Title
Making the Market: How the American pharmaceutical industry transformed itself during the 1940s

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Abstract:
Between 1940 and 1950 the American pharmaceutical industry transformed itself from a collection of several hundred, small, barely profitable firms to a small group of large, highly profitable firms. The object of this paper is to use this case to understand how an industry evolves and, more specifically, to determine how a single industry comes to be dominated by a few large firms. This is in the tradition of recent studies that have examined the role of political, organizational, and social variables in the evolution of American industry(Dobbin 1994; Fligstein 2001; Perrow 2002). The intent here is to analyze different predictors of success following a population-level change, in a new case, one where firm success was previously considered the product of economic efficiency (Temin 1979; Temin 1980). To answer my specific question I employ a random-effect regression analysis on longitudinal data collected on the population of public firms between 1935-1955. I find that while the previous economic explanations may explain subsequent successes, they do not explain the initial change in the industry. Instead, the transformation of the industry into an oligopoly was largely the unintentional result of direct intervention by the US government.

Introduction

In 1940 the American pharmaceutical industry was composed of several hundred small companies, each limited to a particular geographic region and, the largest of which accounted for less than 3% of the total market. 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 and out of a sea of hundreds, fifteen firms had emerged to define the American pharmaceutical industry. These firms were large, highly innovative, highly profitable and together they accounted for 80% of the entire industry's sales and 90% of its' profits. 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 the question: How does a diverse and competitive industry come to be dominated by a few large firms?

Historically, dramatic market transformations have been understood as a product of both political and economic factors (Fligstein 1996; Dobbin and Dowd 1997; Dobbin and Dowd 2000; Perrow 2002; Powell, Koput et al. 2005; Schneiberg 2005). Politically, it was varying policy regimes, or degrees of state strength, that elicited differing forms of competition(Roy 1997; Schneiberg 2005). Charles Perrow provided the basis for what I offer here, by showing that in the late 1800s, a weak state and the advent of a new organizational form combined to produce an American economy dominated by large corporations(Perrow 2002). Dobbin and Dowd's work on Massachusetts railroad foundings echoes this finding, demonstrating the role that policy changes have on the level of competition in an industry(Dobbin and Dowd 1997; Dobbin and Dowd 2000). In each of these cases it is the introduction of new political frames that forces a dramatic change in the organization and level of competition in an industry.

Industrial economists, however, have a different means of explaining such dramatic changes in an industry. While not dismissing the role of regulation, they demonstrate that transformations also occur as the natural product of a market effectively selecting the most efficient firms and removing the remainder (Mahoney 1959; Temin 1979; Temin 1980; Thomas 1990; Grabowski and Vernon 1992; Scherer 1993; Chandler 2005). Competition between these various firms was fierce and the market could only support the few who survived. Business histories, of the pharmaceutical industry in particular, have favored this conclusion and suggested 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(Hirsch 1974; Temin 1979; Chandler 2005).

While both of these explanations offer insight into the pharmaceutical industry of the 1940s, neither alone can fully explain what transpired. Although new regulations were introduced during the period, the industry was already highly regulated for years prior without any resulting consolidation. Similarly, the firms that succeeded were neither the largest, nor the most profitable, nor the most innovative firms at the start of the period suggesting that they had few economic advantages that would have favored their ascendance. Therefore, to better understand what occurred, I intend to juxtapose these theories with an analysis of whether this transformation was brought about by fortuitous organizational changes. During the period of study firms began to invest, for the first time, in research and development laboratories, they incorporated, they hired employees with backgrounds in chemistry and they began forming relationships with research universities. Each of these changes, individually, has been shown to affect firm performance and could together or alone, explain the transformation witnessed here.

Finally, there is the possibility that the transformation of the industry was not the accidental result of political change or the inevitable march of economics, but rather the

direct intent of governmental intervention. In 1942 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 the production of penicillin for the war effort. These firms received assistance in altering their manufacturing plants to produce penicillin and received a several year headstart in studying and producing a drug that would soon be the most profitable in the world. It is possible, but not known, whether being selected for this project enabled a firm to separate itself from the hundreds of similar firms to become one of the handful that would dominate the industry for the next sixty years.

