



**Comments Submitted to the Federal Trade Commission on
the Pfizer-Wyeth and Merck-Schering Plough Mergers**

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Introduction

We are both former Directors of the Bureau of Economics at the Federal Trade Commission, and have studied, lectured and written on the economics of the pharmaceutical industry for many years. As such, we feel obliged to submit these comments to the Commission because, in our judgment, both the Pfizer-Wyeth and Merck-Schering Plough mergers will further retard the rate of pharmaceutical innovation and impose substantial consumer harm.

This is an important matter, and we urge the Federal Trade Commission to consider these issues more fully. Pharmaceutical innovation is critically important for continued improvements in public health.¹ And for many decades, the major pharmaceutical companies have played an essential role in sustaining a rapid pace of pharmaceutical innovation. Society has benefited greatly from their efforts. In recent years, however, the productivity of the innovation process has declined. The leading companies have spent increasing amounts on research and development without showing a corresponding increase in the number of new products introduced. Some companies have responded by seeking refuge in the greater scale achieved

¹ H.E. Frech and Richard D. Miller, *Health Care Matters: Pharmaceuticals, Obesity and the Quality of Life*, American Enterprise Institute, 2004.

through mergers. For the reasons outlined below, we believe that such efforts will merely depress further the rate of innovation.

Many of our views on these matters are contained in two earlier statements posted on the web site of the American Antitrust Institute, with whom we are both affiliated. These statements are attached, and we request that they be included with our Comments. In addition, however, we offer some further considerations which support our position that these mergers are not in the public interest.

Innovation Markets

In guidelines issued jointly by the U.S. Department of Justice and the Federal Trade Commission, the Agencies write: **“An innovation market consists of the research and development directed towards particular new or improved goods or processes, and the close substitutes for that research and development.”** The Agencies continue:

In assessing the competitive significance of current and likely potential participants in an innovation market, the Agencies will take into account all relevant evidence. When market share data are available and accurately reflect the competitive significance of market participants, the Agencies will include market share data in their assessment.... The Agencies may base the market shares of participants in an innovation market on their shares of identifiable assets or characteristics upon which innovation depends, on shares of research and development, or on shares of a related product.”²

Because the proposed mergers will affect competitive conditions in the relevant innovation market, they need to be evaluated in this setting as well.

A relevant question concerns the dimensions of this market. Are the R&D outlays of the major drug companies limited to specific research areas, or do they extend throughout the whole

² U.S. Department of Justice and Federal Trade Commission, *Antitrust Guidelines for the Licensing of Intellectual Property*, April 6, 1995, Paragraph 3.2.3.

range of pharmaceutical products? The answer turns on the degree of dynamic substitutability in their R&D efforts as between disease or therapeutic areas.

Various factors indicate that this market extends across numerous areas. The increasing efforts of major drug companies to engage in cancer research suggest high substitutability. On the front page of *The New York Times* for September 2, 2009, there is the following account:

Pfizer's fortunes in the past were built on cardiovascular drugs, like the cholesterol buster Lipitor and the blood pressure pill Norvasc. But the future of Pfizer, the world's largest pharmaceutical company, may rest ... [on the] 1000 researchers [engaged] for an all-out effort to develop drugs for cancer, a disease the company once largely ignored.

Virtually every large pharmaceutical company seems to have discovered cancer, and a substantial portion of the smaller biotechnology companies are focused on it as well. Together these companies are pouring billions of dollars into developing cancer drugs.³

This report implies that pharmaceutical industry research efforts are fungible across disease areas. Most of the key personnel skills are flexible. Where there are economic incentives to do so, the major drug companies can shift their R&D resources from one area to another. Pfizer and other leading companies have clearly expanded their research activities into cancer research and presumably away from other disease areas. Such actions would indicate that R&D resources are highly substitutable across disease areas.

Recently published economic research supports that conclusion. In an empirical study across therapeutic areas, the authors report that "the retail price of existing drugs induces new drug development. The higher the price in a therapeutic category, the larger the number of drugs in the development pipeline in that therapeutic category."⁴ This finding again suggests high

³ Andrew Pollack, "Taking Big Risks for Big Payoff, Industry Seeks Cancer Drugs," *The New York Times*, September 2, 2009, p. 1.

⁴ Abdulkadir Civan and Michael T. Maloney, "The Effect of Price on Pharmaceutical R&D," *The B.E. Journal of Economic Analysis and Policy*, Vol. 9, Iss. 1, Article 15; available at <http://www.bepress.com/bejeap/vol9/iss1/art15>.

dynamic substitutability in research and development throughout the pharmaceutical industry, and therefore the presence of an industry-wide relevant market.

Competition in the Innovation Market

In our earlier memoranda on this merger, we briefly summarized some economic studies dealing with the pace and determinants of pharmaceutical innovation. We observed there that the pace of pharmaceutical innovation has declined in recent years, which is one reason why the share of generic products now accounts for nearly 70 per cent of all prescriptions filled in the United States.⁵ At the same time, pharmaceutical industry R&D outlays have continued to increase. Between 1998 and 2008, pharmaceutical industry R&D expenditures made in the United States grew from \$17.1 billion to \$38.4 billion, or by more than 100 per cent over a ten year period.⁶ In response, some pharmaceutical companies have sought to offset their lagging productivity problem through mergers and acquisitions. These proposed mergers are merely two examples in a larger merger wave. However, as discussed in our earlier memoranda, there is no evidence that the innovation process has improved as a result of prior large scale mergers.

