggest are often conflated.

The Role of the FDA

The FDA has frequently been cited as a primary scourge of the industry, blamed in the 1960s and again in the 1980s for “drug lags” that prevented medicine from reaching American patients in time. To account for the degree to which this presumed lag discouraged innovation, I include two measures of the FDA’s resources: the total staff of the FDA and the budget specifically allocated to the CDER (Center for Drug Evaluation and Research) or its predecessors, for the evaluation of pharmaceutical products. Although there may be some fear of endogeneity, the FDA staff is actually very distinct from the CDER funding as the FDA has gone through periods where it froze staff levels while the budget increased and other periods when it rapidly added staff but only marginally increased their budget. These data came from the FDA’s annual reports and were crosschecked against the numbers reported in the Federal Budget. As with the firm-level financial data the first-difference of these variables was taken and used in estimation. The summary statistics reports the data for the transformed variables.

Methods

To estimate the effect of a law passed at one point in time is not a trivial matter. Obviously, the first concern is that any effect witnessed occurred as a result of some simultaneous unobserved change. For instance, if a law is passed in the same year that a new technological discovery is made it can be nigh impossible to disentangle the effect of
the discovery from the effect of the policy. Further the response to a new law is rarely immediate and, in the case any time-intensive innovative process, the time when we can expect an effect to become apparent can be opaque. Another way to pose this is to ask: how long after a law is passed would we expect the quality or new drugs to change?

Fortunately, political scientists have developed a number of ways to remedy this problem and to attempt to estimate both the immediate and the delayed effect of a new law. Therefore to answer my question, I borrow from there literature the polynomial distributed lag which estimates both the immediate and the declining effect of a law to the kth period. In particular, in tables 2-4, the effect of each policy is estimated using a Koyck lag model, which is a type of polynomial distributed lag of the form:

\[ Y_i = \alpha + \gamma z_i + \rho Y_{i-1} + \beta X_{ik} + \nu_i, \]

Where |\( \rho | < 1; \( \gamma \) captures the “immediate” effect of the policy and the long run propensity is given by: \( LRP = \frac{\gamma}{(1 - \rho)} \). This allows us to model the process by which each policy gradually created a permanent change in the pharmaceutical market (McDowall, McCleary, Meidinger, and Hay 1980). Because the inclusion of lagged variables can produce problems with multi-collinearity, the equation was estimated using two-stage least squares regression, with robust standard errors reported. This test was preferred to a finite distributed lag model, a model in which the estimates are limited to a specified set of years (for instance, years 1-4 after the passage of a law), after tests revealed that the coefficients for the lagged policy changes were not statistically different from zero, however the probability that the effect was instantaneous is small.\(^{28}\)

These models displayed no heteroskedasticity and weak autocorrelation. Further tests demonstrated no evidence of a unit root. In all the regressions this was modeled through the inclusion of a first-order lag of the dependent variable. A Box-Ljung test confirmed that there was no additional auto-correlation in the revised model.\(^{29}\)

Discussion and Results

The results are presented in three tables: table 5.2 estimates the effect of each policy on the number of NMEs produced, table 5.3 estimates the effect on the number of priority-NMEs produced, and table 5.4 estimates the effect on the percentage of total new drug approvals that qualified for NME status. In tables 5.2-5.4, the first model tested the effect of industry-level controls on each dependent variable. The second model included measures for government support. Models 3-8 test both the immediate and long-term effect of each individual policy on the quality of new drugs produced.

\(^{28}\) Subsequent tests produced identical results using both a finite distributed lag and an Almon lag. These results are available from the author upon request.

\(^{29}\) These models were also estimated using a Prais-Winston AR(1) regression that uses fGLS rather than OLS and adjusts the standard errors to account for any inflation. The results proved almost identical and are available from the author upon request.
In tables 5.2-5.4, models 1 and 2 indicate that the control variables had almost no impact on the number of New Molecular Entities produced in a given year. Fluctuations in the size or profitability of the industry did not translate into variations in the number of breakthrough innovations. Similarly, variations in federal research support also proved to have no significance for the number of new drugs created. The surprisingly negligible impact of these controls found in all models suggests that neither bountiful nor lean years for pharmaceutical companies altered the number of innovative drugs that reached the market.

**INSERT TABLES 5.2-5.4**

The first hypothesis assumed that strengthening regulations would decrease the quality of subsequent innovations. This is based on the prior studies that analyzed total drug output or firm profits and assumed a relationship between the firm’s perception of future profits and its willingness to pursue riskier innovations (Acemoglu and Linn 2004; Cockburn and Henderson 1996). All three measures refute the claims of this hypothesis, showing that while increasing regulation may have reduced the total number of drugs approved it led to an increase in the number of innovative drugs.

In model 3 of table 5.2, the passage of Kefauver Harris produced an initial increase of 4 NMEs (4.61, 2.17). Model 3 of table 5.3 reinforces this finding, estimating that an additional four priority new drugs (4.09, 1.36) emerged as a result of the act. Further, the results show that the long-term effect of this act was to increase the total number of NMEs approved by nine (9.22) and of priority NMEs by nearly five (4.92). Model 3 of table 5.4 indicates the shift in priorities that accompanies Kefauver-Harris, as the percentage of new drugs that were classified as new molecular entities rose over 10% (.118. .027). This rejects the hypothesis that regulation reduced the incentive to innovate, as the number of innovative drugs rose and they became a larger portion of total drug approvals after the passage of the act than they were before.

These results complement earlier economic studies that examined the impact of the 1962 legislation on innovation (Grabowski 1976; Peltzman 1973; Thomas 1990). However, where those studies had focused on the immediate effect of the legislation on NDAs to argue that Kefauver-Harris hampered innovation, here I find that the delayed impact was almost universally positive for the more innovative NMEs.

These findings indicate that the fear that additional regulations, by raising costs, were removing incentives to innovate and would cause a decline in new drug production, may have been overstated. It also, reinforces the claim that any presumed trade-off between wider access to safe and effective drugs and the degree of innovation is not as strictly binary as believed. Additional regulations, intended to require proof of effectiveness, did not produce a decline in the most innovative of medicines and actually may have helped reinforce the firm’s interest in producing them.

The second hypothesis offered a parallel claim: efforts to reduce regulation increase innovation. In theory, reducing regulations is tantamount to reducing the costs of production, and firms would respond by taking greater risks and producing more
innovative drugs. However, the evidence gathered challenges this claim, finding only minimal evidence in support of the hypothesis.

As seen in models 4 and 5, reducing regulatory costs did not yield an increase in the number of innovative drugs. While the coefficients estimated in model 4 have the expected signs, indicating a rise in approved new molecular entities (7.37, 4.62) and priority new molecular entities (1.78, 2.23), they are not statistically significant. Model 5, which tests the 1997 legislation, even reports an unexpected decline in both NME (-23.2, 5.69) and NME-P (-9.36, 3.68). The long-term effects of the legislation are estimated to be even greater for both NME (-32.2) and NME-P (-12.20). Model 5 of table 5.4 also shows a significant decrease in the proportion of NMEs to total new drugs approved initially (-.188, .088) with a greater long term effect (-.27). This suggests that decreasing regulations lead firms to pursue more drugs but less innovative ones. However, these effects are found only for the most recent policy shift, which is by necessity based on the least information. The degree of the effect may therefore be overstated and may be reduced in future analyses with more post-1997 data to include in the analysis.

