
Initial Advantage: the Origins of the Geographic Concentration of the Pharmaceutical Industry in the Mid-Atlantic Region

MARYANN FELDMAN^a AND YDA SCHREUDER^b

(^aInstitute for Policy Studies, The Johns Hopkins University, Baltimore, MD 21218 and ^bDepartment of Geography, University of Delaware, Newark, DE 19716, USA)

In this paper we offer an interpretation of the social and institutional context that promoted the development and evolution of the pharmaceutical manufacturing industry. Our interest is in defining the historical circumstances that led to the geographic concentration of the pharmaceutical manufacturing industry in the Mid-Atlantic region. Our focus is both geographic and institutional as we seek to understand the forces behind geographic localization and the ways in which geographic localization may contribute to the advancement of science and to the evolution of industries. In this paper, we describe the general development of the industry in the Mid-Atlantic region of the nineteenth and early twentieth centuries.

1. The Pharmaceutical Industry in Time and Space

While economists increasingly consider that history and location matter, we have only a limited understanding of the development of industrial geography—the ways in which industrial clusters arise and their impact on the development and evolution of industry. Recent theoretical work by Arthur (1986, 1990), Nelson (1994) and Zysman (1994) suggests that understanding industrial development requires tracing the nature, origin and dynamics of historically rooted institutions. Nelson (1994, pp. 54–55) argues that institutions are specifically important to understanding localized industrial systems as they influence the nature of competition in an industry, the industry's relationships with suppliers and the specific requirements for skills and talents. These factors, in turn, affect both the rate and direction of

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technological change. Jaffe (1989), Mansfield (1995) and Audretsch and Feldman (1996), among others, have observed the importance of geographically mediated spillovers to science-based industrial activity. Most critical is the understanding that geographic proximity advances cooperative relationships, the building of shared resources and institutions, and the types of historical accidents and serendipity that promote scientific advance. Porter (1990) provides a description of localized factors that affect the competitive advantage of industries; however, there is little consideration of the actors, social networks and institutional relationships that organize and define a geographic industrial system, or a consideration of how these relationships evolve over time. Saxenian (1994) argues that regional institutions determine the ability of a region-industry to adapt to changes in markets and technology.

The geographic concentration of the pharmaceutical manufacturing industry in the corridor between Philadelphia and New York City provides an example of an innovative industrial system. Currently, one-quarter of the US pharmaceutical value-added manufacturing originates in this high wage area and this represents one of the most geographically concentrated industries in the country.¹ The headquarters of ten of the world's twenty-five largest pharmaceutical companies are located here along with major research facilities of other major firms.² Many of these companies have long historical roots in the region.³ What is most interesting is that these companies have evolved to accommodate scientific breakthroughs which shifted the product focus from botanical products to alkaloids and biologicals, and finally, to synthetic

¹ Feldman (1994) calculates a location quotient for new product innovations developed by US firms and finds that pharmaceutical manufacturing in New Jersey has a higher geographic concentration than any other industry. Indeed, innovation in New Jersey was specialized in pharmaceuticals at a rate four times greater than would have been expected, given the national number of new pharmaceutical products. Forty percent of new pharmaceutical products were developed by establishments in New Jersey which reflects the large number of R&D labs located there.

² Companies headquartered in the region are Merck and Company, American Home Products (which merged with American Cyanamid in 1994), Pfizer, Warner-Lambert, Bristol-Myers Squibb (Squibb was acquired by Bristol Myers in 1989), Johnson & Johnson, SmithKline Beecham, and Schering-Plough. Prominent companies in the USA that are outside of this area include Eli Lilly, headquartered and based in Indianapolis, IN; Upjohn, headquartered and based in Kalamazoo, MI; Parke Davis, headquartered in Chicago, IL. Noteworthy is Glaxo and Burroughs Wellcome, British firms with US operations at Research Triangle Park, NC. Other firms with substantial presence in the study region include Ciba-Geigy, Sandoz, Hoechst AG, Rhone-Poulenc Rorer, Sterling Drug, Hoffman-LaRoche, Eastman Kodak, Roche Labs and Zeneca. The list of the largest pharmaceutical producers is from Ballance *et al.* (1992, pp. 108–109).

³ See, for example, England (1922), Kremers and Urdang (1940), Shieffelin and Company (1944), Mahoney (1959), Cowen (1974), Foster (1986), Liebenau (1987), Cowen and Helfand (1990) and Sturchio (1991). The industry has maintained a strong presence in the region for as long as manufacturing statistics have been kept. In 1860, ~40% of medicines, extracts and drugs were manufactured in Philadelphia and New York (Department of Commerce, 1865). While Philadelphia and New York were major industrial centers in 1860, this geographic concentration is greater than the concentration for all manufacturing activities and is proportionately greater than that exhibited for other manufacturing industries.

chemicals. Similarly, production technology has shifted competitive advantage from small-scale apothecary shops to dedicated manufacturing plants and, finally, to integrated R&D operations. Concurrent with these changes has been the added importance accorded to marketing and distribution activities.

Why is the pharmaceutical manufacturing industry so strongly concentrated in the Mid-Atlantic corridor? Lichtenberg (1960) noted that the location of the industry is not due to proximity to either raw materials or to the market but to a set of historical circumstances that anchored the industry in the region (p. 40). This paper examines the early origins of the pharmaceutical industry in order to understand the factors that shaped the development of the industry and served to anchor the industry in the region.⁴ Our objective is to illustrate the circumstances and resources that enabled pharmaceutical manufacturing firms in the Mid-Atlantic region to find competitive advantage as scientific breakthroughs occurred, as production technology evolved and as markets expanded. Our focus is both geographic and institutional as we seek to understand how geographic-industrial systems become established and evolve.

This paper provides a broad outline of the development of the pharmaceutical manufacturing industry in the Mid-Atlantic region. We trace the origins of pharmaceutical manufacturing in two separate centers: Philadelphia and New York City. In both cities, institutions and specialized resources develop which perpetuate the initial advantages these cities enjoyed as centers of trade. We find that, over time, the two concentrations coalesced to form an industrial corridor in the state of New Jersey. We conclude by considering how this early history positioned the industry for technological advance in the twentieth century.