Another recent feature of pharmaceutical research is that, increasingly the major drug companies have out-sourced large portions of the R&D process.⁷ Increasing amounts of the drug discovery process are carried out in the laboratories of small biotech firms.⁸ These smaller firms often look to the major drug companies for financial support, usually after but sometimes before discovering promising new molecules. As emphasized in the attached memoranda, there are prospects for substantial synergies from affiliations between the small biotech firms and the major pharmaceutical companies, which should be fostered and encouraged. A considerable

⁵ Generic Pharmaceutical Association, Press Release of May 7, 2009.

⁶ Pharmaceutical Research and Manufacturers of America, *PhRMA Annual Membership Survey*, 2009.

⁷ See William S. Comanor, "The Economics of Research and Development in the Pharmaceutical Industry, in Frank Sloan and C.R. Hsieh, *Pharmaceutical Innovation*, Cambridge University Press, 2007, pp. 54-72.

⁸ F.M. Scherer, "Pharmaceutical Innovation," in Bronwyn Hall and Nathan Rosenberg, *Handbook on the Economics of Technological Change*, North Holland, forthcoming.

danger arising from mergers between and among major drug companies is that with reduced competition in the relevant innovation market, the large companies will be diverted from achieving these synergies.⁹

The cohort of large pharmaceutical companies that comprise the most likely supporters of biotech product development opportunities, either through merger or looser alliances, has become increasingly concentrated during the last two decades. As recently as 1987, government statistics show that the leading eight pharmaceutical companies accounted for 36 percent of U.S. industry shipments of pharmaceutical products. By 2002, however, the share of shipments attributable to the top eight companies had risen to more than 53 percent. Importantly, these figures understate the extent of concentration among research-based companies because they include approximately 18 percent to 24 percent of shipments made by smaller generic product firms.¹⁰

A critical element to be considered in evaluating the innovation consequences of large pharmaceutical mergers is uncertainty. The outcome of pharmaceutical R&D is highly uncertain. At the idea generation stage, tens or even hundreds of possibilities may be evaluated before a single molecule is put into clinical testing. Statistics compiled at Tufts University reveal that only 20 to 23 percent of the new medical entities approved for human tests by the FDA emerge with FDA approval for marketing. When there is so much uncertainty, the optimal strategy is to have laboratories pursuing parallel but independent paths. A recent paper¹¹ by one of us shows that when the project success rate is 20 percent -- i.e., in the bounds of past experience with clinical trials -- the optimal number of parallel paths is on the order of 20. For projects with higher uncertainty, as in pre-clinical stages, the optimal number of parallel paths is considerably higher.

⁹ There have been press reports suggesting that the increased debt Pfizer will assume to acquire Wyeth might preclude it from buying any but the smallest of biotech firms: (<http://www.nytimes.com/2009/01/27/business/27wyeth.html?scp=1&sq=pfizer%20wyeth%20january%2027,%202009&st=cse>.)

¹⁰ U.S. Bureau of the Census, *Concentration Ratios in Manufacturing Industries*, various years.

¹¹ F.M. Scherer, "Parallel Paths Revisited," John F. Kennedy School of Government, Harvard University, Faculty working paper, RWP07-040, September 2007.

The exact optimum number of parallel paths depends on the value of the resulting innovations: the more valuable, the larger the optimal number of parallel but independent R&D paths. The paper referenced above makes no distinction between private and social value. It is well known that the sum of private values appropriated by innovators plus the value conferred in the form of consumer surplus is much larger on average than the private values alone. Given the high social value of pharmaceutical innovations, it is clear that sustaining numerous parallel paths maximizes consumer welfare. By its impact in constricting the number of parallel but independent research groups in any given potential field of therapy, large drug comp[any mergers violate the basic principles of parallel paths logic.

In 2008, Pfizer spent \$7.9 billion on pharmaceutical R&D in 2008 and Wyeth spent \$3.4 billion, for a total of \$11.3 billion. Since neither company reports how much was spent in the United States and how much abroad, we compare these amounts with total industry spending on research and development both in the United States and world-wide. The standard measure of industry spending for research and development is that provided by the Pharmaceutical Research and Manufacturers of America (PhRMA) from their annual surveys of member companies. For 2008, the total amounts reported on their web site are \$38.4 billion and \$50.3 billion respectively. If this merger is permitted to proceed, the new entity will account for 29 per cent of pharmaceutical industry domestic spending on R&D and 22 per cent of this spending world-wide.

In addition to the Pfizer – Wyeth merger, Merck and Co., another leading drug company, recently announced its acquisition of Schering-Plough for just over \$41 billion. In 2008, Merck spent \$4.8 billion on R&D and Schering-Plough spent \$3.5 billion, for a total of \$8.3 billion.¹² This second merger would therefore account for 22 per cent of pharmaceutical industry domestic spending on research and development and 17 per cent world-wide.

