LOCATION AND ORGANIZING STRATEGY:

Exploring the Influence of Location on the Organization of Pharmaceutical Research

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ABSTRACT

The origin and nature of meaningful, persistent firm-specific differences is a central issue in the study of business strategy. I investigate in this paper the role of characteristics physically external to firms, but embodied in their local geographic areas, in driving differences in firms' organizing strategies. Specifically, I examine the extent to which location-specific characteristics affect the organization of pharmaceutical firms' research laboratories. The paper brings both qualitative and quantitative evidence to bear on this issue. Analyses of the histories of several late 19th century drug makers suggest that differences in local institutions, labor markets, and demand structures played important roles in affecting case firms' strategic evolution. For example, while Mulford (Philadelphia PA) exploited the strength of nearby universities and the city's public health system in organizing around leading-edge capabilities in bacteriology, Sterling (Wheeling WV) found that its local environment rewarded investments in marketing and distribution. Panel data analysis on a sample of firms from the late 20th century provides complementary evidence, demonstrating that the scientific orientation of modern drug discovery laboratories is positively and significantly correlated with measures of the strength of the local scientific and technical base. Together, these analyses suggest that location-specific characteristics may be important in driving firm heterogeneity and, ultimately, competitive advantage.

I. Introduction

The origin and nature of meaningful and persistent firm-specific differences are fundamental but incompletely understood issues in strategy. Although leading theoretical perspectives link variation in firm positioning and organizational capabilities to differential performance, they less clearly identify the factors that drive variation in firm strategies. Consistent with theoretical work, empirical research identifying and explaining persistent intra-industry strategic heterogeneity is modest, but draws increasing attention.[1]

Recent empirical work examining firm-specific heterogeneity emphasizes characteristics internal to firms over which managers can exert control (e.g., Cockburn, Henderson, Stern, 2000). This paper takes a somewhat different tack, investigating the role of a specific factor, location, that is *external* to the firm in driving firms' strategic organization. Specifically, this paper suggests that characteristics embedded in local geographic regions can influence firms' choices regarding investments in resources, capabilities, and routines. This proposition is consistent with perspectives on the diffusion of organizing technologies, including sociological and economic models (Rosenberg, 1972; Ryan and Gross, 1943; Coleman, et al, 1957; Griliches, 1957), perspectives on regional competitive advantage (Porter, 1990; Saxenian, 1994), as well as views based in organization theory regarding location-specific institutional pressures (Pouder and St. John, 1996; Sorenson and Audia, 2000; Sull, 2001; Baum and Lant, this volume). Each of these views support the proposition that firms' internal organizing strategies may differ as a function of location-specific characteristics that are, at least in the short-run, beyond the control of local firms. Nonetheless, little empirical research systematically relates particular location-specific characteristics to firm organizing strategies – and no study that I was able to identify tests this hypothesis on a large-scale dataset. In this paper, I employ both qualitative and panel

data analysis to assess the extent to which the characteristics of local environments explain organizing strategies in pharmaceutical research facilities.

A number of factors complicate inquiry into the foundations of firm strategic heterogeneity, including the difficulty in understanding – and measuring – critical strategic components of complex organizations and the difficulty in developing theories disentangling the factors that drive their heterogeneous adoption. To make the issue tractable for study in this paper, I investigate a specific firm activity in an industry that antecedent literature has characterized as strategic and has demonstrated to be important to competitive advantage: drug discovery in the global pharmaceutical industry.

Prior research demonstrates that drug discovery productivity in 1980s and 1990s was positively affected by the adoption of organizing strategies that promoted in-house research in basic science and introduces techniques for measuring this key organizational practice (Henderson and Cockburn, 1994, 1996; Gambardella, 1995). In addition, historical analysis (Liebenau, 1985, 1987) and recent qualitative evidence (interviews reported in Cockburn, Henderson, and Stern, 2000) suggest that pharmaceutical firms' scientific orientations vary according to characteristics of their local environments – in particular, according to the strength of the scientific and technical base in their local geographic region. In this paper I investigate the following propositions: (a) that firm-laboratories' drug discovery strategies vary systematically across locations and (b) that the strength laboratories' local scientific and technical bases constitutes one of the key drivers of this variation.

Numerous perspectives on diffusion may explain these propositions. For example, if the costs of adopting a science-oriented approach to drug discovery are lower (and the benefits are higher) in regions in which the availability of science is greater, economic models of diffusion

would expect regional similarities in organizational practices.[2] Views in organizational sociology and organization theory may expect similar results based on the logic that homogenizing pressures operate more strongly within rather than across geographic regions (Sorenson and Audia, 2000; Sull, 2001) – local mimetic pressures to adopt scientific drug discovery may be stronger in the presence of multiple adopter organizations and local normative pressures may be greater in regions with higher concentrations of scientific and technical personnel (see, also, DiMaggio and Powell, 1983).

In order to evaluate the relationship between location-specific external characteristics and internal organizing strategies I employ both qualitative and quantitative methods. The qualitative analysis consists of illustrative case studies of two drug makers of the early 20th century, Sterling and Mulford, which were founded under similar conditions but pursued vastly different strategic trajectories: Whereas the bountiful research resources in its local Philadelphia environment encourage Mulford to invest in expertise in bacteriology and organize for research-driven drug development, the qualities around Sterling's Wheeling, West Virginia headquarters supported a marketing and distribution-driven orientation.

The quantitative analysis uses a panel dataset reflecting the activities of more than thirty firms over the years 1984-1994 to assess the extent to which drug discovery laboratories during this period pursue a science-oriented strategy in drug discovery varies systematically by region and in a way that correlates with measures of the strength of the local scientific and technical base. The data suggest that lab-level scientific orientation does, indeed, vary by region and is positively related to the strength of scientific and technical bases in the region geographically proximate to the focal laboratory.

The simultaneity of firms' location and strategy decisions is a critical issue in examining the relationship between location-specific characteristics and organizing strategy. In this paper, I have identified cases in which evidence suggests that location decisions predate critical strategy choices. I revisit this assumption throughout the paper and urge caution in interpreting the results. I view the case histories of Sterling and Mulford as illustrative of the potential influence of location-bound characteristics on firm organizing strategies. The quantitative data provide evidence of correlation between the strength of the local scientific base and the extent to which drug research facilities organize to incorporate scientific research. These data do, however, provide evidence suggestive of causality. Sterling and Mulford each selected locations before settling on a their particular organizing strategies and location-specific characteristics appear to condition their investment choices. In the quantitative sample, the majority of the drug discovery laboratories existed before the techniques critical to science-driven drug discovery had been diffused and econometric techniques that correct for initial differences in location-specific characteristics imply that changes in the strength of the local science base correlate with changes in lab-level scientific orientation.

On balance, the results imply a systematic relationship between characteristics local to pharmaceutical research facilities and their strategic organization. Whereas previous research examining the role of location has examined agglomeration and the geography of innovation, among other topics, these results suggest that characteristics of local geographic regions may play an important role in the dynamics of firm heterogeneity.

II. Location and Heterogeneity in Firm Strategy

Although strategy research does not possess a generalized understanding of the impulses that drive strategic heterogeneity (Cockburn, Henderson, and Stern, 2000), researchers are devoting increasing attention to this subject. Much of this emerging work explores how firms' internal qualities impact firm strategies and responses to environmental conditions (see, e.g., Holbrook et al., 2000 and Raff, 2000). This research suggests that characteristics such as firms' technical objectives and aptitudes, managerial leadership, and founder characteristics have an important influence on their organizing strategies.

Somewhat differently, I focus in this paper on the influence of firms' external environments on organizing differences. Because of the high fixed costs of facility relocation, external environmental changes may drive strategic change in a way that is exogenous to the firm in the short term. The view that factors external to a firm can influence its internal structure is common to a number of literatures, including institutional theory (Selznick, 1949; DiMaggio and Powell, 1983; Zucker, 1987), resource dependence theory (Pfeffer and Salancik, 1978), as well as rational models of strategic "fit" (Learned, et. al, 1969). Although these perspectives relate environmental characteristics to internal firm structures, they have, until recently, rarely focused on the particular influence of characteristics associated with local geographic regions.

Research in organizational theory and network sociology has been pioneering in investigating heterogeneity among the multiple facilities of geographically dispersed firms (Baum and Greve, 2001). Authors in these literatures emphasize that practices diffuse more swiftly and that learning occurs more quickly among same-firm facilities than across different firms in the same industry (Greve, 1995, 1996, 1998; Baum and Ingram, 1998; Baum et al., 2000). Recent research also predicts that locally proximate organizations will adopt similar practices and strategies. The local density of social contacts enables organizational practices and

innovations to diffuse more swiftly within narrow geographic regions than across great distances (see, e.g., Sorenson and Audia, 2000; Sorenson and Stuart, 2001). Additional writers propose a similar phenomenon, though by a separate mechanism – Porac and Thomas (1990) Pouder and St. John (1996), and Sull (2001) suggest that institutional pressures or locally shared mental models will lead firms within a region to evidence more similarity than firms in other geographic areas.

Consistent with emerging research in organizational theory and organizational sociology, research in international business has historically predicted location- and firm-specific patterns in strategic organizing practices. For example, Soskice (1993) argues that alternative constellations of national institutional arrangements favor particular firm strategies; Whitley (1992) posits that social institutions, broadly-conceived, determine regional business practices; and Kogut (1991) contends that differing diffusion rates within versus across national borders result in firms' capabilities differing systematically across countries. For the most part, these perspectives consider variation at aggregated geographic levels, such as the country or super-national region, as driving firm organizing differences. Empirical tests of such propositions are difficult, however, because such a large number of characteristics vary across country that it is difficult to identify statistically those factors that impact firm strategies.