The third hypothesis predicted that increasing competition by lowering prices leads to more innovation. The evidence here supports this hypothesis providing evidence for the claim that competition increases innovation. In model 6 of the tables, we find that the increased presence of generic drugs pushed manufacturers to pursue more innovative strategies. The Hatch-Waxman act resulted in greater numbers of new molecular entities reaching the market both in the short (6.20, 2.91) and long (10.16) term. Similarly, it lead to a noticeable increase in the percentage of new drug approvals that qualified for NME status (.147, .040; .173). The results, while still positive, were less robust for the increase in priority new molecular entities (2.55, 1.57). However, the overall effect of the legislation was to move manufacturers away from product-extensions and towards greater innovations, producing 10 more NMEs than would have existed otherwise. This implies that industry member’s were unnecessarily concerned with the effect of greater competition on the production of innovative new drugs. Instead we see that the congressional attempt to reduce prices by increasing competition did not reduce the degree of innovativeness in approved drugs, it increased it.

The fourth hypothesis predicted that congressional attempts to foster collaborations and innovation in the industry would lead to the production of more innovative drugs. The data presented in models 7 and 8 of tables 5.2-5.4 offer qualified support for this hypothesis. In table 2, both the Bayh-Dole Act (4.12, 2.69) and the Orphan Drug Act (5.57, 2.88) correspond to an immediate increase in the overall number of new molecular entities. Further, these two bills have robust long-term effects, helping produce an additional 7 (6.98) and 9 (9.27) NMEs over what would have occurred without their passage. While neither of these effects is significant at the 95% level, they are both significant to the 90% level. Table 3 presents results that are similarly positive in sign and yet not statistically different from zero (2.58, 1.49; 1.90, 161). Table 4 however, offers evidence that that the two bills corresponded to a dramatic shift in the efforts of pharmaceutical companies. Following the passage of the Bayh-Dole Act new molecular entities represented an additional 10% (.110, .034) of new drug approvals,
rising to over 15% (.154). The Orphan Drug Act had a similarly robust effect, initially increasing the ratio of NMEs to total approvals by nearly 15% (.149, .038) a figure that rose to almost 18% (.178) over time. These results suggest that the government was successful in catalyzing a greater degree of innovation from within the pharmaceutical industry. Although the bills were not an unqualified success, they both had similarly positive effects at different points in time.

It is also worth reiterating that changes in the budget of the FDA, the NIH and the NCI, which many people cite as the loci for basic research have extremely minor influence over the numbers of drugs produced. Also increasing the staff at the FDA, which presumably should allow them to speed up reviews does not result in a greater quantity of drugs reaching the market.

Conclusions

On December 6, 1971 the Chairman of the Pharmaceutical Manufacturer’s Association warned Congress that increasing access to new drugs would be detrimental to the industry, he claimed, “If enacted, it would inevitably retard the scientific research which has enabled our industry to make it’s greatest contributions to the public health” (Markus 1972). A similar concern was voiced by his predecessor Dr. Austin Smith, in 1960, who argued that in the long run, it was better to let new innovations bring prices down for the older medicines than to restrict prices (1960). In fact, the claim that policy must favor either innovation or access is so ancient that the New York Times could, in 1931, describe it as the pharmaceutical industry’s “old cry.”

This assumes that regulation is—at best—a necessary evil, a way to ensure safe and effective new products at the inevitable cost of slowing the pace of research. This initial premise resulted in pharmaceutical regulations that sought to balance access, the availability of new drugs, with innovation—the incentives necessary to spur research (Chandler 2005; Temin 1979; Temin 1980b). This presumed mutual exclusion of access and innovation has governed the debates over pharmaceutical regulation from the 1930s through the present day. However, it is not obvious that the primary cost of regulation is to innovation, nor is it clear that regulation and innovation are mutually-exclusive objectives.

“Access vs. innovation” presumes that innovation is primarily, almost exclusively, the product of rational actors seeking greater profits. This discounts the degree to which innovation is the result of prestige-seeking, intellectual curiosity, or the independent developments of science and technology, and it assumes that the potential for profit is the primary motivator for both initial researchers and the corporations that will later bring their ideas to market. Regulation is therefore the bane of future innovations. Ensuring access to safe and effective drugs raises costs and decreases firm profits by requiring additional tests (Reed, Califf, and Schulman 2006). Increasing competition from generics drives down prices and makes drugs more accessible to the public, but simultaneously reduces a firm’s motivation to create new drugs (Vernon 2005). While there are many reasons to believe that this simplification may be erroneous and that pharmaceutical companies, being both international in origin and in their reach, would not be perceptibly swayed by policy changes in one country, the attempt to balance the supposedly
conflicting goals of access and innovation remains the guiding philosophy of U.S. regulatory efforts.

However, the evidence gathered here tells a different story. The controls, presented in models 1 and 2, of all 4 tables, demonstrate the degree to which breakthroughs are insulated from the fluctuations of the market. It would be reasonable to expect that firms enjoying especially profitable years would invest more heavily in research and that this would translate into greater innovation in the future. Or conversely, that firms suffering through particularly lean years would reduce their investments and thereby decrease the number of innovations reaching the market. But neither is the case. The number of innovations does not vary in response to the profits of the industry, they neither decrease when the size of the market contracts, nor increase when it expands. This calls into question the assumption that innovation is driven primarily by the prospect of profit.

The tests of my four hypotheses further complicate our understanding of the relationship between regulation and innovation. In the test of the first hypothesis, we see that firms did not respond to the increased costs and risks associated with new regulation by moving away from innovation. Instead, these regulatory attempts to increase the quality of available drugs resulted in the pursuit of more innovative drugs by the pharmaceutical companies. The new regulations meant that firms could not gain approval for useless drugs and therefore increased the value of useful, more innovative drugs. Rather than curbing innovation, the regulations reoriented firms towards a different concept of what should be researched.

In a similar way, reducing the costs of regulation did not lead firms to greater discoveries. While it remains possible that firms redirected their additional profits into greater R&D activities, it did not correspond to any increase in their productivity. It is impossible to know whether these additional expenditures prevented them from slipping lower than they might have otherwise, but it is clear that the reduction of regulatory costs did not open any metaphorical floodgates, behind which new ideas had become stuck.

The tests of the final two hypotheses further demonstrated that it is possible to reorient firms towards greater innovation and away from reduplicative efforts. The success of these policies argues in favor of competition and collaboration in the place of profit as a driver of innovation. By increasing the degree of competition from generics, Congress forced companies to move more quickly to design improvements to their product lines than they had previously, resulting in a market rise in the number of innovative new drugs. Similarly, by allowing for more collaboration between academics, government scientists and industry, Congress facilitated the movement of new drugs to consumers. Both acts resulted in an increase in the total number of innovative new drugs produced. These results do not indicated that innovation can occur without research, or that research can occur without money. However, it does suggest that the relationship between these variables is highly non-linear.

Given the irrelevance of the majority of variables included here, the question is: Where is the bottleneck? What is preventing us from producing more innovative products? The answer has required two parts: 1) The low-hanging fruit has been plucked, making each subsequent discover exponentially more difficult and expensive 2) The way
to remedy this is to increase the incentives for firms to conduct research by either subsidizing the initial research or by ensuring the promise of high-profits.