Because the Pfizer – Wyeth and Merck – Schering-Plough mergers were announced soon after one another and can therefore be considered contemporaneous, it is instructive to evaluate

¹² Merck and Schering-Plough Annual Reports.

their joint effects on the relevant innovation market for pharmaceuticals. The two new entities would represent fully 51 per cent of total industry domestic R&D spending and 39 per cent of total world-wide spending. In our judgment, this degree of consolidation in the pharmaceutical innovation market will further depress the rate of development and introduction of important new medicines.



The American Antitrust Institute

MEMORANDUM ON THE PROPOSED ACQUISITION BY PFIZER OF WYETH

William S. Comanor¹ and F. M. Scherer²

This memorandum, written on behalf of the American Antitrust Institute, offers a preliminary analysis of the issues posed by the proposed merger between two leading pharmaceutical companies: Pfizer Pharmaceuticals and Wyeth Laboratories. It was prepared without access to the companies' required filings with the Department of Justice and the Federal Trade Commission. Furthermore, because of the grave crises currently facing the American economy, it ranges beyond the conventional scope of merger analyses under U.S. antitrust laws.

We consider the proposed merger in three separate dimensions. First, we examine the macroeconomic consequences of the merger, and second its likely competitive effects in the markets for the two firms' existing product menus. However, as pharmaceutical firms incur large expenditures on research and development (R&D) hoping to develop the next generation of drugs, we also consider the effects of the proposed merger on the relevant innovation markets and the likely effects thereby on the rate of pharmaceutical innovation.

¹ University of California, Santa Barbara and Los Angeles; formerly Director of the Bureau of Economics, Federal Trade Commission, 1978 - 1980.

² John F. Kennedy School of Government, Harvard University, formerly Director of the Bureau of Economics, Federal Trade Commission, 1974 - 1976.

Macroeconomic Consequences

Normally, it is not within the province of antitrust analysis to include the macroeconomic implications of a merger transaction. However, these are not normal times, since the United States is threatened with a credit markets freeze and the worst economic downturn since the 1930s. We therefore proceed where trustbusters generally fear to tread.

On January 25, Pfizer proposed to pay \$68 billion to acquire Wyeth.³ The acquisition would be financed with \$26 billion from Pfizer's internal coffers, \$22.5 billion through loans principally from four large banks, with the remaining \$19.5 billion paid through an exchange of stock. The main banks providing loan financing for the deal are Goldman Sachs, JPMorgan Chase, Citigroup, and Bank of America. These four banks together have received U.S. TARP fund injections thus far of \$95 billion plus credit guarantees (as of January 28) of \$345 billion. As a result, this is a transaction financed at the margin by U.S. taxpayers

The contemplated \$48.5 billion of cash financing is to be paid to Wyeth shareholders in exchange for their shares of the company's common stock. Our first question is: Where will those funds flow, and what are the macroeconomic consequences of these payments as compared with the likely alternatives? We have no data on the institutional distribution of Wyeth shareholders. However, if Wyeth stockholdings are typical of equity holdings for all U.S. corporations, then roughly 33 percent of the value of the shares is held by private individuals, 49 percent by insurance companies, pension funds, and mutual funds, and 13 percent by foreign residents, including sovereign wealth funds.⁴

³ "In Tight Market, Pfizer Agrees to \$68 Billion Deal for Wyeth," New York Times, January 26, 2009, p. A1.

⁴ Statistical Abstract of the United States: 2007, Table 1182, p. 745.

For the approximately one-third of the contemplated payments going to individual stockholders, it is well known that most individual common stockholdings are concentrated among the most wealthy U.S. citizens.⁵ Although some of the cash received by wealthy Wyeth stockholders would come back to the federal government through increased capital gains taxes, most of the remainder would be saved rather than spent. The reason is that the wealthiest individuals have a relatively low marginal propensity to consume, especially out of windfall income, which the proposed transaction would generate. A low marginal propensity to consume means that the transaction would stimulate little additional activity in the "real" sector of the economy, and hence lead to few additional jobs as compared to loans made to support incremental investments in plant, equipment, infrastructure, business inventories, new business formation, and the like. Most of the merger-consummating funds would flow back into securities markets, having a tiny marginal effect in reducing the cost of capital. In an economy caught in a classic Keynesian liquidity trap, as the U.S. economy currently is, a slightly lower cost of financial capital is unlikely to induce any significant job-creating new investment.

Most of the remaining cash transfers would go to financial intermediaries such as pension funds, insurance companies, and mutual funds. Since some pension funds are experiencing cash flow deficiencies, the infusion of Pfizer and bank money from the stock acquisition might marginally increase the funds' ability to maintain payments to retirees and survivors, with a stronger positive impact on the propensity to consume. Most of the transfers are likely to be reinvested in other securities, with the same slight impact on investment and job creation as described in the previous paragraph.

⁵ See F. M. Scherer, "Corporate Ownership and Control," in John R. Meyer and James Gustafson, eds., The U.S. Business Corporation (Ballinger: 1988), pp. 46-48.

