# Two Puzzles Resolved: Of the Schumpeter–Arrow Stalemate and Pharmaceutical Innovation Markets

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*ABSTRACT: One of the most heated discussions in economics in recent years has concerned the relationship between market structure and innovation. After a half-century of debate and innumerable studies, the consensus is that there is no clear answer to the question. On a concrete level, the uncertainty underlies the most fundamental critique of "innovation markets," or markets for research and development ("R&D"). After all, if concentration leads to innovation, then antitrust challenges are not appropriate even for mergers that lead to monopoly.*

*In this Article, I closely parse the economic studies to arrive at a more nuanced answer that highlights factors determining the ideal market structure for innovation. I show that both competition and size play a role in pharmaceutical innovation. In addition, analysis of the pharmaceutical industry rebuts the most cogent critiques of innovation markets.*

*The Article also includes the first empirical analysis of pharmaceutical innovation-market cases. This is particularly instructive because nearly every challenge to innovation-market mergers has arisen in the pharmaceutical industry. For each of the nine cases, I examine the pre-merger treatment for particular conditions, the number of participants in the market and stage of FDA review, and the current market picture. I conclude that approximately half the agency challenges were justified.*

*Finally, I propose a new test to apply to innovation markets. The test examines (1) concentration among firms reasonably likely to reach the market, (2) anticompetitive theories of innovation suppression, and*

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*rebuttals based on (3) rivals' entry, (4) efficiencies, and (5) a "Schumpeterian" need for size. The test thus replaces the current ad hoc approach with a comprehensive framework based on the Merger Guidelines. It also breaks new ground in considering not just the number of firms engaged in R&D, but also the stage (both preclinical and clinical) of FDA review.*

*The debates concerning innovation markets and the relationship between market structure and innovation present some of the most challenging issues in economics and antitrust. My analysis of the economic studies and pharmaceutical innovation-market mergers begins to resolve two crucial, interrelated puzzles.*

## INTRODUCTION

One of the most heated discussions in economic circles in recent years has concerned the relationship between market structure and innovation. After a half-century of debate and innumerable studies, the overwhelming consensus is that there is no clear answer to the question. The diametrically opposed positions of Joseph Schumpeter (favoring concentration) and Kenneth Arrow (favoring competition) both garner support in unending bouts of hand-wringing.

This Article offers at least a partial solution to this puzzle. By closely parsing the economic studies, I isolate several factors that determine the ideal market structure for innovation in specific industries. In particular, I find that competition and size are each important for pharmaceutical innovation.

This nuanced approach promises to pay dividends in the context of "innovation markets," one of the most criticized concepts in antitrust law. Such markets are unique in that they consist not of actual products, but of the research and development ("R&D") directed toward new products. Perhaps because of their novelty, critics have leveled numerous attacks against such markets:[1]

- Innovation is speculative and includes unidentifiable market participants;
- Innovation markets are not needed because conduct can be challenged at a later time;
- The relationship between R&D and innovation is unclear; and
- The market structure most conducive to innovation is unclear.

The approach I offer in this Article addresses these concerns. It also promises to have immediate practical consequences. The antitrust enforcement agencies, for example, have recently been hamstrung by disagreement on innovation markets. In the proposed 2004 merger between Genzyme and Novazyme, the two companies researching Pompe disease (a fatal condition affecting young children), the Federal Trade Commission ("FTC") split 3–1–1 on the question of whether to challenge the merger. In a statement accompanying the majority decision not to challenge the merger, Chairman Timothy Muris refused to "adopt[] [a] presumption[] [of anticompetitive harm] without economic foundation . . . [which] would constitute a major step backward in antitrust law."[2] In contrast,

1. *See infra* Part I.B.

2. Statement of Chairman Timothy J. Muris, In the Matter of Genzyme Corporation/Novazyme Pharmaceuticals, Inc. 25 (Jan. 13, 2004) [hereinafter Muris Statement], *available at* http://www.ftc.gov/os/2004/01/murisgenzymestmt.pdf.

Commissioner Mozelle Thompson's dissent highlighted the dangers of a merger to monopoly.[3]

The common-sense concern about a merger between the two most advanced firms in a market explains not only the dissent in the *Genzyme* case, but also the FTC's eight challenges to mergers (all since 1990) in innovation markets in the pharmaceutical industry. Common sense, however, is not economic foundation, particularly when the relationship between market structure and innovation is as disputed as it is. This Article at last offers the economic foundation that has been missing from innovation-market analysis.

Part I begins by defining innovation markets. It then articulates the most fundamental critiques that have been leveled against the markets. Finally, it rebuts these critiques by emphasizing the realities of the pharmaceutical industry. It explains that

- The high barriers to entry from patents and a lengthy Food and Drug Administration ("FDA") regulatory process allow the relevant innovators to be identified;
- The conduct cannot be challenged at a later time because it is difficult, if not impossible, to observe a lack of innovation in the product market; and
- The question of which market structure is most conducive to innovation can be answered in the pharmaceutical industry.

Part II then focuses on the crucial inquiry involving market structure and innovation. It first articulates the positions of Schumpeter and Arrow. Next, it extracts the most important factors from the economic studies in the past half-century. Applying these factors, this Part finds that the resources needed to survive the lengthy FDA regulatory process demonstrate the importance of size in the industry. But the presence of patents, product innovation, and technological opportunity shows the significance of competition for pharmaceutical innovation. This finding confirms the propriety of antitrust enforcement in innovation markets.

Part III proposes a new five-part test for the agencies to apply to innovation markets. First, the agencies must show that the merger would lead to significant concentration among firms reasonably likely to reach the market. Second, they must offer a theory that the merging firms will suppress innovation. Third, the firms can rebut the prima facie case of concentration by showing that another firm is likely to reach the market.

3. Dissenting Statement of Commissioner Mozelle W. Thompson In the Matter of Genzyme Corporation/Novazyme Pharmaceuticals, Inc. 1 (Jan. 13, 2004) [hereinafter Thompson Statement], *available at* http://www.ftc.gov/os/2004/01/thompsongenzymestmt.pdf.

Fourth, in a narrow range of cases, the merging firms can proffer an efficiencies defense. Fifth, a "Schumpeterian" defense can be offered by small firms that would not otherwise be able to navigate the regulatory process.

The test improves upon the current analysis in several ways. It replaces the current ad hoc approach with a comprehensive framework based on the Merger Guidelines. And it breaks new ground in considering not just the number of firms in R&D, but also their respective stages of FDA review. Given the wildly varying odds of success in reaching the market from the preclinical stage and each of the clinical stages, it is indefensible to continue to neglect this factor.

Part IV presents the results of nine case studies from the past two decades—eight cases challenged and one not challenged by the FTC. These cases are important because they constitute nearly all of the innovation-market cases. In fact, there have been only two challenges outside this arena.[4] In addition, because these matters have all been settled by consent decree, (1) the relevant analysis has taken place not in the courts but in the agencies, and (2) discussion about the cases has, until now, been limited to the facts alleged in the agency complaints.

My empirical analysis examines the treatment of particular conditions before the merger, the number of participants, the merging firms' (and rivals') stage of FDA review, and the state of the market today. It concludes that five of the nine cases were justified but that the remaining four should not have been challenged.

Going forward, application of my test promises to make innovation-market analysis more comprehensive and predictable and to incorporate a more realistic assessment of pharmaceutical development hurdles. By preventing unnecessary challenges, it seeks to ensure the most effective use of limited government resources. And by increasing the odds that certain products will reach the market, it promises to promote innovation.

In short, the debates concerning innovation markets and the relationship between market structure and innovation present some of the most challenging issues in economics and antitrust. By closely parsing the economic studies and conducting the first empirical analysis of innovation-market mergers in the pharmaceutical industry, this Article begins to solve two crucial, interrelated puzzles.

## I. INNOVATION MARKETS

### *A. THEORY*

The concept of innovation markets burst into attention (at least of scholars and the government agencies) in 1995. In that year, the antitrust

4. *See infra* notes 191–92 and accompanying text (describing the two challenges).

enforcement agencies—the U.S. Department of Justice ("DOJ") and FTC—promulgated Intellectual Property ("IP") Guidelines. The most controversial aspect of the Guidelines was the creation of an innovation market, which was defined as

> A[] . . . market [that] consists of the research and development directed to particular new or improved goods or processes, and the close substitutes for that research and development.[5]

"The close substitutes," the Guidelines continued, were "research and development efforts, technologies, and goods that significantly constrain the exercise of market power with respect to the relevant research and development . . . ."[6] The agencies promised that they would "delineate an innovation market only when the capabilities to engage in the relevant research and development [could] be associated with specialized assets or characteristics of specific firms."[7]

The theory behind innovation markets is that a merger between the only two (or two of a few) firms in R&D might increase the incentive to suppress at least one of the research paths. With no other firms ready to enter the market, the merging firms might not wish to introduce a second product that would reduce sales of the first. Moreover, such activity can only be challenged at the R&D stage. Waiting until products appear (or, more likely, fail to appear) in the marketplace is not an effective option.

This concern is heightened given the importance of innovation to the growth of the U.S. economy. Every study in the past fifty years has shown that innovation is far more important than any other economic efficiency in fostering growth.[8] Given the difficulty of measuring innovation, allegations of harm must be considered cautiously. But because innovation is so crucial, we cannot ignore activity that can only be addressed in R&D markets.

To be sure, in most of the cases challenged by the agencies, innovation markets do not play a role. But despite the small number of innovation-market cases, critics have vociferously disparaged the concept.

### *B. CRITIQUES*

Critics have leveled four central attacks against innovation markets: (1) the process of innovation is speculative and does not allow all of the market participants to be identified; (2) we do not know the optimal relationship

5. U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, ANTITRUST GUIDELINES FOR THE LICENSING OF INTELLECTUAL PROPERTY ¶ 3.2.3, at 13 (Apr. 9, 1995) [hereinafter IP GUIDELINES], *available at* http://www.usdoj.gov/atr/public/guidelines/0558.pdf.

6. *Id.*

7. *Id.*

8. *See, e.g.*, Michael A. Carrier, *Resolving the Patent-Antitrust Paradox Through Tripartite Innovation*, 56 VAND. L. REV. 1047, 1060–61 & nn.63–67 (2003) (citing sources standing for the proposition that "innovative efficiencies dwarf those derived from maximizing allocative efficiency and that innovation is the most important factor in the growth of the economy").

between R&D and innovation; (3) innovation markets are not needed because conduct can be challenged at a later time; and (4) we do not know the market structure most conducive to innovation.

First, innovation is speculative. It is "intangible, uncertain, unmeasurable, and often even unobservable, except in retrospect."[9] As a result, it is exceedingly difficult to identify all of the firms that are in a particular innovation market. As Dennis Carlton and Robert Gertner explain, "[B]ecause the results of R&D are so difficult to predict, the analyst may be unable to determine all, or even most, of the relevant firms who might produce competitive products in the future."[10] The authors offer several anecdotes showing the unpredictability of the sources of innovation:

- Experiments on refrigerator gases, which led to the discovery of Teflon;
- Research on wound dressings, which led to the discovery of a breathable, waterproof fabric; and
- A machine developed to analyze brain chemistry, which now identifies the components of fruit juices.[11]

Second, "the optimal amount of R&D is unknown."[12] More R&D does not necessarily result in more innovation. "[A] merger that reduces R&D expenditure may be beneficial if it allows the R&D to be conducted more efficiently."[13] Because competing R&D expenditures might be duplicative, "a merger that eliminates redundancy may lead to the same knowledge produced at lower costs, or even to greater knowledge at lower costs."[14]

Third, innovation-market analysis is unnecessary because the relevant conduct can be challenged at a later stage. It can be challenged at the product-market stage, where we can identify the products and their characteristics. Or it can be challenged at the "potential competition" stage, where at least one firm is on the market and another is about to enter the market.[15] Based on the existence of a potential-competition theory, some have found it "difficult to see"[16] what innovation markets add, while others

9. Richard T. Rapp, *The Misapplication of the Innovation Market Approach to Merger Analysis*, 64 ANTITRUST L.J. 19, 27 (1995).

10. Dennis Carlton & Robert Gertner, *Intellectual Property, Antitrust and Strategic Behavior*, *in* 3 INNOVATION POLICY AND THE ECONOMY 29, 42 (Adam B. Jaffe et al. eds., 2003).

11. *Id.*

12. Rapp, *supra* note 9, at 46.

13. Carlton & Gertner, *supra* note 10, at 38.

14. *Id.*

15. PHILLIP AREEDA ET AL., ANTITRUST ANALYSIS: PROBLEMS, TEXT, AND CASES ¶ 545, at 782 (6th ed. 2004).

16. Ronald S. Katz & Janet Arnold Hart, *Extremism in Defense of Market Definition Is a Vice, in* ANTITRUST/INTELLECTUAL PROPERTY CLAIMS IN HIGH TECHNOLOGY MARKETS 1, 8 (ALI-ABA Course of Study, Jan. 25, 1996), *available at* CA26 ALI-ABA 1 (Westlaw).

call such markets "merely superfluous."[17] Some have even claimed that "the agencies have never found an innovation market."[18]

Fourth, we do not know the market structure most conducive to innovation. As two of numerous commentators explain, "[N]either theory nor empirical work provides [sic] any general justification for an antitrust merger policy aimed at preserving competition in R&D markets,"[19] and "[t]he connection between market structure and innovation has been debated by economists for decades without resolution."[20]

### *C. REBUTTAL*

There is an element of truth in each of the four critiques. In many cases, we do not know all of the potential innovators or the optimal relationship between R&D and innovation. For that reason, an expansive notion of the innovation-market concept is not appropriate. But a narrow version, applied to the pharmaceutical industry, withstands the critiques.

First, in the pharmaceutical industry, innovation is not speculative or carried out by unknown innovators. The barriers to entry provided by patents and, especially, a lengthy regulatory process cabin the universe of potential innovators. Unlike other industries, there are no "garage inventors" that will spring up out of nowhere to create a pharmaceutical product. Because the regulatory process requires a lengthy and costly period of drug discovery, preclinical testing, and clinical trials, an entrant would not be able to "leap-frog" into the market.[21] Rather, it would be required to engage in years of testing before catching up to current R&D efforts.[22]

The pharmaceutical industry therefore meets the requirement articulated in the IP Guidelines that "the capabilities to engage in the relevant [R&D] can be associated with specialized assets or characteristics of specific firms."[23] In addition, cooperation between the FDA and the antitrust agencies has ensured "a wealth of information on the status, approach, and likely effect of each innovation effort."[24]

Second, we know that higher amounts of R&D benefit innovation. Pharmaceutical R&D typically does not suffer from the duplication that

17. Rapp, *supra* note 9, at 20.

18. Lawrence B. Landman, *Competitiveness, Innovation Policy, and the Innovation Market Myth: A Reply to Tom & Newberg on Innovation Markets as the "Centerpiece" of "New Thinking" on Innovation*, 13 ST. JOHN'S J. LEGAL COMMENT. 223, 234–35 (1998).

19. Carlton & Gertner, *supra* note 10, at 40.

20. Rapp, *supra* note 9, at 27.

21. Susan DeSanti & William Cohen, *Competition to Innovate: Strategies for Proper Antitrust Assessments*, *in* EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY: INNOVATION POLICY FOR THE KNOWLEDGE SOCIETY 317, 335 (Rochelle Cooper Dreyfuss et al. eds., 2001).

22. *Id.* at 329 n.69.