Additional research in international management considers firm organization at a more narrowly defined unit of analysis. Specifically, authors suggest that local subsidiaries adapt in order to "fit" with the qualities of local demand and culture (Perlmutter, 1969; Brooke and Remmers, 1970; Hedlund, 1986). Empirical research on this issue is, however, mostly qualitative or prescriptive (e.g., Bartlett and Ghoshal, 1989); though interesting, extant larger-

scale data analysis is cross-sectional and does not focus on practices linked with firm competitive advantage (e.g., Rosenzweig and Nohria, 1994, and Robinson, 1995) in the contexts under study.

In the past decade, a wave of research in mainstream economics and management has reemphasized the importance of location in economic activity. This research has focused in particular on explaining industrial location patterns (Krugman, 1991), proposing reasons for location-specific productivity advantages (Porter, 1990, 1998, and Saxenian, 1994), and exploring aspects of the diffusion of knowledge (Jaffe, 1986, and Jaffe, et al., 1993) and the geography of innovation (Feldman, 1994; Audretsch and Feldman, 1996). Recent research building on these efforts investigates heterogeneity within clusters and regions. For example, McEvily and Zaheer (1999) propose that firms within geographic clusters will vary in their capabilities as a function of the strength of their ties to local institutions. In addition, Shaver and Flyer (2000) and Chung (2001) demonstrate that firms have heterogeneous incentives to locate inside (versus outside) of geographically concentrated industry clusters.

This research acknowledges the possibility, as does some research in organizational sociology and organizational theory, that competition may drive firms to be locally different rather than locally similar.[3] Modeling optimal firm location choices, Flyer and Shaver (this volume) show that direct R&D competition in the presence of agglomeration economies can lead to distant rather than collocation. One implication of this is that firms that do collocate may be sufficiently different that their R&D efforts are not strong substitutes. This is consistent with an alternative view in organization theory that suggests that local competition can lead firms to seek out idiosyncratic niches (White, 1981). By these mechanisms, proximate firms may adopt widely varying organizing strategies.

I propose in this paper that location-specific characteristics (at various levels of geographic aggregation) can affect firms' decisions to adopt particular organizing strategies and evaluates a specific theory of how location affects the adoption decision in the context of drug discovery laboratories. I also introduce a novel methodology to isolate measures location-specific influences from firm-internal influences by considering the firm-facility (rather than the entire firm) as the unit of analysis. The view I propose in this paper is consistent with a number of explanations reviewed above. It is, however, primarily motivated and most similar to research in the economics of the diffusion of production technologies (Griliches, 1957) and historical explanations of the introduction of mass production technology in the United States (Rosenberg, 1972, 1981; Wright, 1990; and Romer, 1996). Specifically, I propose that firm facilities adopt organizational practices according to calculations of the relative costs and benefits of adoption and that this calculation varies according to characteristics of local (as well as more broad) geographic region in which they are located and the remainder of the firm (see Figure 2).

III. Location and Scientific Orientation in Drug Discovery, 1880-2000

Throughout the history of the modern pharmaceutical industry, firms have differed with respect to the extent to which they incorporated scientific pursuits into their research efforts (Liebenau, 1987). In the early years of the industry, this distinction was quite stark: While some firms employed scientists in the search for effective drugs to fight disease, others designed product lines exclusively around combinations of traditional remedies or "snake oils" without exploring their relationships to human physiology. As the state of science progressed and industrial research laboratories developed, the distinction between more and less science-oriented pharmaceutical firms evolved and the geographic sources of science migrated.

Over the course of the 20th century all major pharmaceutical firms established facilities that applied the scientific method in the search for medically active molecules. Nonetheless, substantial differences persisted in the extent to which firms invested in R&D and maintained connections to the scientific community. No company has epitomized the science-oriented firm as consistently as Merck. In the decade between 1946 and 1956 five Nobel Prize winning-scientists were among those who worked closely with Merck and in 1957 the firm accounted for more than 10 percent of total U.S. pharmaceutical research expenditures (Mahoney, 1959, p. 192).

Whereas incorporating scientific processes and personnel into research efforts has proven a viable and often superior strategy for developing new drugs, an emphasis on scientific R&D has not been the singular strategy for success in the industry. Numerous firms expanded rapidly and maintained high levels of profitability over long periods of time by emphasizing alternative capabilities, such as manufacturing, marketing, or distribution. For example, Wyeth Company "never developed a reputation for scientific research or for introducing new medicines, but it did use advanced tableting machines which allowed it to supply convenient dosages of the most popular preparations" (Liebenau, 1987, p. 103).

By the late 1900s, many pharmaceutical firms had developed networks of research laboratories located in North America, Europe, and Asia, often concentrated in geographic clusters (Furman, 2001 and Chacar and Lieberman, this volume). During the final two decades of the century, scientific and technological advances dramatically increased the value of basic science to drug discovery efforts and most firms increased their commitments to scientific inquiry. Nonetheless, important differences remained in the extent to which firms supported *basic scientific research* as part of their internal drug discovery efforts (Henderson and

Cockburn, 1994; Gambardella, 1995). For example, although some firms encouraged their researchers to push the borders of molecular biology and combinatorial chemistry, others preferred that their staff concentrate on tasks more directly related to the search for new drugs.

This paper proposes that location plays an important role in the extent to which pharmaceutical firms incorporate science in their drug discovery efforts. On one hand, national and super-national regional characteristics, such as the nature of health care regulatory systems and other regulatory institutions may be important factors driving these differences. For example, Thomas (1994) and Trumbull (2000) argue that pharmaceutical firm behavior responds to incentives implicit in the regulatory and institutional environments in countries such as France and England. Kyle (2002) demonstrates that price control regulation affects firms' market entry decisions. Determining the influence of national characteristics on firm behavior faces a small-numbers problem, as many key characteristics are country-specific. Evaluating data at more precise geographic levels enables research to identify the influence of the characteristics that vary across local regions. In this paper, I propose that the extent to which firms incorporate science in their drug discovery efforts is correlated with the strength of the scientific base in the local geographic regions in which they operate. I hypothesize that regions that offer extensive scientific resources, such as universities, government laboratories, or collections of private, science-oriented firms, will be more likely to generate science-oriented firms than are those with more limited scientific assets. I expect that high science regions would both attract more science-oriented facilities and also that changes in the strength local science bases would be reflected in the scientific orientation of existing local facilities. I attempt to distinguish these effects in the both the qualitative and quantitative section in order to ascertain whether the result is driven by endogenous location choice, in which firms match the choose locations whose

characteristics match their strategies, or whether the relationship is causal, such that exogenous changes in the local science base would yield adjustment in the organization practices of local laboratories.

A number of theories would predict these outcomes: For example, the enhanced speed and quality of communication that comes from locating drug discovery operations in regions with a high density of researchers may lead to direct productivity gains (Saxenian, 1994; Cohen and Levinthal, 1990; Sorenson and Stuart, 2001). Alternatively, productivity gains may arise in a more indirect way if drug discovery facilities in "high science" regions can acquire the services of higher quality researchers more cheaply (Stern, 1999). In addition, local institutional pressures may drive co-located laboratories to adopt similar organizing strategies (e.g., Sull, 2001). Because multiple theories predict a relationship between location-bound characteristics and lab-level organizing strategy, I focus in this paper on evaluating the phenomenon rather than distinguishing theories of its origin.

IV. Historical Case Comparison: Sterling vs. Mulford, 1880-1918

This section compares the historical development of organizing strategies and capabilities of two pharmaceutical firms, Sterling and Mulford. Sterling and Mulford were two of the most successful pharmaceutical firms of the early 20th century. They were founded at approximately the same time by individuals who graduated from the same academic institution and founded firms in their respective hometowns to sell products advertised to cure medical ailments. I have selected the cases to be illustrative of the phenomenon and to constitute an instructive quasi-experiment: The firms are therefore similar on many observable dimensions but vary with respect to the treatment dimension – location.

Sterling Drug

The company that became Sterling Drug was founded at the turn of the century by William E. Weiss and Albert Diebold. Weiss, who was the firm's primary leader over the coming decades, graduated from the Philadelphia College of Pharmacy (PCP) in 1896. After working for a few years in retail pharmaceuticals, he returned to his hometown of Wheeling, West Virginia and entered into business selling patent medicines with his childhood friend Albert Diebold (Mann and Plummer, 1991). The partners called their new enterprise the Neuralgyline Company, after the firm's first product, neuralgine, which they advertised as a palliative (Mahoney, 1959).

The turn of the century was a generally exciting time in American business, and few industries were as fanciful and imaginative as the patent remedy trade. Somewhat counter-intuitively, patent medicine makers rarely sought patents on the contents of their products, which were often alcohol or narcotics-based combinations of existing drugs and vegetable extracts. The term "patent medicines" derives from some early manufacturers' efforts to patent their formulations in order to gain prestige.[4] Though their scientific bases were unproven (or dubious, at best), such products were extremely popular with consumers and often physicians. Although patent medicine makers could not sell their products on the basis of established efficacy, they were surely among the country's foremost innovators in marketing, advertising, and distribution.

Weiss and Diebold swiftly became leaders in this burgeoning industry segment. Selling from horse-drawn carriages, the industrious pair canvassed the West Virginia countryside, earning $10,000 in their first year of business (Mann and Plummer, p. 50). Prudently, the proprietors reinvested every dollar of their earnings in the company's operations – although not in the traditional way. Rather than reinvesting in physical capital, the owners applied the entirety

of their net income towards the purchase of advertising in two Pittsburgh newspapers. Their promotion-driven strategy proved wildly successful. In only five years the business grew from its $1,000 initial investment into a company valued at half a million dollars. The company's successes facilitated the acquisition of other patent medicine firms, one of which, Sterling Products, gave Weiss and Diebold's organization its new name. By 1912 the firm had achieved a value of $4 million and, based on brand recognition and the strength of its promotional and distributional capabilities, had become the country's foremost patent medicine conglomerate (Mann and Plummer, 1991).