Consider the following counter-factual situation: Suppose the \$22.5 billion of commercial bank loans were made instead to support business inventory maintenance, investments in new plant and equipment, research and development, or the like. Such loans would generate substantial increases in employment, which in turn would lead to further increases in consumer spending. To the extent that the Pfizer loan "crowds out" alternative loans to support investments in business formation and expansion, fewer jobs are created and an important macroeconomic loss incurred.

One might argue that this scenario is unlikely; that the large banks are so paralyzed by credit default risk that they would, absent the merger, leave the funds in their coffers as an additional monetary base. If that were the case, then one must admit that the Treasury's TARP program had largely failed to achieve one of its principal objectives.

Traditional Merger Market Effects

The pharmaceutical industry encompasses a large number of relevant markets, which are traditionally defined in terms of therapeutic categories. Within categories, there should be high degrees of substitutability in consumption, since the various products are used for similar purposes, but low degrees of substitutability across such categories. In a study published in 1998, co-author Comanor reported that increasing the number of rival suppliers in such markets led to significantly lower prices.⁶

A relevant issue therefore is the extent to which the merging parties sell rival drugs in the same therapeutic markets. Currently, there are some markets where their products compete, with

⁶ Z. John Lu and William S. Comanor, "Strategic Pricing of New Pharmaceuticals," *Review of Economics and Statistics*, Vol. 80, No. 1, Feb. 1998. Similar findings are reported in Joseph A. DiMasi and Cherie Paquette, "The Economics of Follow-on Research and Development," *Pharmaceutics*, vol. 22 (2004 supplement), pp. 1-14.

the likelihood that higher prices would result. The most substantial of these is the anti-depressant market, where Wyeth's *Effexor XR* and *Effexor* compete with Pfizer's *Zoloft*. Other such markets include those for anti-bacterials, where Wyeth's *Tygacil* competes with Pfizer's *Zyvox*, and for anti-neoplastics, where Wyeth's *Torisel* competes with Pfizer's *Sutent*. Although the overlapping products may account for a minority of sales by the two companies, there are still likely to be substantial anti-competitive effects resulting from the proposed merger.

Unfortunately, we have no evidence on the extent to which the two companies have prospective products in research, development or testing that would be rivals if and when they receive FDA approval. To the extent that there are developmental overlaps, an innovation market analysis should be undertaken, and if the overlaps are large, that would provide a further basis for opposing the merger. In addition to these issues, there are also larger concerns to be considered.

The Pace of Pharmaceutical Innovation

In recent years, it has become increasingly clear that the pace of pharmaceutical innovation has declined sharply. Iain Cockburn summarizes current concerns at the start of his new survey:⁷

By many accounts, the pharmaceutical industry is experiencing a severe decline in research productivity. More and more money is being invested in R&D, but the rate at which new drugs are introduced is failing to keep pace. Recent years have seen a steady flow of reporting in trade journals and mass media referring to drug companies' "dry," "weak," or "strangled" pipelines, and as the FDA's books closed for calendar 2005 with only 20 new drug approvals, the New York Times concluded ... that the "research drought" had grown worse.

The reverse side of this same story is the increasing research cost of pharmaceutical

⁷ Iain Cockburn, "Is the Pharmaceutical Industry in a Productivity Crisis?" in Adam Jaffe et al., eds., Innovation Policy and the Economy, Vol. 7, National Bureau of Economic Research, 2006, p. 1.

innovation.⁸ Greater amounts are spent on average for each new product, which is merely another reflection of the recent sharp declines in research productivity.

Strikingly, this decline in productivity has accompanied a substantial shift in the structure of pharmaceutical research. There has been an increasing degree of vertical disintegration. The major pharmaceutical companies usually take responsibility for the FDA approval process, including the detailed and highly expensive testing of new drugs. On the other hand, increasing amounts of basic or laboratory research are carried out in much smaller, and often single-product, firms. Often, these smaller research partners are start-up biotech firms.⁹

This pattern is apparent in co-author Scherer's examination of the origins of 85 new medical entities approved by the Food and Drug Administration between 2001 and 2005.¹⁰ Examining the patents supporting the exclusive position of the firms securing FDA approval, he found that 47 percent were issued to firms or non-profit entities with names different from those of the ultimate drug approval recipient. An even higher 54 percent of the earliest patents originated from outsiders. Although it is possible that some of these mismatches involved subtle cross-ownership ties, his main conclusion is that traditional pharmaceutical companies such as Pfizer have come to rely heavily on outsiders for the pharmaceutical innovations they eventually bring to market. These findings reinforce the inference of lagging productivity in the laboratories of the traditional firms.

The traditional firms have tried to offset these problems through mergers and acquisitions. There has been a substantial merger wave in the pharmaceutical industry during the 1990s and early

⁸ Joseph A. DiMasi, Ronald W. Hansen, and Henry G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs" *Journal of Health Economics*, Vol. 22, March 2003, pp. 151-185.

⁹ Co-author Comanor reviewed this new structure of pharmaceutical research. See William S. Comanor, "The Economics of Research and Development in the Pharmaceutical Industry," in Frank A. Sloan and C.R. Hsieh, *Pharmaceutical Innovation*, Cambridge University Press, 2007, pp. 54-72.