23. IP GUIDELINES, *supra* note 5, ¶ 3.2.3, at 11.

24. DeSanti & Cohen, *supra* note 21, at 329 n.69.

might afflict other industries. As one commentator notes, "[I]dentical research tracks and matched future efficacy are unlikely."[25] Even if ten companies test drugs for a particular type of cancer, for example, the projects "are likely to involve different research teams, different concepts, ideas, and directions, different corporate cultures, and other factors affecting the likelihood and degree of eventual success."[26]

Contributing to the absence of duplication, there is a large number of spillovers in the pharmaceutical industry. The industry is marked by high publication rates, and scientists are aware of and influenced by rivals' discoveries.[27] Spillovers have only increased in recent years with the more frequent use of "rational drug design," which anticipates working backward from knowledge of a disease's biochemistry.[28]

Third, innovation-market analysis promises to target activity that could not otherwise be challenged at a later time. Granted, particular mergers may have effects on markets with actual or potential competition. But other activity will remain outside the reach of antitrust. Such a flaw is particularly concerning because the restriction of innovation would appear only as a "non-event."[29] In other words, it will not be apparent after the fact what is missing from the marketplace. We cannot observe the absence of innovation like we can observe higher prices. This is especially worrisome because, as discussed above,[30] research paths in the pharmaceutical industry generally are not duplicative and the innovations are so critical to public health. Moreover, any harms to innovation cannot easily be remedied after the merger has occurred, the research line has been suppressed, and employees have taken on new projects.

Fourth, we can ascertain the market structure most conducive to innovation. Although size is important in the regulatory process, Part II will demonstrate the crucial role that competition plays in pharmaceutical innovation. A close parsing of the economic studies and application to the industry disproves the prospect that only a monopolistic market structure promotes innovation in the industry.

25. Dror Ben-Asher, *In Need of Treatment? Merger Control, Pharmaceutical Innovation, and Consumer Welfare*, 21 J. LEGAL MED. 271, 319 (2000).

26. *Id.* at 319–20.

27. Rebecca Henderson & Iain Cockburn, *Scale, Scope and Spillovers: The Determinants of Research Productivity in Drug Discovery*, 27 RAND J. ECON. 32, 35–36 (1996).

28. GARY P. PISANO, THE DEVELOPMENT FACTORY: UNLOCKING THE POTENTIAL OF PROCESS INNOVATION 64–65 (1997).

29. DeSanti & Cohen, *supra* note 21, at 334.

30. *See supra* notes 25–26 and accompanying text (explaining the reasons that pharmaceutical research usually is not duplicative).

## II. MARKETS, INNOVATION, AND DRUGS

The question of the market structure most conducive to innovation traces back sixty years to the debate between Schumpeter and Arrow. This Part first articulates the two economists' theories. It then discusses more recent studies and extracts the most important factors determining an industry's ideal market structure. It concludes by applying these factors to the pharmaceutical industry.

### *A. SCHUMPETER AND ARROW*

Joseph Schumpeter famously highlighted the role played by concentration in promoting innovation. He explained that perfect competition (a model in which producers lack market power) was "inferior in internal, especially technological, efficiency."[31] The perfectly competitive firm "wastes opportunities" and, because it is less able to develop and evaluate new possibilities, "waste[s] capital."[32] For that reason, "perfect competition is and always has been temporarily suspended whenever anything new is being introduced."[33]

Monopoly, in contrast, affords protection "against temporary disorganization of the market" and secures space "for long-range planning."[34] Monopoly offers "superior methods," such as experience and financial resources, that are not available to competitive firms.[35] It also provides for the "insuring or hedging" activities needed for investment.[36] In fact, the monopolist only can realize its most innovative plans because it is not subject to competition from "heavy capital requirements or lack of experience."[37] In the end, Schumpeter concludes that "the large-scale establishment . . . [is] the most powerful engine of [economic] progress and . . . the long-run expansion of total output."[38]

Some of Schumpeter's arguments—such as the protection against the "disorganization of the market"[39]—envision monopoly. But in several places, the theorist discusses the "large scale unit of control"[40] and advances arguments for which size, not monopoly, is sufficient. For example, he

31. JOSEPH A. SCHUMPETER, CAPITALISM, SOCIALISM AND DEMOCRACY 106 (1942).

32. *Id.*

33. *Id.* at 105.

34. *Id.* at 103.

35. *Id.* at 101.

36. SCHUMPETER, *supra* note 31, at 88.

37. *Id.* at 89.

38. *Id.* at 106.

39. *Id.* at 103.

40. *Id.* at 101; *see also id.* at 106 (discussing the "large-scale establishment or unit of control").

highlights experience, financial resources, and "heavy capital requirements"[41] as essential ingredients for innovation.

In contrast, Kenneth Arrow demonstrated that "the incentive to invent is less under monopolistic than under competitive conditions."[42] Unlike the monopolist, for which some of the profits from the new invention come at the expense of the old technology, the competitor receives all of the returns from a new invention.[43] This conclusion applies with particular force to drastic innovations for which the post-invention monopoly price is less than the pre-invention monopolist's costs.[44] In such a case (in which the old technology is rendered obsolete), the monopolist has "a strong disincentive for further innovation."[45]

The same conclusion holds for a nondrastic innovation. In this scenario, the post-invention monopoly price exceeds the pre-invention costs.[46] The conclusion here is more subtle because the competitor's profits from the new technology are "limited by competition with the former monopolist's old technology."[47]

But because of the declining demand curve, the monopolist's incentive is "less than the cost reduction on the postinvention monopoly output."[48] And because this cost reduction is less than the competitive output, the competitor's incentive exceeds that of the monopolist.[49]

### *B. THE STUDIES*

Economists have conducted countless studies in the past half-century to resolve the market structure–innovation puzzle addressed by Schumpeter and Arrow. This Section examines four of the most critical factors that determine the ideal market structure for innovation in particular industries. Two factors apply to all markets: (1) the distinction between product and process innovation and (2) the distinction between drastic and nondrastic innovation. And two focus on characteristics of particular industries: (3) technological opportunity and (4) appropriability.

One of the most fundamental flaws of the studies is that they do not control for the effect of the factors. In other words, conclusions about

41. SCHUMPETER, *supra* note 31, at 89.

42. KENNETH J. ARROW, *Economic Welfare and the Allocation of Resources for Invention*, *in* ESSAYS IN THE THEORY OF RISK-BEARING 144, 157 (3d ed. 1976).

43. *Id.* at 157–58; Richard Gilbert, *Looking for Mr. Schumpeter: Where Are We in the Competition-Innovation Debate?*, *in* 6 INNOVATION POLICY AND THE ECONOMY 159, 165 (Adam B. Jaffe et al. eds, 2006).

44. ARROW, *supra* note 42, at 157.

45. *Id.* at 158.

46. *Id.*

47. Gilbert, *supra* note 43, at 166.

48. ARROW, *supra* note 42, at 158.

49. *Id.*

whether concentration or competition would maximize innovation are explained more by an application of the four factors than by a blanket assertion about, for example, competitive market structures.[50] My distillation and separate consideration of the factors thus promises to offer a more nuanced view of innovation—one that can offer practical guidance for particular industries.

1. Product or Process

Whether a firm engages in product or process innovation is one of the most important factors determining market structure. Firms typically market product innovations externally and use process innovations internally.[51]

Of the two, product-related R&D more often produces patentable innovations.[52] The patent gives its owner the right to exclude others from making, using, or selling any product embodying the patent.[53] This right also allows the patentee to license the patent.[54] Firms of all sizes are more likely to appropriate their investment in product R&D by exploiting their patents.

In contrast, process innovations are not as likely to be patented. These innovations are more difficult to define and enforce[55] and are easier to invent around.[56] In addition, secrecy is more effective for processes, which are more easily concealed and which may disclose useful business information to competitors.[57] But if processes are not patented, firms need to rely on other mechanisms, such as size, to appropriate their investments. In many cases, monopoly power is just such a mechanism, substituting for legal property rights and preventing misappropriation.[58]

50. For a typical recounting of other flaws, see Jonathan B. Baker, *Fringe Firms and Incentives to Innovate*, 63 ANTITRUST L.J. 621, 640 n.88 (1995) (noting that (1) R&D intensity "may not be a good proxy for innovation rates," (2) seller concentration may not demonstrate market power, and (3) "technological change affects concentration," in addition to the reverse).

51. ORGANISATION FOR ECON. CO-OPERATION AND DEV. & STATISTICAL OFFICE OF THE EUR. CMTYS., OSLO MANUAL: PROPOSED GUIDELINES FOR COLLECTING AND INTERPRETING TECHNOLOGICAL INNOVATION DATA 47 (1997).

52. Albert N. Link & John Lunn, *Concentration and the Returns to R&D*, 1 REV. INDUS. ORG. 232, 233 (1984).

53. 35 U.S.C. § 154(a)(1) (2000).

54. John Lunn, *The Roles of Property Rights and Market Power in Appropriating Innovative Output*, 14 J. LEGAL STUD. 423, 427 (1985).

55. Wesley M. Cohen & Steven Klepper, *Firm Size and the Nature of Innovation Within Industries: The Case of Process and Product R&D*, 78 REV. ECON. & STAT. 232, 233 (1996).

56. Paul Geroski, *Markets for Technology: Knowledge, Innovation and Appropriability*, *in* HANDBOOK OF THE ECONOMICS OF INNOVATION AND TECHNOLOGICAL CHANGE 90, 103 (Paul Stoneman ed., 1995).

57. Cohen & Klepper, *supra* note 55, at 233 & n.5.

58. Link & Lunn, *supra* note 52, at 233.

Monopoly power allows a firm to charge prices in excess of the marginal cost of producing an item, thereby recovering the fixed costs expended in creating the process innovation. Monopoly also may allow a firm to reduce its monitoring costs or to slow the entry of competitors into the industry, both of which encourage research activity.[59] Relatedly, process innovations allow firms to lower their production costs, which could increase concentration.[60]

Many of the economic studies undertaken in the past fifty years have focused on process innovations.[61] Such a focus is largely responsible for the widespread conclusion that concentration is linked with innovation.[62] A careful parsing, then, of the presence of product or process innovations is crucial to determine the role of market structure in innovation. At a minimum, concentration enhances firms' abilities to appropriate process innovations much more than product innovations.[63]

### 2. Drastic or Nondrastic

A second factor underlying the link between market structure and innovation is the presence of drastic or nondrastic innovation. A drastic product innovation is "one that is so superior to existing products in cost or functionality that existing products are not competitive."[64] A drastic process innovation lowers the marginal cost of production by such an extent that firms using a pre-existing process cannot compete with the innovator.[65] Nondrastic innovations, in contrast, typically allow use of both the original and new product or process.[66]

For drastic innovations, competition is superior to monopoly. A monopolist is less likely to introduce a new product that will displace the

59. Lunn, *supra* note 54, at 426. Monitoring costs, which include policing costs and the costs of enforcing contracts, reduce the value of property rights. *Id.* at 425.

60. *See* John Lunn, *An Empirical Analysis of Process and Product Patenting: A Simultaneous Equation Framework*, 34 J. INDUS. ECON. 319, 321–22 (1986).

61. *See* Dirk Czarnitzki & Kornelius Kraft, *License Expenditures of Incumbents and Potential Entrants: An Empirical Analysis of Firm Behavior* 9 (Discussion Paper No. 05-35 2005), *available at* ftp://ftp.zew.de/pub/zew-docs/dp/dp0535.pdf (noting that economic theory "usually discusses process innovation but not product innovation").

62. The studies' conclusions are complicated by dual causation (or, in economic parlance, the endogeneity of the factors). Not only does concentration lead to process innovation, but such innovation also may lead to concentration.

63. *See generally* Lunn, *supra* note 60.

64. Richard J. Gilbert & Steven C. Sunshine, *Incorporating Dynamic Efficiency Concerns in Merger Analysis: The Use of Innovation Markets*, 63 ANTITRUST L.J. 569, 591 (1995).

65. Michael J. Meurer, *Business Method Patents and Patent Floods*, 8 WASH U. J.L. & POL'Y 309, 315 n.36 (2002).

66. *See id.* (discussing how users of a pre-existing process cannot compete with a drastic innovation and how nondrastic innovation is "of a lesser magnitude"); *see also, e.g.*, Gilbert, *supra* note 43, at 166 (noting that a drastic innovation makes the old technology obsolete).

monopoly it currently possesses.[67] The monopolist, in other words, is less likely to cannibalize sales from its existing product. A competitive firm, in contrast, will gain the full benefit of a new drastic innovation without suffering any losses from reduced sales in the prior product.[68]

Jennifer Reinganum has shown that, in the context of drastic innovation, challengers have a greater incentive to invest than monopolists. She demonstrates that if both firms invest marginally less in the new innovation, the monopolist still would receive the revenue flow from its current product, while the challenger would not.[69] As a result, the challenger would be likely to invest more resources in R&D.

Reinganum achieves similar results when considering a sequence of drastic innovations. In that scenario, the length of the current product stage is affected by the monopolist's investment in that stage.[70] The monopolist invests less than the challenger since increased investment shortens the current stage by hastening the discovery of the next innovation.[71] But the monopolist, of course, has "less incentive to shorten the length of its current-stage incumbency."[72]

In contrast, with complementary nondrastic innovations, the old product will not be displaced.[73] The monopolist then will have at least as much incentive as the challenger to invest in R&D. In fact, the monopolist may have greater incentive because, through nondrastic innovations, it can "maintain[] its monopoly profits," as compared to an entrant, who "gains only a share of duopoly profits."[74] This conclusion is strengthened in a model in which a patent is awarded to the highest bidder. In that case, the monopolist may have an incentive to preempt R&D competition by bidding more for a patent than a competitor could invest.[75]

In short, the more the innovation offers a drastic improvement over the previous product, the greater incentive the challenger has to invest in R&D and the less incentive the monopolist has to displace its present monopoly.

The characteristics described in this and the previous Sections explain the results of many of the economic studies. Further elucidation comes from

67. *See* Einer Elhauge, *Defining Better Monopolization Standards*, 56 STAN. L. REV. 253, 299 n.141 (2003) (discussing monopolists' incentives to innovate).

68. *Id.*; *see also supra* notes 42–45 and accompanying text (discussing the lack of incentives for a monopolist to innovate).

69. Jennifer F. Reinganum, *Uncertain Innovation and the Persistence of Monopoly*, 73 AM. ECON. REV. 741, 745 (1983).

70. Jennifer F. Reinganum, *Innovation and Industry Evolution*, 100 Q.J. ECON. 81, 98 (1985).

71. *Id.*

72. *Id.*

73. *See supra* notes 46–49 and accompanying text.

74. Elhauge, *supra* note 67, at 299 n.141.

75. Richard J. Gilbert & David M.G. Newberry, *Preemptive Patenting and the Persistence of Monopoly*, 72 AM. ECON. REV. 514, 514 (1982); *see* Reinganum, *supra* note 69, at 746 ("[T]he certainty model is most appropriate for incremental innovations.").

industry-specific factors. In particular, the factors of technological opportunity and appropriability explain much of the variance in market structures.[76] Technological opportunity "determines the productivity of R&D," while appropriability "determines the fraction of the returns from R&D that the innovator is able to retain."[77]

The relationship between technological opportunity and appropriability, on the one hand, and innovation, on the other, is complex. One difficulty is that the variables are endogenous to market structure. In other words, the variables not only affect innovation, but also are affected by innovation. To the extent, nonetheless, that the two affect market structure, they weaken the link between market structure and innovation. Industries characterized by technological opportunity and high appropriability generally do not need monopoly to encourage innovation.

### 3. Technological Opportunity

Economists have offered several definitions of technological opportunity. One typical definition is "the rate at which more or less exogenous and cumulative advances in science and technology generate profitable new innovative possibilities."[78]

Technological opportunity varies by industry.[79] Industries with rapid changes in scientific knowledge face lower costs of producing innovative output.[80] The greater the technological opportunity, the greater the incentive to engage in R&D and reap the benefits of innovation. Conversely, a slowly advancing and predictable science base could lead to "excessive rivalry" because of fewer opportunities to appropriate investments.[81]

While there is no single formula encapsulating technological development, a Yale University study articulated three sources of contributions to an industry's technological opportunities: (1) the advance of scientific knowledge, (2) "technological advances in other industries," and (3) "positive feedback[]" (and future opportunities) from technological

76. *See* Wesley Cohen, *Empirical Studies of Innovative Activity*, *in* HANDBOOK OF THE ECONOMICS OF INNOVATION AND TECHNOLOGICAL CHANGE, *supra* note 56, at 182, 197 (discussing variables relevant to market structure).

