Innovation and Structural Change in Pharmaceuticals and Biotechnology

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The pharmaceutical industry has long been one of the most innovative industries and, unlike industries such as computers and aircraft, has remained relatively unconcentrated. In recent years, however, there have been contrasting industry developments that could have far-reaching, long-run effects on the industry's structure. This paper examines the impact of the entry of new biotechnology firms, the increasing real cost of innovation, and the recent important mergers among leading firms. Also, a regression analysis reveals disproportionately high innovative contributions from both new biotechnology firms and the very largest multinational pharmaceutical firms.

One of the traditional strengths of the pharmaceutical industry has been the large number of firms engaged in new product development. In many other technologically advanced industries (e.g. mainframe computers and commercial aircraft) there has been a tendency for a few firms to dominate both sales and innovation. By contrast major new product introductions in pharmaceuticals have been generated by a diverse and changing set of firms. As a consequence the overall industry has remained relatively unconcentrated and has been subject to very intensive innovative competition over time. In recent years, however, there have been contrasting industry developments that could have far-reaching, long-run effects on the industry's structure. These involve both significant entry into the industry and consolidation among established firms.

One strong positive development has been the entry of several new biotechnology firms into pharmaceuticals. In most instances these firms were established to exploit fundamental advances in biomedical research that initially took place in university settings. The growth of the biotechnology industry's efforts in pharmaceutical R&D over the past decade has been very impressive. In 1992 there were more than 200 biotechnology firms whose

primary business involved the development of new pharmaceuticals and many others with a secondary focus in those areas. These 200 firms specializing in therapeutics had cumulative R&D expenditures in 1992 of over \$2 billion (Dibner, 1993). To date, the primary contribution of these biotechnology firms has been at the research end of the R&D process in pharmaceuticals. However, there have been some major successful product introductions and several promising products are currently in clinical development. Many of these products in clinical trials involve joint ventures with larger pharmaceutical firms.

A second important industry development has been a movement toward consolidation among the larger established pharmaceutical firms. In this regard, three large mergers occurred at the end of the 1980s. These were the combinations of Bristol Myers and Squibb, Smith Kline and Beecham, and Merrell Dow and Marion. Among the reasons cited for these mergers are the increasing costs of R&D, shorter product life cycles and the highly skewed distribution of sales returns emerging from the pharmaceutical innovation process. A number of the biotechnology firms also have been involved in mergers combining with each other or merging with larger pharmaceutical firms.

A key question, therefore, is how the industry will evolve over the next decade. Will the growth of the biotechnology sector result in a more diversified and less concentrated pharmaceutical industry in the future? Or conversely, will the strong forces toward consolidation in this industry result in a more concentrated structure over the next decade? In this paper, we examine these issues further and consider the likely implications for the pharmaceutical industry. In the next two sections, we analyze the factors underlying entry and consolidation in this industry in greater detail. The third section then looks at the long-term trends in the concentration of innovative output and related measures. The final section presents a brief summary.

1. Innovation and Consolidation in Pharmaceuticals

In an earlier paper, we analyzed the changing structure of the pharmaceutical innovation process that occurred after the 1962 Amendments (Grabowski and Vernon, 1977). We found that this period was characterized by an increased concentration of innovation in large multinational firms and also by fewer individual firms having new drug introductions. In effect there was an exit of smaller firms from the research segment of the pharmaceutical industry and an increase in the minimum threshold size for this segment. Essentially, we found that the larger multinational firms, of which there are

several, were better able to adapt to the increased risks and costs of R&D from both a financial and organizational perspective. A more recent international comparative econometric study by Thomas (1990) also supports this conclusion.

Our recent work on the returns to pharmaceutical R&D suggests the industry adaptation to the more stringent regulatory climate was completed by the mid-1970s. We found that the returns to pharmaceutical innovation increased significantly in the latter part of this decade and into the 1980s (Grabowski and Vernon, 1990, 1994). Ostensibly, this was an attractive time to enter the pharmaceutical industry. Two different types of entry did occur in this period. One was *de novo* entry by the biotechnology group exploiting what can be described as revolutionary advances in basic biomedical science. This is discussed in the next section. The other type of entry was by market acquisition of existing pharmaceutical firms. This was the route chosen by several large chemical firms.