¹⁰ F. M. Scherer, "Pharmaceutical Innovation," John F. Kennedy School of Government working paper 07-04, June 2007.

2000s. The newest mergers have been of two main types: acquisitions of typically small, relatively new biotech companies by traditional "Big Pharma" companies; and acquisition of one sizeable old-line pharmaceutical company by another. Illustrative of the latter are Pfizer's acquisition of Warner-Lambert in 2000, bringing into the Pfizer portfolio inter alia Lipitor, the best-selling ethical drug in world history; the merger in 2000 of Glaxo Wellcome with SmithKline Beecham, themselves the products of earlier large-firm mergers; the 1999 merger of Hoechst and Rhone-Poulenc to create Aventis, which in 2003 added Sanofi to its fold; and the 1997 merger between Sandoz and Ciba-Geigy to form Novartis.

The proposed Pfizer - Wyeth merger is a manifestation of these same circumstances. Pfizer faces the unhappy prospect that few high-selling new drugs will likely appear to replace its best-selling "blockbuster" products, which are approaching their patent expiration dates, with significant sales losses certain to follow.¹¹ According to the New York Times account of the proposed merger, Pfizer's acquisition of Wyeth is designed to smooth a "potential patent 'cliff' into a mere bump in the road."¹²

Furthermore, acquiring Wyeth was considered of interest to Pfizer because a substantial share of Wyeth's sales is derived from biologicals, including vaccines, for which generic substitution following patent expiration is far more difficult and uncertain.

Biotech - Big Pharma Synergies

In their affiliations with small new biotech firms, "Big Pharma" companies frequently have a compelling economic justification. Biotech firms typically enjoy the advantages of a rapidly

¹¹ See also "Bristol-Myers's Heavy Reliance on 3 Drugs Puts Its Prospects for Growth in Doubt," New York Times, January 28, 2009.

¹² "After Acquiring Wyeth, Pfizer Boss Faces a Test," New York Times, January 27, 2009, p.B4.

advancing scientific base, Ph.D.-intensive staffs,¹³ and a vast trove of unexploited medical possibilities, all in sharp contrast to the apparently growing obsolescence of the small-molecule discovery techniques on which Big Pharma companies have traditionally focused. At the same time, Big Pharma companies generally have the resources and expertise needed to undertake large-scale clinical trials, along with the ability to marshal the results obtained through the labyrinthine FDA approval process. Some of these collaborations are organized through outright merger, although there may be difficulties in assimilating the loosely-structured, basic science-oriented researchers of biotech companies into the more bureaucratic and more applications-oriented laboratories of Big Pharma companies. Others are achieved through patent and know-how licensing and alliances, which embody a less formal collaboration.

For this mode of small biotech - Big Pharma collaboration, the proposed Pfizer - Wyeth merger poses a significant danger. A headline in the New York Times following the merger announcement read: "Purchase of Wyeth May Blunt Pfizer's Appetite for Small Biotech Companies."¹⁴ Excerpts from the account follow:

There are probably 5,000 biotech companies out there that are waiting for a deal to save them" [given frozen capital markets] ... Pfizer executives say they remain interested in alliances and deals.... But others say the debt that Pfizer took on to buy Wyeth might preclude it in the short run from buying any but the smallest of biotech companies. And when two big companies merge, talks for deals with smaller companies tend to get put on the back burner, as management's attention is diverted and the newly combined company assesses its research pipeline.¹⁵

The cohort of large pharmaceutical companies that comprise the most likely supporters of biotech product development opportunities, either through merger or looser alliance, has been significantly

¹³ According to the National Science Board, 40 percent of all Ph.D.'s employed in private industry are situated in firms with 99 or fewer employees. Science & Engineering Indicators, 2008, p. 3-23.

¹⁴ New York Times, January 27, 2009, p. B4.

¹⁵ Ibid.

concentrated during the last two decades. There are many fewer heads to consider any given possibility.

This consideration is important because the alliance prospects themselves are highly risky. Only about 23 percent of the drug entities brought into first-stage clinical testing eventually emerge with FDA marketing approval, and even more candidates drop out during animal tests, before human clinical tests begin. Uncertainty is ubiquitous in drug development, and one cannot say ahead of time which drug is the most likely to succeed. What seems clear, however, is that some health-enhancing drugs will be lost as a consequence of the increasing amalgamation of decision-making authority among the major pharmaceutical companies.

The Costs and Benefits of Large Company Mergers

During the past decade, there have been a large number of Big Pharma mergers, which have led to a more concentrated industry than existed before.¹⁶ However, since relevant pharmaceutical markets are more limited than the entire industry, one might argue that increased industry concentration raises few competitive concerns. We disagree, for this point does not apply to an industry where the development of new products is its primary function, and firms often shift among product areas in response to research opportunities and demand structure incentives.