Each of these rationales alone offers a compelling explanation for the movement towards an oligopoly, but the question remains which factors, or which combinations, proved instrumental in both selecting which firms would succeed and limiting the number to so select a group? To answer these I use a random effect regression model on a sample of the eighteen, publicly traded firms engaged in the production of pharmaceutical preparations, from 1935-1955. I find that while organizational changes did lead to more profitable returns, they did not equal the impact of either the regulatory changes or direct governmental intervention by the OSRD. Moreover early size advantages were not beneficial or sustainable, as the largest firms at the start of the study exhibited no greater long-term success than smaller firms with fewer sales. In the end, it was the passage of the Durham-Humphrey Amendment and the receipt of a government penicillin contract that lead to an immediate and significant increase in a firm's size, sales and profits, and helped establish knowledge-based barriers to future competition.

Background

For nearly one hundred years Moody's has offered an annual analysis of every major industry in the US. 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(Silverman and Lee 1974; Scherer 2001). Such a meteoric ascent begs the question: What happened to permit an overlooked division of a few cosmetic companies to become the nations most profitable industry? And, why did the wealth become concentrated in so few hands?

Most examinations of the pharmaceutical industry's historic rise begin in 1945, with the end of WWII (Chandler 2005). The consensus is 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 1980). Previously, most companies maintained their marginal existence by selling nostrums and therapeutic combinations of limited value. There were occasional products, like insulin or morphine, of great value, but these were notable exceptions to the rule. Moreover, these innovations were developed by University professors and merely manufactured by pharmaceutical concerns. Post-WWII companies began introducing more products of their own design and of genuine value. In keeping with this, it is presumed that the companies that succeeded were the ones who adapted to the new environment and moved their resources towards chemical research and the search for new drugs. These firms gained both a scientific advantage and an organizational one, as they developed both chemical expertise and a capacity for navigating the regulatory paths to drug approval. This combination of organizational and scientific knowledge produced a considerable barrier to entry for new firms, helping to further entrench those first few

successful firms and enabling them to remain profitable for as long as the market itself remained the same(Hirsch 1974).

But this accepted history ignores a few important facts. First, if investing in research was what propelled firms to succeed, then how can we explain the failure of so many of their competitors who made similar, and often earlier, investments? Second, if chemical research drove success then why didn't any of the firms with established chemical research divisions experience growth until after WWII? Even if this was an example of Schumpeterian creative destruction, where a radical innovation ushers in a new era of market leaders, why did firms benefit at different rates despite adopting similar responses to the change?

While the economic history suggests that the successful firms were those who best adapted to the situation, my own research into the archives of the Office of Science and Research Development (OSRD) tells a different story. The OSRD was established during WWII to help the US military achieve a number of scientific objectives deemed valuable for military success. Among these goals was the production of penicillin.

Although penicillin was discovered in 1938 and used on patients in 1941, by 1943 there was still no viable way to produce it in large quantities(Elder 1970). After a few years of failure the British government requested the assistance of the American government in solving the question of mass production. Given the high post-injury mortality rate at the time and the, seemingly miraculous, ability of penicillin to curtail precisely the infections that produced these deaths, supplying penicillin to the American forces was considered an issue of great military need. With this obvious a demand, the OSRD was given the authority to involve private corporations in the research and development processes, sharing with these selected firms all the previously classified information about penicillin production. The OSRD obliged by signing a total of seventeen American firms to government contracts in three separate stages, over the course of a few years. These firms ranged from some of the

largest and most successful pharmaceutical companies of the day (e.g. E.R. Squibb & Sons) to several of the smallest (e.g. Merck, Eli Lilly, and Pfizer), to several companies that had no prior experience in the pharmaceutical business at all (e.g. Schenley Industries, Cutter Laboratories). At the same time, the committee purposefully ignored several companies with more established research divisions and more extensive resources to commit to the endeavor. While the process by which these firms were selected is the topic for future research, it is the effects of this decision that are under investigation in this paper.

Of interest here is the degree to which the companies that would come to dominate the post-war era correlate to the companies that were selected by OSRD to participate in the penicillin program. The most obvious explanation for this correlation would arise from the fact that the military likely chose the strongest, most research-intensive companies for their partners. However, this is explicitly not true. Merck and Pfizer, two of the smaller pharmaceutical companies in the 1930s, were both selected because they possessed a rare expertise with deep tank fermentation processes.[1] At this point in time Merck, though already investing in research, was most notable for its line of vitamin B products while Pfizer derived the bulk of its profit not from therapeutic products but from the production of citric acid. In other words, the choice to use these firms was not based on any academic or scientific prowess, but rather out of the need for a specific set of manufacturing equipment.