77. Alvin K. Klevorick et al., *On the Sources and Significance of Interindustry Differences in Technological Opportunities* 3 (Cowles Found., Discussion Paper No. 1052, 1993) (on file with the Iowa Law Review).

78. F.M. SCHERER & DAVID ROSS, INDUSTRIAL MARKET STRUCTURE AND ECONOMIC PERFORMANCE 645 (3d ed. 1990). For another definition, see Cohen, *supra* note 76, at 214 (defining the term as "the set of production possibilities for translating research resources into new techniques of production that employ conventional inputs").

79. Klevorick et al., *supra* note 77, at 6.

80. Lunn, *supra* note 54, at 429.

81. SCHERER & ROSS, *supra* note 78, at 647.

advances.[82] The study also highlighted an ability to renew opportunities at a higher rate as a factor distinguishing high- from low-technological-opportunity industries.[83]

Overlapping with the discussion above, technologically progressive industries are more likely to engage in patentable product innovation, thus reducing the need for concentration.[84] In contrast, the process innovation and secrecy characterizing technologically unprogressive industries typically lead to appropriability through concentration.[85]

Technological opportunity, in short, is a crucial determinant of innovation, one that may explain more than sixty percent of innovation variations.[86] In particular, in technologically progressive industries, "[c]oncentration is not related to research intensity," while the unprogressive industries are characterized by a positive relationship between the two.[87]

### 4. Appropriability

Appropriability signifies a firm's ability to recover its investment. Not surprisingly, a firm's incentive to invest in R&D increases as appropriability increases.[88] In industries characterized by high appropriability, there is less need for monopoly to recover investment.

Much of the discussion about product and process innovation applies to appropriability. For example, appropriability typically is high for firms that patent product innovations. In contrast, reduced appropriability, as more often occurs with process innovations, leads to a need for size to prevent misappropriation.[89] The higher the appropriability, therefore, the more attenuated the connection between size and innovation.

Appropriability varies based on industry. The influential 1987 "Levin" study found that certain industries, such as food processing and metal-

82. Klevorick et al., *supra* note 77, at 8–15; *see also* Lunn, *supra* note 54, at 429 (noting that technologically progressive industries have greater–than-average research activity).

83. Klevorick et al., *supra* note 77, at 8.

84. Lunn, *supra* note 54, at 432.

85. *Id.*

86. P.A. Geroski, *Innovation, Technological Opportunity, and Market Structure*, 42 OXFORD ECON. PAPERS 586, 597 (1990); *see also* F.M. Scherer, *Firm Size, Market Structure, Opportunity, and the Output of Patented Inventions*, 55 AM. ECON. REV. 1097, 1121 (1965) (concluding that "[d]ifferences in technological opportunity . . . are a major factor responsible for interindustry differences in inventive output").

87. Lunn, *supra* note 54, at 431.

88. *Id.* at 424.

89. In many cases, size—not monopoly—is sufficient for appropriability. *See, e.g.*, WILLIAM L. BALDWIN & JOHN T. SCOTT, MARKET STRUCTURE AND TECHNOLOGICAL CHANGE 87 (1987) ("[The] studies indicate[] that economies of scale in industrial R & D . . . are in most cases exhausted well below the largest firm and research establishment sizes examined.").

working, were characterized by a lack of appropriability.[90] In contrast, other industries relied on mechanisms such as patents, secrecy, lead time, moving quickly down a learning curve, and sales or service efforts to recover their investments.[91]

Appropriability generally refers to the recovery of investment after the innovation reaches the market. But the concept also can apply to activity before this time. If hurdles such as an extensive regulatory process or a need for significant capital prevent a firm from reaching the market, then the firm will not even have an opportunity to reach the market to reap rewards. Pre-innovation appropriability, even if it is less apparent than its post-innovation counterpart, thus is an important factor in the analysis.

* * *

In short, myriad conflicting economic studies have built on the Schumpeter–Arrow debate. As this Section has shown, a close parsing of those studies reveals that four factors determine the ideal market structure in particular settings.

One context that has been highly disputed—but until now bereft of connection to the economic studies—is that of innovation markets in the pharmaceutical industry. If application of the four factors shows that size is crucial for pharmaceutical innovation, then mergers in innovation markets might not present concern. If, on the other hand, competition plays an important role, then challenges to innovation-market mergers would be justifiable.

### *C. APPLICATION*

The pharmaceutical industry demonstrates the importance of both competition and size. Most of the factors highlighted in the last Section reveal the benefits of competition for pharmaceutical products. The industry is characterized by product innovation, high post-innovation appropriability, and high technological opportunity. But size plays a role in pre-innovation appropriability by allowing firms to survive a lengthy, expensive FDA regulatory process.[92]

90. Richard C. Levin et al., *Appropriating the Returns from Industrial Research and Development*, 1987 BROOKINGS PAPERS ON ECON. ACTIVITY 783, 802.

91. *Id.* at 794.

92. In most of the challenged innovation-market cases, the factor of drastic or non-drastic innovation does not directly apply because neither of the merging firms had a monopoly in the market for the previous product.

### 1. Product or Process

Pharmaceutical companies devote approximately seventy-five percent of R&D to product innovation.[93] Of even more relevance for our purposes, all of the innovation-market mergers challenged by the FTC involved products. The nine mergers involved (1) a prophylactic herpes vaccine, (2) a rotavirus vaccine, (3) CD-4 based therapeutics used in treating HIV/AIDS, (4) EGFR inhibitors used to treat solid cancerous tumors, (5) enzyme replacement therapies for Pompe disease, (6) fibrin sealants, (7) gene therapy, (8) a noninjectable migraine treatment, and (9) topoisomerase I inhibitors for colorectal cancer.[94]

As shown above, concentration has a much greater effect in encouraging process than product innovations. Because all of the challenged pharmaceutical innovation-market mergers involved products, the first factor counsels in favor of competition promoting innovation.

### 2. Drastic or Nondrastic

For the majority of the mergers, the distinction between drastic and nondrastic innovation does not apply. In five of the nine cases, there was no related product on the market,[95] and in two others,[96] a rival of the merging firms offered a nondrastic but competitive innovation.

Only in two cases did one of the merging companies have a product on a related market. In one, Glaxo had an injectable treatment for migraine headaches that could have been affected by the introduction of a noninjectable migraine treatment being researched by merging firms Glaxo and Wellcome.[97] In the second case, Glaxo Wellcome had a suppressive herpes drug that could have been affected by a prophylactic herpes vaccine being researched by Glaxo Wellcome and SmithKlineBeecham.[98]

Both R&D efforts constituted primarily drastic innovation though they also contained elements of nondrastic innovation. First, because patients naturally preferred oral to injectable delivery, a noninjectable migraine treatment did in fact displace much of the need for injectable treatment.

93. Cohen & Klepper, *supra* note 55, at 232*; see also* Wesley M. Cohen & Daniel A. Levinthal, *Innovation and Learning: The Two Faces of R&D*, 99 ECON. J. 569, 591 n.43 (1989) (finding that seventy-one percent of the R&D expenditures in the sample were dedicated to product innovation).

94. *See infra* Part IV (discussing each of the mergers).

95. *See infra* Sections IV.A, IV.B, IV.F, IV.G, IV.I (discussing the Roche–Genentech, American Home Products–American Cyanamid, Ciba–Geigy–Sandoz, Pfizer–Warner–Lambert, and Genzyme–Novazyme mergers, respectively).

96. *See infra* Sections IV.D, IV.E (discussing the Upjohn–Pharmacia and Baxter–Immuno mergers, respectively).

97. *See infra* note 225 and accompanying text.

98. *See infra* Section IV.H.

But because only injectable treatment worked with certain types of migraines, there was still a need for the old technology.[99]

Similarly, the herpes vaccine largely represented a drastic innovation. Patients who had not contracted the disease would no longer need suppressive treatment after receiving the vaccine. But patients who already had contracted herpes still required the suppressive treatment, thus demonstrating a nondrastic element.[100]

For most of the pharmaceutical innovation-market cases, this factor will not apply. But where it does apply, and where the innovation is drastic, it is more likely that firms will suppress R&D paths. In these cases, competition would best promote innovation.

### 3. Technological Opportunity

The pharmaceutical industry is characterized by high technological opportunity and significant R&D.[101]

Applying the construct described above, the first variable explaining technological opportunity is the proximity of the industry to science. The pharmaceutical industry is one of the most closely linked industries to science. The Levin study, based on a survey of high-level R&D managers, concluded that pharmaceuticals were the industry most linked to a particular science.[102] The sciences of biology and chemistry were closely connected to drugs (scoring at least six-and-a-half on a seven-point scale of relevance).[103] Another study demonstrated a close link between science and the pharmaceutical industry by analyzing the percentage of basic research spending of the total industry R&D spending.[104]

The other two variables also demonstrate high technological opportunity. First, institutions other than private drug companies—in particular, universities and government laboratories—contribute to technical knowledge.[105] Second, there is positive feedback from technological advances, as improving product performance continually spurs innovation in the pharmaceutical industry.

In short, high technological opportunity in the pharmaceutical industry demonstrates the importance of competition.

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99. *See infra* note 235 and accompanying text.

100. *See infra* text succeeding note 312.

101. *See* John Bound et al., *Who Does R&D and Who Patents?*, *in* R&D, PATENTS, AND PRODUCTIVITY 21, 28–29 tbl.2.3 (Zvi Griliches ed., 1984) (demonstrating the high ratio of R&D to sales).

102. Klevorick et al., *supra* note 77, at 22, 40 tbl.2.

103. *Id.* at 45 tbl.7; *see also id.* at 20, 40 tbl.2 (reporting that R&D managers consistently reported the high relevance of science to the "technological progress" of a field).

104. Richard C. Levin & Peter C. Reiss, *Tests of a Schumpeterian Model of R&D and Market Structure*, *in* R&D, PATENTS, AND PRODUCTIVITY, *supra* note 101, at 175, 186, 191 tbl.8.2.

105. Klevorick et al., *supra* note 77, at 32, 43 tbl.5.

### 4. Appropriability

Application of the appropriability factor leads to mixed results in the pharmaceutical industry. Before reaching the market, size is necessary to survive the FDA regulatory process, which demonstrates low appropriability. But after the drug is on the market, appropriability is high, as evidenced by the unique importance of patents in the industry.

Companies need size to surmount the hurdles of the FDA regulatory process. As described in more detail below, the process is lengthy, composed of preclinical testing and three stages of human clinical trials.[106] Large firms are more likely to have the resources—in particular, economies of scale,[107] regulatory expertise,[108] and access to internal funding[109]—to survive this gauntlet. Such firms, for example, have the resources to conduct expensive Phase III clinical trials involving thousands of subjects.[110]

In contrast, small biotechnology companies, even if they can discover compounds and engage in preclinical and early clinical studies, lack the size and resources to go further. They therefore tend to collaborate or merge with larger firms to continue the discovery into large-scale trials.[111] Even the patents that smaller firms may receive during trials do not replace the need for size in surmounting the high regulatory hurdles.

But after the innovation reaches the market, the industry is marked by high appropriability. Numerous studies are consistent in concluding that

- Product and process patents are most effective in the pharmaceutical industry;[112]
- Patents are more effective in the pharmaceutical industry than in almost every other industry;[113]
- More than two-thirds of pharmaceutical R&D in Great Britain in 1968 depended on patent protection;[114] and

106. *See infra* notes 127–44 and accompanying text.

107. Patricia M. Danzon, *The Pharmaceutical Industry*, *in* 3 THE ENCYCLOPEDIA OF LAW AND ECONOMICS 1055, 1083 (Boudewijn Bouckaert & Gerrit de Geest eds., 2000).

108. *Id.*

109. *See* ALFONSO GAMBARDELLA, SCIENCE AND INNOVATION: THE US PHARMACEUTICAL INDUSTRY DURING THE 1980S, at 76 (1995).

110. *See infra* note 134 and accompanying text.

111. *See* Walter W. Powell, *Networks of Learning in Biotechnology: Opportunities and Constraints Associated with Relational Contracting in a Knowledge-Intensive Field*, *in* EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY: INNOVATION POLICY FOR THE KNOWLEDGE SOCIETY 251, 263 (Rochelle Cooper Dreyfuss et al. eds., 2001).

112. *See* Levin et al., *supra* note 90, at 797 tbl.2.

113. *See* Wesley M. Cohen et al., *Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (or Not)* 32 tbl.1 (Nat'l Bureau of Econ. Research, Working Paper No. 7552, 2000) (illustrating that the pharmaceutical industry has the second-highest mean percentage innovation).

- R&D executives would not have developed up to ninety percent of pharmaceutical inventions without patents.[115]

One recent study found that patent protection was sought for more than ninety-five percent of pharmaceutical products.[116] Even more relevant, the products at issue in the challenged innovation-market mergers all were protected by patents. Further increasing appropriability, patents raise the costs of imitation in the industry by thirty to forty percent.[117]

The discrete nature of innovation enhances appropriability. In contrast to complex technologies, which are composed of numerous patented inputs, new drugs contain a "discrete number of patentable elements."[118] The effectiveness of patents in the industry ensures appropriability through commercialization or licensing.[119]

In short, in the pharmaceutical industry, size is important before the innovation reaches the market but, because of the effectiveness of patents, less crucial after that point.

* * *

Most of the factors critical to economists' conclusions demonstrate the significance of competition in the pharmaceutical industry. We thus can conclusively rebut the contention that only a concentrated market structure could maximize pharmaceutical innovation.[120]

To be sure, the need for size in the regulatory process requires that this characteristic be considered in the analysis. But competition's vital role confirms the propriety of enforcement in pharmaceutical innovation markets. In fact, given that mergers between the two firms closest to the market threaten competition as much as any of the firms' activities, antitrust enforcement is essential for pharmaceutical innovation.

114. C.T. TAYLOR & Z.A. SILBERSTON, THE ECONOMIC IMPACT OF THE PATENT SYSTEM: A STUDY OF THE BRITISH EXPERIENCE 202 (1973).

115. Edwin Mansfield, *Patents and Innovation: An Empirical Study*, 32 MGMT. SCI. 173, 174 (1986).

116. Cohen et al., *supra* note 113, at 49 tbl.A1.

117. Edwin Mansfield et al., *Imitation Costs and Patents: An Empirical Study*, 91 ECON. J. 907, 913 (1981) (thirty percent); Levin et al., *supra* note 90, at 811 (forty percent).

118. Cohen et al., *supra* note 113, at 49 tbl.A1.

119. *Id.* at 23. To be sure, research spillovers in the pharmaceutical industry could weaken appropriability. But even this question is more nuanced than is often recognized, since any reduction in incentives from spillovers may be counteracted by an increase in absorptive capacity as firms increase their investment to exploit the knowledge gained from rivals' innovations. *See* Cohen & Levinthal, *supra* note 93, at 593.

120. *See supra* notes 19–20 and accompanying text (discussing the debate concerning the market structure most conducive to innovation).

## III. THE NEW TEST

The agencies currently engage in an incomplete, ad hoc analysis when conducting pharmaceutical innovation-market analysis. Although they emphasize competition, they do not promote the *effective* competition that would most directly offer the innovation benefits described in the previous Section.

In particular, the agencies do not consider the difficulty of bringing a drug to market or the likelihood that the merging firms (or others) will be successful in reaching the market. They also do not consider entry, efficiency, or Schumpeterian defenses that arise out of pharmaceutical innovation and the FDA regulatory process.

This truncated analysis is harmful, as it justifies unnecessary merger challenges that drain finite resources. With a full plate of antitrust (and, for the FTC, consumer protection) issues, unnecessary merger challenges block more-necessary enforcement. And the hazards increase when the agencies challenge mergers that promise to increase the odds of a treatment reaching the market.

In this Part, I offer a new test for the agencies to apply to pharmaceutical innovation-market mergers. The test builds on the insights of the first two Parts of the Article and incorporates a realistic assessment of the hurdles of pharmaceutical development. The goal of the test is to preserve R&D competition where it is most likely to contribute to innovation but most in danger of being suppressed. This competition occurs in the stages of regulatory approval closest to the marketplace.