Sterling's greatest success, however, was yet to be realized. In the aftermath of World War I, the United States Office of the Alien Property Custodian offered for auction the seized U.S. assets of the Bayer Company, the Germany chemical and pharmaceutical giant that had invented aspirin. Bayer had developed aspirin into one of the most successful medical products of its time (and, indeed, of the entire twentieth century). Protecting its sales from counterfeiters and preparing for aspirin's patent expiration, Bayer had invested significantly in branding its medication. As a result, the Bayer cross was a widely recognized icon in North and South America as well as Europe (Mann and Plummer, 1991). At the time of the auction, the brand capital associated with the Bayer name and aspirin trademark were among its most valuable assets, although the company also possessed more than 60 other pharmaceutical products. Dozens of drug makers, banks, and other interested parties participated in the auction, driving the purchase price of Bayer's U.S. assets to just over $5.3 million before the only remaining bidder was Wheeling, West Virginia's Sterling Products.

That Sterling found it worthwhile outbid substantially larger firms like Dupont in order to acquire Bayer's assets is a striking display of its confidence in its marketing and distribution

capabilities – particularly in light of the fact that Sterling's skills in drug-making were so amateurish that it was forced to expend substantial resources soliciting assistance from Bayer simply to manufacture the products, including aspirin, that it had acquired (Mann and Plummer, 1991). With the assistance of the aspirin plant's former owners, Sterling did manage to produce its prized, new product. As the company had projected, Sterling's aspirin business flourished for decades by leveraging its strengths in marketing and distribution.

H. K. Mulford & Company

Like the tale of Sterling Drug, the story of the H. K. Mulford Company begins at the Philadelphia College of Pharmacy (PCP) towards the end of the 19th century. PCP graduates and Philadelphia natives Henry K. Mulford and Milton Campbell founded the firm in 1891, re-organizing and re-incorporating the pharmacy that Mulford had operated after purchasing downtown Philadelphia's "Old Simes" drugstore from his previous boss (Galambos, 1995).

The fledgling firm's first major successes included the development and patenting of a compressed tablet machine, which facilitated mass-production and widespread sale of water-soluble pills, and a further expansion of their medical products and pharmaceutical preparations. Emboldened by their early achievements, the young firm decided to explore a more aggressive project – the synthesis of diphtheria antitoxin.

The effort to synthesize diphtheria antitoxin was particularly ambitious since neither Campbell nor Mulford had sufficient training to participate in the development of the product. Instead, the entrepreneurs responded to their local market in deciding to focus on diphtheria and hired locally available expert researchers to lead the initiative.

As a result of increased density of urban life, bacteriologic illnesses had become increasingly problematic in metropolitan areas. These problems (sometimes referred to as "***The*** Social Problem" of the day) were most pronounced in New York City, whose Public Health Department was an active participant in the community of researchers seeking cures to urban diseases. As the country's third largest city, Philadelphia was also victimized by such problems. Its Municipal Health Department was particularly wary of diphtheria. It had been widely circulating news about the illness and endeavoring to synthesize antitoxin to fight the disease. The city also possessed leading American research institutions, including the University of Pennsylvania, Medico-Chirurgical College, and Pepper Clinical Laboratories of the University Hospital. In the late 1800s, each of these institutions established facilities to conduct research and teach the methods of bacteriology and the Municipal Health Department soon followed suit. (Galambos, 1995; Liebenau, 1987).

Mulford boldly issued new equity in order to finance its own "Biological Laboratory," which it then staffed with faculty from numerous University of Pennsylvania departments. Many of these researchers had connections to researchers in Europe and the New York City Health Department, whose efforts to synthesize diphtheria antitoxin were more advanced than those of any American firm. Led by Joseph McFarland, who had accumulated extensive experience studying pathology and bacteriology in Germany and with the assistance of their network of researchers, Mulford's laboratory was able to successfully produce antitoxin and in 1895 became the first commercial establishment to offer the serum for sale. Its claims of purity and efficacy were bolstered by its having the University of Pennsylvania's Laboratory of Hygiene test the serum regularly for efficacy and safety. Following this tremendous success, Mulford opened a

larger, dedicated laboratory facility and continued to invest in its relationships with university researchers, governmental institutions, and the medical community.

Over the next quarter century, Mulford drew upon those resources to develop substantial in-house capabilities in bacteriology. Though the company also developed considerable expertise in distribution and marketing, particularly in educating the public about its medications (Liebenau, 1987), "the quality of its research, production, and standardization … was the major way Mulford attempted to differentiate itself from its competitors" (Galambos, 1995).

Synthesis: Location and Organizational Strategy in Drugmaking, 1880-1918

Sterling and Mulford were both founded by clever, assiduous entrepreneurs who led their companies to success in drug-making in the early part of the 20th century. Each was founded at around the same time by graduates of Philadelphia College of Pharmacy – each of which was schooled in the business of drug-making but not sufficiently trained to discover and develop therapeutically-active medications. The histories of these two firms suggests that location – i.e., the characteristics of the locations in which these firms operated – was a principal factor driving the strategic profiles adopted by these firms.

The characteristics of Sterling's Wheeling, WV location during the early 20th century were such that the costs of adopting an research-driven strategy would have been relatively high, while the benefits would have been relatively low. Sterling's Wheeling, West Virginia was a small in 1890, compared to other U.S. cities. (With a population less than 35,000, Wheeling ranked behind cities such as St. Joseph, MO and Covington, KY; U.S. Bureau of the Census, 1988.) The largest nearby city, Pittsburgh, into which the firm sought to expand after its initial successes, was also small by the standards of New York and Philadelphia. (Although Pittsburgh

was among the country's fifteen largest cities, its population of nearly 240,000 was less than one-fifth that of Philadelphia and one-tenth that of New York at the time.)

Wheeling's small size and relatively rural surroundings led it to have both a lesser ability to supply research-driven drugs and a lower demand for them. Wheeling lacked both a major medical research facility and a public health system that was organized to develop innovative medicines.[5] Because frontier-level medical research knowledge diffuses slowly across distances (Jaffe et al, 1993) and often requires the large-scale research facilities or local expert researchers (Zucker, Darby, and Brewer, 1998), the costs of the leading-edge knowledge required for a research-driven approach to drug-making was relatively higher in Wheeling, WV than in locations rich in such resources. At the same time, because of Wheeling's relatively low population (and, more importantly, population density), the demand for medications to treat bacteriological illness, which were the few illnesses for which leading-edge science was developing cures, was lower than in cities with high population densities.

Although the costs and benefits research-driven drug-making may have been higher in urban areas, this was not the case for advertising- and marketing-driven patent medicines. Patent remedies had historically high demand in rural areas, and their appeal was facilitated by emerging advertising opportunities in newspapers and other print media (Mann and Plummer, 1991). Thus, the local Wheeling environment contained the key resources Sterling required to organize itself around the production and distribution of patent-medicines, but lacked the resources most essential to a research-driven approach to making drugs.

By contrast, Mulford's Philadelphia home was the "Cradle of Pharmacy" during this period (Mahoney, 1959) and its region provided extensive resources for medical innovation (Feldman and Schreuder, 1996). The city boasted numerous medical research organizations

(including the University of Pennsylvania), German-trained researchers, an active public health service, and a population in acute need of relief from the infirmities associated with urban life. In this environment, the cost of embracing scientific techniques was greatly reduced (particularly relative to rural West Virginia), while the potential benefits were substantially higher. It is not surprising, therefore, that a Philadelphia-based company would follow a strategy designed around research capabilities.

It is important to note, however, that heterogeneity existed within Philadelphia at this time regarding the extent to which firms embraced science. While some Philadelphia firms, including Smith Kline, followed strategies similar to Mulford's, others, such as Wyeth, followed less research-oriented paths (Liebenau, 1987). Further, Philadelphia and New York were not alone in fostering science-oriented firms at the beginning of the twentieth century. For example, Detroit's Parke-Davis and, to a slightly lesser extent, Indianapolis's Lilly were also among the early firms that embraced medical science. The suggestive evidence from an historical review of firms during this time is that the probability of adopting a science-oriented strategy appears to be positively affected by factors external to the firm, but embedded in the geographic region proximate to the firm – most notably, by the quality of the region's medical research institutions. Parke-Davis, Mulford's early competitor in the diphtheria antitoxin market, benefited greatly from cooperation with researchers from the University of Michigan, whereas Lilly formed strong relationships with Purdue's nearby School of Pharmacy. The remainder of the paper investigates this phenomenon in a more formal way, considering the case of drug discovery laboratories in the late 20th century.[6]

V. Investigating the Relationship between the Local Science Base and Laboratory Scientific Orientation

Overview

In the following two sections, I investigate the relationship between location-specific characteristics and drug discovery laboratories' organizing strategies in the late 20th century. Previous research on this time period has characterized the nature of science-oriented drug discovery, identified its importance to research productivity, and introduced quantifiable measures reflecting its extent – at the firm level (Henderson and Cockburn, 1994; Cockburn, Henderson, and Stern, 2000). Specifically, I introduce in this section an econometric methodology that measures the relationship between the characteristics of local geographic regions and the organizational practices of resident drug discovery facilities. Relying on an output-oriented measure of laboratory organizational practices, the methodology tests whether the scientific orientation of drug discovery facilities varies systematically across regions and, if so, whether it varies positively with the strength of the local scientific and technical base. To do this, I conduct the analysis at the level of the *firm-laboratory* (rather than the *firm*) and employ a panel dataset. This enables the analysis to exploit variation both within firms as well as across firms and within and across regions. Further, by allowing us to compare the results that obtain in cross-section analysis with those that are robust to changes over time, the panel enables more precise measurement of the causal influence of changes in location-specific qualities on changes in laboratory organizing practices.