In other words, science is the problem and profit is the answer. It is hard to refute this argument, because—as evidenced by the Orphan Drug Act—if there is no expectation of profitability then firms will not pursue drugs. But the necessity of a base line of profitability and the expectation that additional profitability will yield additional innovation are two distinct arguments. While we may have conflated the two in policy debates, the evidence here argues that the one does not prove the other. In fact, the overall lack of statistical significance for the majority of the variables indicates just how loosely innovation is tied to profitability. This implies that the government ought to focus less on ensuring a potential for profit and more to ensure competition between the firms and to facilitate collaboration between different types of companies.

While these results are based on a study of the pharmaceutical industry, similar fears that regulation must, by its nature, reduce innovation exist across industries. The lesson here is that even in the most research-intensive industries the discovery of breakthrough products is only marginally correlated with the economic success or prospects of the industry. Therefore regulatory reforms are more liable to reorient innovation than they are to reduce or expand it altogether. In the end it is clear, increasing access does not have to cost us innovations.
Chapter Six: Conclusion

Nobody is happy with the pharmaceutical industry. In 2003 Pfizer, the largest pharmaceutical company in the world, earned $8.3 billion dollars in profit (Alpert 2004). To give these numbers a bit of context consider this: that year Pfizer earned more than twice what Toyota, the world’s most profitable automobile company, earned in their best year ever (Taylor 2003). What is perhaps more astonishing than this, is the fact that Pfizer was just barely more profitable than their competitor Merck, who earned slightly over $8 billion in profits, or 60% more than Wal-Mart, the world’s most profitable retailer earned. In a year where neither company introduced a ground-breaking new product, a year in which their research units continued a decade-long decline in productivity, a year in which each of their most valuable products was over ten years old. In this, fairly unremarkable year, these two companies alone earned enough in profits to practically cover the budget of every public school west of the Mississippi for one year. To consumer groups this is proof positive that the industry requires reform.

In 2001, Schering-Plough ranked 36th of the Fortune 500 list, the fifteenth straight year the firm had ranked in the top 100, amassing nearly $2 billion in profits on less than $10 billion in sales. Eight years later, their sales having fallen 80%, Merck bought them before they could go bankrupt, immediately cutting 15% of their workforce. Similar stories can be told for Wyeth, Searle, Smith-Kline and others. To industry-supporters, this is proof positive of how inhospitable the market has become, how damaging regulation has proven, and how willfully we will cut off our nose to spite our face.

Everyone you ask will tell you exactly what is wrong with the drug companies in this country, and everyone will tell you something different. Economists and pharmaceutical executives worry that regulatory costs are too high and prices held too low to encourage innovation. Public health advocates and patients complain that drug costs are too high to allow access to the most beneficial of new medicines. Politicians will warn that government only has limited means to help, doctors will complain that government limits themselves and leaves the public vulnerable, entrepreneurs complain that government limits their ability to grow and forces them to sell out to larger firms. Everyone has a different opinion, but they all agree on one thing: the market is a disaster.

So how do you reach a point where the wealthiest, most advanced country in the history of the world, has a health industry that few people say anything positive about? This is a question that deserves, and has received, a lot of attention. But the attention has focused almost exclusively on the question of health care delivery, or more precisely: of payment. The central question of every attempt at health care reform has resolved around the issue of who should pay for what.

This question focuses on the relationship of doctors to insurers, and raises questions about the prevalence of certain practices, the long-term vs. short-term costs to action and inaction. But it ignores the role of one of the largest players in the debate: the drug companies. To fully understand the system we have and the ways in which it can be improved, we also need to understand the market for prescription drugs we currently experience.
This raises a set of questions that go begging for answers: Why is it that, despite the efforts of hundreds of people over the course of a century that we couldn’t create something better? Did we ever have a market people were happy with? Did we just lose direction along the way? Or was this never a success, just a series of avoided failures?

There are a number of ways of explaining what has happened: Too many people with too many interests and too much to lose to allow anything but incremental change. Someone is benefiting from this and has acted in concert to prevent a wider change. Or, the always popular: we are trying to change the wrong things.

But only one of these really makes sense: we don’t understand how industries and markets change. It is this last one that I am most interested in; because I think it best explains what has happened here. The truth is that this is a complicated industry with millions of moving parts, and each attempt to reorient it is akin to nudging a boulder down a mountain: we know, generally, where it is going to go, but we don’t have any idea how much damage it might cause in the process and whether it bounces to the left and heads straight for town or bounces to the right and heads harmlessly into a meadow is largely the result of forces we can’t see when we’re standing behind the boulder getting ready to push.

So my goal in this dissertation has been twofold: First, to help us step out from behind the boulder, to trace the path that lead it there in the first place, so that we might better understand where it is going to go. To speak without metaphors, the intent has been to document the emergence and the evolution of this vital American industry and to understand why it is that all our past efforts, honest or corrupt as they may have been, produced this: a market as unhealthy as the diseases it exists to cure.

Second, to offer an analysis of why some environmental changes produce significant changes in a market while others, seemingly similar, elicit no response. By offering both detailed analyses of specific events along with comparative studies of multiple events across time, I have been able to take the first steps towards clarifying the mechanism by which an industry transforms. This might seem of limited utility, as industries experience far more incremental change than they do radical change. However, it is through radical transformation that this industry first began, and that other similar industries have arisen and will continue to emerge. It is through this process that new technologies are rejected or incorporated, that political efforts prove instrumental or capable of being mediated, that incumbents fall to challengers, and old ideas give way to new paradigms.

Understanding this process, even if rare, is critical if we seek to understand how evolution can occur at multiple levels (population, organization, individual) at the same time.

What happened here?

With any industry that has been in practice for as long as this one, a historical myopia sets in. In order to replace indifference with outrage every actor (as there are more than the traditional two sides at work here) must present the most recent development as an unparalleled injustice that lacks any historical precedent. A little
perspective can go a long way towards reducing the role of hyperbole and clarifying both which issues remain salient over time and which are recent additions to the landscape.

For instance, adopting a historical lens helps reveal that our concern over the high cost of drugs, though accurate and relevant, is one that was shared by several generations of Americans. This issue, for all its validity, is not a new one and its resonance may have more to do with a cultural discomfort over the concept of establishing a price for health than it does with the actual costs themselves.

Similarly, the repeated concerns of both industry and consumers groups that innovation has declined (either as the result of government interference or industrial malfeasance) suggests a halcyon past that never quite materializes. Instead, a perusal of the archives demonstrates that innovation has never occurred in a linear fashion, as breakthrough ideas prefer to appear sporadically than to remain constrained to the timetable of our expectations. Even during the 1950s, by most present day accounts the “Golden Age” of pharmaceutical innovation, individual firms remained concerned about their commitment to only a few drug products and investors decried their inability to develop more new developments. This means that while we may not be wrong to demand greater degrees of innovation, that we may also not be satisfied—were these wishes to be granted—that enough was yet being done. The hope for a cure is simply a singular economic good and the resulting demand cannot be graphed on any paper, so great is its scale.

Most interestingly even the complaints about “me-too” drugs, which seem so contemporary in character and are often cited as having specific, and recent origins actually echo verbatim the concerns of Americans speaking several generations ago. The very definition of a “me-too” was expressed by the U.S. 4th Circuit Court of Appeals in 1972—nearly thirty years before Nexium—when it defined a “me-too drug” as “one which is equivalent to another, pioneer drug, which preceded it on the market” (1972). Of course, these jurists were taking their cues from a series of complaints in the press and in Congress about the lack of “true innovation” in the pharmaceutical industry that began with an op-ed piece in 1930 stating that it was obvious that the pharmaceutical companies were releasing too few breakthrough drugs and relying too heavily on, what an aspiring newsman in 1917 first called, “me-too drugs.”