Table 1 shows the major acquisitions in the pharmaceutical industry during the 1980s. Part (a) shows market entry acquisitions. Three of the major chemical firms—Dow, Monsanto and Kodak—paid significant market premiums to enter the chemically-related business of pharmaceuticals by acquisition of mid-sized, second-tier firms in the drug industry. These firms decided against the toehold-entry strategy, pursued earlier by Du Pont, as too difficult and economically inefficient in pharmaceuticals. The acquisition of established competitors in the pharmaceutical industry allowed these firms to realize immediate scale economies in both the R&D and marketing areas.

TABLE 1. Major Mergers and Acquisitions in the Pharmaceutical Industry, 1980–1992

(a) <i>Market entry</i>		
1981	Dow Chemical	Richardson-Merrell
1985	Monsanto	G. D. Searle
1988	Kodak	Sterling Drug
(b) <i>Market extension</i>		
1989	Beecham (UK)	Smith Kline
1989	Dow Merrell	Marion
1989	Bristol Myers	Squibb
1990	Rhone-Poulenc (France)	Rorer
1991	Kodak (Sterling Drug)	Sanofi (France)
(c) <i>Biotechnology</i>		
1990	Hoffman La Roche (Switzerland) ^a	Genentech
1991	Chiron	Cetus
1992	American Cyanamide ^a	Immunex
1992	American Home Products	Genetics Institute

^a Acquisition of controlling interest.

These are the traditional areas of scale economies and entry barriers in pharmaceuticals.

The mergers listed in part (b) of Table 1 are very different in character. They involve market consolidation of important competitors in the pharmaceutical industry. In addition to these mergers, there have also been many acquisitions of smaller firms, as well as many joint-venture and co-marketing agreements that were put into place. A recent survey of US pharmaceutical industry executives in the business press found that they predicted overwhelmingly that more industry consolidation would occur and agreed that all remaining mid-sized firms would be subject to mergers or joint ventures in the near future.¹

Of course there can be costs as well as benefits to this consolidation activity. There may be diseconomies in R&D productivity and other adverse side-effects associated with increased firm size and R&D activity.² It is too soon to assess these effects. However, it is clear that the changing nature and economics of the R&D process in pharmaceuticals is one of the primary motivating forces behind this move toward consolidation.

R&D times and costs have increased at a rapid rate over the past decade. In this regard, a recent study by DiMasi *et al.* (1991) analyzed R&D costs for a random sample of new drug candidates first tested in humans between 1970 and 1982. This study found the mean new drug introduction had R&D costs of \$231 million (in 1987 dollars) and took 12 years from synthesis to approval. Furthermore, the R&D costs of the most innovative compounds were greater than those for the typical compound. A comparison of the DiMasi analysis with the results of an earlier study by Hansen (1979) indicates that R&D costs per new drug have more than doubled in a period of less than a decade. There appear to be several factors associated with this increase, including greater expenditures for discovery research, increased emphasis on chronic rather than acute diseases, and greater out-of-pocket expenditures for clinical trials.

Higher R&D costs have not been associated to date with lower returns to pharmaceutical R&D because sales revenues and cash flows have also increased significantly for new drug introductions. There have been more

¹ This story quoted the chief executive of Glaxo as stating that to be a 'big player', a company must have an R&D budget of over 500 million a year and 'those that can't spend that will be left behind or will be good candidates for mergers' (Waldholz, 1991).

² This issue has been investigated historically for pharmaceuticals by a number of authors and with mixed results (Vernon and Gusen, 1974; Schwartzman, 1976; Jensen, 1987). Jensen's analysis covers the most recent time period and utilizes a Poisson distribution regression model. She found that the elasticity of new chemical entity (NCE) introductions with respect to R&D expenditures was not significantly different from one over a wide range of different sized R&D programs. However, it is also important to consider the quality as well as quantity of NCEs emerging from different sized R&D programs, given the highly skewed distribution of innovative outcomes in pharmaceuticals.