Data sources and measures

I have assembled for this project a dataset that chronicles research outputs for thirty-two global pharmaceutical firms over the time period 1984 to 1994. (A complete list appears in Appendix Table 1.) Sample firms were chosen in order to be representative of the population of the world's largest research-intensive pharmaceutical concerns. The sample includes at least one firm from each major pharmaceutical-producing country, including companies headquartered in Europe, Japan, and North America. Twenty of the sample firms were among the world's thirty largest pharmaceutical companies in 1998 (as measured by R&D spending); these twenty firms accounted for more than 70 percent of the total R&D spending of the "top 30" in that year (Mathieu and Foster, 1999). Thus, the sample captures the majority of R&D production by the universe of firms whose organizing strategies might be affected by local conditions.

The size of the firms in the sample and the importance of R&D to their performance suggests attention to the exogeneity of lab location decisions and the extent to which laboratories may alter the characteristics of their local environments. I attempt to address these issues in the econometric analysis by controlling for lab fixed effects and initial conditions; in addition, a number of characteristics of the data suggest that these problems might not be severe. First, the research techniques that increased the value of science-driven drug discovery began to diffuse widely during the sample time frame (Henderson and Cockburn, 1994; Gambardella, 1995). In addition, nearly all of the laboratories in the sample had been in operation for many years prior to the advent of science-driven drug discovery and firms opened or re-located very few laboratories during this period.[7] Thus, it appears unlikely that firms chose the locations of the sample laboratories in a way that was co-determinate with the extent to which they intended to embrace science-driven drug discovery. This is, however, in part confounded by the possibility of longer-term path dependence – that those areas in which research-driven research in the early part of the

century also became the areas in which the local science base most strongly supported science-driven drug discovery. This is difficult to examine empirically in this study, but there is evidence both supporting and refuting this hypothesis. While the local science base in the Philadelphia-New Jersey area remains relatively strong at the end of the 20th century, as it had been during the early part of the century, the scientific bases around Lilly (in Indianapolis) and the former headquarters of Parke-Davis (in Michigan) have lost in relative strength.

The data used to construct measures of laboratory, firm, and region scientific orientation are drawn from the U.S. Patent and Trademark Office (USPTO) and the Institute for Scientific Information's Science Citation Index (SCI). Supplementing those data are measures that describe characteristics of the local scientific and technological bases in the regions geographically proximate to focal laboratories. Table 1 describes the measures used in the paper and Table 2 presents summary statistics. Although much previous location-oriented research is conducted at the national level (or state level within the United States), I focus on sub-national, sub-state regions. Specifically, I perform much of the analysis using the regions within the 35-mile radius of the focal laboratory (using exact lab and city latitudes and longitudes and correcting for the curvature of the earth). I also consider alternative regional units, however, including metropolitan statistical areas (MSAs) in the United States and NUTS regions in Europe. (I describe NUTS regions in the subsection on location-specific factors below.)

Modeling laboratory-level scientific orientation

To measure drug discovery laboratories' scientific orientation, I employ a variable that reflects the lab's scientific outputs, which constitute one manifestation of a laboratory's pursuit of a science-driven approach to drug discovery. This measure, labeled PUBFRAC, reflects the

fraction of pharmaceutical researchers whose names appear on a patent who are also authors on papers published within two years of the worldwide patent application date (Cockburn, Henderson, and Stern (2000) introduce this variable as a firm-level construct; see also Furman (2001) for a more complete description of the variable). PUBFRAC reflects the extent to which a laboratory includes researchers who are actively engaged in the search for new molecules that also participate in the basic scientific activity of publishing academic articles. By employing this variable, I sacrifice the precision with which I capture laboratory organizational practices in favor of gaining the ability to compare laboratory practices across a large number of firms and locations throughout the world.

The data used to compute PUBFRAC consist of patents granted by the U.S. Patent and Trademark Office (USPTO) and publications data recorded by the Institute for Scientific Information's Science Citation Index (SCI). The SCI catalogues publications in nearly five thousand international academic and industry journals, identifying, among other relevant characteristics, authors' names and addresses (which often specify institutional affiliations).

I have identified firm laboratories by reviewing company documents (including web pages), semi-structured interviews with industry experts, and with a careful review of the address fields of the patenting and publications data. Figure 3 identifies drug discovery laboratories in the United States and Europe for all firms in the sample. Over the course of the sample period, 107 laboratories appear in the analysis. These operate in 14 different countries in North America, Europe, and Japan. Forty are located in 14 different states in the United States (13 labs are in the Pennsylvania-New Jersey corridor). Nineteen laboratories are in the UK and seven are in Japan. Consistent with Chacar and Lieberman (this volume), the number of laboratories per firm increases over time, particularly as a consequence of merger activity.

Geographic information in the USPTO and SCI data enable patents and publications to be assigned to the laboratories of their origin. Unfortunately, neither data source directly identifies source laboratories and a number of the features of these data complicate the simple attribution of papers and patents to drug discovery laboratories. First, the SCI dataset lists each of the authors and each of the unique addresses associated with a particular paper separately, but does not match authors to their addresses. Second, patent data identify inventors' home addresses rather than their institutional addresses. Institutional addresses are provided for patent assignees (the companies in which inventors work), but these often refer to company headquarters rather than the particular laboratory in which the relevant research occurred. As a result, it is necessary to infer researchers' laboratory addresses via a complex matching algorithm. In brief, the algorithm uses mapping software to match researchers to the nearest firm-laboratory within a 50 mile radius of the inventor's home.[8]

Laboratory scientific orientation, PUBFRAC, is computed as the fraction of individuals associated with laboratory *i* who are listed as inventors on a USPTO patent and who are also listed as authors on a paper in the SCI within two years of the patent application. Mean PUBFRAC is 0.437.

I model the scientific orientation of the focal laboratory as a function of the scientific orientation of the remainder of its firm as well as characteristics its local regions, controlling for time, and assuming randomly distributed errors. The basic empirical model takes the form:

$$(1)\ \text{PUBFRAC}_{ijt} = \beta X_{-ijt} + \gamma Y_{-jrt} + \delta Z_{ijrt} + \varepsilon_{ijrt},$$

where PUBFRAC reflects the scientific orientation of laboratory *i*, in firm *j*, in year *t*; *X* represents a vector of firm-specific influences; *Y* represents a vector of location-specific influences; and the vector *Z* captures various lab, firm, and time controls. (The subscripts *–i* and

–*j* indicate all firm laboratories other than lab *i* and all firms other than *j*, respectively.) Consistent with previous research, I assume separability among the effects in the primary specification. In the empirical analysis, I examine the robustness of this assumption to alternative specifications of the functional form. As specified, (1) also assumes that the impact of *X* and *Y* on PUBFRAC are contemporaneous; however, I also evaluate models in which the influences on PUBFRAC are lagged.

Influences on Lab Organizing Strategies: Firm-specific factors and indicators of the strength of the local scientific and technological base

Firm-specific factors:

Firm-specific influences are captured by FIRM PUBFRAC, which reflects the average PUBFRAC for all of the *other* laboratories in the focal firm. In order to identify the relationship between location-specific effects and laboratory-level scientific orientation, it is important to "net" out the impact of firm membership on the focal laboratory. As a result, FIRM PUBFRAC is included in all of the models.

Location-specific factors:

The historical case studies presented in Section IV suggest that a number of location-specific factors associated with the strength of the scientific and technological base, including local research institutions, qualities of the labor market, and supply and demand characteristics, are important determinants of the extent to which a region supports in-house research efforts incorporating basic science. In addition, similar to the findings of Zucker and Darby in biotechnology (1997, 1998), the case histories imply that these factors operate within quite narrowly circumscribed geographic regions. As a result, the dataset concentrates on measures reflecting the strength of the scientific and technical base at the local geographic level,

corresponding either to areas within a radius around the focal laboratories or to the MSA in the United States and NUTS regions in Europe.

I measure the strength of the local scientific and technical base in three ways: The first measure, LOCAL PUBLICATIONS, reports the total number of Science Citation Index (SCI) publications that attribute authorship to an address within a thirty-five mile radius of the focal laboratory (subtracting those attributable to the focal laboratory).[9] For example, LOCAL PUBLICATIONS reports for Ciba-Geigy's Basel laboratory the annual number of (identifiable) SCI publications that list an address corresponding to a location within 35 miles of Basel, regardless of whether these are Swiss, German, or French authored publications. LOCAL PUBLICATIONS varies greatly by location. For example, for labs near London, England, such as Amersham's headquarters lab in Amersham, Buckinghamshire and Glaxo's Ware laboratory LOCAL PUBLICATIONS is slightly less than 40,000; by contrast, non-firm LOCAL PUBLICATIONS number fewer than 2,500 for Lilly's Indianapolis headquarters. It is important to note that LOCAL PUBLICATIONS includes *all articles* in the Science Citation Index, not only those relevant to pharmaceutical research. In addition, the limits of computing power require some heuristic simplifications in order to calculate LOCAL PUBLICATIONS. This variable is likely to measure the underlying concept with some noise – it is therefore less likely to identify an existing relationship in the data.