2. Philadelphia: 'The Cradle of Pharmacy'

Philadelphia has been called the cradle of pharmacy because of the large number of early manufacturing firms established there (Mahoney, 1959; Liebenau, 1987). In fact, early in the nineteenth century, the coupling of medical and technical expertise with prowess in distribution and marketing created an environment that was conducive to the advancement of the practice of pharmacy and the subsequent development of a pharmaceutical manufacturing industry. One early advantage that Philadelphia offered was an environment of medical

⁴ Pred (1965) called the type of historical circumstances which give rise to industrial development and economic growth 'initial advantage'—a term we borrow for the title of this paper.

expertise which included the first hospital and the first medical school in the British Colonies of North America. Other cities, notably Boston, also demonstrated similar developing expertise (Baltzell, 1979, pp. 353–363). Philadelphia's unique advantage may be understood from a perspective of the geography of the wholesale trade (Vance, 1970). Philadelphia, of course, was an important colonial port city. In the late eighteenth century, Philadelphia had the advantage over other Atlantic port cities of being the gateway to the Ohio valley, the emerging western frontier, and thus its merchants became major entrepreneurs in the early national period (Lindstrom, 1978). Among the goods traded to the frontier were drugs, and it is from this starting point that the institutional basis of the pharmaceutical industry in Philadelphia finds its origins (Porter and Livesay, 1970, 1971).

In the early national period, American medical care was in a general state of disarray, with an assortment of poorly trained physicians, traveling peddlers, and proprietors of general stores dispensing all kinds of medical advice and products. Frontier life imposed great physical hardship and the geographic dispersion of the emerging American market created demand for medicines that could be easily transported and distributed to the interior.³ The number of trained pharmacists who could compound medicines from crude ingredients was relatively small. In most instances physicians dispensed their own medicines, or medicines were purchased at general stores. Most of the trade relied on imports through a network of personal contacts in the wholesale distribution and retail market.

Quality was often questionable, and it was the so-called reputable drug trade companies which first initiated quality control to promote their commercial interests. General importers and brokers, trading whatever pharmaceutical products they could obtain, dominated the early distribution system. There is some evidence that Europeans exported inferior medicinal products to the American market. Within the USA the distribution system was two-tiered, depending primarily on the size of the order. Wholesalers from the interior typically traveled once or twice a year to the port cities of Boston, Philadelphia or New York to place orders, usually taking their business to several wholesale establishments in order to acquire a range of products. By visiting in person, product quality could be judged before orders were placed. In contrast, individual storekeepers and country physicians did

³ We hypothesize that the lack of trained physicians and pharmacists in the early history of the USA created a market for standardized medicines that could be easily transported and distributed. The majority of the population did not have access to either a physician to recommend medicines (prescriptions were not required for non-narcotics until the late 1930s) or a pharmacist to compound them. These facts may further help to explain the growth and success of American patent medicines and the evolution of pharmaceutical manufacturing.

not have the opportunity to visit before purchasing. Their transactions took place through correspondence directly with the wholesalers. As a result, the reputation of the wholesaler became an important trade asset. The need to establish and authenticate reputation led Philadelphia wholesalers to specialization and to quality certification in the 1820s and 1830s (Higby, 1992, pp. 12–15). In addition, the formation of self-policing pharmaceutical associations promoted product quality standards and furthered their commercial interests (Kremers and Urdang, 1940, pp. 164, 173–186).

The manufacture of pharmaceuticals in Philadelphia found its origins during the Revolutionary War and its aftermath. Great Britain was the major supplier of medicines in colonial times. The disruption of trade during the War of Independence and the War of 1812, and the levying of high tariffs afterwards, provided the opportunity for domestic manufacturing. A trained apothecary had the requisite knowledge to begin manufacturing and it was easy for family apothecary shops to scale-up operations.⁶ In addition, some of the wholesale drug merchants—in order to control product quality and availability—also started manufacturing in the early national period. The production of the most common medicines such as opium powders did not require large-scale capital investment. Technology involved grinding and mixing, and the use of water-powered milling commonly used by other industries in the Philadelphia area was adapted to drug milling and grinding.⁷ The mechanics of the basic batch processing technology enabled small family firms to shift production according to changes in demand. As a result, early drug manufacturers were able to offer a range of medicines at lower cost than small-scale apothecary shops. These manufacturers were well positioned to subsequently take advantage of technological innovation in alkaloid products, such as quinine sulphate, which required greater expertise and production facilities that were more specialized than an apothecary shop could afford. The medicinal importance of these types of products ultimately increased the public's reliance on dedicated manufacturing operations and away from apothecary shops.

Manufacturing process technology advanced quickly in Philadelphia as the use of steam power replaced the use of water power to grind drugs and

⁶ Some of the well-known Philadelphia firms started at this time period are H. K. Mulford, Rosengarten and Sons, and Smith Kline and French.

⁷ In 1812 the first drug mill in the country, and perhaps in the world, was established on the Falls of the Schuylkill River. According to England (1922, pp. 37–38), a druggist named Dr Haral doubtfully entrusted his friend, Charles V. Hagner, with several tons of cream of tartar to turn into powder. Under the traditional method of hand grinding, this work was estimated to occupy several men many months. But in just 12 hours the water-powered mill turned the cream of tartar into finer quality powder than had previously been imagined possible. After this demonstration, the use of water power is noted to have quickly spread across the industry in the area.

stir mixtures. Pharmaceutical manufacturers in Philadelphia, and elsewhere, borrowed process technology from nearby chemical firms and the Philadelphia companies were exceptionally well positioned because the chemical industry was geographically concentrated nearby (MacFarlane, 1912). Specific knowledge of pharmaceutical manufacturing processes appears to have been closely guarded and was not disseminated through textbooks and trade journals. In fact, pharmaceutical production technologies were generally regarded as trade secrets and the first journals dedicated to pharmaceutical manufacturing technology did not appear until the 1970s. The lack of a mechanism to easily disseminate production technology, we hypothesize, provided certain advantages to manufacturers located in close proximity to each other who could thus observe and discuss new technologies, and could easily hire away key personnel in order to initiate new production techniques or new product lines.