FIGURE 1. Present values by decile: 1980–84 NCEs.

breakthrough products in the decade of the 1980s and this has resulted in higher average cash flows for new drugs.³ In effect, the scale of both R&D costs and product revenues has expanded dramatically in pharmaceuticals during the 1980s and early 1990s (Grabowski and Vernon, 1994).

While R&D costs and revenues have been increasing for new products, the distribution of returns from new products has remained very skewed (Grabowski and Vernon, 1990, 1994). This is illustrated in Figure 1, which is based on our most recent analysis of returns for 1980–84 new drug introductions. In particular, the top decile of new drug introductions had discounted returns that exceed average R&D costs by several times, but the median new chemical entity (NCE) does not have returns commensurate with average R&D costs. It is this combination of the increasing scale of innovation and the highly skewed nature of R&D outcomes that has produced one of the strong motivating forces for consolidation in pharmaceuticals.

Another industry development involves the passage of the 1984 Hatch Waxman Act. As a consequence of this legislation and related changes, there

³ Over the past two decades, there has been a strong movement toward a more targeted 'discovery by design' approach to pharmaceutical R&D. Historically, most of the major drug discoveries could be traced to natural occurring compounds, random screening, accidental discoveries, and modification of previously known drugs (Grabowski and Vernon, 1983, ch. 2). Pharmaceutical research is now taking a more rational and fundamental approach to understanding the causes of specific diseases and how drug compounds interact with physiological processes. Several of the major breakthrough products in pharmaceuticals, such as Tagamet, Capoten and Mevacor, have emerged from this targeted approach to R&D. This approach has resulted also in an increasingly interactive and complementary relationship between industry R&D and basic biomedical research activities performed by academic and government programs.

is much greater generic entry and faster erosion of sales revenues on patent expiration (Grabowski and Vernon, 1992). Hence, product life cycles in pharmaceuticals appear to be shortening. Given that this is the case, it is important that firms with significant new drugs achieve faster penetration, in both domestic and foreign markets. This is another factor that has been utilized to justify the mergers and marketing ventures among the pharmaceutical firms. This is discussed further in the next section.

2. The Emerging Biotechnology Sector

The entry of biotechnology firms into pharmaceuticals represents the first significant *de novo* entry into this industry since the early post World War II period. The first successful cloning of foreign DNA (deoxyribonucleic acid) in a host micro-organism took place in 1973. Scientists in the US and other countries immediately began to focus on the possibilities for commercial applications in pharmaceuticals and other areas.

The first firm founded to exploit recombinant DNA technology was Genentech in 1976. This firm was established by scientists from UCSF with venture capital and subsequently had its initial public offering in 1980. Several additional firms were established by scientists at Harvard, MIT, Columbia, Berkeley, Johns Hopkins, Washington, Cal Tech, and other institutions during this period. By the beginning of 1992 there were 48 publicly traded biotechnology companies (and several times this number of smaller non-public companies) specializing in pharmaceuticals and health care.

At the present time, biotechnology applications to pharmaceuticals are thriving. According to a 1991 Pharmaceutical Manufacturers Association survey report, there are over 100 biotechnology medicines currently in clinical development, as well as 21 biotechnology medicines with submitted applications at the Food and Drug Administration (PMA, 1991). Furthermore, about one in three drugs in clinical trials are now based on biotechnology (Bienz-Tadmor, 1992). Sales of biotechnology-derived therapeutic drugs and vaccines in 1991 were \$2 billion and are expected to grow rapidly over the next few years (Dibner, 1993).⁴ These are impressive statistics for an industry that began in earnest only a little over a decade ago.