The five-part analysis I offer is based on the framework of the Horizontal Merger Guidelines. The Guidelines have widely been viewed as providing a coherent, reasonable structure for merger evaluation. Of course, the two contexts are quite different. The Guidelines apply to actual products and justify challenges to mergers that would significantly increase concentration and lead to market power. Analyses in innovation markets of "concentration," "competitive harm," and "entry" thus do not apply in exactly the same manner as in product markets. But innovation markets nonetheless present analogous concerns. As I will elaborate in this Part, I propose the following framework to govern innovation-market analysis:

- First, the agencies must show that the merger would lead to significant concentration among firms reasonably likely to reach the market.
- Second, the agencies must offer a theory that the merging firms will suppress innovation.
- Third, the merging firms can rebut the prima facie case of concentration by demonstrating that at least one other firm is likely to reach the marketplace.

- Fourth, in a borderline case, the firms can demonstrate efficiencies from the merger.
- Fifth, in a borderline case, the firms can offer a Schumpeterian defense that size is needed to complete the regulatory process.

The agencies currently ignore parts of the first and second, and all of the third, fourth, and fifth factors. In doing so, they engage in an unnecessarily truncated (and harmful) analysis. Such analysis may lower implementation costs but only at the cost of neglecting the realities of pharmaceutical innovation. Nor can the agencies justify such an abbreviated analysis as a type of "per se" rule. Courts apply such bright-line rules because of the severe anticompetitive effects and unlikely procompetitive justifications of certain activities. But innovation-market mergers do not demonstrate such effects and, thus, call for a more nuanced analysis than they have received.

### *A. STEP 1: EVALUATE THE CONCENTRATION OF THE MARKET*

The "unifying theme" of the Merger Guidelines is that "mergers should not be permitted to create or enhance market power or to facilitate its exercise."[121] Mergers cannot have this effect unless they "significantly increase[] concentration and result[] in a concentrated market."[122] As described further below, a concentrated market increases the likelihood of collusion, by which competitors can increase price and reduce output.[123]

There are no actual markets in an innovation-markets analysis. It is not possible to ascertain consumer demand or to determine the effect of a "small but significant and nontransitory" increase in price.[124] Nonetheless, concentration similarly leads to concern in these markets.

As the R&D markets get significantly concentrated, the odds of more than one firm reaching the marketplace decrease. Consequently, the likelihood of product market competition decreases. Arrow recognized the innovation benefits brought about by even one nonmonopolist competitor in a market.[125] The product market innovation promised by the competitive firm assuages concerns that, after the merger, the merged firm will suppress innovation.

121. U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, HORIZONTAL MERGER GUIDELINES § 0.1 (rev. Apr. 8, 1997) [hereinafter MERGER GUIDELINES], *available at* http://www.usdoj.gov/atr/public/guidelines/hmg.htm.

122. *Id.* § 1.0. The market is defined in terms of demand substitution—in other words, consumer responses. *Id.*

123. *See infra* note 150 and accompanying text (discussing the potential effects of diminishing competition as a result of mergers).

124. *Id.*

125. ARROW, *supra* note 42, at 156–60.

As discussed below, where the merging firms are the only ones close to the market, they would have greater ability and incentive to suppress one (and, in some cases, both) of their R&D paths.[126] This would tend to increase the likelihood of either a product absence or monopoly on the market. In short, the competition that is necessary for pharmaceutical innovation is thwarted.

The most important factor in determining the likelihood of reaching the market is the stage of FDA review. Firms in the pharmaceutical industry face daunting hurdles at each of the stages. A brief background on the review process demonstrates just how difficult it is to reach the market.

### 1. FDA Review Process

The FDA approval process is lengthy, proceeding through numerous stages. First, a company engages in discovery, selecting a target for a potential medicine and searching for a molecule that can act on the target.[127] Upon finding such a molecule, the company enters preclinical testing, which utilizes tissue cell cultures, computer-based data analyses, and live animals to determine whether the chemical compound will be safe and effective for human use.[128] The odds of success in the discovery and preclinical stages are low: only 1 out of every 1000 tested compounds makes it to clinical studies.[129] And because, as I show below, only 1 out of every 4 compounds (at most) in clinical trials ever makes it to the market, the odds of a compound in preclinical development reaching the market are less than 1 in 4000.

If the company does manage to succeed in the preclinical stage, then it files an Investigational New Drug Application ("IND") at the FDA.[130] And if a board of "scientists, ethicists, and health-care specialists approves the sponsor's study protocol" and the FDA "finds the approach promising," it accepts the IND, and the drug begins three stages of clinical studies.[131]

126. *See infra* text succeeding note 155 (discussing how merging firms in an innovation-market context may wish not to introduce new products).

127. PHRMA, DRUG DISCOVERY AND DEVELOPMENT: UNDERSTANDING THE R&D PROCESS 3 (2007), *available at* http://www.innovation.org/drug_discovery/objects/pdf/RD_Brochure.pdf.

128. JOHN R. THOMAS, PHARMACEUTICAL PATENT LAW 303 (2005).

129. *See* FOOD & DRUG ADMIN., DEP'T OF HEALTH & HUMAN SERVS., JUST THE FACTS PUBLICATION NO. FS 02-5, FDA AND THE DRUG DEVELOPMENT PROCESS: HOW THE AGENCY ENSURES THAT DRUGS ARE SAFE AND EFFECTIVE (2002) [hereinafter FDA AND THE DRUG DEVELOPMENT PROCESS] ("No more than 5 in 5,000 tested compounds pass these preclinical trials and are proposed for clinical studies."). In its complaints, the FTC does not distinguish between discovery and preclinical testing. As used in this Article, "preclinical development" or "preclinical studies" encompasses both stages.

130. THOMAS, *supra* note 128, at 303–04.

131. FDA AND THE DRUG DEVELOPMENT PROCESS, *supra* note 129.

Phase I investigations focus on the safety of the drug and involve closely monitored studies of twenty to eighty healthy individuals.[132] Phase II trials evaluate safety and effectiveness for patients who have the disease and involve up to several hundred participants.[133] Phase III studies typically involve many large-scale trials with thousands of patients and are designed to establish effectiveness and discover infrequently occurring side effects.[134] Some trials straddle the phases. Phase II/III trials, for example, occur where "Phase II-like trial[s are] sufficient to produce statistically sufficient data for approval, removing the need for a Phase III trial."[135]

Upon completion of clinical testing, the firm prepares a New Drug Application ("NDA") and submits it to the FDA for review.[136] NDA applicants also are required to identify any patent that claims the drug, with these patents listed in the "Orange Book" upon FDA approval.[137]

The likelihood that a drug will reach the marketplace increases significantly with each stage of review. Several studies have documented this likelihood from each of the three stages of FDA review. Four of the most comprehensive studies reveal the following odds:

132. 21 C.F.R. § 312.21(a) (2004).

133. *Id.* § 312.21(b).

134. *Id.* § 312.22(c); Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151, 156 (2003).

135. Ark Therapeutics, Glossary, http://www.arktherapeutics.com/main/glossary.php?content=glossary#P (last visited Sept. 26, 2007) (defining relevant terms including "Phase II/III").

136. THOMAS, *supra* note 128, at 306.

137. *Id.* at 306–07.

Table 1. Likelihood of Reaching the Market from Particular Clinical Stages[138]

| Study | Date Range | Sample | Phase I | Phase II | Phase III |
|---|---|---|---|---|---|
| DiMasi (2001)[139] | 1987–1992 | 24 firms with self-originated new chemical entities | 23% | 33% | 79% |
| Adams/Brantner (2003)[140] | 1989–2002 | 3,328 drugs that entered clinical trials | 12% | 17% | 38% |
| Kola/Landis (2004)[141] | 1991–2000 | The 10 largest drug companies | 11% | 38% | 55% |
| Abrantes-Metz et al. (2004)[142] | 1989–2002 | All drugs with a known entry date that began the FDA process during the period | 26% | 32% | 57% |
| Aggregate (mean) figures | | | 18% | 30% | 57% |

The mean percentage likelihood of reaching the market from each of the three stages of clinical studies thus is 18% from Phase I, 30% from Phase II, and 57% from Phase III. Although the percentages are similar for most drugs and methods of administration, some—such as anti-cancer and anti-HIV drugs, and administration through alimentary (digestion), parenteral (injection), and topical (skin) routes—are more likely to reach the market.[143] Other products, such as anti-Alzheimer's drugs, are less likely to reach the market.[144]

138. Figures are rounded off to the nearest percentage point.

139. Joseph A. DiMasi, *Risks in New Drug Development: Approval Success Rates for Investigational Drugs*, 69 CLIN. PHARMACOLOGY THERAPEUTICS 297, 303 (2001).

140. Christopher P. Adams & Van V. Brantner, *New Drug Development: Estimating Entry from Human Clinical Trials* 20 tbl.4 (Fed. Trade Comm'n Bureau of Econ., Working Paper No. 262, 2003), *available at* http://papers.ssrn.com/sol3/papers.cfm?abstract_id=428040.

141. *See* Ismail Kola & John Landis, *Can the Pharmaceutical Industry Reduce Attrition Rates?*, 3 NATURE REVS. 711, 711–12 (2004).

142. Rosa M. Abrantes-Metz, Christopher Adams, & Albert D. Metz, *Pharmaceutical Development Phases: A Duration Analysis* 9 tbl.B.2.A (Fed. Trade Comm'n Bureau of Econ., Working Paper No. 274, 2004), *available at* http://papers.ssrn.com/sol3/papers.cfm?abstract_id=607941.

143. *See id.* (providing figures for Phases I, II, and III, respectively, of 42%, 48%, and 66% for anti-cancer drugs; 50%, 58%, and 94% for anti-HIV/AIDS drugs; 49%, 55%, and 71% for alimentary administration; 47%, 51%, and 69% for parenteral administration; and 50%, 56%, and 71% for topical administration (figures rounded to the nearest whole number)).

144. *See id.* (reporting results of 16%, 20%, and 33%, rounded to the nearest whole number, in Phases I, II, and III, respectively).

### 2. Concentration

The previous subsection demonstrated how difficult it is for chemical compounds to reach the market. In particular, it traced the divide between preclinical and clinical development and the importance of the product's clinical stage.

The astronomical odds confronting firms in preclinical development call for caution in emphasizing Arrow's exhortation to competition. If the odds are less than 1 in 4000 that a firm will reach the market from preclinical development, there is less concern about the firm reducing its R&D paths in a way that would affect the likelihood of a product reaching the market.

In preclinical development, for example, the odds of reaching clinical studies are approximately 1000 to 1. Industry realities thus do not show a race between competitors but rather a solitary quest to surmount the steep odds of making it to clinical trials. Drugs in preclinical development are so unlikely to succeed that merger challenges do not effectively promote competition. I therefore part company with the agencies and commentators in concluding that the agencies should not consider firms with products in preclinical development in determining the concentration of the R&D market.[145]

A few examples illustrate the point. Where the merging firms only have products in preclinical development, the staggering odds that either one would reach the market, let alone both, counsels the agencies not to challenge the merger. Nor does a merger between a firm with a product in advanced trials (say, Phase III) and one in preclinical development raise concern. Even if—as the FTC alleged in several challenges I discuss below—those two firms are "closest" to the market, the improbability that the latter will ever reach the market reduces concern. Assertions of proximity to market that ignore the stage of review are overbroad and unrealistic. Thus, under my test, the agencies must show that the merger would lead to significant concentration among firms reasonably likely to reach the market. Firms with products in preclinical development do not satisfy this test.

Once the market is limited to products in clinical trials, the most important factors in determining market concentration become (1) the number of firms with products in these stages and (2) the specific stage of FDA review. The greatest concern applies when the number of competitors is low and the parties are at an advanced stage of FDA review. This occurs when a merger is proposed between the only two firms in clinical studies, both of which are in Phase III. In this case, no potential entry is anticipated

145. Nor should agencies and commentators be concerned that firms in preclinical studies are more likely to have a significant share of future products that reach that stage. None of the challenged mergers discussed in Part IV involved firms in preclinical studies that had a monopoly over—or even unique ability to develop—particular types of treatments.

for the foreseeable future, and the firms are reasonably likely to reach the market. As discussed in the next Section, because the firms are close to the market, they would have the greatest ability and incentive to suppress a research path.[146]

To be sure, it is not certain that each of the merging firms in Phase III would have reached the market absent the merger. But there is a reasonable likelihood that they would have done so. And if the dangers of suppression apply anywhere, it is in this case.

It is conceivable that the agencies could demonstrate concentrated markets where the merging parties have products in earlier stages. But such challenges should be rare. As the last subsection demonstrated, there is roughly an 18% chance of making it to market from Phase I, 30% from Phase II, and 57% from Phase III. Because it is unlikely that firms in Stage II and, especially, Stage I will reach the market, challenges should be limited to categories such as anti-cancer drugs and AIDS drugs in which there is a greater likelihood of reaching the market or to other exceptional cases in which the anticompetitive harms seem particularly acute.[147]

Finally, and as discussed more fully below,[148] where there is at least one firm other than the merging companies in clinical studies, the harm would tend to decrease. The closer to the market the competitor is (and the more numerous the rivals), the greater the odds of success and the less the concern.

The market concentration test I propose improves upon the agencies' version in two important ways. First, it takes into account the realities of the pharmaceutical industry. Drugs in preclinical development that have a 1 in 4000 chance of making it to the market do not present significant concern. Second, the test looks at not only the number of competitors in the market, but also the stage of FDA review. Given the markedly different odds confronting firms in each of the three stages, the test thus more effectively incorporates the realities of pharmaceutical development.

### *B. STEP 2: ASSESS COMPETITIVE HARM*

Under the Merger Guidelines, the agencies must demonstrate potential adverse competitive effects from the merger.[149] The most important of these effects is the danger of collusion. As the number of firms in the market decreases, it becomes easier to reach an agreement to reduce supply

146. *See infra* text accompanying note 150.

147. *See supra* notes 139–44 and accompanying text (describing various drug categories' percentage chance of reaching the market).

148. *See infra* Part III.C.

149. MERGER GUIDELINES, *supra* note 121, § 2.0.

(thereby increasing price) and to police the terms of that agreement.[150] In short, the likelihood of collusion increases.

A second competitive harm occurs even in the absence of collusion. According to the theory of "unilateral competitive effects," the firms may—regardless of the actions of the other market participants—raise price and reduce output.[151] This is of particular concern where the products of the merging firms are similar.[152]

In innovation markets, the danger of collusion is markedly reduced. First, reaching an agreement is difficult. In contrast to fixing a price on homogeneous products, the multiple dimensions of R&D significantly decrease the likelihood of coordinating its direction or speed.[153] Second, it is easier to cheat because innovation typically is "conducted in secret."[154] Finally, the manifest rewards of successful innovation encourage cheating.[155]

But there is an analogue in the innovation-market context to unilateral competitive effects. In certain cases, the merging firms might—regardless of the actions of other firms—not wish to introduce new products. Especially as the similarity of the products increases, the likelihood of suppression increases.

The second requirement of my test is that the agencies allege a theory of competitive harm. That theory typically will involve the potential suppression of a research path. As the concentration in the market increases and the products get closer to market, the incentive and ability to suppress one of the research paths increases.

The *incentive* increases because it is more likely that a product will reach the market. Suppression matters most for probable future products (as opposed to speculative research paths). Once success appears likely in the product market, firms naturally would recognize that suppression would have an effect. In contrast, in the early stages, the incentive to suppress is much more attenuated because it is not needed: the staggering odds of the regulatory process itself create the same result.

The *ability* to suppress also increases as the product gets closer to the market. The determination of the ability to suppress should incorporate the likelihood that suppression will have an effect. Of course, a firm technically

150. Such coordinated interaction includes activity that is profitable "only as a result of the accommodating reactions of the [other firms]." *Id.* § 2.1.

151. *Id.* § 2.2.

152. *See id.* § 2.211 (explaining "market concentration measures" and when to rely on the data to show a significant share of sales in the market by "consumers who would be adversely affected by the merger").

153. PREPARED STATEMENT OF M. HOWARD MORSE BEFORE THE ANTITRUST MODERNIZATION COMMISSION HEARING ON ANTITRUST AND THE NEW ECONOMY 11 (Nov. 8, 2005), *available at* http://www.amc.gov/commission_hearings/pdf/Statement_Morse_revd.pdf.