A question here arises as to whether or not the government realized the value of the information and assistance it was providing. However, the notes taken by the OSRD suggest that they were fully aware of what they were doing and the advantage it would provide to those selected(Adams 1943). There are two reasons why this did not produce a pause in their actions: first, they did not see any plausible alternative and the need for more penicillin

[1] At the time this was there were only two methods for penicillin production and this, the deep-tank fermentation method, was considered a more likely avenue for mass production.

far outweighed any economic concerns about the future of the pharmaceutical industry. Second, they felt that by selecting a broad range of companies they were ensuring themselves of a competitive market and preventing any one company from garnering the lion's share of the profits.[2]

Theory and Hypotheses

There are two nested questions that motivate this paper, the first asks specifically: What happened, during the 1940s, to catalyze the US pharmaceutical industry? The second asks more broadly: How do markets originate and how are they transformed? In the organizational literature these types of population-level changes are often precipitated by an environmental change (Chandler 1977; Pfeffer and Salancik 1978; Baum and Singh 1994; Stuart and Sorenson 2003). These exogenous shocks can take on a variety of forms ranging from: the introduction of a new political regime, to the appropriation of a new organizational model, to the innovation of a new technology (Galambos 1970; Piore and Sabel 1984; Lamoreaux 1985; Roy 1997; Galambos 2005). In each case a change in the environment alters the population of organizations by selecting a new set of incumbents either from those most able to adapt or from those best suited to capitalize on the new developments.

During the 1940s, the pharmaceutical industry experienced several such exogenous shocks, as new technologies were invented, new regulations introduced, and governmental oversight changed tactics. Combined, these shocks resulted in a drastic change to the market for pharmaceutical products, and any one of these alone many have been sufficient to produce the oligopoly that emerged. However, what we do not know is which firm-level and which population-level changes mattered in elevating a disorganized, unprofitable,

[2] Their expectation may have been accurate but several pharmaceutical companies were later prosecuted by the FTC and found guilty of price-fixing, a practice that prevented the competition the government anticipated from ever taking place, and helped these firms to solidify their advantage over the non-selected firms.

uninnovative industry into the most profitable, stable, innovative industry of the past fifty years. To answer these questions, I will discuss the different environmental changes that created the potential for a transformation of the market and then I will hypothesize which firms would benefit most from which changes.

Environmental Change: Political and Technological

Shocks produce change in a variety of ways, most often, they isolate/segregate one set of organizations from another and split the population(Stinchcombe 1965; Freeman and Hannan 1989; Baum and Singh 1994). This creates precisely the kind of population-level change that occurred with pharmaceuticals, where a small subset of firms emerged following the division to control the industry. But each type of shock, from political to technological, operates in a unique way and results in different types of population-level change.

The most frequently examined shock occurs through a political action. 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(Fligstein 1990; Roy 1997; Dobbin and Dowd 2000).

In particular, Dobbin and Dowd, in their study of Massachusetts railroad companies, find that different policy regimes produce different forms of competition (Dobbin and Dowd 1997). They demonstrate how the introduction of additional forms of regulation can transform the market and affect which companies succeed and which fail by favoring certain organizational forms over others. In later work, Dobbin and Dowd build on this to show that the prevailing business model is not the product of efficient selection, but result from social processes that are structured by political change (Dobbin and Dowd 2000). This complements work done by Fligstein who shows that changes in the regulatory framework promote different concepts of efficient organizations (Fligstein 1990; Fligstein 1996). In

both cases, we could expect to find that changes in the regulatory environment might favor some firms and disadvantage others, altering the population and producing a new constellation of dominant organizations, though who would be favored would vary depending upon the type of governmental change.

Further, in the pharmaceutical industry there were two significant legislative changes during the period of study. The first, in 1938, arose out of the Massengill tragedy, and required that all new drugs be proven safe before they were marketed. The second, the Durham-Humphrey Amendment of 1951, established a permanent distinction between two classes of medicine: those that could be sold over the counter and those that required the consultation and approval of a physician. How these environmental changes affected the market is not immediately clear, but will become more so later when we discuss the differences between existing organizations.

Although regulatory changes raised additional barriers to entry for new firms, and raised the cost of business for existing ones, few studies of this period acknowledge them as having caused a change in the population of firms. Instead, business historians tend to date the origins of the industry to 1945 when penicillin provided a dramatic technological shift, what Schumpeter earlier described as a "creative destruction"(Schumpeter 1947; Temin 1980; Liebenau 1987; Chandler 2005).