Biotechnology can be used in different ways in the drug discovery and development process. First, recombinant DNA techniques can be used as a production process to produce natural or modified human proteins. Most currently approved biotechnology drugs fit this categorization. Biotechnology

⁴ As for pharmaceuticals, the distribution of sales for biopharmaceuticals is highly skewed. In 1991, three biopharmaceuticals (insulin, Epogen and TPA) accounted for the majority of overall sales.

also can be used on the rational design of synthetic molecules, such as in the cloning of genes that produce receptors which can then be used to study receptor-binding compounds. In this case, biotechnology is used to understand the disease mechanism and to facilitate rational drug design (OTA, 1991). Several pharmaceuticals currently being researched by biotech firms and established pharmaceutical firms utilize this approach.

TABLE 2. New Biopharmaceuticals Approved in the United States, 1982–1992

Drug	Originating firm ^a	Therapeutic indications	Year
Insulin	Genentech (Eli Lilly)	diabetes	1982
Human growth hormone	Genentech	human growth hormone deficiency	1985
Interferon-alpha-2a	Genentech (Hoffman La Roche)	cancer, viral infections	1986
Interferon-alpha-2b	Biogen (Schering-Plough)	cancer	1986
Anti-T-Cell (CD3)	Ortho	kidney transplant rejection	1986
Hepatitis B vaccine	Chiron (Merck)	hepatitis B prevention	1986
Human growth hormone	Eli Lilly	human growth hormone deficiency	1987
TPA	Genentech	cardiovascular disease	1987
Erythropoietin	Amgen (Ortho)	anemia	1989
Interferon alpha n3	Interferon Sciences	genital warts	1989
Hepatitis B vaccine	Smith-Kline Beecham	hepatitis B	1989
Interferon-gamma	Genentech	cancer, infections and inflammatory diseases	1990
G-CSF	Amgen	chemotherapy effects	1991
GM-CSF	Immunex (Hoechst-Roussel)	infections related to bone marrow transplantation	1991
Interleukin-2	Chiron/Cetus	cancer	1992
Factor VIII	Genetics Institute (Baxter Healthcare)	hemophilia	1992

^a Originating firm is shown first; firms collaborating in the development of a drug are shown in parentheses.

Sources: PMA, 1991; the NDA Pipeline (various issues).

The first biotechnology product, human insulin, was approved in 1982. From 1982 through to 1992, 16 biopharmaceuticals have been approved for the US market by the FDA. These products are listed in Table 2. Collectively these products have 23 approved indications. Several drugs have approved indications in the cancer area. Among these biotechnology drugs there are

also some major commercial successes. These include erythropoietin used to treat anemia in end stage renal diseases and AIDS, granulocyte colony stimulating factor for neutropenia, insulin for diabetes, TPA to dissolve blood clots in acute myocardial infarction, and human growth hormone for children with growth deficiencies.

Most of the biopharmaceuticals approved for the US market originated in dedicated biotechnology firms. This reflects the strength of these firms in the research phase. At the same time, a majority of these products were developed in collaboration with an established pharmaceutical firm, and many are marketed in whole or part by large drug firms. This latter situation illustrates the differences as well as the current nature of the interactions between the smaller biotechnology firms and the larger vertically integrated pharmaceutical industry.

These differences are also reflected in analyses of the clinical development of biotechnology drugs during the 1980s. A recent study by Bienz-Tadmor *et al.* (1992) examined the sources of and expected success rates for 95 biotechnology drugs that entered clinical trials in the US between 1980 and 1988. Of this total, only 15 drugs were developed solely by pharmaceutical firms, 36 drugs were developed solely by biotechnology firms, and 44 drugs were developed jointly by biotechnology and pharmaceutical firms. Bienz-Tadmor *et al.* also found that the clinical success rate of drugs self-originating in pharmaceuticals was markedly lower than for biotechnology firms.

These data show that the US pharmaceutical industry took a fairly cautious approach to biotechnology R&D during its early years. Pharmaceutical firms were already engaged in broad-based R&D programs in a number of therapeutic areas. Rather than restructure existing in-house R&D programs to implement what was perceived as a risky new technology, most pharmaceutical firms chose instead to provide investment financing to the new biotechnology firms and develop products in joint ventures with them as the potential for these new approaches became apparent.

