

## Pharmaceutical Company Mergers and Research Productivity

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### ***Abstract***

*Several major econometric studies that looked at mergers and acquisitions (M&As) across various industries concluded that, in general, there is no synergy created or released by M&A activity. This paper utilizes research and development (R&D) performance in the pharmaceutical industry as a measure of output to examine the impact of M&A activity on corporate productivity.*

*After several decades of relative stability in the pharmaceutical industry, there occurred three distinct “waves” of pharmaceutical company mergers. The first took place in the late 1980s/early 1990s, the second happened in the mid-1990s, and the third occurred at the beginning of the 21<sup>st</sup> century. This paper examines the effect of the first two waves of corporate mergers in the pharmaceutical industry on research performance. Rather than focusing on conventional econometric/financial indicators, this study considers chemically novel drugs approved by the United States Food and Drug Administration (FDA), as well as patents acquired in the United States, as upstream indicators. Chemically novel drug data, employed in the study as R&D output indicators, were weighted according to the FDA’s evaluation of each approved drug’s clinical significance as a means of identifying genuine innovation. R&D expenditures of each pharmaceutical organization included in the study were utilized as the R&D input indicator.*

*Preliminary findings indicate that when compared to those companies within the pharmaceutical industry that did not experience merger activity during the same time period, as well as to the industry as a whole, pharmaceutical companies that merged were able to achieve more favorable post-merger productivity scores (i.e., viable new drugs per research dollar expended) than were attained prior to their merger. From a research output perspective, both the first and second waves of mergers within the pharmaceutical industry appear to have been relatively successful. Patent data show the accomplishment of synergy, as well as the implementation of effective merger strategy, for the second wave of mergers. These phenomena contradict the conclusions of the*

*majority of the econometric literature relating to mergers. They are examined in some detail and possible explanations are discussed.*

## **Introduction**

The issue of productivity within the pharmaceutical industry has been an area of great interest for the last several decades. The work of Comanor (1965) was a seminal piece of research. It concluded, based on econometric analysis, that there were diseconomies of scale in pharmaceutical research and development (R&D). This conclusion was influential in the United States Government's decision to oppose the proposed merger of Warner Lambert and Parke Davis. Subsequent work, commencing with that by Koenig and Gans (1975), has tended toward the opposite conclusion (i.e., there are economies of scale in pharmaceutical R&D).

One possible reason for the difference in conclusions is that while Comanor drew his conclusion from sales figures in a domain where, in many cases, the products are not capable of being substituted (e.g., a drug for diabetes can not be substituted for a drug for hypertension), Koenig and Gans, in the initial analysis to do so, looked at R&D production (i.e., the number of drug entities themselves) rather than at sales. Vernon and Gusen (1974) and Schwartzman (1976) also found economies of scale using New Chemical Entities (NCEs) that were modest in the first case, but more significant in the latter. Both studies weighted NCEs by sales, a useful technique from an economic perspective, but one that obscures strict analysis of productivity. Jensen (1987), using NCEs that had not been weighted, found a positive relationship between R&D expenditures and innovation, but no scale effect (i.e., no indication that economies of scale were related to firm size). More recently, Graves and Langowitz (1993) also found slight diseconomies of scale using NCEs as a principal measure. When considered collectively, these studies appear to indicate that no significantly discernable effect upon productivity results from economies of scale.

Certainly the wave of mergers in the pharmaceutical industry indicates that (1) the industry sees advantages to mergers, presumably including economies of scale in R&D, and (2) government regulators have become much more hospitable toward merger activities in the pharmaceutical industry, presumably, in part, because they no longer have the perception that mergers are antithetical to R&D productivity. Thompson (2001) reported that pharmaceutical companies that merged experienced slower sales growth (2% to 12%) than non-merged companies (15% to 20%). But, Thompson, Vice-President of Corporate Strategy at Eli Lilly, did not set forth his data and presents his findings in an article extolling Lilly's growth strategy without recourse to merger. A recent financial study by McKinsey & Co. cited in *Business Week* (Barrett & Capell, 2002) finds no correlation between return on investment and company size in the pharmaceutical industry.