During this same era, Philadelphia established a complementary reputation as a pre-eminent center of pharmaceutical expertise (Proctor, 1850, p. 189). In 1821, the Philadelphia College of Pharmacy, the first school of pharmacy in the USA, was established by an alliance of 60 apothecaries, wholesalers and manufacturers. The mission of the college was to provide pharmaceutical education and improve the conditions of the practice of pharmacy. At the time of the foundation of the College of Pharmacy in 1821, Philadelphia counted 130 establishments identified with the drug trade and professional practice. Most important, this association promoted educational and professional standards. In 1825, the College founded the first US pharmaceutical journal; the *Journal of the Philadelphia College of Pharmacy*. In 1826, the College issued the first *Druggist's Manual*, a handbook for the drug trade, with lists of drugs, medicines and prices, as well as other useful commercial information for the druggist. The College served to unite the various interests of the Philadelphia pharmaceutical community and to disseminate commercial and scientific information among the members.

The scientific credibility of the Philadelphia pharmaceutical community was established by the publication of several key documents and journals. The *USA Pharmacopoeia*, convened and published in Philadelphia in 1820 by the Authority of the Medical Societies and Colleges, sought to establish national standards for pharmaceutical products. The perceived importance of the document is evident in the introduction, which states that the document covers 'the whole *Corpus Medicum* in these free, independent, and USA', and declares itself 'the first performance of the kind. . . compiled by the authority of the faculty throughout a nation' (Cowen and Helfand, 1990, p. 137).

Indeed, in 1906 the Pure Food and Drug Act made the specifications of the *Pharmacopeia* the legal standard of acceptability for pharmaceutical products. The *Pharmacopeia* was complemented by a series of textbooks, professional journals and trade journals which further augmented Philadelphia's reputation as a center for medical expertise.⁸ This material was easily disseminated as Philadelphia was already a prominent center for publishing, with a focus in medical publishing that continues today.

In addition to these and other factors, Philadelphia was generally recognized as the pre-eminent place to receive pharmaceutical education (Brooke, 1956, pp. 280–301). There is evidence of a synergy between the pharmaceutical educational establishment and commercial interests. A number of firms, both in the region as well as nationally and internationally, were established by graduates of the Philadelphia College of Pharmacy. Companies in Philadelphia maintained strong ties with the College by establishing scholarships and prizes for students, by allowing the College to use their facilities, and by incorporating faculty of the College of Pharmacy and the Medical School as directors and employees (Liebenau, 1987, pp. 16–19).

Philadelphia's academic lead was coupled with its expertise in the marketing and distribution of pharmaceutical products. For example, in 1861 the Philadelphia Drug Exchange was founded to provide a central location for the sale of wholesale drugs. The Exchange developed into a manufacturers' trade association which sought to control competition between the Philadelphia merchants and united them for 'the protection and advancement of their common interests' (*Philadelphia Drug Exchange Circular*, 1888). The Exchange sponsored the national distribution of a company directory and a fortnightly flier that contained business and marketing advice in addition to product pricing information.

Wholesale operations changed significantly after the Civil War due to the use of the telegraph and the railroads. These developments challenged Philadelphia's hegemony in the industry, particularly from New York wholesalers. In response, the Philadelphia companies innovated. For example, Smith Kline and Company revolutionized distribution with a system that set the industry standard by filling an order within a week, using a system remarkably similar to modern just-in-time delivery. H. K. Mulford and

⁸ In 1825 the College of Pharmacy began a journal which was reformulated in 1835 as the *American Journal of Pharmacy*. Other prominent publications include *The Philadelphia Druggist and Chemist*, which began national distribution in 1878. Prominent textbooks include Thomas D. Mitchell, MD, *Medical Chemistry; or, a Compendious View of the Various Substances Employed in the Practice of Medicine, that Depend on Chemical Principles for their Formation* (Philadelphia, 1819); Wood and Batsch, *The Dispensatory of the U. S. of America* (Philadelphia, 1833); Edward Parish, *Introduction to Practical Pharmacy* (Philadelphia, 1856); and Joseph Remington, *The Practice of Pharmacy* (Philadelphia, 1885).

Company, another prominent Philadelphia company, changed the emphasis of marketing and distribution with the introduction of 'detail' men who provided personal visits and service to their clients. These two companies also began to advertise extensively to the public, projecting an image that their products were science-based as a way to differentiate themselves from their competitors and to create corporate identity.

Philadelphia had developed as the prominent center of the pharmaceutical industry by the mid-nineteenth century. In 1860, 35% of the value of products for medicines, extracts and drugs in the USA were produced by the 40 manufacturing firms in the city of Philadelphia (US Bureau of the Census, 1865). In contrast, only 5% of the value of products was manufactured in New York in 1860. The Philadelphia firms were, on average, larger and better established than their counterparts elsewhere.