This is all a way of saying, as I did at the beginning, that there are no new complaints about the pharmaceutical industry. For nearly one hundred years Americans have complained bitterly that the products weren’t effective enough, that developments came along too rarely, that access was too limited by high prices, and that the drug companies themselves were too profitable as a result. The companies themselves have responded, for one hundred years, quite simply: if you want any innovation then this is the price. One deal was offered and, despite a century of negotiation, it is this same deal

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30 Recent articles have claimed that the protests against “me-too” drugs, the practice of incrementally modifying a drug to earn a new patent rather than pursuing new breakthroughs, began in either 1983, with Zantac; in 1991, with Zocor; or in 2001 when Nexium was approved.
that sits before us today. The question I have posed in this dissertation is what has changed and why haven’t things changed more?

It is hard to imagine an industry more central, more vital, to the future of the nation than this one. It employs millions of people, accounts for hundreds of billions of dollars in sales, and its one and only goal is to improve the standard of living. In a word, it is the one industry for which their business truly is health. And yet, or perhaps as a result of this, no one is very happy with the way that it operates.

My object, on a theoretical level, was to use this industry as a case through which to examine the emergence and evolution of an industry. To test prior assumptions and hypotheses concerning the relationship between changes in the external environment and the manifestation of these changes in a population of firms. More concretely, I hoped to explain how the various political, social, and technological efforts of the past century have combined to produce the market for prescription drugs that we so vigorously curse today.

What did I find?

In each chapter I have tried to explore the ways in which the pharmaceutical industry evolved, adapting to new environments, new regulations and old complaints, to remain so profitable and so reviled. It has always struck me as a curious combination that something could be so profitable, so important, and so widely disliked. Why, I wondered, can we not find a better way to do all of this? And so, in these chapters I discuss the different attempts, large and small, successful and failed, to find a better way to do this: to produce innovative new drugs and still make them available. This research has produced a range of findings, of which I would like to highlight three.

#1: Government intervention was critical in the early stages but proved more protective and less transformative later.

The market for drugs in the 1800s was an unmitigated disaster. The initial federal attempts to mitigate this, was to induce greater competition. But the market failed to transform through these competitive pressures, and only through direct intervention by the federal government could the market transform into the modern industry we have today. However, just as important as these federal efforts proved in lifting the industry out of its primordial morass and catalyzing the evolution that resulted in this giant, profitable, innovative oligopoly. Later efforts proved less relevant in explaining the changes in the industry. While the passage of regulation ensuring safe and effective medicine was instrumental in altering the types of products on the market and, most importantly, helped remove a number of “predator firms” from competition, the effect on the remaining firms was less pronounced.

This appears counter-intuitive, given the multiple studies documenting how many fewer drugs reached the market after each law was passed. But, however true that might be, the behavior of individual firms—of the handful that even in 1960 accounted for the vast majority of sales, barely changed as a result of regulations. Even in 1960 the largest
firms were focused on both breakthrough innovations and product extensions. The model for a successful firm from penicillin forward was a firm that earned the bulk of its profits from only a few drugs. Only a brief, as discussed in chapter five, dalliance with diversification marred this history and even that, though important in reducing their pharmaceutical output, had no ill effect on their profits or their position.

Although new regulations were debated in Congress each year, and the threat of price controls remained present in the distance, the actual regulations that passed had only a minimal impact on the firms themselves. For instance, although the Kefauver-Harris Act prevented the sale of ineffective medicines, the other, noninnovative, drugs that the firms were forced to stop releasing were neither that important to their profits, nor that reflective of their efforts. They were just a way to make something out of byproducts. The effect of these later regulatory changes was not to hinder the performance of the old firms but to erect larger barriers to entry for new firms.

The one exception to this, the Hatch-Waxman Act, generally did revolutionize the industry by introducing a new form of competition: external generic companies. These new players were not bound by the gentleman’s agreements that prevailed in the industry and by which firms maintained prices even after their patents expired. The introduction of generic competition meant firms had to introduce patentable modifications to the drugs at a regular pace, or risk losing their customers. It is not clear that this change lead to an increased rate of breakthrough innovations, but it is clear that it forced firms to adjust their behavior and lead to the market we see today.

#2: Informational changes proved more transformative than changes in incentives

Removing barriers to generics did not bring about either demand for generics or a spate of generic founding. Even with the financial incentives in place a generic industry simply failed to emerge in the U.S. Instead, the confusion pharmaceutical firms created over the safety and effectiveness of generic drugs served as a sufficient barrier to entry. Even now, decades after the passage of the Hatch-Waxman Act helped improve generic competition, consumers demonstrate a strong preference for brand-name drugs.

In fact, the role of patients and the information granted to them and expectations for them, are among the features of the market that have undergone the most dramatic changes. Originally it was assumed that patients were capable of determining, on their own, both which medicines to take and which to avoid. The governing assumption for 150 years was that patients did not require the assistance of government in becoming informed. The first major regulatory effort was, in fact, entirely unrelated to financial incentives and sought only to better inform patients by requiring accurate labels on the sides of medicine.

This pattern continued throughout the 20th century as subsequent regulatory battles rarely included sections on price controls or forced licensing—these financial measures were almost always eliminated early in political debates—but instead focused on changes in information. As a result, the 1938 Act insured that drugs were safe before
being sold; improving confidence, but also giving patients more information about the
Drugs they were buying and reversing the assumption that it was incumbent upon them to
inform themselves. The 1962 Act continued this pattern, again informing patients that all
the drugs they receive will be proven effective, and reversing the assumption that doctors
alone were capable of determining effectiveness. Each of these major acts, the ones that
calmed the greatest debate and consternation in the industry had more to do with changes
in information than in the financial structure of the market. This pattern continues
through this day, as experts fear that the dual introduction of the Internet and Direct-to-
Consumer advertisements has reintroduced the illusion of the informed consumer and
served to undermine the informational gains of the previous fifty years.

These changes in the availability of information also affect in which way in which
firms behaved, more so than any prior or subsequent changes in the financial incentives
for performance. Requiring firms to share information during WWII was instrumental in
moving a subset from process and towards product innovation. More than the financial
gains of penicillin, which dissipated quickly following the war (the price fell 1,000% in
two years), it was the change in the firms’ mode of operation that helped establish and
perpetuate their success. And this came about not from the financial incentives, which
had long been in place, but through the required collaborations of the penicillin effort.

Similarly, the movement of the industry towards and away from a more
diversified model of business did not arise as a means of hedging against future losses or
exploiting opportunities for economies of scale. Surprising though it may be, there are
few economies to be found in moving from cholesterol medicines to film production.
Instead, the movement occurred as small and medium-size firms followed the lead of the
larger firms. They remained diversified not until the returns diminished, for several firms
the returns never materialized, they remained there until they learned that the leaders had
adopted a new strategy: allying with biotech firms and pharmacy benefit management
firms.