In Schumpeter's story, markets evolve by paths of creative destruction whereby new technologies emerge that render the old manner of business obsolete. Firms then need to adapt to the new environment or close. Penicillin provided precisely this kind of technological breakthrough, offering a product considerably more effective than anything else available for a range of common ailments. Moreover, it elevated the value of training in

chemistry as both penicillin and the subsequent antibiotics were derived through attempts to chemically produce penicillin in a modified, and therefore patentable, form.

Galambos and Sturchio, in a more recent history of the pharmaceutical industry return to this theory and find that the introduction of biotechnology produced a similar moment where firms had to reorient themselves around the new technological possibilities of biological-based research or risk their demise (Galambos and Sturchio 1998). 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 et al. 1996).

Both these political, and this technological, changes altered the environment, creating an opportunity for a few firms to rise up from the ranks of their competitors and become dominant. But different theories assume that very different factors would determine *which* firms made the leap successfully. My hypotheses will be derived from the predictions of different theoretical responses to the question of what determines success following such a large-scale change.

Adaptation or Selection

The most obvious answer would be that the firms most able to adapt to these environmental changes would be the firms most likely to succeed. However, a review of studies on the benefits of adaptive organizational change shows at best inconsistent results(Baum and Shipilov 2006). Hannnan and Freeman offer a cogent argument that while firm adaptations may matter, firms are unlikely to know which will be the most favorable beforehand(Freeman and Hannan 1984). This would suggest therefore that when an environmental change occurs, the firms that succeed would be the ones best situated for the change, not the ones best at adapting.

Business historians and economists who have studied this field favor the Hannan and Freeman argument. They contend that the firms that were in the best position beforehand were the ones most likely to benefit from the new environment. This could mean, as Hirsch has shown, that pharmaceutical firms benefit from economies of scale and that, post-penicillin, it was the largest firms that would achieve the greatest success(Hirsch 1974).

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, where marketing prowess enabled the sale of many goods of dubious effectiveness. These changes require 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/largest firms are the most insulated from the changes and therefore best able to survive in new environments(Freeman, Carroll et al. 1983; Carroll and Swaminathan 2000; Baum and Silverman 2004).

Taken together, this would suggest that, although there were hundreds of similarly-sized firms in 1935, those that were larger and 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 1: The largest and most profitable firms would benefit most from environmental change and show the greatest growth.

While acknowledging the relevance of the size and age of a firm, several scholars have focused more attention on the role that a firm's subsequent strategic choices have on

that firm's survival(Pfeffer and Salancik 1978). Their work contends that it is the ability to adapt to a new environment that determines whether a firm will survive. Change at the population level occurs as firms are either too slow or too inert to adapt their organizations to their new surroundings(Porter 1980).

Charles Perrow explains a change similar to what transpires here in his study of the rise of the large corporation in America(Perrow 2002). He attributes this transformation to two central factors: the weakness of the state and, simultaneously, the decision by firms to incorporate. This is not monocausal as the two issues worked very much in sync, but it does demonstrate how a particular organizational adaptation produced the rise of larger corporations in the place of a formerly dynamic market. Between 1935 and 1955, there were three comparable 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 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.

Similarly, while raising capital helped insulate firms, many historians argue that it is how firms invested that capital that proved crucial in determining which firms succeeded. Temin and Chandler both claim that following the invention of penicillin what mattered was not the size of the firm but the size of their investment in chemical research(Temin 1979;

Temin 1980; Chandler 2005). Firms needed to move away quickly from marketing nostrums and towards producing more drugs like insulin and penicillin. To do this firms needed to acquire an expertise in chemistry and the easiest way to do this would be through the hiring of new employees and the creation of R+D laboratories. Both authors, in concert with most studies of the period assume that pre-1945, few pharmaceutical firms had invested significantly in research laboratories. Firms were less vertically-integrated then and there was a clear separation between universities, where research was done, manufacturers, who produced the chemicals and the pharmaceutical houses that sold them.

Even though these are "core changes" of the kind that Hannan and Freeman found can reintroduce liabilities of newness, studies of the industry argue that firms that do not make these changes cannot—to borrow Hirsch's idea—finance or find the "hits" that will enable them to profit (Freeman and Hannan 1984). Therefore, it is reasonable to assume that the firms who adapted to the new environment by building laboratories, increasing their R+D investments, or by hiring scientists would be more likely to succeed.

Hypothesis 2: The firms that adopted any of these organizational changes were more likely to succeed in the new environment than those that did not.