Many pharmaceutical firms are now expanding their in-house R&D efforts in the biotechnology area (Dart, 1989). In this regard, the R&D expenditures of the pharmaceutical industry for biotechnology in 1992 exceeded that of dedicated biotechnology firms for the first time, according to an ongoing survey of these firms (Dibner, 1993). Relative to the dedicated biotechnology firms, pharmaceutical firms have focused particularly on the use of biotechnology as a tool for a more rational approach to conventional drug development.

If established pharmaceutical firms were laggards in the biotechnology R&D process, the new biotechnology firms (and their investors) often underestimated the long time frames and resources involved in the clinical de-

velopment, regulatory approval and market launch of new drugs. Their entry into pharmaceuticals was science driven. As such most of the employees of biotechnology were, and still are, engaged in research. Biotechnology firms were very successful in obtaining financing from venture capitalists, R&D partnerships and stock offerings to research particular technologies and product applications. Most of these firms, however, lacked the resources and expertise necessary to conduct product development over the long time frames necessary to obtain regulatory approvals.

Biotechnology firms, therefore, also had strong incentives to engage in joint ventures with the established pharmaceutical industry as their products moved out of the research phase and into clinical development. Frequently, the pharmaceutical firm will take primary responsibility for the final stages of clinical development and regulatory approval. As part of these agreements, the originating biotechnology firms may maintain some US marketing rights to the product and cede foreign marketing rights to its pharmaceutical firm partner. Alternatively, the collaborating pharmaceutical firm may obtain all marketing rights and pay a royalty from product revenues to the biotechnology firm originating the compound. Many biotechnology firms view these licensing arrangements as interim measures toward the development of fully integrated company structure.

While biotechnology-derived drugs seem assured of a strong role in pharmaceutical R&D in the future, the future evolution of the dedicated biotechnology segment of firms is somewhat uncertain. It would appear that these firms are likely to incur significant consolidation in future years. As shown in Table 1, this process has already begun with both significant mergers between biotechnology firms (Chiron and Cetus), as well as the acquisition of biotechnology firms by pharmaceutical firms (Hoffman La Roche's acquisition of a controlling interest in Genentech).

The stated original intentions of many biotechnology firms were to become fully integrated pharmaceutical firms. To date, however, most biotechnology firms are still basically research companies focused on niche markets and without salesforces of their own. Only two firms, Amgen and Genentech have managed to integrate vertically in particular industry segments, and one of these firms is no longer an independent entity (Genentech). A recent survey by Ernst and Young found that 39% of all biotechnology firms surveyed now expect to be acquired by a large firm within the next five years, and another 32% expect to merge with an equal-sized firm within five years (Ernst and Young, 1990).

At this time, it is much too soon to assess the long-term implications for the competitive structure of the pharmaceutical industry from the wave of *de novo* entry by biotechnology firms that began in 1976 with the founding of

Genentech. A small number of these firms may succeed eventually in becoming broad-based global pharmaceutical competitors. Others may be able to survive as specialty research-oriented firms that license their patented products to larger pharmaceutical firms for development and marketing in exchange for royalty income. Many other firms are likely to become subsumed within the existing structure of the pharmaceutical industry through mergers and acquisitions.

3. Changes in Innovative Structure over Time

While it is too early to assess the long-run effects of the consolidation and entry that has taken place in pharmaceuticals in recent years, it is instructive to investigate what has been happening to innovative structure in this industry. To do so, we focus in this section on what we term 'innovative output'. Innovative output is defined as the sum of the first three years of sales for each of the NCEs introduced by a firm in a given time period.⁵ Hence, total innovative output is the sum of this measure over all firms with NCE introductions and essentially weights the introduction of an NCE by its economic importance. The basic question is what has been the trend in the combined share of total innovative output by the leading innovative firms.