The one prominent exception to this is the passage, in 1984, of the Orphan Drug
Act, which did help create a flood of important new drugs. However, the long-term
benefits of this act have been, unsurprisingly, less pronounced. The initial wave of new
drugs arose from the fact that many pharmaceutical companies were “sitting on” potential
cures until they found a more profitable way to sell them. The Orphan Drug Act made
unprofitable markets profitable enough for the firms to release cures they already had,
but not enough to entice them to pursue cures for small-market diseases. In other words,
the basic structure of the market provides strong incentives for firms to maintain their
traditional mode of behavior and these episodic attempts to push the firms a few degrees
in a new direction, via small subsidies or penalties, has no effect. Even the Orphan Drug
Act proved so incapable of enticing firms to develop orphan drugs that non-profit
organizations have emerged with the specific purpose of buying the rights to these drugs
from companies who have created them but elect not to distribute them. In this way the
regulation helped produce a new organizational entity, but not to change the market.
“Access vs. Innovation” fails to capture the diversity of sources behind breakthrough innovations.

Although useful and logical as a rhetorical device, a comparison of the effects of different policies over time reveals “access vs. innovation” to be an extraordinarily limited portrayal of the market. While the phrase suggests the relevance of financial incentives in securing innovation and argues for a dichotomy separating greater access from the discovery of new breakthroughs, the evidence fails to uphold this claim. Instead, we find that efforts to increase access can function without reducing innovation. Some because they operate without decreasing firm profits, some because they operate without harming any of the other, multiple, sites of innovation for the industry. Our reliance upon this framework reinforces the notion that pharmaceutical firms have succeeded in creating the illusion of a legitimate market, where discussions about how to remedy perceived problems are only visible when seen through a particular, in this case “access vs. innovation”, framework. This, I argue, is one of the main reasons why, despite a century of change in the organization of firms, behavior of doctors and patients, and structure of regulation around the industry, the complaints we hear remain the same ones first given voice in the 1920s.

How then can we understand the history of this industry? And, why does the market look the way it does today? The answer is simple: because we have a poor understanding of how to change it. The important thing to recognize is that this market has changed; the industry has not been the same over time. And the changes have occurred both because of and despite the influence of the pharmaceutical firms and their lobbyists. Despite the popular claims, PhRMA has not won every battle they have fought, and it is a mistake and misleading to consider today’s market only in light of the ways in which it benefits the pharmaceutical companies. What is interesting about the evolution of this market is just how unpredictable the transformative moments prove to be. PhRMA lost battles it should have won, it won against technologies that probably should have usurped it. And yet through it all it has remained profitable, the pace of innovation has remained relatively constant, and the complaints have remained loud and unceasing.
Cited References


Figure 2.1: Average Sales of OSRD and Non-OSRD Firms

- Selected Firms
- Non-selected Firms

Duration of Penicillin Program
Figure 2.2:

1941: The Profitability of Selected Firms

Profits (millions USD)

Note: Selected Firms are highlighted in black, unselected firms are in light grey.
Figure 2.3:

1946: The Profitability of Selected Firms

Note: Selected Firms are highlighted in black, unselected firms are in light grey.
Table 2.1: Population Statistics

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Note: This table is based on 892 observations of a total of 46 publically traded American pharmaceutical firms between January 1935 and December 1955. “Firms in Study” counts the number of firms included in this study operating in a given year. “Selected Firms” refers to firms that were selected to participate in the OSRD program. Exit occurs when a firm is acquired or becomes insolvent. Exited Moody’s indicates that firms were no longer classified as “Drug, Medicine, or Cosmetic” firms by Moody’s Industrial Analysis.
Table 2.2: Descriptive Statistics

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1  Age (years)  -
2  Incorporation  -.07  -
3  Creation of Research Lab  .36  .16  -
4  Hired Chemist  .44  .27  .49  -
5  1938 FDA Act  .15  .22  .10  .16  -
6  Durham-Humphrey Act  .07  .39  .13  .17  .21  -
7  World War II  .02  -.11  -.02  -.03  .26  -.24  -
8  OSRD Contract  .11  .34  .35  .31  .24  .31  .05  -
9  Income (mil.)  .15  .32  .39  .28  .24  .35  .04  .63  -
10  Profit (mil.)  .16  .34  .39  .31  .19  .32  -.16  .63  .95  -
11  Sales (mil.)  .32  .07  .38  .27  .22  .22  -.05  .48  .82  .79  -
12  Employees (thou.)  .19  .11  .44  .37  .16  .17  -.04  .56  .68  .68  .76  -
13  1935 Sales (mil.)  .49  -.24  .31  .24  .00  -.08  .02  .02  .28  .29  .71  .52  -
14  1935 Profits (mil.)  -.03  .28  .22  .16  .00  -.04  .37  .53  .59  .36  .55  .31  -
15  1935 Scientists (thou.)  .32  -.13  .39  .28  -.02  -.11  .02  .30  .32  .34  .49  .67  .57  .35  -

Note: This table is based on 892 observations of 46 publically traded American pharmaceutical firms between January 1935 and December 1955. OSRD Contract is a dummy variable referring to whether or not a firm was selected to participate in the penicillin program. Hired chemist and Incorporation are count variables, counting from the year a firm first hired scientists or incorporated respectively. Creation of research lab is a dummy variable counted 0 up until a firm established a research laboratory and then as 1 thereafter.
Table 2.3: Selection for the Penicillin Program

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>.007 (.012)</td>
<td>.009 (.013)</td>
<td>.003 (.013)</td>
<td>.005 (.014)</td>
<td>.007 (.012)</td>
<td>.009 (.015)</td>
</tr>
<tr>
<td><strong>Organizational</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorporation</td>
<td></td>
<td>.025 (.019)</td>
<td></td>
<td>.025 (.021)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creation of Research Lab</td>
<td></td>
<td>.609 (.815)</td>
<td></td>
<td>.395 (.917)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(dummy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hired Chemist</td>
<td></td>
<td>.005 (.019)</td>
<td></td>
<td>-.006 (.023)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1940 Science Employees</td>
<td></td>
<td></td>
<td>.005 (.006)</td>
<td></td>
<td>.004 (.007)</td>
<td></td>
</tr>
<tr>
<td>(thou.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Initial Advantage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sales (mil.)</td>
<td>-.008 (.009)</td>
<td>-.005 (.009)</td>
<td>-.008 (.009)</td>
<td>-.008 (.009)</td>
<td>-.005 (.009)</td>
<td>-.003 (.010)</td>
</tr>
<tr>
<td>Profit (mil.)</td>
<td>.418** (.151)</td>
<td>.369* (.154)</td>
<td>.389* (.155)</td>
<td>.409** (.155)</td>
<td>.337* (.176)</td>
<td>.306 (.184)</td>
</tr>
<tr>
<td>Constant</td>
<td>-3.47 (.883)</td>
<td>-4.53 (.133)</td>
<td>-3.57 (.914)</td>
<td>-3.45 (.883)</td>
<td>-3.56 (.913)</td>
<td>-4.70 (1.44)</td>
</tr>
<tr>
<td>Observations</td>
<td>112</td>
<td>112</td>
<td>112</td>
<td>112</td>
<td>112</td>
<td>112</td>
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<td>Firms</td>
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<td>39</td>
<td>39</td>
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<tr>
<td>Log Likelihood</td>
<td>-31.5</td>
<td>-30.7</td>
<td>-31.2</td>
<td>-31.4</td>
<td>-31.1</td>
<td>-30.3</td>
</tr>
</tbody>
</table>

Note: Models 1-6 in this table present random-effects logit regressions of the likelihood of selection to participate in the penicillin program. The data evaluates 39 firms who were at risk of selection between 1941, when the program was first announced, until 1943, when the final firm was selected.