As emphasized above, the pharmaceutical research and development process is highly risky. Only about one molecule brought into human tests out of four or five succeeds in gaining entry to the market. In pre-clinical work, uncertainties are even greater. Estimates vary widely, but it is not excessive to suggest that success rates at the molecular synthesis stage are less than one in one hundred. When uncertainty abounds in this way, and when success can lead to important societal

¹⁶ From various issues of the U.S. Census Bureau publication, Concentration Ratios in Manufacturing, one finds that the eight-firm sales concentration ratio for pharmaceutical preparation manufacturing (previously pharmaceutical preparations) rose from 36 percent in 1987 to 53 percent in 2002. More recent data are not yet available.

and health benefits, a "parallel paths" research strategy is almost surely optimal.¹⁷

Under a "parallel paths" approach, alternative molecules are researched and tested in the hope that at least one will yield therapeutic and commercial success. At the pre-clinical stage, such strategies are widely employed by pharmaceutical companies. It is less likely, however, that the companies will carry more than one or two alternate molecules aimed at a particular therapy through the far more expensive stages of clinical testing.

However, even when individual firms shun parallel paths testing, parallelism continues across the set of all pharmaceutical companies. DiMasi and Paquette show that 72 first-in-class drugs introduced in the United States between 1960 and 1998 were soon followed by at least 235 new and approved drugs in the same narrow therapeutic categories.¹⁸ Further analysis reveals that many of these drugs must have been in clinical testing stages in parallel, despite the disparate timing of their FDA approvals. Thus, the degree of parallelism is on the order of 3.25 molecules per therapeutic class. But recognizing that at best only one drug in four proceeds through clinical trials to FDA approval, the degree of parallelism at clinical trial stages must have been on the order of 13 drug candidates per narrow therapeutic category. Co-author Scherer furthermore shows that for drugs that will yield significant therapeutic benefits, the optimal number of parallel paths with such success probabilities is on the order of 20.¹⁹ Because of the pharmaceutical merger wave of the 1990s and 2000s, the number of companies pursuing in parallel the clinical testing of drugs for a

¹⁷ There is ample evidence that winning solutions are most frequently achieved from a diversity of approaches despite the apparent higher costs associated with "duplicated" efforts. See Burton Klein, *Dynamic Economics*, Harvard University Press, 1977. This phenomenon was initially emphasized in various RAND Corporation publications by Klein, Charles Hitch, and Roland McKean. An early model is found in Richard R. Nelson, "Uncertainty, Learning, and the Economics of Parallel Research and Development Efforts," *The Review of Economics and Statistics*, Vol. 43, No. 4, Nov. 1961, pp. 351-364.

¹⁸ Joseph A. DiMasi and Cherie Paquette, "The Economics of Follow-on Research and Development," *Pharmacoeconomics*, vol. 22 (2004 supplement), pp. 1-14.

¹⁹ F.M. Scherer, "Markets and Uncertainty in Pharmaceutical Development," John F. Kennedy School working paper 07-0039 (September 2007); and "Parallel R&D Paths Revisited," John F. Kennedy School working paper 07-040 (September 2007). Both are accessible on the Kennedy School faculty working paper web site.

new area of therapy may already be below the optimum. A merger of the world's largest pharmaceutical company with its tenth-largest rival will further constrict the likelihood of pursuing optimal parallel paths.

To be sure, it is possible that the benefits of parallel pharmaceutical research are outweighed by the gains from economies of scale and scope to be realized by combining the Pfizer and Wyeth research establishments. The possibility of such "synergies" has been suggested in early press accounts of the merger. It merits careful attention.

At the outset, however, there are grounds for skepticism as to the presence of appreciable synergies. As noted above, the leading pharmaceutical companies have sustained a substantial merger wave during the past two decades. Many of these mergers were made with the stated expectation of improving the success of their research and development efforts. Yet this result has not occurred, and there is disappointment over the number and importance of new medical entities that have followed. To be sure, this fact alone does not prove causality.

In recent years, there have been important contributions to the economic literature showing that larger scale and scope for pharmaceutical companies can lead to higher research and development productivity. In their seminal 1996 paper, Cockburn and Henderson observed that larger firms and firms operating in a more diverse set of therapeutic categories were more productive in generating fruitful new research outcomes.²⁰ They found, however, that over time, the pure size effect dwindled to insignificance, and there were diminishing returns in the scope effect.

In a prior article that rests on the same research, Henderson provided a graph showing that research productivity (measured by patents obtained per program) peaked in firms with eight diverse

20 Rebecca Henderson and Iain Cockburn, "Scale, Scope and Spillovers: The Determinants of Research Productivity in Drug Discovery," *RAND Journal of Economics*, vol. 27 (1996), pp. 32-59.

programs.²¹ Measured productivity fell by roughly half when a company encompassed twenty diverse programs. These results, we note, came from a period during which biotech firms, with quite different research strategies, had not yet become prominent.

In a later analysis, Henderson and Cockburn focused on the success of pharmaceutical firms in bringing new drug ideas through clinical testing phases and leading to the receipt of FDA approval. They found no benefits to larger size *per se*, although higher success rates ensued for firms with more diverse therapeutic portfolios (scope).²² However, a further analysis cast doubt on even this result. They concluded that the seeming advantages of scope were confounded causally with the fact that some firms appear to have unique skills and insight that let them be more successful than others in bringing new molecules through the testing pipeline to FDA approval.