154. *Id.*

155. *Id.*

can suppress a research path at any point. But suppression is more likely to have an effect as the likelihood of reaching the market increases. In addition, the ability to suppress also rises with a reduction in the number of firms in the market because suppression will have a more direct effect in the absence of competitors.[156] Incentive and ability to engage in anticompetitive effects thus will largely track the first inquiry concerning market concentration.

There are two additional factors that increase the likelihood of suppression: cannibalization and similar products.

First, if one of the merging firms has a currently existing treatment for a condition, that firm may have a lower incentive to introduce a new product. In many cases, sales of the new product would reduce the sales of the current product.[157] The distinction between drastic and nondrastic innovation articulated above is instructive here.[158] The monopolist has less incentive than the competitive firm to introduce a drastic innovation because such an innovation would displace its monopoly in the market for the previous product.[159]

In most of the challenged mergers, this factor would not have applied since (1) there was no current treatment or (2) the treatment was offered by a nonmerging firm. But in two of the cases, one of the merging firms had market power in the previous generation's product.[160] Where this is the case, and particularly where the firm's R&D appears directed to a drastic innovation, it is more likely that there will be competitive harm.

The second factor involves the relationship between the two products. The closer the products are, the greater the incentive to suppress one of the products. This conclusion overlaps with the Merger Guidelines' recognition that the similarity of the merging firms' products increases the likelihood of unilateral competitive effects.[161] As the similarity of R&D paths increases, the need for both decreases. As a result, the merging firms have a greater incentive to suppress one of them.

156. *See* Ben-Asher, *supra* note 25, at 314 (noting the increased specialization in the industry and "R&D-related barriers to entry").

157. *See* ARROW, *supra* note 42, at 157–59.

158. *See supra* notes 64–75 and accompanying text (contrasting the two types of innovation).

159. *See* Elhauge, *supra* note 67, at 299 n.141 ("[A]n existing monopolist has less incentive to create drastic innovations because when it makes such innovations it replaces its existing monopoly profits to some extent, whereas an entrant who makes such a drastic innovation reaps full monopoly profits with no replacement offset.").

160. *See infra* note 301 and accompanying text (discussing the merger between Glaxo Wellcome and SmithKline Beecham, the companies most advanced in developing a prophylactic herpes vaccine); *see also infra* note 234 (discussing the effect of Glaxo's monopoly in injectable migraine treatment in an innovation market for noninjectable migraine treatment).

161. MERGER GUIDELINES, *supra* note 121, § 2.211.

In short, the theory of competitive harm will largely depend on the level of concentration of the R&D market and the stage of FDA review of the merging and nonmerging firms. But two additional factors increase the likelihood of anticompetitive harm: (1) a merging firm's market power in the previous generation's product (especially for drastic innovations) and (2) similar research paths.

### *C. STEP 3: EVALUATE THE ENTRY DEFENSE*

In the Merger Guidelines, entry negates the adverse effects of concentration. If entry into the market is easy, then firms cannot sustain price increases, and it is less likely that the merger would lead to the creation of market power.[162] In the parlance of the Guidelines, entry would "deter an anticompetitive merger in its incipiency" or "deter or counteract the competitive effects of concern."[163]

In the innovation-market context, in contrast, there is no currently existing product market that an outside firm could enter. But the underlying policy of the Guidelines nonetheless applies. If another firm in addition to the merged firm makes it to the market, then, by definition, there will be competition. Competition is important for pharmaceutical innovation, and the presence of a competitor reduces suppression concerns. Even if competition is not as robust as it would be in a more atomistic market, the presence of a single non-monopolist competitor in the market increases the likelihood of innovation.

To be sure, the determination of entry is speculative in both the product and innovation-market contexts. The Merger Guidelines require entry to be "timely, likely, and sufficient in its magnitude, character and scope to deter or counteract the competitive effects of concern."[164] Determining these characteristics for a future occurrence is speculative. Similarly, in the innovation-market context, we do not know which companies eventually will make it to the market. But significant guidance is offered by the odds of success at each stage of the FDA review process.

The merging firms therefore are able to offer a defense based on the likelihood that another firm will enter the market. The identity of products in various stages is public information that is easily discoverable.[165] And the stage of review provides an instructive guide to the odds of reaching the market.

Firms in Phase III are the most likely to reach the market, with approximately a 57% likelihood of success. If two firms other than the

162. *Id.* § 3.0.

163. *Id.*

164. *Id.*

165. For example, the National Institutes of Health "provides regularly updated information about federally and privately supported clinical research in human volunteers." ClinicalTrials.gov, http://clinicaltrials.gov (last visited Oct. 10, 2007).

merging companies are in Phase III, then there is roughly an 81% chance that at least one of the nonmerging firms will reach the market (a 32% likelihood of success for both, plus a 49% likelihood of success for one).[166] In this case, because the 81% chance demonstrates a significant likelihood that there will be competition in the market, the agencies should recognize entry as a very powerful defense.

Where there is only one nonmerging firm in Phase III, the odds of that firm making it to the market (and thereby offering competition) are approximately 57%. In this case, though it is less certain that there will be competition, it is still a reasonable possibility. The agencies thus should accept a more qualified defense, which could make a difference in close cases.

This type of qualified defense also would apply in other cases with similar odds of success. For example, if two firms are in Phase II, then the odds of success are 51% (a 9% likelihood of both and a 42% chance of one).[167] Different permutations determine the odds of entry.

### *D. STEP 4: EVALUATE THE EFFICIENCIES DEFENSE*

An additional defense that the merging firms could offer is that the merger will lead to efficiencies. The Merger Guidelines recognize several types of efficiencies: an enhanced ability and incentive to compete, the introduction of new or improved products, and "a better utilization of existing assets" that allows the combined firm to lower its costs.[168] The Guidelines explain that marginal cost reductions resulting from shifting production among facilities are the most substantial and verifiable type of efficiency.[169] R&D efficiencies "are potentially substantial" but "less susceptible to verification."[170]

In order to be considered, the efficiencies must be "merger-specific," achievable only through merger. The agencies consider whether cognizable efficiencies would be "sufficient to reverse the merger's potential to harm consumers in the relevant market."[171] The efficiencies tend to achieve this result when the likely adverse competitive effects are "not great."[172] In

166. The odds of both firms making it to the market are .57 * .57 = .3249. The odds of only one firm succeeding are 2 * (.57 * .43) = .4902. Therefore, the odds of at least one firm making it are .3249 + .4902 = .8151.

167. The odds of both firms making it to the market are .30 * .30 = .09. The odds of only one firm succeeding are 2 * (.30 * .70) = .42. Therefore, the odds of at least one firm making it are .09 + .42 = .51.

168. MERGER GUIDELINES, *supra* note 121, § 4.

169. *Id.*

170. *Id.*

171. *Id.*

172. *Id.*

particular, they "almost never justify a merger to monopoly or near-monopoly."[173]

In the innovation-market context, there are no products for which marginal cost can be reduced. But the introduction of new products is the goal of pharmaceutical R&D. The relevant efficiency thus takes the form of an increased likelihood that the firms will be able to reach the market. In certain cases, the merging firms may be able to combine complementary knowledge and expertise in a way that would increase the likelihood of success.

Of course, pharmaceutical firms merge for numerous reasons other than achieving efficiencies in R&D markets. In the late 1990s, for example, there was significant consolidation in the industry, with mergers driven by pressures to reduce costs and "bolster drug pipelines" in the face of decreasing profit margins.[174] Other firms merged to utilize excess capacity or as an "exit strategy when faced with financial trouble."[175]

But sometimes the merger will help firms in the particular R&D market. For example, benefits were offered in the merger between Genzyme and Novazyme, two companies researching Pompe disease, a fatal and difficult-to-treat disease affecting infants and young children.[176] The merger made comparative experiments possible, as the companies could engage in a "comprehensive, blinded pre-clinical analysis comparing all four [relevant] enzymes."[177] The merger also "provided information that enabled the Novazyme program to avoid drilling dry holes" and relatedly accelerated the Novazyme program.[178] Finally, it allowed Novazyme to gain access to a Genzyme assay, to use Genzyme cell lines scalable for a Pompe enzyme, to measure glycogen reduction, and to learn patients' reactions to earlier Pompe products.[179] Because only Genzyme had this experience with Pompe disease, no other company could offer these benefits.

Where it is particularly difficult to reach the market, and where there is no currently existing treatment, the agencies should most seriously consider the efficiencies claim. For example, in the Genzyme–Novazyme merger, there was no available treatment for a fatal disease. Of equally significant concern, Pompe disease is one of forty-one diseases known as lysosomal

173. MERGER GUIDELINES, *supra* note 121, § 4.

174. Andrew Ross Sorkin, *Glaxo and SmithKline Agree to Form Largest Drugmaker*, N.Y. TIMES, Jan. 17, 2000, at A1.

175. Patricia M. Danzon et al., *Mergers and Acquisitions in the Pharmaceutical and Biotech Industries* 32–33 (Nat'l Bureau of Econ. Research, Working Paper No. 10536, 2004), *available at* http://www.nber.org/papers/w10536.

176. Muris Statement, *supra* note 2, at 1.

177. *Id.* at 17 & n.42.

178. *Id.* at 17.

179. Douglas L. Wald & Deborah L. Feinstein, *Merger Enforcement in Innovation Markets: The Latest Chapter—Genzyme/Novazyme*, THE ANTITRUST SOURCE, July 2004, at 9, *available at* http://www.abanet.org/antitrust/at-source/04/07/Jul04-Feinstein7=23.pdf.

storage disorders ("LSDs").[180] Developing drugs to treat LSDs is particularly challenging: As of late 2006, there was a treatment for only four of the forty-one diseases, with each of these developed by Genzyme.[181] The most important goal in these cases thus should not be to ensure the presence of two products on the market, but to increase the likelihood that one product reaches the market.[182]

In general, the efficiencies defense would have the greatest effect when the firms are furthest from the market. This mirrors the Merger Guidelines' direction to consider efficiencies most seriously "when the likely adverse competitive effects, absent the efficiencies, are not great."[183] In contrast, just as "[e]fficiencies [in product markets] almost never justify a merger to monopoly or near-monopoly,"[184] they typically will not sanction an innovation-market merger where there is a significant concentration of firms reasonably likely to reach the market.

In short, the merging firms can proffer efficiencies that increase the likelihood that the product will reach the market. The agencies should most seriously consider these efficiencies as market concentration decreases and as the difficulty of reaching the market increases.

### *E. STEP 5: EVALUATE THE SCHUMPETERIAN DEFENSE*

The final defense bears some overlap with the current "failing firms" defense. The Guidelines state that "a merger is not likely to create or enhance market power or to facilitate its exercise, if imminent failure . . . of one of the merging firms would cause the assets of that firm to exit the relevant market."[185] The rationale is simple: "In such circumstances, post-merger performance in the relevant market may be no worse than market performance had the merger been blocked and the assets left the market."[186]

Small firms in innovation markets may not be in danger of failing. But they face a related challenge in the towering hurdles of the regulatory process, which can block development. As discussed above, the process is lengthy, with Phase III trials in particular requiring thousands of subjects. For that reason, a merger might allow a smaller firm to pursue expensive and administratively complex clinical trials that otherwise would be

180. *Id.* at 2.

181. GENZYME, *Genetic Diseases*, *in* ANNUAL REPORT (2006), *available at* http://genzyme.com/2006_ann_rpt/genetic.asp (reporting the launch of Myozyme, the fourth LSD therapy marketed by Genzyme).

182. The efficiencies defense also could apply to vaccines and to drugs subject to the Orphan Drug Act, 21 U.S.C. § 360bb(a)(2) (2000), which provides seven years of market exclusivity to products treating rare conditions.

183. MERGER GUIDELINES, *supra* note 121, § 4.

184. *Id.*

185. *Id.* § 5.0

186. *Id.*

impossible. Absent a merger or other collaboration, in other words, the firm would not be able to proceed through the development process.

Allowing a defense for such firms is a concrete manifestation of Schumpeter's theoretical construct and incorporates the Part II finding that size is important in navigating the FDA process. Schumpeter emphasized the importance of size in offering financial resources and investment.[187] Although some of his arguments applied only to monopolies, most were satisfied by large firms.[188] In fact, the hurdles of the FDA regulatory process demonstrate the need for size, particularly in conducting Phase III trials. Even if monopoly is not necessary to navigate the process, size is.[189]

In many mergers, this defense will not apply. Firms merge for many reasons, such as cost pressures and emptying pipelines.[190] Even in innovation-market cases, companies often focus on product markets, with millions of dollars in sales. In addition, many of the cases involve large pharmaceutical companies that could easily conduct clinical studies. Merging firms that are in Phase III studies have already shown the ability to navigate the regulatory process.

But where a small firm with a promising compound could not otherwise pursue clinical trials, the agencies should consider such a defense. The firm could demonstrate an inability to proceed by introducing evidence of reasonably objective factors like market capitalization, assets, and profits. Like the efficiency defense, the Schumpeterian defense would be most persuasive where there is only modest concentration among firms reasonably likely to reach the market.

* * *

In short, the proposed framework builds on the current merger analysis, adapting it to account for the realities and hurdles of the pharmaceutical regulatory process.

The most important factor in the agencies' case is the first, by which the agencies must show that the merger would lead to significant concentration among firms reasonably likely to reach the market. Where this factor is met, the second factor, by which the agencies must offer a theory that the merging firms will suppress innovation, likely is satisfied. And where it is absent, competitive harm is not a real concern.

The third, fourth, and fifth elements allow the merging parties to present defenses to the agencies' claims. The third, by which the merging firms can demonstrate that at least one other firm is likely to reach the marketplace, is the most important since a rival's entry promises to

187. SCHUMPETER, *supra* note 31, at 101.

188. *Supra* notes 40–41 and accompanying text.

189. *See supra* notes 106–10 and accompanying text (noting the resources available to large firms).

190. *See supra* note 174 and accompanying text.

introduce the desired competition into the market. The fourth (merger-specific efficiencies) and fifth (Schumpeterian defense for small firms) factors will not apply in many cases. But when they do, the agencies will need to balance the threat from concentration against the proffered benefits. That they currently do not engage in such a nuanced comparison demonstrates what is missing in the analysis today.

## IV. EMPIRICAL STUDIES

There have been ten challenges to (and one prominent refusal to challenge) mergers in innovation markets. Two of these challenges occurred outside the pharmaceutical industry. In 1993, the U.S. Department of Justice (in its only innovation-market case) challenged General Motors' attempt to sell one of its divisions to ZF Friedrichshafen AG on the basis that the two firms were the primary producers of heavy-duty automatic truck and bus transmissions.[191] Two years later, the FTC challenged Sensormatic's acquisition of Knogo, claiming that the two firms were the only ones conducting R&D for the next generation of antishoplifting equipment.[192] Every other innovation-market challenge occurred in the pharmaceutical industry.

The nine pharmaceutical mergers (of which eight were ultimately challenged), of course, involved many product lines. In addition to R&D markets, some mergers involved products that were in actual competition (i.e., both merging parties had products). Others involved potential competition (i.e., one of the merging firms had a product). But the universe of pharmaceutical merger challenges in which there was at least one overlapping research line for which there was not yet a product on the market is limited to these nine cases.

Until now, most of the discussion of these cases has been limited to the facts alleged in FTC complaints. Because these matters have been resolved by consent agreement, there has been remarkably little information beyond the agreement that has been subject to debate. There are no court cases examining the validity of the FTC's allegations. Even scholarly analysis has not challenged the allegations.

In addition, the entities most likely to question such determinations—the merging firms themselves—have not done so. As mentioned above, the companies typically have numerous reasons to merge, such as cost pressures and disappearing pipelines.[193] In addition, the innovation market usually is one market out of many affected by the merger. Multiple product markets, with millions of dollars in current sales, are the parties' primary concern.