The success of Philadelphia as a center for the pharmaceutical manufacturing industry may be traced to an initial advantage in medical and manufacturing technology and to marketing and distribution expertise. The building of institutions that promoted the industry's interests was critical. Boston and New York were among the first to follow the example of Philadelphia in the organization of the pharmacy trade. Boston and New York were also major port cities where medicines were imported during the nineteenth century. Several of the same problems with quality control and standards existed in these centers, and both Boston and New York founded Colleges of Pharmacy in the 1820s modeled on the Philadelphia College. The constitution of the Massachusetts College of Pharmacy (1823) stressed the same points emphasized in the Philadelphia charter of 1821. Likewise, the College of Pharmacy of the City of New York (1829), was founded as 'an association of pharmacists, druggists, and others interested in the progress of the profession, for purposes of mutual instruction, protection and assistance in all matters pertaining to their professional welfare' (Wimmer, 1929, p. 5). The list of founders of the College of Pharmacy of the City of New York shows that wholesale druggists were prominent among those promoting professional pharmacy.⁹ Other large cities that could support the practice of pharmacy followed this example during the middle decades of the nineteenth century, when four more Colleges of Pharmacy were founded in Baltimore (Maryland College of Pharmacy, 1841), Cincinnati (Cincinnati College of Pharmacy,

⁹ There is much rich detail which illustrates the evolution of relationships in the industry and region. The person credited with initiating plans for the New York school was John D. Keese, who was a clerk in the drug wholesale firm of Lawrence and Schieffelin at that time, and later a partner in Lawrence, Keese and Company, another drug wholesale firm in New York. Keese had attended the Philadelphia College of Pharmacy and was selected as the first president of the New York College, while his employer, Henry H. Schieffelin, was one of three vice-presidents. See, Schieffelin and Company (1944, pp. 27-28).

1850), Chicago (Chicago College of Pharmacy, 1859) and St Louis (St Louis College of Pharmacy, 1864). These cities developed drug and chemical manufacturing industries by 1880 but were never able to match the scale and the intensity of the industry in the Mid-Atlantic region.

After the Civil War, pharmaceutical trade and practice started coming of age. The country's western frontier was becoming settled, and the industry began to serve rapidly developing national markets. Pharmaceutical companies that operated through New York became prominent during this era. The development of the industry in New York, while showing similarities to the early history of pharmacy in Philadelphia, showed significant differences in the later decades of the nineteenth century.

3. The Development of the Industry in New York

In the second half of the nineteenth century, most imported pharmaceutical products entered the US market through New York, offering wholesalers located there a clear advantage over their Philadelphia counterparts.¹⁰ Only in major cities along the East Coast, such as Boston, New York, Philadelphia and Baltimore, or inland gateway centers, such as Cincinnati, Chicago and St Louis, did pharmacists find a niche among health care practitioners, and in these cities pharmaceutical manufacturing developed (Feldman and Schreuder, 1996). Firms in these cities relied on fine chemicals supplied by importers. New York attained primacy as the wholesale center in pharmaceutical products and fine chemicals in the second half of the century and as the gateway city to the Midwest (Albion, 1939). Most of these products distributed through New York's wholesale distribution network were manufactured in Germany until World War I (Kremers and Urdang, 1940, pp. 320–323), and German immigrants and their descendants played a prominent role in both the drug trade and the medical and pharmaceutical community at large.¹¹

In 1850 the German immigrant population constituted nearly 26% of the foreign-born population in the USA and in 1860 this percentage was over 31%. German immigrants were found throughout the Eastern Seaboard, with significant concentrations in Philadelphia, Baltimore and New York City. At

¹⁰ Porter and Livesay (1970, p. 355) describe how Troth and Company, a Philadelphia wholesaler, paid freight in order to make their drugs competitive.

¹¹ Other cities, such as Baltimore, Cincinnati and St Louis, in which there were substantial German populations also developed a pharmaceutical manufacturing industry, although none were as successful as the New York companies (Feldman and Schreuder, 1996).

the end of the 1850s the German population of New York City was estimated at 100,000 with a well developed social network of 20 churches, 50 schools, 10 bookstores, five printing establishments, and numerous drugstores and apothecaries (Wittke, 1939, p. 198). Many of the refugees from the German revolutions of 1830 and 1848 were professionals and this community had a higher percentage of people in the professions than other immigrant groups. Indeed, after the 1848 German uprising, 30 physicians and 20 apothecaries are noted to have left the principality of Baden alone (Kremers and Urdang, 1940, p. 183). Since New York was the main point of arrival, many of these immigrants stayed there. In addition, German immigrants concentrated in the Midwestern cities of Cincinnati, Milwaukee and St Louis, which were in the path of the emerging trade hinterland of New York City. For example, of the 47 retail drug stores and the 10 wholesale establishments which existed in St Louis in 1852, 24 retail drug stores and 2 wholesale establishments were owned by German immigrants. In contrast, in New York City in 1852 there were 273 retail drugstores and 51 wholesale drug companies, and there was reputedly a German pharmacy for every 50 families (Wittke, 1939, p. 388).

The German influence on the development of the US pharmaceutical industry in New York City is apparent as early as the mid-nineteenth century (Eberle, 1907, p. 187). The German pharmacists founded the *New Yorker Pharmazeutischer Leseverein* (New York Pharmaceutical Literary Society) in 1851.¹² This association was the first US pharmaceutical association concerned with improving the scientific and professional standards of its members.¹³ Evidence of the influence of German educational standards was witnessed in 1872, when New York City introduced the first test to measure the professional and scientific knowledge of pharmacists. Of the 270 candidates of German birth 207 proved to be qualified, while only 76 of the 276 US-born candidates passed the test (Kremers and Urdang, 1940, pp. 294–295). American-born pharmacists are noted to aspire to apprentice with a German-trained pharmacist as a means to establish credibility.

Many German pharmacists had university training and, in 1861, a delegation of practitioners led by Johann Michael Maisch were recruited to revise the curriculum at the New York College of Pharmacy (Wittke, 1939, pp. 387–388). Many members of the Society of German Physicians of New York were 1848 immigrants, and synergies between German physicians and German pharmacists contributed to the vitality of building and sustaining

¹² The *Veren* changed its name to *Deutscher Pharmazeutischer Verein* 6 months later.

¹³ Kremers and Urdang (1940, pp. 184–185) Some of the other state and local pharmaceutical associations concerned with qualification standards are branches of the American Pharmaceutical Association and the National Association of Retail Druggists, which came into existence after 1900.

institutions, libraries and professional societies. In 1864, the *Deutsche Pharmazeutische Verein* became the *New-Yorker Apotheker-Verein* in order to open up membership to second-generation German pharmacists who had not been trained in Germany but still followed the traditional scientific method (Schleussner and Lehman, 1926).