The current study continues the tradition of examining pharmaceutical R&D productivity by considering concrete outputs, such as approved new molecular entities

and patents, rather than sales. The central question is: Was any synergy created or increased efficiency realized by the numerous mergers that took place in the pharmaceutical industry in recent years?

Econometric studies have tended to conclude that there is no synergy overall from mergers. They conclude that, while some mergers do indeed produce positive effects, there are at least as many instances where the effect is negative (“The Trouble with,” 1994). This conclusion received perhaps its most visible presentation in the somewhat infamous September 10, 1994 issue of *The Economist*. Its cover photo showed two camels “consummating” their “corporate marriage.” Within the issue, “lovelorn company bosses” were advised to “take your time” and “play the field” when contemplating mergers that could cause them to “end up in bed with a camel” (“The Trouble with,” 1994). The issue’s feature article declared that econometric studies (Shleifer & Vishny, 1990; Mitchell & Lehn, 1990) indicate that, on average, no synergy is produced from mergers (“Making a Meal,” 1994). When mergers occur, there are as many losers as winners. A study by KPMG International (Bruner, 1999) concluded that 83% of the 700 most expensive acquisitions during the period 1996 to 1998 were unsuccessful in producing any major benefit with regard to shareholder value. Were the same study to be conducted today, following the bursting of the dot.com bubble, its conclusions would undoubtedly be more negative than those originally reached.

The intent of this study is to examine whether synergies can be detected in mergers when they are examined from a scientometric, rather than an econometric, point of view.

## **Background**

The spate of late 20<sup>th</sup> and early 21<sup>st</sup> century mergers have occurred in three distinct “waves.” The first took place in the late 1980s/early 1990s, the second happened in the mid-1990s, and the third occurred at the beginning of the 21<sup>st</sup> century. These mergers represented a dramatic change in the landscape of the pharmaceutical industry. A landscape which had been structurally stable for almost half a century, from the initiation of change caused by appropriations of foreign assets in World War II until the first wave of mergers in 1989.

The first merger wave consisted of the Bristol-Myers Squibb and Smith-Kline Beecham mergers. The second wave of mergers occurred in the years 1994 to 1996. American Home Products merged Ayerst and Wyeth in 1994, two subsidiaries that had been run independently. This was followed by: Glaxo Wellcome in 1995, Pharmacia and Upjohn in 1995, Hoechst A.G. in 1995, and Novartis, previously Ciba-Geigy and Sandoz, in 1996. The third wave commenced in 2000 when Pfizer merged with Warner Lambert, a far larger merger than the proposed Warner Lambert - Parke Davis merger that the United States Government had opposed in the 1960s.

The phenomenon of mergers occurring in waves is an interesting one. It is a general phenomenon that is not limited to specific industry segments, such as the pharmaceutical industry (Shleifer & Vishny, 1990). Why mergers occur in waves may be an unsolvable question. According to *The Economist*, “No study has been able plausibly to explain why mergers happen in waves.” It suggested that they arise whenever: (1) an industry is under stress and (2) “economies are buoyant and “company bosses have money to spend (or can raise it more easily) and worry less that shareholders will call them to account for what they do with it” (“Making a Meal,” 1994). This explanation appears to be as reasonable as any other explanation that has been proposed to date.

## **Discussion of Data**

Drug data was obtained from the United States Food and Drug Administration (FDA). The drugs specifically examined were those considered by the FDA to be New Molecular Entities (NMEs). Minor modifications of known drug entities were excluded. The use of this particular data has the advantage of limiting the analysis to those new therapeutic agents that are likely to represent a significant research component and excludes possible noise created by companies focusing more on capitalizing upon their already patented compounds by devising minor variations.

The FDA breaks down drug data further into what are regarded as more or less important drugs. Prior to 1992, the FDA classified new drug approvals by whether they were considered to represent (1) an important therapeutic gain, (2) a modest therapeutic gain, or (3) little or no therapeutic gain. Beginning in 1992, the FDA ceased making these distinctions and began distinguishing between those new drug applications (NDAs) that would receive priority review and those that would receive merely a standard review. This change was prompted by the activism of those campaigning for a review process that would allow AIDS drugs to be reviewed and made available more promptly. It also avoided awkward questions about drugs described with the phrase “little or no therapeutic gain.”