191. Complaint, United States v. Gen. Motors Corp., No. 93-530 (D. Del. Nov. 16, 1993), *available at* 1993 WL 13610315.

192. Sensormatic Elec. Corp., 119 F.T.C. 520, 520 (1995) (consent order).

193. *See supra* note 174 and accompanying text.

In short, there has been no comprehensive analysis of the FTC's pharmaceutical innovation-market challenges. This Part offers the first such assessment. Four questions frame the analysis:

- What was the pre-merger treatment (if any) for the condition?
- At the time of the merger, in which stage of preclinical or clinical review were the merging companies?
- Were there other companies in preclinical or clinical studies at the time of the merger?
- What does the market look like today?

For each merger, I answer these questions. I then apply my test to determine whether the FTC correctly challenged the mergers. I conclude that the agency was correct in five out of the nine cases. But application of my test would have altered the outcome in four of the nine cases—the mergers between Roche and Genentech, AHP and American Cyanamid, Ciba-Geigy and Sandoz, and Pfizer and Warner Lambert.

### *A. ROCHE–GENENTECH*

#### 1. Case Study

In November 1990, the FTC entered into a consent decree with Roche and Genentech.[194] The relevant market covered "CD4-based therapeutics for the treatment of AIDS and HIV infection."[195] Human Immunodeficiency Virus ("HIV") attacks a patient by attaching itself to the protein CD-4, a receptor on the surface of immune cells that helps the virus gain entry into the cell.[196] Experimental drugs allowed an engineered CD-4 protein to circulate in the bloodstream, picking up the virus before it could affect living immune cells.[197]

The FTC alleged that Genentech was "the most advanced of a limited number of companies developing CD4-based therapeutics for use in the treatment of AIDS/HIV infection."[198] Roche was "also engaged in" similar R&D and "ha[d] patent applications pending on its products."[199]

At the time of the merger, Genentech was in Phase I studies.[200] Roche was in preclinical studies.[201] A rival, Biogen, was in Phase I/II trials.[202] As a

194. *In re* Roche Holding Ltd., 113 F.T.C. 1086, 1086 (1990).
195. *Id.* at 1087.
196. Joseph Palca, *New AIDS Drugs Take Careful Aim*, 246 SCI. 1559, 1559 (1989).
197. *Id.*; Laura Jereski, *Biogen's New Moneymaking Genes*, BUSINESSWEEK, June 19, 1989, at 94.
198. *Roche*, 113 F.T.C. at 1088.
199. *Id.*
200. Laura Evenson, *Genentech Merger Gets FTC's OK*, S.F. CHRON., Sept. 1, 1990, at B1.
201. *Id.*

result of the consent agreement, the FTC required Roche to grant nonexclusive patent licenses for its version of CD-4.[203]

But because of unsuccessful studies and exorbitant costs, these companies abandoned their CD-4 efforts shortly after the merger.[204] Today, there are no first-generation CD-4 products on the market. The closest product is Hoffman La Roche's Fuzeon, which was developed by Trimeris and approved by the FDA in March 2003.[205]

### 2. Application

Application of my test shows that the FTC should not have challenged this merger. In particular, the agency would not have been able to demonstrate the first step of a concentrated market. Genentech was in Phase I, and Roche was in preclinical studies. Of the nine cases, this is the weakest case of concentration because it was unlikely that either firm would have reached the market.

As it turns out, the compulsory licensing requirement imposed on Roche was not beneficial. In fact, because of unsuccessful studies and exorbitant costs, each of the merging firms abandoned their CD-4 efforts shortly after the merger. Although a related drug was approved in 2003, there are no drugs similar to those of Roche and Genentech on the market today.[206]

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202. *See Biogen Inc. Signs Funding Agreement with New York Life Insurance Co.*, APPLIED GENETICS NEWS, Nov. 1, 1989, *available at* 1989 WLNR 1234342 (noting that Biogen conducted tests on its drug in Phase I/II clinical trials).

203. Evenson, *supra* note 200.

204. *See Progenics Developing CD4-IgG2 for HIV-Infection*, ANTIVIRAL AGENTS BULL., June 1995, *available at* 1995 WLNR 3761267. The article noted that

> [b]esides Progenics, Genentech, Biogen and SmithKline Beecham had previously licensed CD4 from Columbia Univ. and pursued development of recombinant soluble CD4 and related agents for treatment of HIV-infection. . . . [T]he lack of sufficiently dramatic efficiency noted with CD4 in clinical trials and the high dosages (and associated cost) at which indications of efficacy were observed has caused CD4 and related first generation CD4-immunoglobulin fusion proteins to be abandoned.

*Id.*

205. *FDA Grants Traditional Approval for Fusion Inhibitor for HIV Treatment*, IMMUNOTHERAPY WKLY., Nov. 17, 2004, at 102, *available at* 2004 WLNR 7585320; *Timeline Set for Development of T-20 for HIV-Infection*, ANTIVIRAL AGENTS BULL., Oct. 2001, *available at* 2001 WLNR 7846734. In contrast to CD-4 products, which attach to the AIDS virus before reaching other cells, Fuzeon creates a barrier between the virus and healthy cells. Press Release, Roche Pharmaceuticals, U.S. FDA Approves Fuzeon; First Drug to Block Entry of HIV into Immune Cells (Mar. 14, 2003), *available at* http://www.roche.com/inv-update-2003-03-14.

206. *See supra* note 205 and accompanying text (noting that Hoffman La Roche's related drug, Fuzeon, was approved by the FDA in 2003).

### *B. AMERICAN HOME PRODUCTS–AMERICAN CYANAMID*

#### 1. Case Study

In November 1994, the FTC approved the merger of American Home Products ("AHP") and American Cyanamid ("Cyanamid"). The agency initially had alleged an effect on an innovation market for a vaccine to treat rotavirus, "a diarrheal disease that causes thousands of children's deaths annually."[207] In particular, it claimed that the merging companies were "two of only three producers of vaccines with research projects either in or near the clinical trial stage" of FDA review.[208] It required that AHP license Cyanamid's rotavirus vaccine research to a third party.[209]

At the time of the merger, AHP was in Phase II/III studies.[210] Cyanamid appeared to be in preclinical studies.[211] A third company, Virus Research Institute ("VRI"), also appeared to be in preclinical studies.[212]

For several years after the merger, there were no products on the market. Although the FDA approved AHP's product, RotaShield, in 1998,[213] the firm pulled the product less than one year later because of an increased risk of intussception, a rare blockage or twisting of the intestine.[214] Cyanamid's product did not reach clinical trials in the United States and was

207. Press Release, Fed. Trade Comm'n, American Home Products Settles FTC Charges in American Cyanamid Acquisition (Nov. 10, 1994) (on file with the Iowa Law Review).

208. *Id.*

209. *Id.*

210. *American Home: Finally a Pharma Company*, MARKETLETTER, Dec. 7, 1992, *available at* 1992 WLNR 1948153. For a description of Phase II/III, see *supra* text accompanying notes 132–35.

211. It is difficult to document Cyanamid's precise development stage. But unlike the record for products that make it to clinical studies, I have been unable to uncover evidence—through news articles, securities filings, and general Internet searches—that Cyanamid's product made it to that stage.

This result is confirmed by the allegation in the FTC complaint that AHP and Cyanamid had products "in or near the clinical trial stage." Hon. Christine A. Varney, Commissioner, U.S. Fed. Trade Comm'n, The Federal Trade Commission and International Antitrust, Remarks at the Fordham Corporate Law Institute 23rd Annual Conference on International Antitrust Law and Policy (Oct. 17, 1996), *available at* http://www.ftc.gov/speeches/varney/fcli_96.shtm. The FTC did not use this language when challenging any of the mergers where the firms both had products in clinical studies. In this case, because AHP was in clinical studies, it seems reasonable to assume that Cyanamid was the treatment "near" clinical review (i.e., in preclinical studies).

212. *New Adjuvant Enters Trials with Influenza Vaccine*, ANTIVIRAL AGENTS BULL., Nov. 1, 1996, *available at* 1996 WLNR 4238765 (noting that, as of November 1996, VRI had recently entered Phase I/II trials).

213. *The Hunt Continues*, MED. AD. NEWS, Nov. 1, 1998, *available at* 1998 WLNR 5455043.

214. Joseph Brown, *The Power of the Pipeline*, MED. AD. NEWS, Oct. 1, 1999, *available at* 1999 WLNR 5478723.

divested in October 1996 to Korea Green Cross Corporation.[215] VRI (which later became Avant Immunotherapeutics) partnered with GlaxoSmithKline to receive approval of its treatment in Mexico and several European countries,[216] though it has not received FDA approval in the United States.[217]

A fourth company, Merck, increased its development efforts for its own vaccine, RotaTeq, after AHP pulled its product.[218] The FDA approved this vaccine on February 3, 2006.[219] It is currently the only vaccine for rotavirus approved for use in the United States.

#### 2. Application

Application of my test shows that the FTC should not have challenged the merger. Again, the agency would not have been able to demonstrate the first step of a concentrated market. Even though AHP was in Phase II/III, Cyanamid was in preclinical development.

An ex post review confirms that the merger challenge was not necessary. Although Merck's Rotateq received FDA approval in February 2006, this development was related to the merger challenge only in that the *failure* of AHP's product prompted Merck's development. AHP's product made it to the market in 1998 but was pulled because of complications. And Cyanamid's divested product never reached clinical trials in the United States.[220]

### *C. GLAXO–WELLCOME*

#### 1. Case Study

In June 1995, the FTC entered into a consent decree with merging parties Glaxo and Wellcome.[221] The parties each were developing noninjectable 5HT-1D agonists, which treat migraine attacks.[222] Migraine is "an often debilitating, biological disease characterized by severe pain,

215. Press Release, Fed. Trade Comm'n, Announced Actions for October 4, 1996, *available at* http://www.ftc.gov/opa/1996/10/petapp58.htm; *see supra* note 211.

216. Brady Huggett, *Avant Raises $14M Through Shelf to Develop Products*, BIOWORLD TODAY, Oct. 18, 2001, *available at* 2001 WLNR 4215262; *Rotarix GlaxoSmithKline Marketed, UK*, R&D FOCUS DRUG NEWS, June 12, 2006, *available at* 2006 WLNR 9933602.

217. *Annual Report: 10 Best Pipelines: GlaxoSmithKline*, PHARMABUSINESS, Jan. 2001, at 48, *available at* 2001 WLNR 7835705.

218. David Shook, *New Jersey-Based Drug Maker Says New Items Will Counter Expected Losses*, REC. N. N.J., Dec. 10, 1999, *available at* 1999 WLNR 5501766.

219. *FDA Approves New Vaccine to Prevent Rotavirus Gastroenteritis in Infants*, FDA NEWS, Feb. 3, 2006, http://www.fda.gov/bbs/topics/news/2006/NEW01307.html.

220. *See supra* notes 214–15 and accompanying text.

221. In the Matter of Glaxo PLC, 119 F.T.C. 815, 815 (1995).

222. *Id.* at 816.

usually on one side of the head," with attacks that "occur periodically and . . . last from [4] to 72 hours."[223]

The FTC alleged that the merger would "[d]ecreas[e] the number of [R&D] tracks for non-injectable 5HT-1D agonists" and "[i]ncreas[e] Glaxo's ability to unilaterally reduce [R&D] of non-injectable 5HT-1D agonists."[224]

At the time of the merger, Glaxo had an injectable migraine treatment, Imitrex,[225] but there were no noninjectable migraine drugs on the market. Wellcome's 311C was in Phase III trials,[226] and Glaxo's Naramig was in either Phase II or Phase III.[227] As a condition of the merger, the FTC required the companies to divest Wellcome's 311C.[228]

In 2006, Glaxo's Imitrex had 56% of the migraine drug market.[229] Products with at least 10% of the market included Merck's Maxalt, Pfizer's Relpax, and Zeneca's Zomig.[230] These figures show increasing competition as compared to figures from 2003 (when Imitrex had 60%, Zomig had 11%, and Maxalt had 8%)[231] and, especially, 1999 (when Imitrex had 83%, Zomig had 7%, Glaxo Wellcome's Amerge had 3%, and Maxalt had 1%).[232]

### 2. Application

The FTC correctly challenged this merger. Because Wellcome was in Phase III and Glaxo was in either Phase II or Phase III, the agency could have demonstrated the first step, significant concentration among firms reasonably likely to reach the market.

It also could have satisfied the second step by offering a theory of anticompetitive harm in the form of innovation suppression. Such a

223. *FDA Approves Amerge for Migraine Treatment*, DOCTOR'S GUIDE, Feb. 11, 1998, http://www.docguide.com/dg.nsf/PrintPrint/2877C3E773686229852565A80060754A.

224. *Glaxo*, 119 F.T.C. at 817.

225. In the Matter of Glaxo PLC, Agreement Containing Consent Order, File No. 951-0054, n.1 (F.T.C. Mar. 7, 1995), *available at* 1995 WL 140769.

226. Commission Regulation 4064/89, Case No. IV/M.555 (Glaxo v. Wellcome), 1995 O.J. (C 65) 3, at ¶ 28 (EC), http://ec.europa.eu/comm/competition/mergers/cases/decisions/m555_en.pdf.

227. Glaxo, Annual Report (Form 20-F), at 9 (Sept. 26, 1994).

228. *Glaxo*, 119 F.T.C. at 820–21.

229. Andy Stone, *No More Headaches?*, FORBES.COM, Apr. 17, 2006, *available at* http://www.forbes.com/2006/04/13/pozen-trexima-migraine-cz_as_0417pozen_print.html.

230. Stan Hull, Senior Vice President, US Pharmaceuticals-RTP, PowerPoint Presentation, at slide 41 (June 7, 2006), *available at* http://gsk.com/investors/presentations/2006/06072006-roundtable-hull.pdf.

231. Al Branch, Jr., *A New Headache for Imitrex*, HIGHBEAM RESEARCH, June 1, 2003, *available at* http://www.highbeam.com/DocPrint.aspx?DocId=1G1:104577998.

232. *The Fast Growing Migraine Drug Market*, 3 ASIA PAC. BIOTECH NEWS 62, 62 (1999) (on file with the Iowa Law Review). None of the market share figures distinguish between injectable and noninjectable treatments.

conclusion naturally follows from the finding on market concentration.[233] And it is bolstered by Glaxo's monopoly in the previous injectable migraine treatment. The new product primarily resembles a drastic innovation because most patients will prefer oral to injectable treatment.[234] Even though there are elements of nondrastic innovation (because of the need for injectable treatment for migraines with nausea or vomiting, "morning migraines," and "rapidly escalating migraines"),[235] the significant improvement offered by noninjectable treatment demonstrates the type of drastic innovation bolstering the conclusion of anticompetitive harm.

Nor would the merging parties be able to offer defenses sufficient to reverse this outcome. No rivals were in clinical studies, let alone poised to enter the market. The efficiencies defense would not apply because there was already an injectable treatment on the market. And the size of the firms would prevent the use of the Schumpeterian defense.

An ex post analysis confirms that the FTC correctly challenged the merger. There is currently a robust market for noninjectable migraine treatment, as four companies (Glaxo, Merck, Pfizer, and Zeneca) each possess at least 10% of the market.[236] Of particular significance, Wellcome's divestiture played a direct role in Zeneca's presence on the market today.

### *D. UPJOHN–PHARMACIA*

#### 1. Case Study

In February 1996, the FTC entered into a consent agreement with Upjohn and Pharmacia Aktiebolag ("Pharmacia").[237] The merging parties were researching topoisomerase I inhibitors, a class of chemotherapy drugs that inhibited the multiplication of cancer cells in the body.[238] In particular, the drugs targeted colorectal cancer, which had not previously responded well to chemotherapy.[239]

Solid cancerous tumors usually are removed through surgery and treated with radiation therapy and/or chemotherapy.[240] For colorectal

233. *See supra* notes 156–59 and accompanying text (discussing the relationship between innovation suppression and market concentration).

234. *See* Carl G.H. Dahlof, *Zolmitriptan Nasal Spray—An Important New Development in the Acute Treatment of Migraine, Business Briefing*, EUR. PHARMACOTHERAPY 80, 80 (2005) (noting that oral formulations accounted for more than ninety percent of sales of migraine treatment in 2003 and 2004).