One of the difficult distinctions 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 organization literature, the division between selection and adaptation assumes that firms adapt to the new environment and that those adaptations help the firm to survive. 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 important to know how when the firms first made their organizational changes, to determine whether those organizational changes only mattered once the environment had changed. 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.

Intervention

Finally, a firm might have survived neither because the environment selected them nor because they adapted properly. 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. Curiously, for a market whose history is as well documented as the pharmaceutical industry, no scholar argues for this position. Instead, the dispute remains between whether the most adaptive firms succeeded or whether the most well-positioned firms benefited from fortunate environmental changes, but no one has examined whether the government actively moved to transform the market(Silverman and Lee 1974; Temin 1980).

However, there is ample reason to believe that it was governmental intervention that first created the modern market for pharmaceuticals. As discussed previously, the OSRD selected a group of 17 firms to participate in a top-secret program to produce penicillin.

Unsurprisingly there is a high degree of correlation between the 17 firms selected to participate in the program and the largest firms in 1950. The most logical explanation for this correlation would be that the government selected the best firms for its program and so their success was not caused by the program, but preceded it. This is however, explicitly untrue. Of the 17 firms selected, 3 had no experience producing pharmaceutical products, 4 had no prior experience conducting pharmaceutical research and 6 were not yet selling $1million worth of products(Adams 1943). In other words, these companies were not uniformly large, scientifically driven, or competent. About the only thing they had in common was that they were all selected for the OSRD program.

However, the decision by the federal government to become actively involved in guiding and funding pharmaceutical research could easily have benefited the companies fortunate enough to receive this assistance. These companies would have had a several year advantage in manufacturing and researching the antibiotics that would later provide the bulk of pharmaceutical revenues. These companies would have completed manufacturing facilities years ahead of their competitors and scientific expertise that would not be easily equalized even once the information itself was made public. Despite the best efforts of the OSRD to leave the market unaffected by their program, it is certainly possible that it worked as a filtering mechanism.

Hypothesis 3: The firms selected by OSRD were most likely to succeed.

Data

I began by assembling a list of all companies engaged in the production of pharmaceutical products between 1935 and 1955 from Moody's Industrial Reports and the National Research Council Industrial Surveys. For my sample, I included all eighteen pharmaceutical firms that were publicly traded for the duration of the period of study. Of

these eighteen, nine were selected to participate in the OSRD and nine were not. This will produce a slight bias in my results against the effect of the OSRD contract as the control firms represent the largest and most successful firms of their era(as evidenced by their ability to go public). Therefore we would expect these firms to succeed irrespective of their inability to gain an OSRD contract and we would expect the firms who received a contract to experience only a mild advantage.

In order to operationalize the "success" of a firm during the period of study, data were collected on the firm's annual sales, income and, employee figures for every year available. This produced three disparate dependent variables, each measuring a different performance-related outcome and is consistent with previous studies of growth at the firm-level(Uzzi 1996; Stuart 2000). Unfortunately, due to inconsistencies and omissions in the reporting of employees, those models are based on a set of only 216 observations whereas the first two sets are based upon 338 observations, both from the same 18 firms. This amounted to the difference between a bi-annual and semi-annual reporting of data and is not believed to have impacted the ability to compare between tables. 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 data.

INSERT TABLE ONE

Controls

One plausible explanation for which firms succeeded is that firms are capable of growth once they reach a maturation point and that, what we find in the 1940s is that, the oldest firms are the ones that are growing the fastest. This could be due to the fact that they've had more time to experiment with different models or that they simply have more financial or scientific resources. To control for this, I included a variable for the age of the firm, 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, I include a dummy variable to measure the effect of the period during which the US was involved in WWII.

Independent Variables

To address the findings of organizational theorists I included four distinct organizational variables: date of incorporation, date of investment in chemistry, a dummy variable for whether or not they established a research laboratory, and the number of employees with backgrounds in the natural sciences, employed in 1945. The date of incorporation is determined by the year in which the firm first chose to incorporate itself. The date of the investment in chemistry is taken from annual reports and documents the first record of a contract with a University chemistry department or the hiring of a trained chemist to guide research. The date of laboratory founding, similarly, 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. The number of employees trained in science helps distinguish between the effect of a small, but early investment in the new methods and a large, but late one.[3] Dates were found and confirmed using a range of data sources including, but not limited to: annual reports, published corporate histories, and individual biographies.[4]

To evaluate the role that economies of scale played in selecting winners I use three variables: profitability at time t0, sales at t0, and employees at t0. These four variables allow me to address the most obvious explanation for success: that the firms who succeeded were

[3] Ideally, I would like to gather annual data on the number of employees with backgrounds in science, but thus far I've only found sporadic data.