For the purpose of this analysis, we considered “priority review” drugs to be the equivalent of “important therapeutic gain” drugs, since these drugs are likely to have an important therapeutic impact for which the FDA will assign a priority review. On the same grounds, we treated “standard review drugs” as the equivalent of the combined previous classes of “modest therapeutic gain” and “little or no therapeutic gain”. This is convenient, but probably not a perfect mapping.

It appears that the FDA was more discriminating in its selection of important therapeutic gain (ITG) drugs, 15% of all approved drugs, than it is in selecting drug candidates for priority review, 44% of all approved drugs, since not all candidates selected for priority review may reach the approval stage. Some of this variation is quite logical. ITG drugs were designated after having been fully examined and with substantial data in hand. Priority review drugs are selected further upstream, near the beginning of the review process when they have been only partially examined. It is only

logical for the FDA to be less selective, or perhaps more hopeful, at what one might call the “likelihood stage.” Other factors may be the activism mentioned above, the increasing public scrutiny under which the FDA operates, and the FDA’s disinclination to be seen as giving short shrift to anything that may have real potential, particularly for diseases in the public spotlight.

Patent data was supplied by CHI Incorporated. They kindly “deconstructed” their data by backing out the individual company data before mergers occurred.

R&D financial data was obtained from a number of sources including corporate annual reports, United States Securities and Exchange Commission (SEC) 10-K and 20-F reports, *Moody’s Manuals*, Mergent’s *FISOnline*, and Disclosure’s *Worldscope*. All R&D expenses stated in foreign currencies were converted to United States (U.S.) dollars using exchange rates for the particular year as reported in “Table B-110.—Foreign exchange rates, 1981-2001” of the 2002 *Economic Report of the President* published by the United States Government Printing Office. U.S. Consumer Price Index (CPI) data obtained from the U.S. Federal Reserve Bank of Minneapolis was used to convert reported R&D expense data for all companies into present-day (i.e., 2002) dollars adjusted for inflation.

## **Methodology**

An index of pharmaceutical research productivity was compiled for each merged company. Simply stated, the index represents FDA drug approvals or patents obtained per research dollar expended. The FDA drug approval index was further refined by (1) including only those drugs categorized by the FDA as NMEs and (2) giving increased weight to those drugs (a) judged by the FDA to be important therapeutic gains or (b) selected by the FDA for priority review.

Overall, there were approximately 2.5 times more drugs in the lesser category (i.e., 185 modest, little, and standard drugs) than there were in the superior category (i.e., 75 important and priority drugs). We have used that ratio, 2.5 to 1, to weight the superior category drugs. In other words, in our measure of overall drug output, we have given important/priority drugs a weight 2.5 times that of modest/little/standard drugs.

The rationale for weighting the drug data is that drugs classified by the FDA as being an important therapeutic gain or a priority review drug are more important by definition than modest or little therapeutic gain or standard review drugs from a societal viewpoint. A metric that accords greater weight to more important drugs is likely to be a better metric of that company’s performance or utility of output. The question is: What weight factor should be utilized? Observing that important/priority drugs are 2.5 times less frequent than modest/little/standard drugs, and perhaps 2.5 times more difficult to develop, a factor of 2.5 was selected. While this is a “rational” approach, there is no specific correlation between difficulty of development and degree of social utility for important/priority drugs. Consequently, the choice of a weighting factor is arbitrary.

Changes in a pharmaceutical company's productivity following merger activity were compared to changes in productivity for other major pharmaceutical companies that had not been involved in mergers during the same period, as well as to such changes for an aggregate of all major companies within the pharmaceutical industry. This metric has been used in previous studies (Koenig, 1983, 1992).

### **Limitations and Caveats**

This study contains two major limitations. The first is that the size of the population is modest. For example, only two mergers, the Bristol-Myers Squibb and Smith-Kline Beecham mergers occurred in the first wave. If this were merely a sample, it clearly would be too small for drawing generalizations. However, it is not a sample; it is the entire population. Nevertheless, it is important to note that any generalization or extendibility of conclusions drawn from this study is limited. The data, while accurately describing a particular company or wave, should only be used to draw extendible conclusions that can be applied as a single piece of evidence, among many, concerning the merger phenomenon in general.