235. *Migraine—FDA Approves New Formulation of Imitrex (Sumatriptan Succinate) Injection*, MED. NEWS TODAY, Feb. 6, 2006, *available at* http://www.medicalnewstoday.com/printerfiendlynews.php?newsid=37154.

236. *See supra* notes 229–30 and accompanying text.

237. In the Matter of Upjohn Co., et al., 121 F.T.C. 44, 47–48 (1996).

238. *Id.* at 45–46.

239. *Id.*

240. *Id.* at 45.

cancer, the treatment before the merger involved a combination of chemotherapy agent 5-fluorouracil ("5-FU") and leucovorin or levamisole.[241] Generic equivalents of 5-FU had been on the market since the 1980s.[242]

Topoisomerase I inhibitors were "expected to increase the rate of survival" of colorectal cancer patients.[243] The FTC anticipated that sales of topoisomerase I inhibitors for treatment of colorectal cancer would "exceed $100 million by 2002."[244]

At the time of the challenge, each of the merging parties was in clinical studies. Upjohn's product, CPT-11 ("Camptosar"), was "expected to be the first topoisomerase I inhibitor for the treatment of colorectal cancer on the market in the United States."[245] In particular, it was in Phase II/III studies.[246] Pharmacia's product, 9-aminocamptothecin ("9-AC"), was to be considered for FDA approval "within the next few years."[247] At the time, it was in Phase II.[248] As a condition of allowing the merger, the FTC required the companies to divest the R&D assets of 9-AC.[249]

Today, the market for colorectal cancer treatments has many competitors:

- Pfizer's Camptosar (approved by FDA in October 1998),
- Roche's Xeloda (May 2001),
- Sanofi-Synthelabo's Eloxatin (August 2002),
- Imclone and Bristol-Myers Squibb's Erbitux (February 2004),
- Genentech's Avastin (February 2004), and
- Amgen's Vectibix (September 2006).[250]

241. *Id.*

242. Carla Lazzareschi, *IPP Receives Federal OK to Sell Generic Form of Drug*, L.A. TIMES, Mar. 18, 1986, at 2.

243. *Upjohn Co.*, 121 F.T.C. at 45.

244. *Id.*

245. *Id.* at 46.

246. Pharmacia & Upjohn, Inc., Statement of Earnings (Form S-4/A), at 109 (Sept. 15, 1995) [hereinafter Pharmacia & Upjohn, Earnings Statement], *available at* http://www.sec.gov/Archives/edgar/data/949573/0000950123-95-002652.txt.

247. *Upjohn Co.*, 121 F.T.C. at 46.

248. Pharmacia & Upjohn, Earnings Statement, *supra* note 246, at 148.

249. *Upjohn Co.*, 121 F.T.C. at 50.

250. CenterWatch, Drugs Approved by the FDA: Camptosar, http://www.centerwatch.com/patient/drugs/dru499.html (last visited Oct. 2, 2007); CenterWatch, Drugs Approved by the FDA: Xeloda, http://www.centerwatch.com/patient/drugs/dru717.html (last visited Oct. 2, 2007); CenterWatch, Drugs Approved by the FDA: Eloxatin, http://www.centerwatch.com/patient/drugs/dru795.html (last visited Oct. 2, 2007); FDA, *New Treatments for Colorectal Cancer*, FDA CONSUMER MAG., May–June 2004, *available at* http://www.fda.gov/fdac/features/2004/304_cancer.html (Erbitux); CenterWatch, Drugs Approved by the FDA: Avastin, http://www.centerwatch.com/patient/drugs/dru851.html (last visited Oct. 2, 2007); CenterWatch, Drugs Approved by the FDA: Vectibix, http://www.centerwatch.com/patient/drugs/dru933.html (last visited Oct. 2, 2007).

Although exact market share figures are difficult to ascertain, it is clear that there are many competitors in the market for colorectal cancer treatment today.[251]

### 2. Application

The FTC correctly challenged the merger. Because Upjohn had a product in Phase II/III and Pharmacia was in Phase II, the agency could have demonstrated significant concentration among firms reasonably likely to reach the market. The theory of anticompetitive harm in the form of innovation suppression naturally follows from this conclusion on market concentration.[252]

Nor would the merging parties be able to offer defenses to reverse this outcome. No rivals were in clinical studies, let alone poised to enter the market. The efficiencies defense would not have applied because the conditions did not pose unique challenges. And the size of the firms would have prevented the use of the Schumpeterian defense.

Finally, an ex post analysis demonstrates that the market for topoimerase I inhibitors for colorectal cancer is competitive, with market participants Amgen, Genentech, Imclone/BMS, Pfizer, Roche, and Sanofi-Synthelabo.[253]

## *E. BAXTER–IMMUNO*

### 1. Case Study

In March 1997, the FTC challenged Baxter's acquisition of Immuno.[254] The agency alleged that the two companies were "two of only a small number of companies seeking FDA approval to market [f]ibrin [s]ealant in the United States."[255]

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251. There are several reasons for the difficulty in assessing market shares. First, drugs have different levels of effectiveness for various cancer stages. Second, patients often take several drugs together. For example, Camptosar is more effective when combined with 5-FU and leucovorin, as is Eloxatin. Am. Cancer Soc'y, Detailed Guide: Colon and Rectum Cancer: Chemotherapy, http://www.cancer.org/docroot/CRI/content/CRI_2_4_4x_Chemotherapy_10.asp?rnav=cri (last visited Oct. 17, 2007). Finally, the drugs treat colorectal cancer in different ways. Xeloda is an oral version of 5-FU that is preferred by the many patients who wish not to take 5-FU intravenously. *Id.* Erbitux is a targeted therapy that "attacks the epidermal growth factor receptor (EGFR), which often appears in high amounts on the surface of cancer cells." *Id.* And Avastin is "directed against vascular endothelial growth factor (VEGF), a protein that helps tumors form new blood vessels to get nutrients." *Id.*

252. *See supra* text following note 155 (demonstrating the connection between market concentration and incentives and ability to suppress research paths).

253. *See supra* note 250 and accompanying text.

254. *See generally* In the Matter of Baxter Int'l Inc., 123 F.T.C. 904 (1997).

255. *Id.* at 906.

Fibrin sealant is "extracted from human plasma" and "used in surgical procedures to arrest bleeding and as an adjunct to wound healing."[256] At the time of the Baxter–Immuno merger, the products were used in Europe and Japan for these purposes.[257] In the United States, there were no commercial fibrin sealant products. Surgeons had prepared homemade fibrin sealants, but these products were not "standardized or consistent" and were "virally inactivated."[258]

At the time of the merger, Baxter's Sealagen was in Phase II/III.[259] Immuno's Tisseel appeared to be in either Phase II or Phase III.[260] A third company, Vitex, had completed Phase II studies and was about to commence Phase III.[261] The FTC required Baxter to grant a nonexclusive, royalty-free license of Immuno's Tisseel to an approved licensee.[262]

The FDA approved Tisseel in May 1998.[263] One month later, Baxter marketed the product as Tisseel, and Haemacure (the licensee) marketed the identical product as Hemaseel.[264] Other fibrin sealants on the market today are manufactured by Aventis and Omrix.[265] Exact figures are difficult

256. Haemacure Corp., 2000 Annual Information Form (Form 6-K), at 1 (Apr. 12, 2001), *available at* http://sec.edgar-online.com/2001/04/18/0000897069-01-500079/Section4.asp.

257. Press Release, Fed. Trade Comm'n, FTC Decision in Baxter/Immuno Acquisition to Preserve Competition in Two Markets for Plasma Products Ensuring Lower Prices for Consumers and Continued Research and Development (Dec. 19, 1996), *available at* http://www.ftc.gov/opa/1996/12/baxter.htm.

258. U.S. Food & Drug Admin., *FDA Talk Paper: New Fibrin Sealant Approved to Help Control Bleeding in Surgery*, May 1, 1998, http://www.fda.gov/bbs/topics/ANSWERS/ANS00865.html.

259. BAXTER INT'L, ANNUAL REPORT 4 (1996), *available at* http://www.baxter.com/about_baxter/investor_information/annual_report/1996/bax96ar_t.pdf.

260. Although the stage is not clearly documented, the strongest available evidence comes from a meeting of the Blood Products Advisory Committee of the Center for Biologics Evaluation and Research, which approves biologic products. The minutes of one meeting describe the results of three clinical trials, each with more than 100 participants, and conclude that "[t]he sum of these studies is that the efficacy of . . . [Tisseel] has been demonstrated as a topical hemostatic agent, as an aid to surgeries involving the pancreas and as a tissue sealant in colostomy patients." U.S. Food & Drug Admin., Ctr. for Biologic Evaluation and Research, Blood Prods. Advisory Comm., 57th Meeting, Dec. 11, 1997, at 23, *available at* http://www.fda.gov/ohrms/dockets/ac/97/transcpt/3361t1.pdf. Further bolstering the conclusion that the product was in advanced clinical studies, the minutes reveal that there were only two steps remaining for approval: product labeling and "corrective actions that [were] . . . fairly straightforward" to comply with "Good Manufacturing Practices." *Id.* at 23–24.

261. V I Techs., Annual Report (Form 10-K), Ex. 10.20 at 3 (Mar. 31, 2000), *available at* http://sec.edgar-online.com/2000/03/31/16/0000927016-00-001138/Section29.asp.

262. In the Matter of Baxter Int'l Inc., 123 F.T.C. 904, 920–21 (Mar. 24, 1997). Baxter retained exclusive rights to Tisseel outside the United States. *Baxter's Fibrin Sealant Ready*, MED. MATERIALS UPDATE, May 1, 1998, *available at* 1998 WLNR 3599648.

263. Haemacure Corp., Annual Report (Form 20-F), at 24 (Dec. 12, 2001), *available at* http://sec.edgar-online.com/2001/12/12/0000897069-01-500639/Section5.asp.

264. *Id.*

265. D. Paul Cohen, *Dirty Dozen Research: No Agenda*, at 29 (Oct. 12, 2001), *available at* http://www.cohenresearch.com/reports/kool_10-12-01.pdf.

to ascertain, but Baxter appears to be the market leader, holding a "large share" of the market.[266]

### 2. Application

The FTC correctly challenged the merger. Because Baxter had a product in Phase II/III and Immuno was in Phase II, the agency could have demonstrated significant concentration among firms reasonably likely to reach the market. Although there is modestly less concern because the merging firms were not quite in the final stages of review, that is not enough to prevent the conclusion of a significantly concentrated market. And a theory of innovation suppression, though slightly less persuasive because neither firm was in Phase III, would have followed from the showing of market concentration.

At the time of the merger, another firm, Vitex, was in Phase II. While this provides some solace, it does not rise to the level of likely entry by another firm. Nor would the efficiencies and Schumpeterian defenses have applied.

Finally, the suitability of the FTC's licensing requirement is borne out by a robust market that includes not only market leader Baxter and competitors Aventis and Omrix, but also Haemacure, the licensee that received Baxter's product.[267]

## *F. CIBA-GEIGY–SANDOZ*

### 1. Case Study

In March 1997, the FTC entered into a consent decree with Ciba-Geigy and Sandoz.[268] The companies were "two of only a few entities capable of commercially developing gene therapy products."[269] In particular, they were the only ones that "control[led] the substantial proprietary rights necessary to commercialize gene therapy products."[270]

Gene therapy "enables the patient's own body to produce a desired protein by inserting the gene for that protein into the patient's cells."[271] The

266. *U.S. Tissue Sealants Are Set to Boom*, BIOMEDICAL MATERIALS, May 1, 2002, *available at* 2002 WLNR 4969980. In 1999, Baxter had approximately 75% of fibrin sealant sales and Haemacure had 25%. HAEMACURE, ANNUAL INFORMATION FORM 3–4 (1999), *available at* http://www.haemacure.com/rtecontent/document/Rap99A.pdf (noting that Haemacure was "one of only two approved marketers of fibrin sealant" and that it had "captured . . . approximately a 25% share of the . . . market").

267. *See supra* note 265 and accompanying text.

268. In the Matter of Ciba-Geigy Ltd., 123 F.T.C. 842, 842 (1997).

269. *Id.* at 846.

270. *Id.*

271. Chiron Corp., Annual Report (Form 10-K), at 5 (Mar. 30, 1998), *available at* http://www.sec.gov/Archives/edgar/data/706539/0001047469-98-012226.txt.

agencies alleged harm not only to a general market for gene therapy, but also to four specific markets, which covered "(a) [h]erpes simplex virus-thymidine kinase ("HSV-tk") gene therapy for the treatment of cancer; (b) HSV-tk gene therapy for the treatment of graft versus host disease; (c) [g]ene therapy for the treatment of hemophilia; and (d) [c]hemoresistance gene therapy."[272]

At the time of the merger, Sandoz had acquired Genetic Therapy Inc., which was conducting research on HSV-tk gene therapy in Phase II/III trials.[273] Ciba-Geigy had a 49.9% stake in Chiron; Chiron's subsidiary, Viagen, was in preclinical development.[274] A third company, Systemix, had received FDA approval to begin Phase I/II trials of a gene therapy protocol for the treatment of HIV.[275]

In the specific markets for HSV-tk and hemophilia gene therapy products, the FTC required the merging companies to grant a nonexclusive license to Rhone-Poulenc Rorer.[276] In the general market for gene therapy, the FTC required the parties to license at a low royalty rate the important Anderson ex vivo patent, which "cover[ed] the entire category of gene therapy treatment involving cell modification that takes place outside the body."[277]

Today, there is no approved human gene therapy product offered in the United States.[278] Difficulties that confront gene therapy include the "[s]hort-lived nature of gene therapy," difficulties triggered by the immune system's response to a foreign object, problems with the viruses that carry the genes, and multigene disorders.[279] And there have been many setbacks,

272. *Ciba-Geigy*, 123 F.T.C. at 844–45.

273. Eleanor J. Morgan, *Innovation and Merger Decisions in the Pharmaceutical Industry*, 19 REV. INDUS. ORG. 181, 187 (2001); *see also* Commission Regulation 4064/89, Case No. IV/M.737 (Ciba-Geigy v. Sandoz), 1997 O.J. (L 201) 1, 8 (EC) [hereinafter ECCR Ciba-Geigy v. Sandoz], *available at* http://eur-lex.europa.eu/LexUriServ/LexUriserv.do?uri=CELEX:31997D0469:EN:HTML.

274. ECCR Ciba-Geigy v. Sandoz, *supra* note 273, at 16; *see also Ciba-Geigy*, 123 F.T.C. at 843–44; *Id.* at 846–47 (stating that each of the products is "either in clinical development or near clinical development" for several of the markets); *supra* note 211.

275. *HIV Rev M10: Gene Therapy from SyStemix Enters Trials*, ANTIVIRAL AGENTS BULL., Dec. 1, 1996, *available at* 1996 WLNT 4230764.

276. *Ciba-Geigy*, 123 F.T.C. at 873–77.

277. Press Release, Fed. Trade Comm'n, FTC Accord in Ciba Geiby/Sandoz Merger to Prevent Slowdown in Gene Therapy Development & Preserve Competition in Corn Herbicides, Flea-Control Markets (Dec. 17, 1996), *available at* http://www.ftc.gov/opa/1996/12/ciba.htm.

278. In 2003, China's State Food and Drug Administration approved gene therapy medication Gendicine for the treatment of head and neck squamous cell carcinoma. *The Genesis of Gendicine: The Story Behind the First Gene Therapy*, BIOPHARM INT'L, May 2004, at 42, 43.

279. *Id.*

such as the death in 1999 of an eighteen-year-old who was participating in a gene-therapy trial.[280]

### 2. Application

Application of my test shows that the FTC should not have challenged the merger. The agency would not have been able to demonstrate the first step of a concentrated market. Even though Sandoz was in Phase II/III, Ciba-Geigy was in preclinical development.