Throughout the second half of the nineteenth century, continental European and, in particular, German methods and practices in pharmacy gained prominence over British-based American methods and practices. Nowhere was this more evident than in the development of the pharmaceutical literature. In 1846, when the Philadelphia College of Pharmacy created a professorship of pharmacy and gave William Proctor Jr, a well-known and highly respected Quaker pharmacist, the responsibility to develop a curriculum, Proctor could find no English language text or reference materials that would fulfill the requirements of a scientific training in pharmacy (Kremers and Urdang, 1940, pp. 206–207, 277–281). Gradually, German textbooks were translated and the *Pharmacopoeia*, inspired by the recognition of continental practices, gained ground as a text in the practice of pharmacy (Kremers and Urdang, 1940, pp. 255–257). Of interest to note is that one of the most important textbooks in the 1890s, the *Handbook of Pharmacy* (Coblentz, 1894) relies on German source materials. Nineteen of the 25 books mentioned were German texts, and two were English adaptations of German books (Kremers and Urdang, 1940, p. 281). These influences combined to give American pharmacy a distinctly German character which was complementary to the large-scale import of German pharmaceutical products.¹⁴ German companies had the benefit of patent legislation, favorable tariff rates and a tradition of scientific research in organic chemistry that American companies lacked (Beer, 1959, pp. 103–114).

Seizing the marketing opportunities in New York City and the emerging hinterland, pharmaceutical manufacturing began. Chas. Pfizer Company, the antecedent of Pfizer Incorporated, provides an example of the German connection. Charles Pfizer came to the USA from Germany in 1848. The company began producing santonin, a de-worming botanical, to meet local need. Within a few years, Pfizer and his cousin Erhart were manufacturing and distributing a range of fine chemicals and pharmaceutical products. Most of their ingredients were imported from Germany. Some members of the Philadelphia pharmaceutical community moved in to fill the growing New York demand. For example, E. R. Squibb & Sons was formed in 1859 by a

¹⁴ Based on an analysis of products in the 1912 *Druggist Circular*, Schreuder and Feldman (1996) find that 80% of all pharmaceutical products were imported from Germany through the Port of New York.

Philadelphia pharmacist who had been responsible for the testing of government pharmaceutical purchases at the Brooklyn Naval Hospital (Blochman, 1958, pp. 101–127). When Squibb's laboratory was discontinued for lack of funds, the New York medical community, recognizing the need for medicinal products, provided loans and the promise of purchase orders. Subsequently, Squibb set up his business in Brooklyn near his former location at the Naval Yard. During the Civil War, the demand for pharmaceuticals increased and protective tariffs, established in 1862, increased the price of imported medicines which further stimulated domestic production.

In large part, the historical development of the pharmaceutical industry in New York is due to the emergence of New York City as the major port of entry for products entering the American market from Europe. In the course of the nineteenth century, New York had become the American center in the wholesale trade. Wholesale specialty firms, such as McKesson and Robbins (established 1833) and Schieffelin Brothers and Company (established 1794), began manufacturing drugs in the 1850s as government and frontier customers began to demand standardized products and ready-made pharmaceuticals. In order to further control the product flow, the major drug wholesale firms in the New York region were also instrumental in establishing professional manufacturing and marketing associations, such as the Manufacturing Chemists' Association in 1872 and the Western Wholesale Druggists' Association in 1876—renamed the National Wholesale Druggists' Association in 1882. The more successful wholesale establishments used traveling salesmen or detail men who provided customer service and information on new products in order to build greater market share. The development of the national railway and communication network, both assisted and required this new type of sales agent as competition between domestic and foreign manufacturing interests grew. Toward the end of the nineteenth century, the position of wholesale companies became more uncertain as manufacturing companies established their own sales offices staffed with trained pharmacists.

Difficult relationships with pharmaceutical wholesalers in the New York region, in fact, forced some foreign companies to establish their own sales offices and distribution centers.¹⁵ The USA was experiencing rapid economic

¹⁵ E. Merck and Company from Darmstadt in Germany had first used the wholesale firm of Lehn and Fink of New York to sell and distribute its products. This relationship began before F. W. Fink emigrated to the USA in 1866 and is an example of the reliance on personal ties to reduce risk in a time of poor communications and slow transportation (Galambos and Sturchio, 1992). In 1887 E. Merck was forced to terminate the relationship because Lehn and Fink had been counterfeiting E. Merck labels and placing them on inferior goods. E. Merck decided to set up its own US marketing department in New York and

growth which provided lucrative new markets.¹⁶ In addition, increasingly high tariffs on fine chemicals and pharmaceutical products during the late nineteenth century gave the German companies great incentive to establish manufacturing plants in the USA. In 1896, Republican President McKinley, who was known for his stand on restricting imports of manufactured goods, came to power. The trade legislation that followed was the most restrictive in the history of the USA (Summers, 1935, pp. 43–55, 57–66; Terrill, 1973, pp. 184–200, 201–210).

Against this background several German pharmaceutical firms transferred manufacturing to branch plants in the New York area. Among them was *Farbenfabriken Bayer* (Mann and Plummer, 1991, pp. 15–30). The German firm began selling in the USA in 1863 when the company was known primarily for its dye business. By 1899 the company had recognized the therapeutic uses of aspirin, a dye by-product. In the USA the drug was in widespread use, distributed through Schieffelin and Company and through a sales office known as *Farbenfabriken of Eberfeld Company*. A manufacturing plant was established in the New York area when the patent on aspirin was about to expire so that Bayer would avoid import duties and could compete with domestic producers. In 1903 Bayer built a manufacturing plant in Troy, NY, where the company had purchased partial ownership in the Hudson River Aniline and Color Works at Rensselaer in 1881. The site was noted to be accessible to both rail and river transportation and in close proximity to the New York market. Like Merck's facility in Rahway, NJ, built along the Pennsylvania Railroad Line, Bayer established its manufacturing plant close to its wholesale distribution center with easy access to the New York market and national transportation network.¹⁷