The second measure of the strength of the scientific base reports the counts and densities of scientists and engineers (S&E) by laboratory region. As administrative agencies' efforts to collect S&E data at sub-national levels of aggregation have only recently begun in earnest, the availability of useful data is limited. For this dataset, I have been able to compile data for laboratory-regions in the United States and Europe, but not for Japan. For the United States,

sub-national employment counts by occupational group are available from the decennial census's Equal Employment Opportunity files. I therefore collected MSA-level data from the 1980 and 1990 census.[10]

A recent European Union (EU) effort compiles national and regional economic and social data collected by national statistical agencies in the New Cronos database. Science and technology data, including counts of scientists and engineers are among the categories of data collected. U.S. regional data distinguish scientist from engineering employment; the EU data do not. Regional data are disaggregated within countries according to various levels of NUTS (Nomenclature of Territorial Units for Statistics) regions. The level of aggregation each NUTS level differs somewhat across countries: For example, the NUTS-1 level includes 77 entities, which correspond to states (*Länder*) in Germany and "standard regions" in the United Kingdom. On balance, NUTS-1 levels are somewhat larger than U.S. MSAs (although they are smaller than U.S. states).[11] The 203 regions at the NUTS-2 level include districts in Germany (*Regierungsbezirke*) and "groups of counties" in the U.K. In terms of geographic scope, these are more similar to the size of U.S. MSAs than are NUTS-1 regions.

In addition to specifying the geographic scope of NUTS regions somewhat differently, countries vary in the regularity and precision with which they report scientist and engineering data by NUTS level. For example, Denmark reports S&E employment in every odd-numbered year from 1985 to 1995 at both the NUTS-1 and NUTS-2 level, whereas the U.K. reports data disaggregated by NUTS-1 region only for 1993 and not at all for NUTS-2 regions. As the NUTS-1 data are more complete, the empirical results section reports only estimates made using these data; it is useful to note, however, that similar results obtain on analysis in which NUTS-2 data are used where available. Where necessary, data have been imputed for missing years.

The United States's efforts to systematically collect scientist and engineering data by local geographic regions are also in an early stage. The National Science Foundation (NSF) reports state-level estimates of scientists and engineering employment only for the most recent years. Historical estimates can be obtained, however, by converting data from the Census Bureau's Equal Employment Opportunity files, which are available for 1980 and 1990. These report employment by occupation (disaggregated by gender, race, and ethnicity) for all MSAs in the year of the census. As definitions appear to change from the 1980 to 1990, I use data only from the 1980 census, which includes the count of scientists by MSA.

I normalize both the European and U.S. human capital data by the population in their regions in order to be reflect the intensity of human capital devoted to the scientific and technical base. The variable for Europe, labeled S&E/POP–EU, reflects the annual number of scientists and engineers per 10,000 population in each NUTS-1 year. The variable for the United States, SCI/POP–US1980, reflects the number of scientists per 10,000 population in each MSA in 1980. The fact that the data include engineers as well as scientists is apparent when comparing summary statistics. Whereas SCI/POP–US1980 averages only 2.8, the mean for S&E/POP-EU exceeds 10.6.

Some of the most science-intensive MSAs in the United States are in Connecticut. For example, Bristol-Myers Squibb's Wallingford, CT laboratory and Pfizer's Groton, CT laboratory are in MSAs with that average more greater than 4.4 scientists per 10,000 persons in the early 1990s . At the lower end of the scale, Miles-Sterling's Wheeling, WV laboratory lies in an MSA that averages approximately 1.0 scientists per 10,000 persons. In Europe, London, England and Frankfurt, Germany are among the regions with the highest S&E intensity. Each of these regions averages more than 10.0 scientists and engineers per 10,000 residents in the early 1990s and each

hosts laboratories from multiple firms. By contrast, the region around Glaxo's Verona, Italy laboratory averages only approximately 2.2 scientists and engineers per 10,000 residents during this period.

As a final indicator of the strength of the local scientific and technical base, I examine the explanatory power of counts of U.S. Patent and Trademark Office patents in the region within the 35 mile radius of the focal laboratory, LOCAL PATENTS, which I compute in a manner similar to that described for SCI publications. Total patents (PATENTS), as well as patents listed in USPTO chemical classes (CHEM PATENTS), and patents attributed by the USPTO to university inventors (UNIV PATENTS) are considered separately in the analysis. Whereas SCI publications are often used as indicators of scientific progress, patents are more closely related to technological advance. A measure that emphasizes the technical base provides a useful check on the results obtained from publications and S&E data and is of interest on its own. The variation in LOCAL PATENTS across locations is similar to that for LOCAL PUBLICATIONS: Over the sample period, the database includes an annual average of more than 12,000 inventors from the region surrounding the Yamanouchi and Bristol-Myers laboratories in Tokyo, Japan, but fewer than 50 inventors per year from the area around the Organon facility in Newhouse, Scotland.

VI. Empirical Results

Tables 3 though 7 report the paper's empirical results. Taken together, the results provide evidence that the scientific-orientation of a focal laboratory is positively and significantly correlated with the strength of the scientific and technical base in its local geographic region over the sample period. The models in Tables 3 through 5 use OLS, which

allows for the most straightforward interpretation of the findings. Table 6 demonstrates the robustness of these results to alternative assumptions about functional form. Supplementing the laboratory-level analyses in Tables 3-6, Tables 7 and 8 present additional exploratory analyses at the firm and regional level.

Laboratory-level analysis

The first model examined in the paper, (3-1), establishes that both firm and location effects are statistically significant and quantitatively important predictors of LAB PUBFRAC. The coefficients on FIRM PUBFRAC and REGION PUBFRAC are similar to elasticities. For example, the coefficient on FIRM PUBFRAC implies that nearly 22 percent of differences in the scientific orientation of other firm laboratories are reflected in LAB PUBFRAC. Relative to a laboratory whose FIRM PUBFRAC is at the mean, a lab whose FIRM PUBFRAC is one standard deviation above the mean will receive a boost in predicted LAB PUBFRAC of 3.8 percent. (This is equal to the coefficient on FIRM PUBFRAC, 0.218, multiplied by the standard deviation of FIRM PUBFRAC, 0.174.) In this model, as in the rest of the models in this paper, I control for intertemporal differences in PUBFRAC by employing year fixed effects. In nearly every specification, these are significant and increasing over time.

The remainder of the models in Table 3 examine the sensitivity of laboratory-level scientific orientation to regional and country effects. Equation (3-2) adds to the base model of (3-1) dummy variables for representing each country in which drug discovery labs are located and tests the joint restriction that the coefficients associated with these regions are zero. The set of country fixed effects is significant. These measured differences suggest that lab-level scientific orientation varies significantly across country; it is possible, however, that country

dummies proxy for differences in the way the components of PUBFRAC are measured across countries. The significance of regional and country effects in (3-3) and (3-4) demonstrates that scientific orientation differs systematically across countries as well as across regions within country.

The models in Table 3 demonstrate that observed laboratory scientific orientation varies across locations, but do not identify factors that drive these differences. The specifications in Table 4 explore the hypothesis that characteristics of the scientific and technical base in the area around a focal laboratory have an influence its scientific orientation. A number of indicators of the local scientific and technical base are significant in explaining LAB PUBFRAC. Throughout the paper, these variables appear in logarithmic form; as a result, their coefficients are similar to elasticities.

In (4-1), ln(LOCAL PUBLICATIONS) is insignificant, though of the expected sign. This variable does demonstrate significance in later models on a set of interesting sample sub-groups. In (4-2), ln(LOCAL CHEM PATENTS) enters positively and significantly, while ln(LOCAL UNIV PATENTS) enters negatively. The result for ln(LOCAL CHEM PATENTS) matches with expectations, although the effect for ln(LOCAL UNIV PATENTS) is the opposite of that hypothesized. The sensitivity of LAB PUBFRAC to UNIV PATENTS is greater than that to CHEM PATENTS, but since the mean value of CHEM PATENTS is substantially larger than the mean for UNIV PATENTS, the effective impact of local university patenting on lab-level scientific orientation is less than that of local chemical patenting. Equation (4-3) includes variables reflecting the concentration of scientific human capital in US and European regions. Both ln(S&E/POP-EU) and ln(SCI/POP-US1980) are found to positively affect LAB PUBFRAC. The elasticity of the US measure greatly exceeds that for Europe. This is not

surprising, however, as the European measure includes scientists and engineers and the US variable records scientists only.

The final model of the table (4-4) includes each measure of the scientific and technical base. Measures reflecting the technically trained workforce and university patenting remain significant in the analysis, although chemical patenting and local publication are insignificant. Although the impact of ln(LOCAL UNIV PATENTS) is small relative to the other measures of the scientific and technical base, its unexpected sign is confounding. This may reflect substitution between university commercialization efforts and laboratory scientific efforts. In the main, however, these findings suggest a positive relationship between the strength of the local scientific and technical base and the extent to which laboratories adopt science-oriented practices.

Models that explore the robustness of the core findings to various laboratory characteristics underscore this relationship in Table 5. Specifically, equations (5-1), (5-2), and (5-3) demonstrate a significant and positive relationship between ln(LOCAL PUBLICATIONS) and LAB PUBFRAC for headquarters laboratories, home country laboratories (as opposed to foreign subsidiaries), and large laboratories (those with annual patents greater than the median). That both the magnitude and the significance of LOCAL PUBLICATIONS is substantially greater for these sample subgroups suggests that they are more sensitive to the characteristics of the local science base than the overall population of laboratories. This is consistent with prior research in international management emphasizing the differential roles played by different laboratories (Frost, 1998; Kuemmerle, 1999).