* indicates p<.05, ** p<.01, *** p<.001.
### Table 2.4: Fixed Effect Regression Results

<table>
<thead>
<tr>
<th>Income</th>
<th>Profit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.909</td>
</tr>
<tr>
<td>Incorporation</td>
<td>-0.844</td>
</tr>
<tr>
<td>Creation of Research Lab (dummy)</td>
<td>0.20</td>
</tr>
<tr>
<td>HIred Chemist</td>
<td>0.145</td>
</tr>
<tr>
<td>Employees</td>
<td>0.265 (2.26)</td>
</tr>
<tr>
<td>Political</td>
<td></td>
</tr>
<tr>
<td>1938 FDA Act</td>
<td>-0.001 (0.866)</td>
</tr>
<tr>
<td>Durham-Humphrey Act</td>
<td>0.253 (0.932)</td>
</tr>
<tr>
<td>World War II</td>
<td>0.667 (0.561)</td>
</tr>
<tr>
<td>Intervention</td>
<td></td>
</tr>
<tr>
<td>OSRD Contract (dummy)</td>
<td>3.25** (1.04)</td>
</tr>
<tr>
<td>Plant Built for the Firm (dummy)</td>
<td>0.934 (1.49)</td>
</tr>
<tr>
<td>Contracted to Research (dummy)</td>
<td>3.29* (1.33)</td>
</tr>
<tr>
<td>Contracted to Manufacture (dummy)</td>
<td>4.39*** (1.36)</td>
</tr>
<tr>
<td>Interactions</td>
<td></td>
</tr>
<tr>
<td>Employees*OSRD</td>
<td>4.19 (2.238)</td>
</tr>
<tr>
<td>Lab*OSRD</td>
<td>-0.811 (2.11)</td>
</tr>
<tr>
<td>First Order Lag of DV</td>
<td>778*** (0.03)</td>
</tr>
<tr>
<td>Constant</td>
<td>-25.04 (33.9)</td>
</tr>
<tr>
<td>Observations</td>
<td>951</td>
</tr>
<tr>
<td>Units</td>
<td>42</td>
</tr>
</tbody>
</table>

Note: Models 1-7 of this table present fixed-effect regressions of the impact of selection on four measures of firm growth. OSRD Contract indicates whether or not a firm was selected to participate in the Penicillin Program. Model 5 distinguishes between firms given research and those given manufacturing contracts. Models 7 and 8 include interaction effects between selection and size, and selection and the prior establishment of a research laboratory. * indicates p<.05, ** p<.01, *** p<.001.
Table 2.4 (continued)

<table>
<thead>
<tr>
<th>Sales</th>
<th>Employees</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.13</td>
</tr>
<tr>
<td>Organizational</td>
<td>Incorporation</td>
</tr>
<tr>
<td>Creation of Research Lab (dummy)</td>
<td>9.86**</td>
</tr>
<tr>
<td>Hired Chemist</td>
<td>.455</td>
</tr>
<tr>
<td>Employees</td>
<td>3.76***</td>
</tr>
<tr>
<td>Political</td>
<td>1938 FDA Act</td>
</tr>
<tr>
<td>Durham-Humphrey Act</td>
<td>.265</td>
</tr>
<tr>
<td>World War II</td>
<td>4.87**</td>
</tr>
<tr>
<td>Intervention</td>
<td>OSRD Contract (dummy)</td>
</tr>
<tr>
<td>Plant Built for the Firm (dummy)</td>
<td>8.95*</td>
</tr>
<tr>
<td>Contracted to Research (dummy)</td>
<td>9.05*</td>
</tr>
<tr>
<td>Contracted to Manufacture (dummy)</td>
<td>8.14*</td>
</tr>
<tr>
<td>Intertwines</td>
<td>Employees*OSRD</td>
</tr>
<tr>
<td>Lab*OSRD</td>
<td>.266</td>
</tr>
<tr>
<td>First Order Lag of DV</td>
<td>297***</td>
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<tr>
<td>Observations</td>
<td>617</td>
</tr>
<tr>
<td>Units</td>
<td>41</td>
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</table>
Table 2.5: Random Effect Regression Results

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<tr>
<th></th>
<th>Income</th>
<th>Profit</th>
<th>Sales</th>
<th>Employees</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Age (years)</td>
<td>-0.008</td>
<td>(0.009)</td>
<td>-0.037</td>
<td>(0.010)</td>
</tr>
<tr>
<td>Organizational</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorporation</td>
<td>0.012</td>
<td>(0.013)</td>
<td>0.013</td>
<td>(0.015)</td>
</tr>
<tr>
<td>Creation of Research Lab (dummy)</td>
<td>2.09***</td>
<td>(0.659)</td>
<td>1.63**</td>
<td>(0.585)</td>
</tr>
<tr>
<td>Hired Chemist</td>
<td>-0.014</td>
<td>(0.014)</td>
<td>-0.016</td>
<td>(0.015)</td>
</tr>
<tr>
<td>Primarily a Pharmaceutical Company (dummy)</td>
<td>0.11*</td>
<td>(0.484)</td>
<td>0.59*</td>
<td>(0.718)</td>
</tr>
<tr>
<td>Research &amp; Development Division (dummy)</td>
<td>0.308</td>
<td>(0.593)</td>
<td>-0.562</td>
<td>(0.671)</td>
</tr>
<tr>
<td>Initial Advantage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1935 Sales</td>
<td>0.009</td>
<td>(0.111)</td>
<td>0.009</td>
<td>(0.111)</td>
</tr>
<tr>
<td>1935 Profit</td>
<td>0.306**</td>
<td>(0.113)</td>
<td>0.444***</td>
<td>(0.130)</td>
</tr>
<tr>
<td>1940 Science Employers</td>
<td>-0.004</td>
<td>(0.025)</td>
<td>-0.056*</td>
<td>(0.028)</td>
</tr>
<tr>
<td>Political</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1938 FDA Act</td>
<td>0.590</td>
<td>(0.647)</td>
<td>0.748</td>
<td>(0.670)</td>
</tr>
<tr>
<td>Durham-Humphrey Act</td>
<td>0.349</td>
<td>(0.653)</td>
<td>0.615</td>
<td>(0.694)</td>
</tr>
<tr>
<td>World War II</td>
<td>0.378</td>
<td>(0.591)</td>
<td>0.418</td>
<td>(0.575)</td>
</tr>
<tr>
<td>Intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OSRD Contract (dummy)</td>
<td>2.27*</td>
<td>(0.716)</td>
<td>2.97*</td>
<td>(0.771)</td>
</tr>
<tr>
<td>Contracted to Research (dummy)</td>
<td>3.40***</td>
<td>(0.945)</td>
<td>2.48**</td>
<td>(1.02)</td>
</tr>
<tr>
<td>Contracted to Manufacture (dummy)</td>
<td>3.40**</td>
<td>(0.945)</td>
<td>2.48**</td>
<td>(1.02)</td>
</tr>
<tr>
<td>First Order Lag of DV</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Constant</td>
<td>0.875**</td>
<td>(0.026)</td>
<td>0.818**</td>
<td>(0.029)</td>
</tr>
<tr>
<td>Observations</td>
<td>545</td>
<td>519</td>
<td>519</td>
<td>628</td>
</tr>
<tr>
<td>Units</td>
<td>41</td>
<td>37</td>
<td>37</td>
<td>42</td>
</tr>
</tbody>
</table>

Note: Models 8-10 present a random-effect regression that tests the impact of pre-selection success and organizational structure on post-selection status.
Table 2.6: Survival Analysis