The second limitation is the "lag" phenomenon. There is certain to be a delay between the consummation of a merger and the merger's effect upon the R&D process. Additionally, because of the extended clinical trials required before a new therapeutic agent can be approved for use, a considerable period of time will often elapse between a drug's "discovery" and its approval for clinical use. In other words, an extended development period can exist between the research phase and any measurable output that would be available for analysis (e.g., a new drug approval). As a result, this study required the examination of drug output data for a number of years after the date of each merger. Because of this limitation, it was possible to consider the first and second wave of pharmaceutical company mergers during this inquiry, but not the third wave.

### **Analysis of Data**

When pre-merger (1981-1989) company performance, as measured by constant dollar cost per weighted NME, is compared to post-merger (1990-2000) performance for the first wave of mergers (**TABLE 1**), first wave companies appear to be performing better than both non-merged companies and the overall pharmaceutical industry. The cost per weighted NME in constant dollars for merged first wave companies *increased* by only 29%, while the cost *increased* 43% for non-merged companies and 41% for all companies. When the *non-weighted* constant dollar cost per NME is considered, the relationship among the three classes of companies was similar. Cost per NME for first wave merged companies *increased* 65%, while non-merged companies and all companies experienced a 101% and 81% *increase* respectively. Generalizing from these results is dangerous since the two mergers that make up the total Wave 1 population performed

differently. SmithKline Beecham's cost per NME *decreased* 13%, while Bristol-Myers Squibb's *increased* by 72%.

If analysis of Wave 1 data is performed in a manner that is comparable to the limited analysis that is currently possible for Wave 2 data (i.e., five years subsequent to the merger wave), Wave 1 mergers appear substantially more successful. Comparing data for the years prior to Wave 1 mergers (1981-1989) to the five years subsequent to the first merger wave (1990-1994), cost per weighted NME in constant dollars *decreased* by 22% for those companies that merged, while the cost *increased* 15% for non-merged companies and 19% for all companies.

When pre-merger (1981-1995) company performance is compared to post-merger (1996-2000) performance for the second wave of mergers (**Table 2**), second wave companies also appear to be performing better than both non-merged companies and the overall pharmaceutical industry. The constant dollar cost per weighted NME for the five companies that constitute the second wave *increased* by only 1%, while the cost *increased* 48% for non-merged companies and 34% for all companies. When the constant dollar cost per *non-weighted* NME is considered, the relationship among the three classes of companies was similar. Cost per NME for second wave companies *increased* 17%, while non-merged companies and all companies experienced a 93% and 61% *increase* respectively. When utilizing NME drugs as a standard of measure, it may be concluded that productivity increases following merger activity.

The results are more ambiguous, making conclusions more difficult to reach, when studying patent data. When pre-merger (1981-1989) company performance, as measured by constant dollar cost per patent, is compared to post-merger (1990-2000) performance for the first wave of mergers (**Table 3**), first wave companies appear to be performing worse than both the non-merged companies and the overall pharmaceutical industry. The cost per patent for merged first wave companies *increased* by 303%, while the cost *increased* 281% for non-merged companies and 244% for all companies.

If analysis of Wave 1 patent data is performed in a manner that is comparable to the limited analysis that is currently possible for Wave 2 data, Wave 1 mergers appear to be less successful. Comparing data for the years prior to Wave 1 mergers (1981-1989) to the five years subsequent to the first merger wave (1990-1994), constant dollar cost per patent *increased* 61% for those companies that merged, while the cost *increased* for 35% for non-merged companies and 38% for all companies.

When pre-merger (1981-1995) company performance is compared to post-merger (1996-2000) performance for the second wave of mergers (**Table 4**), second wave companies appear to be performing better than both non-merged companies and the overall pharmaceutical industry. Constant dollar cost per patent for the five companies that constitute the second wave *decreased* by 21%, while there was a 3% cost *increase* for non-merged companies and an 8 % cost *decrease* for all companies. When utilizing patents as a standard of measure, companies that merged in the first wave lost ground to

non-merged companies, while companies that merged in the second wave gained ground over non-merged companies.