[4] I owe a special note of thanks to the Lehman Brothers Collection at the Baker Library at Harvard for their collection of corporate histories.

simply the largest, most successful firms. If economies of scale matter then we should see that the most profitable and most innovative firms possessed a distinct advantage.

In response to the claim that political changes are responsible for the alteration of the market, I introduced two additional variables. 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.

The final variable is a dummy variable that indicates whether a company was granted a government contract for the production of penicillin. The date for this arose from the contracts signed by the OSRD and the contracted party.

Methods and Results

For each of my three dependent variables I produced three models that I tested with a random effect regression. I chose random effects over fixed effects due to the fact that several of my variables remained constant during the period of study and a Hausman test showed that there was no bias in the model.[5] The first model tested the effect of my three controls on each dependent variable; in no case did this explain more than 43% of the variance. The second model included all the variables with the exception of whether or not the firm had a government contract. The third model included a measure for whether a firm received a

[5] The models were also run as fixed-effect regressions with no significant variance in the results. Those results are available from the author upon request.

government contract, along with the previously tested variables. This final model explained over 60% of the variance for all three of my dependent variables.

INSERT TABLE TWO

The first hypothesis assumed that economies of scale determined the success of firms in this period and that the largest and most profitable firms would therefore benefit most from changes. However, the models do not offer support for this hypothesis as only once do any of the three measures of firm size help predict the growth of the firm. In model 9, each additional million in profits corresponded to an increase in employees (1.09, $p<.05$) but the other measures both proved statistically insignificant. Early profitability also had a positive effect, in model 6, on future sales, but not to a statistically significant degree. In earlier models(1, 4, and 7) these factors did prove significant, but their significance decreased substantially as other variables were added to the model suggesting that size, while beneficial, was really a proxy for other changes within the firms.

The second hypotheses proposed that firm growth resulted from the adoption of organizational changes and that the earlier these changes were adopted the better. But again, the models do not offer support for these hypotheses as in all six models show that being quick to incorporate, build a research facility, or hire employees trained in the natural sciences did not result in more revenue, profit or employees. Initially the total number of employees with a science background hired by a firm proves advantageous, in models 2 and 8, in increasing income(.059, $p<.01$) and expanding the firm(.021, $p<.05$). However, the significance of this decision disappears when the OSRD contracts are included in the calculation. Suggesting that whatever benefit was gained from having a large research staff was more than offset by the benefit of getting, or cost of not-getting, an OSRD contract. Pfizer might be the best example of this type of firm, as it was both late to build a research

lab and ended the period of study with relatively few scientific staff, yet it received an OSRD contract and its profits, sales, and staff grew almost immediately.

The final hypothesis proposed that direct governmental intervention, measured by the signing of penicillin contracts with the government, proved critical in determining which firms succeeded. The evidence presented in columns 3, 6 and 9 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. In model three, we can see that receipt of a government contract (10.61, $p<.001$) equaled the impact on income of having nearly 300 more scientific employees. Similarly, model six reveals that a government contract (71.84, $p<.001$) produced the same effect as a nearly 5 million dollar advantage in profits (16.23, $p<.1$). While, in today's dollars, that seems like an insignificant amount, it should be mentioned that only one firm earned more than $5 million in profits at the start of the period. Finally, model nine shows that receipt of a government contract resulted in more than a 3,000 employee differential (3.87, $p<.001$), more than a three million dollar advantage in initial profitability (1.09, $p<.05$).

What I do not hypothesize, but does prove relevant, is that the political changes which helped introduce these environmental changes, also affected the profitability of the industry. Surprisingly, these two laws did not function as might be assumed. For instance, while the 1938 amendment introduced significant barriers to entry for new firms, it did not provide any corresponding boost in sales or income for the existing firms. It did however correspond to an increase in the number of employees (1.01, $p<.01$) which may have resulted from the considerable additional scientific work required prior to introducing a product to market. In contrast, the 1951 Durham-Humphrey Act, which introduced a relatively modest change to the market, did have a large and significant positive effect on income (6.22, $p<.001$), sales (32.45, $p<.001$) and employees (1.28, $p<.01$). Unfortunately, this is not enough information

to determine whether they were beneficial for some firms and not others and, as presently structured, the evidence cannot be construed to either support or dismiss the belief that the shock alone helped determine who succeeded.