We used this measure first in an article that covered three five-year periods from 1957 to 1971 (Grabowski and Vernon, 1977). As discussed earlier, innovative output became more concentrated in the period after the 1962 Amendments were enacted. Table 3 reproduces the results from that article and includes new results for successive five-year periods beginning in 1970 and going through to 1989. The table shows the share of innovative output for the leading 4, 8 and 20 firms. The total number of NCEs and firms with at least one NCE are presented as well.

The major finding is that there is no trend apparent in the data. Indeed, innovative output is actually somewhat less concentrated in the 1980s compared to immediately preceding periods. There are also more individual firms with NCEs in the 1980s compared to these earlier periods.

One factor reducing the concentration of innovative output in the 1980s is the increasing presence of foreign firms in the US market. This is reflected, for example, by the fact that in the 1980–84 period, four of the leading eight innovative firms were basically foreign firms that had previously had only minor sales in the US market (Glaxo, Hoechst, ICI/Stuart and

⁵ An alternative way of weighting the importance of new drug introduction is to base it on the international diffusion of new drugs across countries. This measure is positively correlated with one based on market sales (Barral, 1987; Grabowski, 1989; Thomas, 1991). In this regard, Barral found that quality measures based on sales performance, international availability and the rankings of medical experts were positively correlated and led to similar findings in terms of international competitiveness.

TABLE 3. Trends in Innovative Output

Period	Total no. new NCEs	No. firms with NCE	Innovative output concentration		
			4 firm	8 firm	20 firm
1957-61	233	51	46.2	71.2	93.2
1962-66	93	34	54.6	78.9	97.7
1967-71	76	23	61.3	81.5	98.5
1970-74	45	26	57.8	75.6	98.7
1975-79	55	29	65.7	81.1	98.2
1980-84	67	32	48.0	64.8	92.2
1985-89	73	36	49.1	69.5	93.9

Sources: Grabowski and Vernon, 1977; authors utilizing original sales data from IMS.

Beecham—in terms of US sales rank, they were numbers 59, 23, 27 and 34 respectively in 1980). While it is true that all of these firms were represented in the US market in prior periods, there has been a distinct movement by European firms to develop and market their major products in this country during the 1980s rather than rely on licensing arrangements.

A second phenomenon apparent in the last period, 1985-89, is the presence for the first time of biotechnology firms with major innovation shares. In particular, two biotechnology firms (Amgen and Genentech) were among the top eight firms in terms of innovative shares. As discussed in the last section, the innovative importance of new biotechnology products is likely to intensify in the period ahead. Whether it will be a major deconcentrating force, however, in the pharmaceutical industry's innovative structure remains to be seen.

Another issue that we investigated in our prior study was the relation of innovative output to firm size. We found that in the post-1962 period there was a tendency for innovative output to be shifted in favor of the large-sized firm. The issue of firm size and innovation is an especially pertinent one, again given the contrasting developments in recent years discussed in sections 2 and 3 above.

In order to examine this issue for the most recent period, we performed a polynomial regression analysis on a sample of 45 pharmaceutical firms. In this analysis we utilized a Tobit analysis to regress each firm's share of innovational output over the 1985-89 period, *IS*, on its US market sales share in 1984, *MS*. The best-fitting equation was a quadratic which is shown below⁶ (standard errors are shown in parentheses).

$$IS = 0.012 - 1.10 MS + 37.8 MS^2$$

(0.010) (0.99) (16.2)

⁶ Interestingly, a 1987 study (Pavitt *et al.*, 1987) found a similarly U-shaped relationship between innovation and firm size for over 4000 significant innovations in the UK. Their study covered a wide cross-section of British industries.

FIGURE 2. Estimated relation of innov-Q to market share.

We should observe that, in the best of worlds, the equation would be embedded in a structural model and derived rigorously. For our purposes, however, we believe that a regression that simply enables us to describe efficiently the 'stylized facts' of innovative structure is justified. Also, by measuring the size variable at an earlier date (1984) than the innovation variable (1985-89), simultaneity bias should be minimized.