sent a trusted employee, Theodore Weicker, and a family member, George Merck, to organize the company's operations and establish Merck and Company—New York in 1891. In 1899 Merck began to manufacture drugs in the USA and established its American operations in Rahway in northern New Jersey. George Merck, the American company's founder, meticulously developed a niche in the American market by building a loyal, mostly German-speaking workforce and customer base, and by emphasizing the German parent company's reputation for producing high-quality products. Other German pharmaceutical companies made similar location decisions, and changed from importing their German-manufactured products to manufacturing their products in the USA at about this same time. This strategy established Merck in the USA, and had another significant effect on the industry. In 1905, Weicker, who began his career working as an apprentice for Merck in Darmstadt, became President of E. R. Squibb & Sons. In 1905, the year that E. R. Squibb died, Weicker and his father-in-law Lowell M. Palmer bought controlling interest in Squibb for \$900,000.

¹⁶ The German chemical companies were searching for new medical products due to the crash of the red dye markets in the late nineteenth century. Red-dye was a fine chemical made from coal tar and many of the dye manufacturers also made medicines. See Beer (1959) and Meyer-Thurrow (1982).

¹⁷ Merck also established a plant in St Louis, MO, where the Herf and Frerichs Chemical Company had a plant for lease. St Louis also had a large German-immigrant population and seemed to be a good site to serve the growing western regional market. But Merck shortly consolidated all of its manufacturing at Rahway in order to achieve economies of scale. The St Louis facility was used for warehousing and subdividing chemicals.

In some instances the newly transplanted German pharmaceutical firms transferred scientific and technical personnel directly from the German parents. These German employees were originally assigned to work on product quality but their responsibilities soon expanded to include work on new product development. Although the pharmaceutical firms did not have dedicated R&D labs until the 1930s, the Biological Control Act of 1902 required pharmaceutical firms with biological products to have testing facilities.¹⁸ This requirement added scientific and technical staff which provided the capacity to move into more scientific-based product development. While the company's early product development efforts were typically a matter of recombination of existing compounds, scientific breakthroughs in bacteriology, immunology and synthetic chemicals gradually shifted the companies' attention to more technology-intensive activity.

As observed with more recent Japanese auto transplants, the German pharmaceutical companies continued to conduct most of their basic scientific research as well as their high value-added production in their home country (Graham and Krugman, 1991, pp. 76–78). World War I brought an embargo on imported German chemicals that provided American firms with the opportunity to replace the synthetic organic products that had been previously obtained from Germany. As a result, American firms increased their investment in research and development in order to produce the wide array of embargoed products. The pharmaceutical companies recognized that the prevailing anti-German sentiment created support for their undertakings. Situations such as the relapses of epileptics who had previously successfully controlled their diseases using German Luminal were well publicized and helped prompt the American scientific community to action (Tainter and Marcelli, 1959, pp. 399–401). Initially, American product development was frustrated by the fact that many of the patents on key products were held by German firms (Steen, 1995).¹⁹ A swift political resolution to that barrier presented itself. In 1919 the US Alien Property Custodian seized the properties of German individuals and companies with the intent that the companies would become 'thoroughly Americanized'.²⁰ These included all of the assets and patents of the German

¹⁸ Firms in the patent medicine or synthetic chemical business, with the exception of firms producing arsphenamine, were required to have a chemist only to analyze and control contents. Typically these chemists had only completed high school.

¹⁹ The American pharmaceutical industry of this era is noted to have disdain for the patenting of drugs and medicines. This contrasts with the German strategy of patenting new discoveries as a strategy to prevent future competition (Liebenau, 1988).

²⁰ This was the intent of Federal Judge A. Mitchell Palmer, who was appointed as Alien Property Custodian.

chemical and pharmaceutical companies. These assets were subsequently sold at an auction and provided a major impetus for the growth of the American chemical and pharmaceutical industry. Through this action, the ties to the German parent companies were broken and the American pharmaceutical industry was positioned for its own advance.

4. Some Speculation on Why New York Overtook Philadelphia

Why did the balance of competitive advantage shift to favor New York as the predominant center for the pharmaceutical industry? Part of the explanation is that the New York firms developed superior marketing and distribution capabilities as New York became the undisputed center of import and domestic trade during the second half of the nineteenth century. In addition, the existence of a highly competent pharmaceutical German immigrant community provided conduits for successful German fine chemical and pharmaceutical companies into the American market during a time of rapid market expansion. Finally, New York firms were more receptive to the breakthroughs in bacteriology that occurred in Germany and France. We may hypothesize that the commercial success of Philadelphia firms limited their receptivity to the synthetic chemical technology.²¹ One interpretation that deserves further attention is that public institutions such as the New York City municipal Public Health Department Laboratories and proactive public policy, especially the support and funding of state and municipal governments, provided an advantage to the development of the pharmaceutical industry in New York (Liebenau, 1987).

In the 1880s diphtheria was a major world health problem. A remedy for diphtheria, an antitoxin, was discovered at the Koch Institute in Berlin in 1890 and knowledge of this breakthrough diffused rapidly. Laboratories throughout the world proceeded to work on the development and large-scale manufacture of a vaccine. The laboratory of the New York City Department of Public Health and the Philadelphia Public Health Laboratory did pioneering work on the development of the antitoxin. The Philadelphia Public Health Laboratory was dominated by advocates of the public sanitation movement who were not initially as receptive to bacteriology as their New York counterparts. In part, the antitoxin development effort in New York was more successful because the project benefited from greater influence of bacteriologists who were able to garner the funding and political

²¹ The Philadelphia firms merged with, or were acquired by, other firms, notably from New York (Feldman and Schreuder, 1996).

support necessary to quickly begin research and then manufacturing. Additional impetus for the support of this project in New York may have been due to the perceived health threat that was posed by the great numbers of immigrants arriving through the Port of New York (Kraut, 1994). During this time, the Hygienic Laboratory at Staten Island Marine Hospital did pioneering work in applied bacteriology. The Laboratory flourished as part of the US Public Health Services and became a front-line defense against cholera brought in by immigrants by virtue of its location at the main point of entry to the USA (Koshland, 1987; Weatherall, 1990).²²

The New York Public Health Service further provided pioneering work in bacteriology and in technology to manufacture large quantities of the diphtheria antitoxin. Public institutions were in a unique position to foster these endeavors at a time when the commercial potential of the new technology was uncertain and the resources needed to support new ventures were extensive, especially in light of the uncertainty and unknown efficacy of the drug. As a result of public support, the New York Public Health Service was able to produce antitoxin for commercial sale throughout the country.