In each of these three cases, receipt of a penicillin contract provides the largest positive impact of any of the included independent variables; it also corresponds to a dramatic improvement in the ability of the model to account for the variance. In each case adding this one variable provides at least a 10% improvement in the model.

Conclusion

I began this paper with a deceptively simple question: what caused the pharmaceutical industry to transition from a market of hundreds of small firms to a cluster of a few large firms? My intent was to use this case to understand the broader question of how a market transforms from a primitive, chaotic state to a highly structured, oligopolistic one. To answer these questions I examine four hypotheses testing different theories of how population level changes occur following an environmental shock: through different organizational changes, political intervention, or economies of scale. My findings suggest that the answer is a combination of all three; firms that combined a government contract with a history of research came to dominate the industry just as regulations made it more difficult for competitors to enter and technology made it more profitable for those who remained.

What transpired was a series of population-level changes to the political and scientific environment that created the possibility for a new kind of pharmaceutical market, one drastically different from the marketing-driven model that preceded it and one based more on scientific prowess and innovation. However the firms that succeeded in this new market were not necessarily those who initially appeared in the best position to do so: the victors were neither the largest, nor the most profitable, nor the most innovative. The successful

firms were also not those who demonstrated a greater adaptability than their peers. These were not the firms who were quickest to adapt, nor were they the firms who made the most significant investments in change. Instead, the successful firms were the ones provided a significant advantage by the federal government. Continued success was dependent upon subsequent firm-level change, but those changes absent governmental help were not enough, no matter how significant the change, to overcome the disadvantage. This is contrary to past work that has limited the discussion to a question of adaptation or selection. Here, we introduce a third possibility: that the markets are political constructions and, as such, success in them can be politically determined even before economics enters in.

In a metaphorical sense, the US government created an opening and then allowed a select group of firms to try to pass through. Whether or not they made it through depended not on the prior status of the firms, nor upon what organizational decisions they had made, but entirely on political preference. Eventually everyone got their chance, but that head start proved critical and the firms that made it to the other side first are the firms that still dominate the industry to this day.

In more specific terms, I found that being selected to produce penicillin was tantamount to be selected to participate in the industry. Of the ten largest pharmaceutical firms in 1979, nine had participated in the OSRD penicillin program. By 2005, twelve of the seventeen still existed and they comprised all ten of the largest American pharmaceutical firms. The firms that were not chosen struggled to recover and, only those who consolidated via a merger movement 1950s were able to remain even loosely competitive.

The most obvious criticism of this finding is that the government merely selected the most capable and efficient companies from within the industry. And, it is clear that there was an advantage accorded to more established firms, though it proved less important how old or

large one was and more important how profitable. But while being more profitable at the start of the study proved valuable, it was more important to have invested in chemical research. As most firms had been conducting research for several decades and were barely earning over a million in profits, the advantage some firms gained by being profitable was balanced by other firm's investments in research.

More importantly, neither the size, nor the profits nor the history of research proved to be related to which firm was selected(Younkin 2007). A similar finding of note is that there is little correlation between hiring scientists early, or hiring a lot of scientist, and the prior success of the firm. In other words, firms that had high sales, high numbers of employees or high profitability were not more likely than other firms to invest early or heavily in scientific research. This confirms previous work which has shown larger, more established firms to be laggards in adapting to population-level change. Also, it confirms that while later FDA reforms made size a critical factor in maintaining success (as Hirsch shows), size was not a critical factor in achieving that initial success.

It is important here to reiterate that being chosen was merely the first in what proved to be a two-stage assault. Selling penicillin provided an immediate boost, a short-term, but dramatic rise in the profitability of the companies, but it was their next set of developments that cemented this advantage into a class separation. This second, and greater, financial success came through the fruits of their own research and their own laboratories. In essence, technological discoveries transformed the possibilities of the market, increasing the potential returns to extraordinary heights. Regulatory changes introduced new boundaries, limiting the number of firms who could succeed in the new environment. Governmental intervention provided a vital advantage to a handful of firms, but the degree to which they had altered their organization determined whether or not they could capitalize upon this.