Equation (5-4) examines the robustness of the results to the inclusion of laboratory fixed effects. Adding laboratory fixed effects imposes a "high bar" on additional variables, requiring

that intertemporal variation be sufficient to identify a significant effect. FIRM PUBFRAC does remain significant in this model and, although ln(LOCAL PUBLICATIONS) remains positive, it is significant only at the 15 percent level. In an additional model including laboratory fixed effects and S&E intensity (not included in the tables), S&E/POP-EU enters positively and significantly, suggesting that intertemporal changes in the technical workforce may drive increases in laboratory scientific orientation (at least in European laboratories). This model is the most restrictive in the analysis and go the longest way towards mitigating potential endogeneity problems.

The next table in the econometric analysis, Table 6, explores the robustness of the results to alternative specifications of (1). Equations (6-1) and (6-2) correct for initial conditions in various measures of local characteristics. In so doing, they attempt to separately identify the impact of cross-sectional and intertemporal influences on LAB PUBFRAC. Interestingly, in each model, all measures of initial conditions (i.e., the values of the local characteristics in 1984) are insignificant, although some time-varying measures enter significantly. For example, the coefficient on ln(LOCAL CHEM PATENTS) and ln(LOCAL CHEM PATENTS-1984) in (6-1) implies that the level of LAB PUBFRAC is not determined by the initial level of LOCAL CHEM PATENTS but does respond to different levels of LOCAL CHEM PATENTS over time.

To account for the mass of observations where LAB PUBFRAC equal zero or one, equation (6-3) estimates a two-sided Tobit model. The results for this specifications are similar to those obtained in previous tables, particularly for the scientific and technical workforce measures. Equation (6-4) modeling laboratory scientific orientation according to an S-curved diffusion process. The results of this model also resemble those of core models. Although the core results demonstrate robustness to these alternative specifications, they weaken when the

relationship between LAB PUBFRAC and measures of the scientific base are lagged. (These models do not appear in the Tables, but are available from the author.) This implies that the relationship between lab scientific orientation and the strength of scientific base is contemporaneous.

Firm-level analysis

Whereas the previous tables examine the influence of the local scientific and technical base on organizational practices at the laboratory level, Table 7 explores their influences at the firm level. Specifically, the models in Table 7 examine the overall firm profile as a function of the weighted average of the qualities of the locations in its laboratories are located. In so doing, it inquires whether overall *firm* strategies respond to conditions local to the firm's multiple facilities. Table 7 uses FIRM PUBFRAC as the dependent variable, where FIRM PUBFRAC is computed as the firm-level equivalent of LAB PUBFRAC. Equations (7-1) and (7-2) model FIRM PUBFRAC as a function of weighted averages of scientific and technical base in the regions in which firm laboratories are located (where weights are assigned based on the intensity of a firms patenting activities). For example, if 60% of a firm's patents come from Laboratory A and 40% from Laboratory B , then FIRM-LOCAL PUBLICATIONS equals [0.6* Lab A's(LOCAL PUBLICATIONS)] + [0.4 * Lab B's(LOCAL PUBLICATIONS)]. When all indicators are included, none are significant; in models with only the patenting variables, however, FIRM-LOCAL CHEM PATENTS enters positively and significantly.

It is possible that headquarters laboratories play a particularly large role in firm strategy-making, and that the firm's overall strategy is shaped more by its headquarters' environment than by the environment around its other laboratories. To examine this question, I model FIRM

PUBFRAC as a function of the qualities of the scientific base local to firms' headquarters laboratory only. In most of these models, coefficients on the characteristics local to headquarters' laboratories are insignificant. Equation (7-3) presents one model in which EU S&E intensity is positive and significant. The analysis in this paper does not suggest that headquarters' environments exert a disproportionate influence on overall firm strategic profiles. Overall, the analysis tentatively suggests that FIRM PUBFRAC does respond to the weighted average of its laboratories' local characteristics and that HQ environmental conditions may have an influence. More extensive analysis is warranted before definitive conclusions should be reached; this may be a useful avenue for future research.

VII. Discussion

I evaluate in this paper both qualitative and quantitative evidence regarding the influence of characteristics embedded in the local environment on the strategic organization of drug discovery laboratories. Using case histories, I compare two firms, Sterling and Mulford, that resemble each other on numerous dimensions, but differ with respect to the strength of the scientific base in the locations in which they are founded. These histories suggest that the organizational practices that they adopt and the capabilities in which they invest were greatly affected by the resources available in their local environments. Using panel data reflecting pharmaceutical laboratories' outputs during the latter years of the 20th century, econometric analysis demonstrates (1) that laboratories differ systematically across locations and (2) that various measures of the strength of the scientific and technical base in the regions geographically proximate to drug discovery laboratories are positive and significant factors explaining laboratory scientific orientation. Each form of analysis contributes evidence supporting the

hypothesis that the strength of a region's scientific base is positively and significant related to the scientific orientation of laboratories in that region.

The evidence is strong in the cross section, and is suggestive though not dispositive of causality. Indeed, interpreting these results requires considerable caution. Although the case histories appear representative of the experiences of firms in the industry, I have written them based on secondary sources, examining but two of the scores of firms in the pharmaceutical industry. The quantitative analysis is quite ambitious with respect to the level of regional detail at which the data are examined and, as a result, faces limitations with respect to the precision of the data it employs. Although the majority of the results are robust and consistent with expectations, the results are not universally as hypothesized and the robust negative coefficient on UNIV PATENTS recommends further attention.

Considering the imprecision of the location-specific measures of the scientific base, the extent to which these measures enter sensibly and as expected in the analysis is noteworthy. Their success in this analysis recommends additional work using narrowly defined measures of location-specific characteristics.

The role of competition in driving within-region strategic heterogeneity receives little attention in this analysis, but warrants examination in future work. A strong science base may both draw laboratories to a region and support science-driven organizing strategies. At the same time, however, competitive forces may draw less-science oriented laboratories that attempt to appropriate rather than generate spillovers (Frost, 1998; Kuemmerle, 1999); as the number of laboratories in a high-science region increases, the ability of each lab in the region to adopt a high science approach may decline. Incorporating a nuanced view of competition into the

analysis does become difficult, however, as lab-based competition occurs at the level of the therapeutic class, which is an even more fine-grained level of detail.

The relationship between regional characteristics and firm investments is another issue that may warrant future research. In their time, Sterling and Mulford were small relative to their environments and the histories I present of these firms cover a period short enough that the firms' investments likely had little impact on their local environments. Over past hundred years, however, larger firms, such as Lilly and Merck, have played significant roles in shaping the characteristics of the science base around their principal laboratories. The results of this paper suggest a number of implications: Firms located within "high science" areas will have incentives to invest in these areas in order to increase the strength of the scientific base on which they can draw. At the same time, facilities located initially distant from "high science" face the choice of moving their laboratories, investing locally in order to improve the quality of their local scientific bases, investing distantly in order to tap the strengths of distant researchers (as has Lilly; see Walcott, 1998), or remaining committed to "low science" strategies, trading off the relocation and switching costs associated with becoming a "high science" organization with the reduced productivity benefits associate with less science oriented discovery efforts.

Finally, the results of this paper raise an interesting possibility regarding a mechanism driving location-specific competitive advantage. If, as suggested by these results, the adoption of organizational practices varies systematically according to characteristics of geographic regions and, as is the case with scientific orientation in drug discovery research, organizational practices are tied to productivity differences, then competitive advantages may arise in locations whose characteristics favor the adoption of more productive organizational practices. This possibility raises interesting considerations for public policy as well as strategy.

ENDNOTES

[1] Initial efforts at identifying heterogeneity in within-industry firm conduct include Hatten and Schendel (1977); more recently, the 2000 special issue of the *Strategic Management Journal*, "The Evolution of Firm Capabilities," (ed., Constance E. Helfat, ed., 21(10-11)) brings these issues into greater focus.

[2] Note that this is consistent with research on the local nature of knowledge spillovers (Jaffe, 1986; Jaffe et al, 1993).

[3] The idea that firms respond to competition by seeking different "positions" traces back at least as far as Hotelling (1929).

[4] Some firms also applied for patents to protect the "look-and-feel" of their products, e.g., the shape and color of their packaging, their labeling information, and their promotional materials.

[5] Even Pittsburgh, part of Sterling's target market, lacked the facilities present in Philadelphia and New York. (In fact, the Pittsburgh City Council engaged the New York Bureau of Municipal Research to conduct a review of its city's Public Health and other city services (Pittsburgh City Council - New York Bureau of Municipal Research, 1913)).

[6] Sterling and Mulford also appear in some form in the 20th century sample, although with different corporate identities: In 1994 Bayer acquired the over-the-counter business of Sterling-Winthrop, thus reasserting its ownership over the North American trademark to Bayer Aspirin, after more than three-quarters of century. Sharp and Dohme purchased Mulford in 1929 and subsequently merged with Merck in 1953.

[7] In the years since the end of the sample period (1995-2002) a number of firms have built or planned major, new drug discovery facilities. Interestingly, these have been disproportionately located in areas such as Boston that have an extensive scientific base.

[8] A precise description for the matching algorithm is available from the author. Note that the algorithm addresses issues associated with the spelling of inventor and city names.

[9] In order to count the number of publications in the area within the radius of a focal laboratory, it is necessary to generate (a) a list of all town names within that radius and then (b) compare the complete set of "local town names" to each of the city names in every record of the Science Citation Index. Thus, the computational intensity required to compute LOCAL PUBLICATIONS is immense, and increases dramatically with the size of the radius that defines "local" publications. A thirty-five mile radius was therefore chosen in order to be large enough to be representative of the strength of the local science base, but economical enough with respect to computing time, to be tractable for use in the thesis.