Grabowski and Kyle provide an admirable study of the impact of both mergers and research scope (as measured by the number of R&D projects per company) on the rate of pharmaceutical innovation.²³ Their analysis begins at the individual project level, with projects assigned to the originating company. Since their sample includes more than 4,500 companies, smaller biotech companies clearly receive appreciable weight. They analyze progressions of research projects through each of three successive clinical trial stages, and from the third stage to FDA approval.

From this work, Grabowski and Kyle report appreciable scope effects, especially from Phase III to product launch, although the effects turn statistically insignificant when merger indicators are included. Projects that originated prior to a merger are insignificantly less likely to proceed to

²¹ Rebecca Henderson, "Managing Innovation in the Information Age," *Harvard Business Review*, January-February 1994, p. 103.

²² Rebecca Henderson and Iain Cockburn, "Scale and Scope in Drug Development: Unpacking the Advantages of Size in Pharmaceutical Research," *Journal of Health Economics*, vol. 20 (2001), pp. 1033-1057.

²³ Henry Grabowski and Margaret Kyle, "Mergers and Alliances in Pharmaceuticals: Effects on Innovation and R&D Productivity," in Klaus Gugler and B. B. Yurtoglu, eds., *The Economics of Corporate Governance and Mergers*, Edward Elgar: 2008, pp. 262-287.

subsequent phases. However, projects that originated after a merger are more likely to progress to later trial and marketing phases. The authors' conclusion is that there is "a benefit to merging that is independent of size alone."²⁴

Because of the high incidence of biotech firm acquisitions by larger firms in their data set, this result might reflect the known advantages of integration into a larger company for small drug originators. However, the difference between projects that originated pre-merger and post-merger may also reflect organizational politics. That is, the champions for projects are more successful if they are embedded within the organization carrying out the clinical research, while outsiders can only hope for the needed support. The concluding interpretation by Grabowski and Kyle of their results is that "very small firms with only a few projects in their R&D portfolio can gain the most benefits from mergers with more experienced firms in developing new drug introductions." They are more skeptical of the advantages of large-firm mergers, and conclude that "there is little evidence to date that [mergers intended to solve short-run pipeline problems] increased long-term R&D performance."

In his reassessment of the evidence, Cockburn also expresses skepticism that large-firm mergers have contributed much to solving depleted pipeline problems. He reiterates his earlier findings with Henderson that "productivity benefits from increasing size and diversity were exhausted at much smaller scale than the research efforts of today's industry leaders."²⁵

The Pfizer – Wyeth Merger

Turning now to specific evidence on Pfizer and Wyeth, we find scant reason to believe that

²⁴ Ibid. p. 282.

²⁵ Supra note 9 at p. 22 (NBER report).

this proposed merger is likely to improve their R&D productivity. Each of the two is already large and diverse in scope -- well into the stage of diminishing returns to R&D productivity as identified by Henderson and Cockburn. According to their most recent 10-K reports, both companies have some laboratories associated with production facilities. Ignoring these and counting only free-standing laboratories, Pfizer has eight laboratories employing more than 8,900 persons spread across three nations. Wyeth has five laboratories, most of which are distant geographically from each other and from their Pfizer counterparts.

Will the merger lead to productivity-increasing interactions among personnel at the decentralized laboratories? Or will it merely introduce increased coordination difficulties and bureaucratic delays? A New York Times column quoted Pfizer's CEO as saying that the Wyeth merger would be different. "'We have obviously learned a lot from our prior acquisitions,' he said, conceding that they had 'hurt morale and hurt productivity.'"²⁶ An earlier Business Week analysis concluded that "Pfizer's old approach was disjointed and bureaucratic."²⁷

Other observations reported in the press support our inclination towards skepticism. The Economist quotes an industry consultant as believing that consolidation "did absolutely nothing" for pharmaceutical companies other than taking out some costs and adding more bureaucracy.²⁸ Another consultant quoted in the same article said that "bosses may have hurt the discovery process with an orgy of deal-making that has turned Big Pharma into [centralized and bureaucratic] 'Enormous Pharma.'"²⁹ Business Week quoted the observations of Glaxo's new CEO, asserting that

26 "After Acquiring Wyeth, Pfizer Boss Faces a Test," New York Times, January 27, 2009, p. B4.

27 "The Big Rethink at Pfizer," Business Week, December 18, 2006, p. 42.

28 "Billion Dollar Pills," The Economist, January 27, 2007, p. 71.

29 *Ibid.*

"Research teams became less like teams and more like assembly lines, passing drug ideas from chemists to biologists to other specialists in the hope that great products would emerge at the other end. Bureaucracy overpowered braininess."³⁰ Another Glaxo R&D executive observed earlier that "The very thing that was supposed to bolster the labs' output -- the merger -- has instead hampered it... It's a disaster."³¹ Observing that "giantism" could impair the research productivity of pharmaceutical firms, Business Week quotes the managing partner of a leading consulting firm as saying that "Without real management diligence, [pharmaceutical companies] can get slow, ineffective, and infrastructure-bound."³² At a National Institutes of Health conference in 2004, an NIH leader attributed the dwindling new medical entity productivity of the U.S. drug industry to excessive concentration of industry R&D efforts through mergers.