This success did not go unnoticed by the pharmaceutical industry. In 1902, a delegation of druggists and manufacturing chemists presented a petition of protest against the city's competition with private enterprise to the Mayor of New York. The petition was signed by more than a thousand of the city's physicians and the Mayor responded by limiting the department's production of antitoxin and the sale of antitoxin by the Public Health Service outside of the city of New York. This action subsequently created a large commercial market for the pharmaceutical companies.

At the transition from public production, many of the New York Public Health Service scientists and professionals found employment with private companies. For example, Ernst Lederle began his career in the New York City Department of Health's bacteriology labs when it was formed in 1892. He advanced to become the New York City Health Commissioner. In 1906, after the first of his two terms as Health Commissioner, he formed a private firm called Lederle Labs.²³ The new company's first product, diphtheria antitoxin, was a commercial success.²⁴ The development of this local expertise appears to have especially benefited the New York industry.

²² The Laboratory was moved to Washington, DC, and later to Bethesda, MD, and eventually developed into the National Institutes of Health (see Harden, 1986).

²³ Lederle Labs is currently a division of American Home Products.

²⁴ Ernest Lederle provides one example of the interesting career involvement of the pharmaceutical entrepreneurs. Lederle was of German descent and was a volunteer to the Alien Property Custodian, where his knowledge of German was cited as helpful for American firms in producing chemicals that had previously been imported from Germany.

Safety concerns regarding the antitoxins had further wide-reaching effects for the development of the pharmaceutical manufacturing industry. In 1902, after incidents of contaminated antitoxin led to deaths in St Louis and Camden, NJ, the first American legislation regulating the manufacturing of medicines and the licensing of their producers was passed. The Biological Control Act of 1902 required the government to monitor the production of new medicines and required companies to set up laboratories for testing and inspection purposes. The Act changed the nature of competition in the industry as those marginal producers who could not meet the standards were driven out of business (Liebenau, 1987). In addition, firms could use testing labs and standards to differentiate their products on the basis of quality, and testing labs provided companies with a mechanism to conduct research for new products. Most importantly, with the imposition of responsibility for quality and standards, American products grew in stature, nationally and internationally.

5. New Jersey: The Formation of the Industrial Corridor

While the development of the pharmaceutical industry began as two separate complexes in the cities of Philadelphia and New York, over time these two centers coalesced to form an industrial corridor. This pattern of growth reflects the historical development of the pharmaceutical industry and also reflects a broad pattern of development common to American industry, including the suburbanization of industry along developing transportation corridors, first rail and then highway, a series of mergers and acquisitions (Lamoreaux, 1985), and the evolution of hierarchical and decentralized organizations (Chandler, 1990).

The first pharmaceutical company to locate outside of New York was Johnson & Johnson. Robert Mead Johnson, the founder, and his brothers located their start-up firm in New Brunswick, NJ in 1886.²⁵ This company was unique among pharmaceutical manufacturers in that none of the founders had any chemical, medical or pharmaceutical training. Their location decision is noted to have been motivated by an affordable lease for a vacant industrial building. The company's first product was sterile bandages, however, the company quickly moved into more sophisticated products. Their choice of location—roughly midway between Philadelphia and New York—turned out to be a favorable one. Situated along rail and canal routes, it proved to be

²⁵ Johnson & Johnson's first product was antiseptic surgical dressings. The firm grew rapidly and diversified its product line. Within 2 years the workforce was 125 employees, and in 5 years, in 1894, it was 400. The company established a bacteriological laboratory at Highland Park, NJ in 1891.

most opportune in its proximity to both Philadelphia and New York. In the late nineteenth century other companies followed and the industrial landscape in the corridor filled in. As mentioned before, in 1899 Merck built a plant in Rahway, NJ, along the Pennsylvania Railroad Line. Merck's location decision appears to have been influenced by the fact that Theodore Weicker, the co-founder of Merck's American operations, owned land in Rahway and was an advocate for the community.

Newcomer (1924) remarks on the concentration of large pharmaceutical companies in Brooklyn—among them E. R. Squibb and Sons, McKesson and Robbins, New York Quinine and Chemical Works, and Charles Pfizer and Company. Since Brooklyn offered limited opportunities for physical expansion, companies branched out in other locations. The Brooklyn plants are noted to be dedicated to small batch manufacturing and those commodities which required skilled labor. Newcomer notes that when it became profitable to manufacture a product continuously, production was moved to plants in New Jersey where there was greater available space. Newer industrial facilities were essential to accommodate the specialized machinery necessary for the so-called mass production of drugs (Newcomer, 1924, pp. 23–24).

The early decades of the twentieth century witnessed the location of company facilities, first manufacturing and later R&D, to New Jersey. For example, Hoffman-La Roche Inc., a Swiss company, began distributing pharmaceutical products through agent wholesalers in New York in 1900, and in 1905 the company established a distribution office in New York City. The company's success is witnessed by three moves to successively larger quarters within New York City before 1920. Then, in 1928, the company purchased 20 acres of land at Nutley, NJ, 'a pleasant residential town about fourteen miles outside of New York City' (Maltbie, 1937, p. 151). This site provided sufficient acreage and facilities for 'a model plant for the pharmaceutical industry' and, from this site, the company expanded. In addition, pharmaceutical company subsidiaries and new firm spinoffs have stayed in close proximity. For example, Roche Diagnostics, a subsidiary of Hoffman-La Roche specializing in medical instruments, is located in Montclair, NJ, just a few miles away from the Nutley site. Other companies followed a similar pattern of geographic expansion (Cowen, 1974).