<table>
<thead>
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<th></th>
<th>Merger/ Bankruptcy</th>
<th>Exit Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Age (years)</td>
<td>-.002 (0.13)</td>
<td>-.004 (0.14)</td>
</tr>
<tr>
<td><strong>Organizational</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorporation</td>
<td>-.013 (0.17)</td>
<td>-.01 (0.19)</td>
</tr>
<tr>
<td>Creation of Research Lab (dummy)</td>
<td>-.333 (0.746)</td>
<td>-.139 (0.960)</td>
</tr>
<tr>
<td>Hired Chemist</td>
<td>.003 (0.018)</td>
<td>.006 (0.021)</td>
</tr>
<tr>
<td>Primarily a Pharmaceutical Company (dummy)</td>
<td>2.39* (1.04)</td>
<td>2.64* (1.3)</td>
</tr>
<tr>
<td>Research &amp; Development Division (dummy)</td>
<td>-1.69* (0.859)</td>
<td>-2.02 (1.09)</td>
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</tbody>
</table>

**Initial Advantage**

<table>
<thead>
<tr>
<th></th>
<th>1935 Sales</th>
<th>1935 Profit</th>
<th>1935 Science Employees</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>.015 (0.016)</td>
<td>-1.51 (0.866)</td>
<td>-.002 (0.039)</td>
</tr>
<tr>
<td></td>
<td>.011 (0.015)</td>
<td>-1.76 (0.936)</td>
<td>-.028 (0.041)</td>
</tr>
<tr>
<td></td>
<td>.059 (0.039)</td>
<td>-.714** (0.269)</td>
<td>.087 (0.063)</td>
</tr>
<tr>
<td></td>
<td>.057 (0.041)</td>
<td>-.653* (0.292)</td>
<td>.079 (0.057)</td>
</tr>
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</table>

**Note:** Models 1-4 present a cox proportional hazard regression for acquisition or bankruptcy. Models 5-8 present a fixed-effect logit regression estimating the likelihood a firm would remain classified (SIC:2834) as a pharmaceutical company at the end of the period of study.
Figure 3.1: State Repeals of Anti-Substitution Laws

Figure 3.2: Industry Profitability

- Most States Had Anti-Substitution Laws
- Most States Repealed Anti-Substitution Laws
Figure 3.3:

![Chart showing New Molecular Entity Production with years range from 1957 to 2007](image)
Figure 3.4: 1970-82 Industry Profits, Products, and State Support
Figure 4.1

Acquisitions by Type, 1950-90

Note: This chart presents the total number of acquisitions, by type, for all the firms in the pharmaceutical industry.
Figure 4.2

Articles on "Diversification" in the *New York Times*

- Dotted line: Total Articles
- Solid line: Positive Articles
Table 4.1

<table>
<thead>
<tr>
<th>Pharmaceutical Firm</th>
<th>Acquired</th>
<th>Products</th>
<th>Acquired</th>
<th>Divested</th>
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</thead>
<tbody>
<tr>
<td>AHP</td>
<td>Chef Boy-Ar-Dee</td>
<td>Food</td>
<td>1946</td>
<td>1996</td>
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<tr>
<td>AHP</td>
<td>Wrigley Gum</td>
<td>Candy</td>
<td>1950</td>
<td>1984</td>
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<tr>
<td>Bristol-Myers</td>
<td>Luziers</td>
<td>Cosmetics</td>
<td>1955</td>
<td>1974</td>
</tr>
<tr>
<td>Bristol-Myers</td>
<td>Clariol</td>
<td>Cosmetics</td>
<td>1959</td>
<td>2001</td>
</tr>
<tr>
<td>Merck</td>
<td>Calgon</td>
<td>Water Treatment</td>
<td>1961</td>
<td>1993</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Barbasol</td>
<td>Shaving Cream</td>
<td>1962</td>
<td>2001</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Coty Cosmetics</td>
<td>Cosmetics (Stetson, Musk)</td>
<td>1963</td>
<td>1992</td>
</tr>
<tr>
<td>Abbot Labs</td>
<td>Faultless Rubber</td>
<td>Golf Balls</td>
<td>1966</td>
<td>1972</td>
</tr>
<tr>
<td>AHP</td>
<td>Brach &amp; Sons</td>
<td>Candy</td>
<td>1966</td>
<td>1986</td>
</tr>
<tr>
<td>Schering-Plough</td>
<td>Maybeleine</td>
<td>Cosmetics</td>
<td>1967</td>
<td>1989</td>
</tr>
<tr>
<td>E.R. Squibb</td>
<td>BeechNut</td>
<td>Candy</td>
<td>1968</td>
<td>1972</td>
</tr>
<tr>
<td>E.R. Squibb</td>
<td>LifeSavers</td>
<td>Candy</td>
<td>1968</td>
<td>1981</td>
</tr>
<tr>
<td>Smith-Kline</td>
<td>Love (created)</td>
<td>Cosmetics</td>
<td>1969</td>
<td>1980</td>
</tr>
<tr>
<td>American Cyanamid</td>
<td>Shulton</td>
<td>Cosmetics (Old Spice)</td>
<td>1970</td>
<td>1990</td>
</tr>
<tr>
<td>Bristol-Myers</td>
<td>Palomar Pictures (created)</td>
<td>Film Studio</td>
<td>1970</td>
<td>1974</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Elizabeth Arden</td>
<td>Cosmetics</td>
<td>1970</td>
<td>1987</td>
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<td>Vicks-Richardson-Merrill</td>
<td>Oil of Olay</td>
<td>Cosmetics</td>
<td>1970</td>
<td>1985</td>
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<td>Parke-Davis</td>
<td>Revlon</td>
<td>Cosmetics</td>
<td>1970**</td>
<td></td>
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<td>E.R. Squibb</td>
<td>Charles of Ritz</td>
<td>Cosmetics</td>
<td>1971</td>
<td>1986</td>
</tr>
<tr>
<td>Norton Simon</td>
<td>Max Factor</td>
<td>Cosmetics</td>
<td>1973</td>
<td>1983</td>
</tr>
</tbody>
</table>

** Proposed, but the merger was never completed
Figure 4.3

Distribution of Acquisitions and Divestments

Number of Actions

- Non-Medical Acquisitions
- Non-Medical Divestments
Figure 4.4

Percent of Pharmaceutical Industry Diversified
This table is based on 890 observations of 25 publicly traded American pharmaceutical firms between 1950 and 1990. Initial Acquisitions is an indicator variable, which is 0 until a firm acquired their first non-medical firm. Annual Acquisitions is a yearly indicator for whether a firm acquired a non-medical firm in a given year. Initial and Annual Divestments are similar indicators counting the initial decision to divest non-medical firms, and an annual indication of divestment. Industry Diversification is a measure of the percent of firms currently pursuing a diversification strategy.
Table 4.3