Therefore it was the combination of the initial advantage provided to a privileged few by the government and those firm's own organizational changes that allowed them to succeed. Their selection by the government helped firms to gain knowledge about antibiotics and to develop the capacity to both examine and produce penicillin. Further, it gave them a momentary influx of capital with which to finance the research they were now capable of undertaking. This dual combination of a capital and informational influx enabled their nascent research laboratories to achieve greater insights than previously possible. The second wave of antibiotics, and the oligopoly it produced, was a result therefore not merely of economic efficiency or of a Darwinian struggle to fill a final niche, but of governmental intervention creating a limited set of opportunities and the fortunate, and capable, firms capitalizing.

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Table One: Regression Variable Summary Statistics

	Observations	Mean	SD	Min	Max
Income (millions)	354	9.3	11.39	0.124	83.29
Sales (millions)	378	44.13	59.84	0.283	451.1
Employees (thousands)	230	3.57	4.08	0.25	25.5
Age (years)	441	54.95	24.74	3	106
1935 Sales (millions)	378	8.43	8.1	0.283	29.287
1935 Profit (mililons)	378	2.24	2.79	0.1	10.292
1935 Employees (thousands)	399	2.18	3.26	.28	13.37
Organizational Change:					
1945 Science Employees	441	73.14	80.69	0	325
Time since first science employee (years)	441	23.16	18.38	0	73
Time Since Incorporation (years)	420	41.1	22.2	0	109
Built Research Facility (dummy)	441	0.59	0.49	0	1
Political Change:					
1938 Food and Drug Act	441	0.81	0.393	0	1
1951 Durham-Humphrey Act	441	0.24	0.43	0	1
Governmental Intervention					
Penicillin Contract	441	0.29	0.45	0	1

Table Two: Random Effect Regressions

	Pre-Tax Income			*Sales*			*Employees*		
	1	2	3	4	5	6	7	8	9
Age (years)	.334*** (.05)	.014 (.035)	-.02 (.031)	1.82**** (.245)	.35 (.252)	.046 (.253)	.145*** (.016)	.0115 (.016)	-.004 (.015)
World War II	-01.08 (1.07)	-.345 (1.1)	-.389 (.989)	-14.03* (5.76)	-9 (5.79)	-9.14 (4.93)	-.694* (.348)	-.935* (.391)	-.847** (.31)
Initial Advantage:									
1935 Sales (million)	-1.44*** (.43)	-.276 (.384)	-.132 (.347)	-8.23*** (2.19)	-2.67 (2.87)	-4.79 (2.87)	-.711*** (.2)	-.109 (.178)	-.251 (.173)
1935 Profits (million)	6.09*** (1.21)	.270 (1.16)	1.22 (.1.04)	31.96*** (6.19)	11.87 (8.6)	16.23 (8.5)	2.91*** (..558)	.824 (.533)	1.09* (.518)
1935 Employees (thousands)	.562 (.48)	-.036 (.368)	-.107(.33)	4.71 (2.44)	3.96 (2.82)	3.01 (2.85)	.528* (.224)	.338* (.17)	.331 (.172)
Organizational Change:									
1945 Scientific Employees		.059** (.019)	.032 (.017)		.142 (.139)	.006 (.138)		.021* (.009)	.01 (.008)
First Scientific Employee		-.069 (.053)	-.038 (.048)		.093 (.386)	.294 (.377)		-.009 (.02)	-.003 (.022)
Incorporation		-.1.01* (..04)	.054 (.037)		-528 (.295)	.146 (.296)		.009 (.02)	-.008 (.018)
Built Research Facility (dummy)		.329 (1.48)	-.117 (1.33)		-1.33 (8.88)	-8.4 (7.88)		-.346 (.529)	-.214 (.436)
Political Change:									
1938 Food and Drug Act		4.25** (1.28)	.1.94 (1.18)		22.38** (7.34)	7.91 (6.37)		1.79*** (.432)	1.01** (.363)
1951 Durham-Humphrey Act		7.46*** (1.12)	6.22*** (1.19)		39.33*** (6.4)	32.45*** (5.63)		1.58 *** (.356)	1.28*** (.293)
Governmental Intervention									
Penicillin Contract			10.61*** (1.19)			71.84*** (6.44)			3.87*** (.371)
Constant	-12.19 (3.27)	-7.67 (2.31)	.913 (1.62)	-67.37 (16.89)	-49.63 (16.97)	-1.17 (17.5)	-5.89 (1.32)	-1.95 (1.04)	.423 (1.04)
r-squared	.249	.549	.648	.194	.456	.609	.429	.705	.807
Firms=18							Firms= 18		
Observations= 338							Observations=216		