[10] Note that the 1998 Occupation and Employment Survey also reports occupational data by MSA. These data are less comprehensive than the Census data and have been complied according to different definitions and standards. As a result, this paper relies on Census data for regional counts of U.S. scientists.

[11] Whereas the average population of laboratories' U.S. MSA regions is slightly more than 2.25 million, the NUTS-1 regions with drug discovery laboratories have an average of 6.5 million residents. (By contrast, the average population in U.S. states with drug discovery labs in the sample is nearly 11 million.)

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TABLE 1
DEFINITIONS OF KEY VARIABLES

VARIABLE NAME	DEFINITION	SOURCE
LAB-LEVEL		
LAB PUBFRAC	The fraction of a laboratory *i*'s inventors (individuals whose names appear on a USPTO patent in year *t*) who publish an article cataloged in the Science Citation Index within two years of patent application.	Author computations based on Science Citation Index (SCI) and U.S. Patent & Trademark Office (USPTO)
Annual PATENTS	The number of USPTO patents with inventors attributed to laboratory *i* in year *t*	USPTO
Annual INVENTORS	The total number of USPTO inventors that appear on patents attributable to laboratory *i* in year *t*	USPTO
FIRM-LEVEL		
FIRM PUBFRAC	The fraction of firm *j*'s inventors *not affiliated with laboratory i* who publish an article cataloged in the Science Citation Index within two years of patent application.	Author computations based on SCI and USPTO data
Annual PATENTS	The number of USPTO patents with inventors attributed to firm *j* in year *t*	USPTO
Annual INVENTORS	The total number of USPTO inventors that appear on patents attributable to firm *j* in year *t*	USPTO
REGION-LEVEL		
REGION PUBFRAC	For laboratory *i*, the fraction of inventors *not affiliated with firm j* whose addresses are within a 100-mile radius of the focal laboratory who publish an article cataloged in the Science Citation Index within two years of patent application.	Author computations based on SCI and USPTO data
LOCAL PUBLICATIONS	The total number of SCI publications attributable to locations within a 35 mile radius of laboratory *i*	Author computations based on SCI data
LOCAL PATENTS	The total number of USPTO patents attributable to individuals residing within a 35 mile radius of laboratory *i*	Author computations based on USPTO-TAF data
LOCAL CHEM PATENTS	The total number of USPTO patents in chemical attributable to individuals residing within a 35 mile radius of laboratory *i*	Author computations based on USPTO-TAF data
LOCAL UNIV PATENTS	The total number of patents classified by the USPTO as universities patents issued to individuals residing within a 35 mile radius of laboratory *i*	Author computations based on USPTO-TAF data
EU - S&E / POP*	For laboratories in EU countries only, the number of scientists and engineers per 10,000 persons in the NUTS-1 region in which laboratory *i* is located	EuroStat, New Cronos database
US – S&E / POP (1980)*	For laboratories in the USA only, the number of scientists per 10,000 persons in the MSA in which laboratory *i* is located	U.S. Bureau of the Census, EEO Reports, 1980

TABLE 2
MEANS & STANDARD DEVIATIONS
(N=737)

VARIABLE	MEAN	STANDARD DEVIATION	MIN	MAX
LAB-LEVEL				
Annual PATENTS	23.431	26.483	1	158
Annual INVENTORS	57.982	79.027	1	472
LAB PUBFRAC	0.439	0.299	0	1
FIRM-LEVEL				
Annual PATENTS	61.792	45.541	1	259
Annual INVENTORS	227.588	209.767	2	1035
FIRM PUBFRAC	0.429	0.174	0	1
REGION-LEVEL				
REGION PUBFRAC	0.423	0.221	0	1
LOCAL PUBLICATIONS	12248.250	10709.750	10	52978
LOCAL PATENTS	1758.890	2351.997	17	17849
LOCAL CHEM PATENTS	140.470	173.100	0	975
LOCAL UNIV PATENTS	28.061	39.562	1	222
S&E/POP – EU*	10.647	7.865	2.21	55.05
SCI/POP – US 1980*	2.813	0.731	0.97	4.51
CONTROLS				
YEAR	89.286	3.176	84	94

* Note that these are based on administrative designations (MSAs in the USA and NUTS-1 regions in the EU), whereas other region-level variables describe characteristics of the area circumscribed by the 35 miles radius around the focal laboratory.

TABLE 3
EXAMINING REGIONAL VARIATION IN LAB-LEVEL SCIENTIFIC ORIENTATION

	Dependent Variable = LAB PUBFRAC$_{i,j,t}$			
	(3-1) Firm & Region PubFrac, with Year Fixed Effects	**(3-2)** Firm PubFrac, with Regional Fixed Effects	**(3-3)** Firm PubFrac, with Country Fixed Effects	**(3-4)** Firm PubFrac, with Regional and Country Fixed Effects
FIRM CHARACTERISTICS				
FIRM PUBFRAC	**0.218 (0.069)**	**0.230 (0.061)**	**0.214 (0.065)**	**0.205 (0.065)**
REGIONAL AND COUNTRY CHARACTERISTICS				
REGION PUBFRAC	**0.108 (0.055)**			
REGIONAL FIXED EFFECTS*+		F(38,687)= 2.81 **Pr>F=0.00**		F(36,676)= 2.13 **Pr>F=0.000**
COUNTRY FIXED EFFECTS*			F(13,712)= 5.18 **Pr>F=0.000**	F(13,676)= 3.06 **Pr>F=0.000**
CONTROLS				
YEAR FIXED EFFECTS*	F(11,664)= 6.40 **Pr>F=0.00**	F(11,664)= 9.29 **Pr>F=0.000**	F(11,712)= 2.72 **Pr>F=0.000**	F(11,676)= 2.46 **Pr>F=0.000**
R-squared	0.704	0.743	0.729	0.756
Adjusted R-Squared	0.698	0.724	0.719	0.734
Observations	677	737	737	737

^ Throughout the tables, boldface type indicates coefficients significant at least the 5% level. Bolded and italicized text denotes coefficients significant at least the 10% level.

* Reports results of Wald test of joint restrictions.

+ Note that regional fixed effects are computed using dummies for each MSA (USA) and NUTS (EU) region.

TABLE 4
EXPLORING THE IMPACT OF MEASURES OF THE LOCAL SCIENCE BASE^

	Dependent Variable = LAB $PUBFRAC_{i,j,t}$			
	(4-1) FirmPubFrac, with LOCAL PUBS	**(4-2)** FirmPubFrac, with CHEM & UNIV PATS	**(4-3)** FirmPubFrac, with S&E EMPLOY-MENT	**(4-4)** FirmPubFrac, PUBS, PATS, & S&E EMP
FIRM CHARACTERISTICS				
FIRM PUBFRAC	**0.239 (0.066)**	**0.247 (0.079)**	**0.244 (0.065)**	**0.245 (0.078)**
LOCAL CHARACTERISTICS				
ln(LOCAL PUBLICATIONS)	0.005 (0.009)			0.008 (0.010)
ln(LOCAL CHEM PATENTS)		**0.021 (0.010)**		0.010 (0.010)
ln(LOCAL UNIV PATENTS)		**-0.032 (0.009)**		**-0.026 (0.013)**
ln(S&E/POP – EU)º			0.039 (0.025)	**0.115 (0.059)**
ln(SCI/POP – US 1980)º			**0.226 (0.093)**	**0.245 (0.105)**
CONTROLS				
YEAR FIXED EFFECTS*	F(11,721)= 2.65 **Pr>F=0.002**	F(11,530)= 4.81 **Pr>F=0.000**	F(11,721)= 12.59 **Pr>F=0.000**	F(11,522)= 2.97 **Pr>F=0.001**
R-squared	0.702	0.703	0.716	0.716
Adjusted R-Squared	0.697	0.695	0.710	0.705
Observations	734	544	737	541

^ Throughout the tables, boldface type indicates coefficients significant at least the 5% level. Bolded and italicized text denotes coefficients significant at least the 10% level.

º Dummy variables accompanying these variables not reported.

* Reports results of Wald test of joint restrictions.

TABLE 5
EXPLORING ROBUSTNESS TO LABORATORY CHARACTERISTICS^

	Dependent Variable = LAB PUBFRAC$_{i,j,t}$			
	(5-1) Headquarters Labs only	**(5-2)** Home Country Labs only	**(5-3)** Large Labs only	**(5-4)** Including Lab Fixed Effects
FIRM CHARACTERISTICS				
FIRM PUBFRAC	**0.174 (0.080)**	***0.121 (0.073)***	**0.252 (0.068)**	**0.171 (0.069)**
LOCAL CHARACTERISTICS				
ln(LOCAL PUBLICATIONS)	**0.025 (0.011)**	**0.020 (0.011)**	**0.017 (0.009)**	0.018 (0.014)
CONTROLS				
LAB FIXED EFFECTS*				F(88,633)= 2.48 **Pr>F=0.000**
YEAR FIXED EFFECTS*	F(11,281)= 1.47 Pr>F=0.107	F(11,463)= 1.37 Pr>F=0.184	F(11,486)= 1.74 **Pr>F=0.062**	F(11,633)= 2.02 **Pr>F=0.024**
R-squared	0.776	0.736	0.802	0.779
Adjusted R-Squared	0.766	0.729	0.796	0.743
Observations	294	476	499	734

^ Throughout the tables, boldface type indicates coefficients significant at least the 5% level. Bolded and italicized text denotes coefficients significant at least the 10% level.

* Reports results of Wald test of joint restrictions.