<table>
<thead>
<tr>
<th>Model Type</th>
<th>H1a: Initial</th>
<th>H1a: Degree</th>
<th>H1b: Initial</th>
<th>H1b: Degree</th>
<th>H1c: Initial</th>
<th>H1c: Degree</th>
<th>H1d: Initial</th>
<th>H1d: Degree</th>
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<td>FE Logit</td>
<td>FE Logit</td>
<td>FE Logit</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Sales</td>
<td>.125***</td>
<td>-.001**</td>
<td>.039***</td>
<td>.000</td>
<td>.004</td>
<td>.000</td>
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</tr>
<tr>
<td></td>
<td>(.021)</td>
<td>(.000)</td>
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Note: These results were estimated using fixed effect logit and cox proportional hazard models on a population of 25 firms from 1950-1990. The results presented are the unexponentiated coefficients, not the hazard rates. The dependent variable is time to adoption/abandonment of the new strategy. *p<.05, **p<.01, ***p<.001.
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| First Five to Divest        | 1956-65      | 17.7         | 53.9         | 165        | 113        | 242        | 810        |
| Last Five to Divest         | 1977-87      | 25.5         | 32.5         | 102        | 62         | 202        | 620        |
| Remaining Firms             | 1977-87      | 20.3         | 29.9         | 85.6       | 85.9       | 185        | 612        |
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Note: these results were estimated using cox proportional hazard models on a population of 25 firms from 1950-1990. The results presented are the unexponentiated coefficients, not the hazard rates. Sales and profits are estimate for the year prior, family-run firm is an indicator for whether or not the CEO was related to the founder, Pharmaceutical Executive indicates that the CEO had a background in pharmacy science, dedicated pharmaceutical means the firm did not begin as a diversified firm. FDA recall indicates whether or not the firm had a product recalled by the FDA the year prior. Antitrust suit indicates whether or not the firm was investigated by the FTC in the preceding year. In models 2 and 3 the covariates were estimated separately, but presented in one model for comparison.
Table 4.7

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<td>1</td>
<td>2</td>
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<tr>
<td>Diversified (1950-54)</td>
<td>35.5 (23.5)</td>
<td>-7.41 (39.6)</td>
<td>80.4** (27.8)</td>
<td>-7.07 (24.8)</td>
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<td>Diversified (1955-59)</td>
<td>13.9 (23.9)</td>
<td>-23.4 (40.5)</td>
<td>49.5 (28.2)</td>
<td>2.77 (26.1)</td>
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<tr>
<td>Diversified (1960-64)</td>
<td>19.9 (24.1)</td>
<td>-13.7 (35.4)</td>
<td>76.1** (29.6)</td>
<td>18.2 (26.7)</td>
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<tr>
<td>Diversified (1965-69)</td>
<td>17.4 (27.2)</td>
<td>-12.1 (40.7)</td>
<td>52.7 (32.3)</td>
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<td>Diversified (1970+)</td>
<td>11.2 (32.4)</td>
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<tr>
<td>Divested (pre-1960)</td>
<td>26.2 (22.1)</td>
<td>.706 (34.2)</td>
<td>81.0 (78.9)</td>
<td>-20.2 (68.8)</td>
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<td>Divested (1960-65)</td>
<td>46.5* (23.3)</td>
<td>28.9 (31.4)</td>
<td>57.7 (79.7)</td>
<td>15.3 (67.3)</td>
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<td>Divested (1966-71)</td>
<td>13.8 (20.2)</td>
<td>2.82 (30.5)</td>
<td>79.3 (78.3)</td>
<td>38.3 (66.4)</td>
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<td>Divested (1972-76)</td>
<td>-3.19 (29.4)</td>
<td>.654 (40.9)</td>
<td>22.7 (81.8)</td>
<td>30.4 (73.2)</td>
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<td>Divested (1977-81)</td>
<td>5.84 (20.2)</td>
<td>-1.65 (28.8)</td>
<td>45.4 (78.4)</td>
<td>35.5 (66.2)</td>
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<td>Divested (1982+)</td>
<td>31.1 (27.9)</td>
<td>47.5 (38.6)</td>
<td>68.8 (81.7)</td>
<td>91.5 (73.1)</td>
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<td>Count of Non-Medical Acquisitions</td>
<td>4.13*** (1.31)</td>
<td>2.48 (1.83)</td>
<td>15.3*** (1.31)</td>
<td>8.42*** (1.41)</td>
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<td>Count of Non-Medical Divestments</td>
<td>11.9*** (2.84)</td>
<td>9.99** (3.83)</td>
<td>49.0*** (3.07)</td>
<td>47.11** * (3.90)</td>
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<td>1.06 (21.9)</td>
<td>8.79 (6.60)</td>
<td>9.79 (5.73)</td>
<td>7.94 (17.8)</td>
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<td>757</td>
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<td>r^2</td>
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Figure 5.1: Legislative History and Effect

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<th>Year</th>
<th>Legislation</th>
<th>Purpose</th>
<th>Primary Intended Effect</th>
<th>Annual NME Before</th>
<th>Annual NME After</th>
<th>NME-P Before</th>
<th>NME-P After</th>
<th>% NME Before</th>
<th>% NME After</th>
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<tr>
<td>1962</td>
<td>Keating-Harris</td>
<td>Required proof of efficacy before a drug could be marketed for sale in the US.</td>
<td>Increase Quality</td>
<td>20.00</td>
<td>21.72</td>
<td>6.23</td>
<td>9.40</td>
<td>0.09</td>
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<td></td>
<td>(1970 effective following SC decision in Upjohn v. Finch)</td>
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<tr>
<td>1979</td>
<td>Bayh-Dole</td>
<td>Allowed private companies control of intellectual property discovered with government funding</td>
<td>Increase Innovation</td>
<td>17.37</td>
<td>25.88</td>
<td>6.50</td>
<td>11.15</td>
<td>0.17</td>
<td>0.30</td>
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<tr>
<td>1983</td>
<td>Orphan Drug Act</td>
<td>Created tax incentives for drug companies to create new drugs for diseases that affect small populations</td>
<td>Increase Innovation</td>
<td>17.71</td>
<td>26.91</td>
<td>6.56</td>
<td>11.91</td>
<td>0.18</td>
<td>0.32</td>
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<td>1984</td>
<td>Hatch-Waxman</td>
<td>Reduced requirements for generic drug approval and extends patent length for brand name drugs.</td>
<td>Increase Competition</td>
<td>17.83</td>
<td>27.14</td>
<td>6.63</td>
<td>12.05</td>
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<td>1992</td>
<td>Prescription Drug User Fee Act (PDUFA)</td>
<td>Requires manufacturers to pay fees for product applications, intended to speed FDA review</td>
<td>Decrease Regulatory Costs</td>
<td>19.00</td>
<td>29.00</td>
<td>7.56</td>
<td>12.31</td>
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<td>1997</td>
<td>Direct to Consumer Advertising</td>
<td>Reauthorization of PDUFA allows for public advertising of prescription meds</td>
<td>Decrease Regulatory Costs</td>
<td>20.50</td>
<td>26.25</td>
<td>8.00</td>
<td>12.63</td>
<td>0.22</td>
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Figure 5.2:

New Drug Introductions

Note: This table is based on the number and kind of drugs approved by the FDA between 1950-2005.
### Table 5.1: Descriptive Statistics

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<td>33140</td>
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<td>Minimum</td>
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<td>.319</td>
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<td>9 US Prescription Drug Sales (million)</td>
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<td>.491</td>
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Note: This table is based on the number and kind of drugs approved by the FDA between 1950-2005.
Table 5.2: Effect of Policy on New Molecular Entities

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Note: These tables present koyck lags estimated with a two-stage least square regression on industry-level data collected between 1950-2005. The coefficient for each policy estimates the initial effect of the policy, while the LRP captures the long-term effect on the total number of NMEs approved. Coefficients with robust standard errors are reported. *** p<.001, ** p<.01, * p<.05.
Table 5.3: Effect of Policy on Priority New Molecular Entities

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Table 5.4: Effect of Policy on NMEs as a Percent of All New Drug Approvals

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