Conclusions

That the merger of Pfizer with Wyeth will benefit consumers is far from a foregone conclusion. There is ample reason to believe that it will make an unsatisfactory bureaucratic situation even worse, while it enriches the company managers and the banks that allocate funds to support the merger -- funds for which American taxpayers bear ultimate responsibility. There is also evidence supporting an inference of more traditional anti-competitive effects. A careful and skeptical investigation by the responsible antitrust agency is very much in the national interest.

30 "Pharma's Law of the Jungle," Business Week, November 10, 2008, p. 46, quoting Glaxo CEO Andrew Witty.

31 "Where Are All the New Drugs," New York Times, October 5, 2003, Section 3, p. 1. The same article quotes the CEO of AstraZeneca as stating that "distraction among scientists is 'a huge problem' during mergers," leading, according to unnamed scientists, to "months, and even years, of uncertainty and indecision."

32 "Big Pharma: Getting Too Big for Its Own Good," Business Week, July 29, 2002, p. 74.



The American Antitrust Institute

Date: April 7, 2009

To: Federal Trade Commission

From: William S. Comanor and F.M. Scherer

Re: Pharmaceutical Industry Consolidation

This supplements our memorandum dated February 9, 2009, available at <http://www.antitrustinstitute.org/Archives/PfizerWyeth .ashx>.

The pharmaceutical industry has conferred enormous benefits on consumers. It has allocated billions of dollars to the development and testing of new drugs which are significantly responsible for striking improvements in public health during the past few decades.ⁱ To cite only one example, a study by Professor Frank Lichtenberg of Columbia University reports that new medicines account for more than half of the 25% increase in six-year cancer survival rates that occurred between 1975 and 1995.ⁱⁱ

There is considerable risk in developing new medicines. Most research projects fail, and even when they succeed, the resulting drugs often do not offer the breakthrough results that were anticipated. And this effort appears to have become increasingly costly. Despite increased spending on pharmaceutical research and development, the number of new therapeutic molecules introduced into US markets has remained stable at between 20 and 30 per year, with most offering few substantial therapeutic gains over existing drugs.

In this setting, the recent efforts towards industry consolidation are particularly troublesome.

Not only has Pfizer, the industry's largest company, sought to acquire Wyeth for \$68 billion, but now

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Merck would acquire Schering-Plough for just over \$41 billion. And strikingly, both merger proposals are financed in part by banks receiving TARP funds. Additional merger proposals in this industry are either in the works or being discussed in the media.

These acquisitions follow a whole line of earlier ones that have led this once diffuse industry to a far more concentrated structure. As recently as 1987, government statistics reveal the leading 8 pharmaceutical companies accounted for 36 percent of U.S. industry shipments. By 2002, the share of the largest 8 companies had risen to more than 53 percent.ⁱⁱⁱ These figures, moreover, understate the extent of concentration among research-based companies since they include roughly 18 to 24 percent of shipments made by smaller generic manufacturers.

This trend is particularly problematic because of its likely impact on the rate of pharmaceutical innovation and hence on impairing consumer welfare. Because of the considerable risk and uncertainty inherent in developing new drugs, the pursuit of “parallel paths” is essential.^{iv} Under this strategy, different research approaches to a given therapeutic problem are followed at different laboratories and companies. While many will fail, the likelihood is that at least one path will yield both a therapeutic and commercial success. There is ample evidence that winning solutions are most frequently achieved when diverse approaches are pursued, despite the higher costs resulting from overlapping efforts.

Increased concentration among large pharmaceutical companies not only reduces the extent of desirable parallel-paths R&D, but also it limits the number of buyers who can purchase new potential pharmaceuticals from scientifically prolific biotech firms which are generally too small to finance full-scale clinical trials and the related marketing efforts. In recent years, such startups have been key sources of innovative drugs – contributing as many as half of the total number of new drugs ultimately introduced into U.S. markets. Especially in a period of financial crisis, when biotech startups have

experienced difficulty in obtaining research-sustaining funding, "thinning" the market for licensing or purchase of such firms' research output is likely to inhibit innovation.^v

The American Antitrust Institute recommends that the Federal Trade Commission pursue an integrated approach to analyzing the pharmaceutical mergers over which it has jurisdiction, taking into account not only the consequences of the individual mergers but also their broader systemic effects on pharmaceutical innovation.

ⁱ Richard D. Miller and H. E. Frech, *Health Care Matters Pharmaceuticals, Obesity and the Quality of Life*, 2004.

ⁱⁱ Frank R. Lichtenberg, "The Expanding Pharmaceutical Arsenal in the War on Cancer," Columbia University and National Bureau of Economic Research, 2004.

ⁱⁱⁱ U.S. Bureau of the Census, *Concentration Ratios in Manufacturing Industries*, various years.

^{iv} See Burton Klein, *Dynamic Economics*, Harvard University Press, 1977; and F.M. Scherer, "Markets and Uncertainty in Pharmaceutical Development," John F. Kennedy School working paper 07-0039 (September 2007); and "Parallel R&D Paths Revisited," John F. Kennedy School working paper 07-040 (September 2007).

^v Anna Levine, "Licensing and Scale Economies in the Biotechnology Pharmaceutical Industry," 2008.