TABLE 6
EXPLORING ROBUSTNESS TO FUNCTIONAL FORM^

	Dependent Variable = LAB $PUBFRAC_{i,j,t}$			
	(6-1) Correcting for initial PUBS & PATS	**(6-2)** Correcting for initial S&E levels	**(6-3)** Using 2-sided Tobit	**(6-4)** Using Log-Odds
FIRM CHARACTERISTICS				
FIRM PUBFRAC	**0.247** **(0.090)**	**0.245** **(0.065)**	**0.342** **(0.107)**	0.260 (0.305)
LOCAL, REGIONAL, AND COUNTRY CHARACTERISTICS				
ln(LOCAL PUBLICATIONS)	0.020 (0.014)		0.011 (0.014)	-0.003 (0.037)
ln(LOCAL PUBLICATIONS-1984)	-0.009 (0.014)			
ln(LOCAL CHEM PATENTS)	**0.072** **(0.028)**		0.010 (0.014)	***0.057*** ***(0.033)***
ln(LOCAL CHEM PATENTS-1984)	-0.015 (0.033)			
ln(LOCAL UNIV PATENTS)	**-0.048** **(0.018)**		**-0.035** **(0.017)**	-0.028 (0.044)
ln(LOCAL UNIV PATENTS-1984)	-0.017 (0.025)			
ln(S&E/POP – EU)º		**0.066** **(0.037)**	**0.148** **(0.076)**	**0.401** **(0.212)**
ln(S&E/POP – EU-1984)º		-0.048 (0.050)		
ln(SCI/POP – US 1980)º		**0.226** **(0.094)**	**0.339** **(0.141)**	**0.720** **(0.357)**
CONTROLS				
YEAR FIXED EFFECTS*	F(11,332)= 2.16 **Pr>F=0.016**	F(11,719)= 12.37 **Pr>F=0.000**	F(11,523)= 2.28 **Pr>F=0.010**	F(11,375)= 3.66 **Pr>F=0.001**
R-squared	0.742	0.717		0.214
Adjusted R-Squared	0.728	0.710		0.174
Observations	350	737	541	394

^ Throughout the tables, boldface type indicates coefficients significant at least the 5% level. Bolded and italicized text denotes coefficients significant at least the 10% level.

* Reports results of Wald test of joint restrictions.

TABLE 7
EXPLORATORY ANALYSIS:
FIRM PUBFRAC AS A FUNCTION OF WEIGHTED AVERAGE OF REGIONAL CHARACTERISTICS^

	Dependent Variable = FIRM PUBFRAC$_{i,j,t}$		
	(7-1) With all indicators	**(7-2)** Patent data only	**(7-3)** Impact of HQ region
FIRM-LEVEL WEIGHTED AVERAGES OF LOCAL CHARACTERISTICS			
ln(FIRM-LOCAL PUBLICATIONS)	0.036 (0.071)		
ln(FIRM-LOCAL CHEM PATENTS)	0.006 (0.008)	***0.013*** ***(0.008)***	
ln(FIRM-LOCAL UNIV PATENTS)	0.006 (0.012)	-0.0001 (0.010)	
ln(FIRM-S&E/POP – EU)º	0.003 (0.017)		
ln(FIRM-SCI/POP – US 1980)º	-0.018 (0.016)		
LOCAL CHARACTERISTICS IN REGION OF HEADQUARTERS LAB			
ln(HQ REGION PUBLICATIONS)			0.010 (0.009)
ln(HQ REGION TOTAL PATENTS)			-0.006 (0.009)
ln(HQ REGION S&E/POP – EU)º			**0.041** **(0.024)**
ln(HQ REGION SCI/POP – US 1980)º			-0.105 (0.102)
CONTROLS			
YEAR FIXED EFFECTS*	F(11,301)= 13.31 **Pr>F=0.000**	F(11,306)= 27.80 **Pr>F=0.000**	F(11,303)= 23.60 **Pr>F=0.000**
R-squared	0.876	0.872	0.876
Adjusted R-Squared	0.868	0.867	0.869
Observations	321	321	321

^ Throughout the tables, boldface type indicates coefficients significant at least the 5% level. Bolded and italicized text denotes coefficients significant at least the 10% level.

º Dummy variables accompanying these variables not reported.

* Reports results of Wald test of joint restrictions.

FIGURE 1
LOCATION AND SCIENTIFIC ORIENTATION IN DRUG DISCOVERY

	Firm/Lab		
Region	Scientific Orientation	Lo	Hi
	Hi		Mulford
	Lo	Sterling	

FIGURE 2
FIRM AND REGIONAL FACTORS AFFECTING THE ORGANIZATION OF RESEARCH UNITS

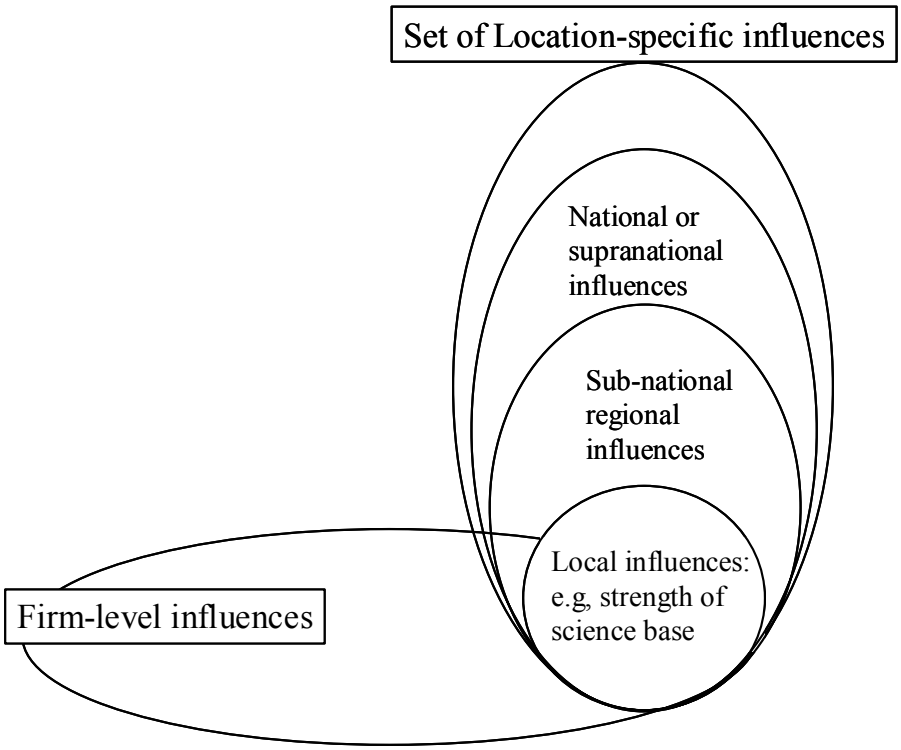
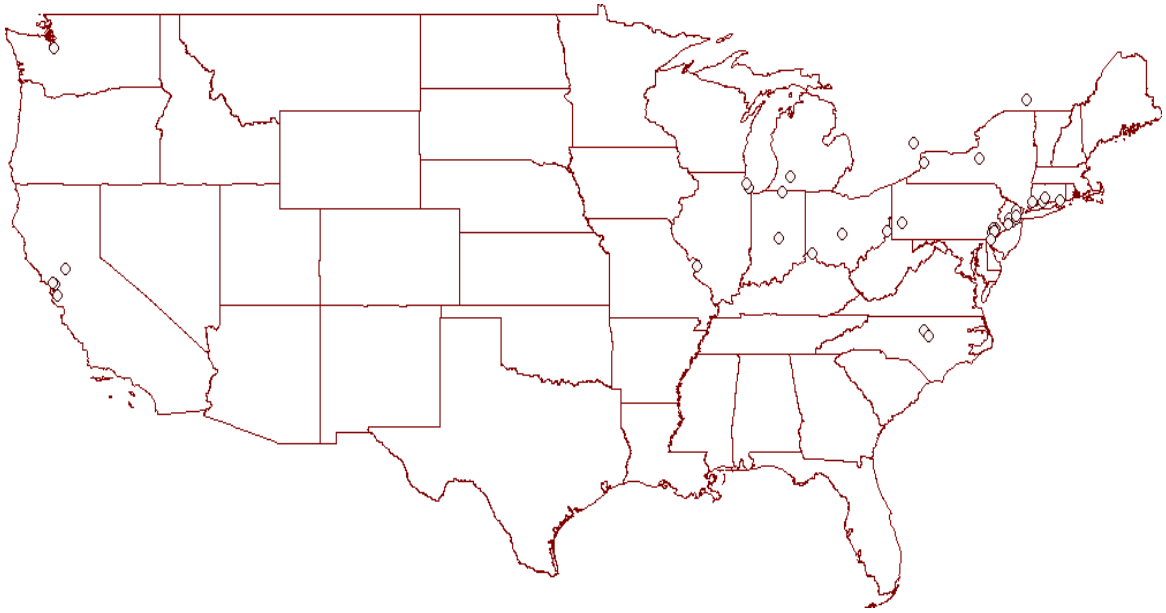


FIGURE 3

DRUG DISCOVERY LABORATORIES IN NORTH AMERICA



DRUG DISCOVERY LABORATORIES IN EUROPE

APPENDIX TABLE 1
FIRMS INCLUDED IN THE STUDY

Abbott	Ciba-Geigy	Nycomed	Searle
Amersham	Glaxo	Organon	SmithKline
Astra	Hoechst	Pfizer	Solvay
Bayer	Lilly	Pharmacia	Squibb
Beecham	Merck	Rhone	Takeda
Boehringer Ingelheim	Miles	Sanofi	Upjohn
Boehringer Mannheim	Nordisk	Schering	Yamanouchi
Bristol-Myers	Novo	Schering-Plough	Zeneca