The quadratic equation is plotted in Figure 2, along with a 45° line from the origin. As shown in Figure 2, the descriptive equation indicates that market shares below 1% and those above 5% are associated with innovative shares in excess of firm market shares, while the reverse is true for market shares between 1 and 5%.⁷

The main reason for the strong showing of firms at the low end of the market share spectrum was the large innovation shares in the 1985-89 period for the two biotechnology firms, Amgen and Genentech. These firms ranked third and seventh in terms of innovation shares for this period, even though they started the period with no pharmaceutical sales at all. At the same time, several of the industry leaders accounted for disproportionate innovation shares in the 1985-89 period. In particular, Merck and Lilly, both ranked among the top four firms in market sales, had the two largest firm innovative shares of 21 and 12% respectively for this period (compared

⁷ We also estimated this equation using ordinary least squares (OLS), and the differences in the estimated equations were minor. In particular, the OLS estimated equation was:

$$IS = 0.017 - 0.95 MS + 33.8 MS^2 \quad R^2 = 0.32$$

(0.009) (0.87) (14.3)

to 6% shares in terms of sales). This helps to explain the increasing segment of the fitted curve between firm market shares and innovation output observed in Figure 2.

The estimated structural equation in Figure 2 nicely illustrates some of the opposing forces currently impinging on the pharmaceutical industry that were discussed in the earlier sections. This curve suggests that traditional pharmaceutical firms with small to mid-sized market shares generally have not been strong performers in terms of innovative output; and this is consistent with the consolidation wave currently occurring in this industry. By contrast, however, the new biotechnology firms have been successful in making some major innovative advances in recent years, even though they started with no established presence in this industry.

It is also important to emphasize that there is a large variability in innovative output in the case of pharmaceuticals, both across firms and over time. Size is certainly no guarantee of firm innovativeness. In this regard, our data indicate several instances in which a leading sales firm had no NCE introductions over a particular period.

One way of showing this dynamic volatility in innovation is given in Figure 3. Here we have selected the 10 largest firms by sales rank in the year 1982, which is the mid-year of our 1975–1989 period. The largest firm is indicated at the left by the number 1, the second largest by 2, and so on. The three bars show for each firm the shares of innovative output that each firm obtained in each of the three periods: 1975–79, 1980–84 and 1985–89. Clearly, there is considerable diversity in innovative performance by these leading firms.

FIGURE 3. Innov-Q shares for 10 largest firms.

If we arbitrarily take 10% as representative of a major share of innovations, four firms had such periods while several of these industry sales leaders had less than 5% shares in all three periods. When we examine the 10 leading firms in sales, in 1989, it is interesting to note that all the firms with major innovations remained in the top 10; however, two of the firms without such innovations dropped out. There is, therefore, considerable movement in firm rankings over time which is related to their innovative performance.

In terms of future research agendas, it is important to note that the pharmaceutical industry is increasingly a worldwide industry, and that there are a large number of major pharmaceutical companies worldwide. As indicated above, foreign-owned multinational companies can enter the US market quickly with significant impact through innovation even though they may only have tiny sales shares here at the time. In future research, it would be interesting to consider the shares of the major pharmaceutical firms from a global perspective. In particular, it would be interesting to see whether worldwide shares are becoming more or less concentrated as a consequence of the different factors discussed above.

4. Summary and Conclusions

The pharmaceutical industry has been subject to both significant entry from start-up biotechnology firms and consolidation among established drug firms in recent years. These developments are associated in turn with more fundamental changes in the R&D process in pharmaceuticals. It is still much too early to assess the effects of these developments on the long-term structure of the industry.

Nevertheless, an analysis of the innovative output dating back to the 1950s and extending through the 1980s indicates continuing volatility in the set of firms making major innovative contributions to the US pharmaceutical market. Furthermore, innovative output became less concentrated during the 1980s largely as a consequence of several important new drug introductions from new industry entrants. Finally, a structural equation relating a firm's innovative share to its market share for the most recent five-year period, 1985–1989, revealed disproportionate innovative contributions from both new biotechnology firms and the very largest US multinational firms. It will be interesting to see how the different forces currently at play in this industry sort themselves out during the rest of the 1990s.

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