While patents are important to a pharmaceutical company, they are merely tools with which to stake a claim to a new drug entity. The pharmaceutical industry axiom "the NDA is the name of the game" is indicative of the far greater value placed on approved New Drug Applications (NDAs). Based upon currently available NME data, the conclusion that mergers within the pharmaceutical industry have resulted in increased corporate productivity is a persuasive one.

## **Discussion and Further Research**

There has been substantial discussion in the business press about the spate of pharmaceutical company mergers. Speculation has focused on why the mergers took place and whether they have been beneficial both overall and for the individual companies involved in each discrete merger. Most of this discussion is decidedly non-scholarly, but a number of intriguing speculations have been put forward.

One interesting viewpoint is that the first wave of pharmaceutical mergers resulted from necessity, while the second wave represented attempts to capitalize on opportunities. The data presented above is not inconsistent with this hypothesis, but does not confirm it. It does, however, indicate that the second wave was more successful than the first.

The contrast between the NME drug data and the patent data is intriguing. Remember the axiom "the NDA is the name of the game." Pharmaceutical companies depend on a few "blockbuster" drugs for the majority of their revenue. Comparatively short patent lives and the constant threat that an existing drug will be superceded by a more efficacious drug, even during the life of the drug's patent, require pharmaceutical companies to keep their pipelines full. Consequently, it has been frequently claimed that the principal goal of a merger is to acquire or combine with a company whose pipeline appears healthy. This logic is compelling for a company with a weak pipeline and makes smaller companies with a comparatively strong pipeline an attractive candidate for merger and/or acquisition activity. If this type of strategic thinking plays a primary role in pharmaceutical industry mergers, overshadowing such factors as buoyant economic conditions and shareholder scrutiny, we would expect to see results much like what has been found in this study.

Increased merger synergy, when measured by drugs rather than by patents, is not at all inconsistent with this scenario. Once again, remember the "name of the game." Companies are much more likely to be evaluated as potential merger candidates based on their pipeline rather than on their patent portfolio. This is true in spite of the fact that the patent portfolio may be a better indicator of fundamental research strength (Narin, Noma, & Perry, 1987). That patent portfolio, however, is more difficult to evaluate. The



number of NDAs that are ultimately approved is very small. One estimate is that the ratio is 5,000 to 1 (Pollack, 2002).

It is also not inconsistent with this scenario to observe improved performance over the five-year post-merger period for the two individual companies that experienced merger activity during Wave 1. However, only SmithKline Beecham maintains this improvement over the next decade. Bristol-Myers Squibb's performance deteriorates noticeably over the same period. This is not inconsistent with the "pipeline" hypothesis. This limited sample suggests that, while there is evidence of short-term utility in merger activity, there is no real evidence of long term synergy when measured by approvals for NME drugs. Continued study of the companies that comprise Wave 2 is necessary to gather additional evidence of long-term synergy. The passage of time will also provide data for an analysis of the third wave of merger activity.

If the assumption is made that NMEs are drugs that have been synthesized in the past, while patents are closer to being a measure of current activity, the improved patent position of the five companies that merged during Wave 2 may be taken as evidence that synergy arises not only from "pipeline opportunism," but also from the merger itself. This hypothesis leads to an area for additional research that can be carried out in the immediate future. Since an acquiring and a target company are clearly identifiable in most mergers, post-merger products might be examined to determine the source of the patents used to develop each new product. This could be accomplished through an examination of the patent history of each compound. If the hypothesis is correct, a higher proportion of new post-merger products will have been generated from target company patents.

Using patent family and patent classification data to examine pre-merger and post-merger emphases could further extend the current research. Such data might also be helpful for examining any possible changes in patenting strategy. If changes are evident, this data could be used to determine whether they "muddy" the patent data.

Building on the work of McMillan and Hamilton (2002), an additional opportunity to elucidate the "pipeline opportunism" vs. synergy debate would be the use of publication and citation analysis to enrich this study. The authors used such analysis in previous work (Koenig, 1983). They expect to continue work in this area and invite collaboration.

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A revised version of this contribution has been published as:

Michael E.D. and Elizabeth M. Mezick (2004). Impact of Mergers & Acquisitions on Research Productivity within the Pharmaceutical Industry. *Scientometrics*, 59(1) 157-169.