In the 1920s, following a period of rapid growth in the industry, several major pharmaceutical companies reorganized and restructured their operations which led to further suburbanization of the industry. George W. Merck introduced a plan in 1926 to decentralize and departmentalize the company along functional lines. R&D, laboratory testing, and marketing and

manufacturing became separate entities, and Merck and Company was reorganized to handle a larger and more complex business. Further expansion came with the acquisition of Powers-Weightman-Rosengarten, a large Philadelphia fine chemical manufacturer. With a broad manufacturing base, Merck and Company increased R&D investments and marketing outlays. In 1933 the Merck Institute of Therapeutic Research was built at Rahway to house the research of Dr Hans Molitor, previously Professor of Pharmacology from the University of Vienna. A number of scientists, seeking to leave Germany in the 1930s, found employment in American pharmaceutical companies and this transformed the status of working in the industry.

The changes in the industry's research capabilities and reputation led to further alliances with academic research and cooperative ventures in the 1940s and 1950s. For Merck, this included antibiotic research, led by Professor Selman A. Waksman, of nearby Rutgers University, and Alfred Newton Richards, at the School of Medicine of the University of Pennsylvania, who served as a general consultant to Merck and Company for more than 30 years. The success of the joint venture with Waksman at Rutgers University led to the discovery of streptomycin—the drug to combat tuberculosis—and two new production plants: a factory to produce streptomycin in Elkton, VA, and a new finishing facility at Rahway. The relationship with Richards led to the development of various vitamins and hormone research and joint projects with scientists at Princeton University, the Carnegie Institute and the Rockefeller Institute. The ultimate goal of Merck and Company was to build an institutional base for research to improve relations between universities and industry in biology, pharmacy and medicine (Swann, 1988, pp. 45–49). As part of this strategy, Merck scientists regularly presented scientific papers at professional meetings and published their work in academic and professional journals. The period between World War I and World War II is thus marked by several examples of collaboration between industry and universities, and may be recognized as a systematic endeavor conducted by the American chemical and pharmaceutical industry to improve their R&D capacity and to build scientific resources (Swann, 1988). While Martin Arrowsmith's professional integrity was considered compromised by working for a pharmaceutical company lab (Lewis, 1930), by the 1940s company researchers were full participants in the scientific research community.

During World War II, federal government officials recognized that the geographic concentration of the pharmaceutical industry provided a potentially vulnerable air-strike target. Given the strategic importance of the industry to the war effort, the government urged the pharmaceutical companies to establish operations outside of the Mid-Atlantic region and the

companies complied. The operations which were decentralized were mainly branch plants engaged in routine production. Company headquarters, R&D facilities and high value-added manufacturing remained concentrated in the Mid-Atlantic region.

6. *Reflective Conclusions*

A series of historical circumstances in the early nineteenth century gave the pharmaceutical industry an initial start in the Mid-Atlantic region. The early location of the pharmaceutical industry was influenced by diverse factors such as transportation and trade patterns, migration and settlement patterns, as well as a certain amount of serendipity and personal predilections. From these initial advantages, specialized resources and informational networks developed which promoted the growth of the industry. The success of the industry, while due to entrepreneurial efforts, relied in large part on the building of institutions, notably professional and trade associations, and the setting of industry standards. Over time, a social and economic landscape of specialized inputs, subsidiary firms, labor pools and informational networks evolved which augmented and complemented the activity of the industry. These, in turn, contributed to the industry's growth and evolution. A sustained advantage was created for the industry in the Philadelphia–New York corridor. Local events and social interactions which occurred in the Mid-Atlantic region had permanent effects on the development of the industry nationally.

Companies in this industry evolved to incorporate technological advance which shifted the production of drugs and medicines from apothecary shops to dedicated manufacturing plants and then to integrated R&D operations. Those engaged in pharmaceutical manufacturing have always considered their field to be based on science, crude as it may seem by today's standards. The reliable supply of efficacious and reputable medicines has always been important to society. Professional organizations in the Mid-Atlantic region were among the first in the new American nation to recognize this and to create institutions to promote these product quality standards and education and training. The sheer size of the American continent and the lack of trained physicians and pharmacists created special needs for standardized and easily transportable medicines. This created a strong early influence for the wholesale trade and influenced the direction of technological change. Wholesalers integrated backward into manufacturing activity and brought a sense of commercial expediency to the ways in which the industry evolved.

Further, government played a decisive role in the development of the

industry. Since the industry was recognized to be of strategic national importance, government actions and legislation played an important supportive role. Protective tariffs were enacted to stimulate and protect the domestic pharmaceutical industry. The nationalization of the German pharmaceutical companies during World War I formed a critical point in the industry's development and catapulted the scientific basis for the industry in the Mid-Atlantic region. In addition, the Pure Food and Drug legislation had a decisive effect in promoting the industry standards, product quality and increased consumer acceptance which gave those companies that had the best equipped testing labs and R&D facilities the edge over small producers. Subsequently, the larger pharmaceutical firms set the tone, bought up the smaller companies and established joint ventures with universities in the region.

This pattern of development reflects a broader pattern of change common to American industry, including the evolution of hierarchical and decentralized organizations, a series of mergers and acquisitions, and the suburbanization of industry along developing transportation routes—first rail and then highway. This industry appears to be unique in that it does not disperse to other regions. In fact, our findings suggest that unique capabilities developed in the region. These capabilities anchored the industry in the region and provided a springboard for the development of the industry. The pharmaceutical industry has been characterized as one of the most innovative and economically successful in the USA. From the initial advantage described here, the pharmaceutical industry was positioned and poised for growth in the twentieth century.

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