And despite the compulsory licensing ordered in the merger, there still is no effective gene therapy treatment on the U.S. market today. Of course, the difficulties of gene therapy treatment prevent a confident assertion that there would have been success absent a merger challenge. But these very difficulties point to an efficiency defense that the parties could have offered.[281] In any event, the challenge did not prevent anticompetitive harm or lead to market success.[282]

## *G. PFIZER–WARNER-LAMBERT*

### 1. Case Study

In June 2000, the FTC entered into a consent agreement with Pfizer and Warner-Lambert. The companies were developing "Epidermal Growth Factor receptor tyrosine kinase [EGFR] inhibitors for the treatment of solid cancerous tumors."[283] Such tumors generally include "head and neck, non-small-cell lung, breast, ovarian, pancreatic and colorectal cancers."[284] EGFR inhibitors "target the EGFR oncogene that regulates cancer cell growth" and seek to inhibit the "cell division signal transduction that results in cancer cell proliferation."[285]

The FTC alleged that Pfizer and Warner-Lambert "produce[d] two of the most advanced EGFr-tk inhibitors currently being developed, and are

280. Oak Ridge Nat'l Laboratory, Human Genome Project Information*:* Gene Therapy, http://www.ornl.gov/sci/techresources/Human_Genome/medicine/genetherapy.shtml#status (last visited Oct. 2, 2007).

281. *See supra* note 272 and accompanying text.

282. One can question whether the merger between Ciba-Geigy and Sandoz even was a true innovation-markets case. Because Ciba-Geigy lacked an alternative gene therapy technology, there was no anticompetitive overlap with Sandoz. Mary Azcuenaga, Commissioner, Fed. Trade Comm'n, Remarks Before the American Law Institute and the American Bar Association, Antitrust and Intellectual Property: Recent Highlights and Uncertainties (Apr. 24, 1997), *available at* http://www.ftc.gov/speeches/azcuenaga/aliaba97.htm#N_21. Rather, the concern seemed simply to be the breadth of the Sandoz patent. *Id.*

283. Analysis of Proposed Consent Order to Aid Public Comment, Pfizer Inc., and Warner-Lambert Company, File No. 001 0059 (Fed. Trade Comm'n, June 19, 2000), *available at* http://www.ftc.gov/os/2000/06/pfizeranalysis.htm.

284. *Id.*

285. *Id.*

among a relatively small number of companies working on these types of drugs."[286] The agency claimed that, as a result of the merger, "Pfizer could delay or simply fail to develop one of the two competing drugs, leading to less product innovation, fewer consumer choices and higher prices in the marketplace."[287]

At the time of the merger, there were four companies with EGFR inhibitors in clinical studies. Pfizer's CP-358,774 compound was in Phase II trials.[288] Warner-Lambert's CI-1033 was in Phase I.[289] And AstraZeneca and Imclone each had products in Phase III.[290] The consent order required Pfizer to divest its EGFR inhibitor to its development partner OSI.[291]

Today, there are three firms on the market with an EGFR inhibitor.[292] The FDA approved Imclone's Erbitux in February 2004 for colorectal cancer and in March 2006 for cancer of the head and neck.[293] OSI's Tarceva was approved in November 2004 for advanced non-small cell lung cancer[294] and in November 2005 for certain types of pancreatic cancer.[295] And the FDA approved Amgen's Vectibix in September 2006 for colorectal cancer.[296]

286. Press Release, Fed. Trade Comm'n, FTC Order Clears Way for $90 Billion Merger of Pfizer Inc. and Warner-Lambert Company (June 19, 2000), *available at* http://www.ftc.gov/opa/2000/06/pfizer.htm.

287. *Id.*

288. OSI Pharms., Inc., Current Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 (Form 8-K), at 2 (June 19, 2000), *available at* http://www.sec.gov/Archives/edgar/data/729922/000095012300005877/0000950123-00-005877-0001.txt.

289. *See id.* (stating that a Warner-Lambert EGFR inhibitor is "currently in early Phase I studies").

290. *Id.* at 3.

291. *See id.* at 2 (stating that Pfizer "agreed to grant all development . . . rights to OSI . . . for CP-358,774" to meet FTC requirements for its merger with Warner-Lambert).

292. A fourth product, AstraZeneca's Iressa, came to the market in May 2003 but was pulled in December 2004 after a post-marketing clinical study failed to show a survival benefit. *Cf.* Press Release, U.S. Food and Drug Admin., FDA Statement on Iressa (Dec. 17, 2004), *available at* http://www.fda.gov/bbs/topics/news/2004/new01145.html (stating that the FDA would determine whether to withdraw Iressa from the market after evaluating recent study results indicating Iressa's ineffectiveness).

293. Press Release, U.S. Food and Drug Admin., FDA Approves Erbitux for Colorectal Cancer (Feb. 12, 2004), *available at* http://www.fda.gov/bbs/topics/news/2004/new01024.html; Press Release, U.S. Food and Drug Admin., FDA Approves First Head & Neck Cancer Treatment in 45 Years Data Shows Treatment with Erbitux Extends Survival (Mar. 1, 2006), *available at* http://www.fda.gov/bbs/topics/news/2006/new01329.html.

294. Press Release, U.S. Food & Drug Admin., FDA Approves New Drug for the Most Common Type of Lung Cancer (Nov. 19, 2004), *available at* http://www.fda.gov/bbs/topics/news/2004/NEW01139.html.

295. Press Release, Genentech, FDA Approves Tarceva in Combination with Gemcitabine Chemotherapy for Treatment of Locally Advanced, Inoperable or Metastatic Pancreatic Cancer (Nov. 2, 2005), *available at* http://www.gene.com/gene/news/press-releases/display.do?method=detail&id=9067.

296. CenterWatch, Drugs Approved by the FDA: Vectibix, http://www.centerwatch.com/patient/drugs/dru933.html (last visited Oct. 17, 2007).

### 2. Application

The FTC should not have challenged the merger, which did not threaten significant concentration among firms reasonably likely to reach the market. Neither of the merging firms had reached the final stage of FDA review: Pfizer was in Phase II and Warner-Lambert was in Phase I. Even if the market likelihood percentages are adjusted upward to take into account the higher success rates of anti-cancer treatments, they still only demonstrate 48% and 42% likelihood, respectively.[297] While Pfizer's development partner eventually was able to bring the divested product to market, the merged company did not encounter such success with Warner-Lambert's Phase I product.[298]

In addition, the merging firms could have offered a powerful defense based on likely entry by competitors. Two firms, Astra-Zeneca and Imclone, each were in Phase III, making it very likely that at least one of the firms would reach the market and offer competition. In fact, both products did reach the market. Although Astra-Zeneca's Iressa was pulled from the market after a disappointing clinical trial, Imclone's Erbitux is still on the market.[299]

## *H. GLAXO WELLCOME–SMITHKLINEBEECHAM*

### 1. Case Study

In December 2000, the FTC entered into an agreement with merging parties Glaxo Wellcome ("Glaxo") and SmithKline Beecham ("SKB").[300] The companies were the most advanced in the effort to develop a prophylactic

297. Without such adjustment, the figures would be thirty and eighteen percent. *See supra* note 143 and accompanying text (noting that "anti-cancer . . . drugs . . . are more likely to reach the market").

298. *See supra* notes 292–96 and accompanying text (listing the EGFR inhibitors that are on the market today).

299. *See supra* note 292–93 and accompanying text; *see also* Erbitux, http://www.erbitux.com/erbitux/erb/home/index.jsp?BV_UseBVCookie=Yes (last visited Nov. 8, 2007). The challenge also was plagued by a questionable market definition, as the relevant market appeared to cover patients' conditions, not drug delivery mechanisms. The FTC defined a market even though EGFR inhibitors targeted different cancers and worked in different ways. If the agency had defined the market according to the type of condition being treated, there likely would have been no challenge. For example, colorectal cancer could be treated through not only EGFR inhibitors but also other types of similarly effective treatment, which today are offered by Amgen, Genentech/Roche, Imclone/BMS, and others. *Market Report, Cancer Market: Overview, Strong Sales Growth Drives the Market*, PHARMACTIVES, Jul. 8, 2006 http://www.pharmactives.com/article.cfm?ref=577.

300. Decision and Order, Glaxo Wellcome PLC & SmithKline Beecham PLC, No. C-3990, (F.T.C. Dec. 15, 2000), *available at* 2000 WL 1860065.

herpes vaccine.[301] Genital herpes is a sexually transmitted disease characterized by lesions and chronic, lifelong infection.[302]

At the time of the merger, SKB was in Phase III,[303] and Glaxo, in conjunction with partner Cantab Pharmaceuticals, was in Phase II.[304] As a condition of the merger, Glaxo divested to Cantab "all rights and information and results from clinical trials that are necessary for Cantab to develop a prophylactic herpes vaccine."[305]

Today, there is no prophylactic herpes vaccine on the market. In 2002, Cantab's vaccine failed a Phase II trial, and Wyeth discontinued a vaccine in Phase I.[306] GlaxoSmithKline's Simplirix vaccine, which is in Phase III, currently is the closest to the market.[307]

Although there are no prophylactic herpes vaccines, there are suppressive herpes drugs that treat the disease. One year before the merger, Glaxo Wellcome's Valtrex had approximately a 30% market share, while SmithKline Beecham's Famvir had approximately 17%.[308] As a condition of the merger, the FTC required Glaxo and SKB to divest Famvir.[309] Today, GlaxoSmithKline's Valtrex is the market leader,[310] and other market participants include the company's Zovirax and Novartis's Famvir.[311]

### 2. Application

The FTC correctly challenged this merger. It could demonstrate significant concentration among firms reasonably likely to reach the market since SKB was in Phase III and Glaxo was in Phase II.

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301. Complaint ¶ 22, Glaxo Wellcome PLC & SmithKline Beecham PLC, No. C-3990, (F.T.C. Dec. 15, 2000), *available at* 2000 WL 1860065.

302. L.R. Stanberry, *Control of STDs—The Role of Prophylactic Vaccines Against Herpes Simplex Virus*, 74 SEXUALLY TRANSMITTED INFECTIONS 391, 391 (1998).

303. *SmithKline Beecham's Pharmaceutical Pipeline*, PHARMABUS., Nov. 1, 1998, at 210, *available at* 1998 WLNR 5260829.

304. Complaint, *supra* note 301, ¶ 22; *Cantab Phase II Trials*, EUR. CHEMICAL NEWS, Nov. 22, 1999, at 42, *available at* 1999 WLNR 306136; *Therapeutic HSV-2 Vaccine Abandoned*, ANTIVIRAL AGENTS BULL., Feb. 1, 2002, *available at* 2002 WLNR 9153655.

305. Analysis of Proposed Consent Order to Aid Public Comment, Glaxo Wellcome PLC & SmithKline Beecham PLC, No. C-3990, (F.T.C. Dec. 15, 2000), *available at* 2000 WL 1860065.

306. *Therapeutic HSV-2 Vaccine Abandoned*, *supra* note 304 (Cantab); *Vaccine, Gene-Based, Herpes Simplex Virus Wyeth Discontinued*, R&D FOCUS DRUG NEWS, Feb. 7, 2005, *available at* 2005 WLNR 22405913 (Wyeth).

307. *Prophylactic Vaccines for Selected Infectious Diseases*, 40 FORMULARY 356, 356 (2005).

308. *GW Highlights Current Status of Its Antiviral Portfolio*, PHARMACEUTICAL COMPANIES ANALYSIS NEWS, Apr. 30, 1999, *available at* 1999 WLNR 262936 (providing figures for March 1999).

309. Order at Part III.A, Glaxo Wellcome PLC & SmithKline Beecham PLC, No. C-3990, (F.T.C. Dec. 15, 2000), *available at* 2000 WL 1860065.

310. Gillian Law, *Generic Brands and Weak Dollar Hit GSK*, EVENING NEWS, July 28, 2004, at 2 ("Valtrex has been consistently increasing its market share and remains the market leader.").

311. Herpes-Coldsores.com, Herpes Treatment, http://www.herpes-coldsores.com/herpes_treatment.htm (last visited Oct. 2, 2007).

The theory of anticompetitive harm in the form of innovation suppression naturally follows from this conclusion on market concentration.[312] And it is bolstered by Glaxo's Valtrex, which had a monopoly in pre-merger suppressive herpes treatment.

In comparison to Valtrex, the vaccine offered elements of both drastic and nondrastic innovation. The innovation would be drastic for patients who do not have herpes and thus would not need suppressive treatment. But it would be nondrastic for patients who already have herpes because it would be too late for a vaccine and the patients would still need suppressive treatment. The factor therefore demonstrates moderate cannibalization concerns, buttressing concerns of anticompetitive harm.

Nor would the defenses have reversed this outcome. No rivals were in clinical studies, let alone poised to enter the market. And the size of the firms would have prevented the use of the Schumpeterian defense.

Under my test, the parties could offer an efficiency defense based on the difficulty of developing vaccines, which is confirmed by the absence of a herpes vaccine on the market today. But this efficiency would not outweigh the concentration demonstrated by one firm in Phase II and the other in Phase III.

## *I. GENZYME–NOVAZYME*

### 1. Case Study

Genzyme acquired Novazyme in September 2001.[313] At the time of the merger, both companies were engaged in preclinical studies to develop a treatment for Pompe disease, a rare and fatal genetic disorder affecting infants and children.[314] Because there are few patients with the disease, therapies fall under the Orphan Drug Act, which provides seven years of market exclusivity to the first therapy to receive FDA approval.[315]

The FTC began to investigate the matter shortly after the merger was completed.[316] In January 2004, it voted 3–1–1 not to challenge the merger. There were three separate statements. Chairman Muris emphasized that

312. *See supra* text following note 150 (describing the theory of "unilateral competitive effects" and resulting competitive harm).

313. Muris Statement, *supra* note 2, at 1 n.1.

314. *Id.* at 6 n.14; Press Release, Fed. Trade Comm'n, FTC Closes Its Investigation of Genzyme Corporation's 2001 Acquisition of Novazyme Pharmaceuticals, Inc. (Jan. 13, 2004), *available at* http://ftc.gov/opa/2004/01/genzyme.htm.

315. Press Release, Fed. Trade Comm'n, *supra* note 314.

316. Muris Statement, *supra* note 2, at 1 n.1. The firms fell below the threshold for notifying the agencies of the merger because Novazyme had less than $10 million in assets. George Chester, *All You Need To Know About the FTC's Recent Genzyme/Novazyme Decision in Under 10 Minutes*, Mar. 5, 2004, at 1, *available at* http://www.cov.com/Publications (follow "Author" drop-down menu to "Chester Jr., George M."; then follow "Go" hyperlink; then follow title hyperlink).

"because there is currently no treatment for Pompe disease, the most important goal for patients is to get one effective treatment for Pompe disease on the market as soon as possible."[317] He also warned that "[t]he adoption of presumptions without economic foundation would constitute a major step backward in antitrust law."[318] Commissioner Thompson, in contrast, worried about the "consummated merger to monopoly in the research and development of a highly specialized drug," the dangers of which were exacerbated because "entry of a new market participant [wa]s not likely to replace the innovation competition eliminated by the merger."[319] Commissioner Harbour abstained because she had joined the FTC in its final stages of review, but emphasized the importance of innovation competition in the pharmaceutical industry.[320]

At the time of the merger in 2001, and even at the time of the decision to close the investigation in 2004, there was no treatment for Pompe disease.[321] Novazyme, which had been in preclinical studies at the time of the merger, was still in that stage in January 2004.[322] Genzyme, which was in preclinical testing at the time of the merger, had reached Phase II/III clinical trials by 2004.[323] Genzyme had previously acquired two other companies researching the disease, but those products had both been abandoned by 2002.[324]

In April 2006, the FDA approved Genzyme's Myozyme, the first treatment for Pompe Disease.[325]

### 2. Application

The FTC correctly decided not to challenge the merger. This result is consistent with my analysis: even though Genzyme was in Phase II/III, Novazyme was only in preclinical studies. Because of the staggering odds that a firm in preclinical studies will reach the market, I would not include

317. Muris Statement, *supra* note 2, at 18.

318. *Id.* at 25.

319. Thompson Statement, *supra* note 3, at 1.

320. Statement of Commissioner Pamela Jones Harbour, Genzyme Corporation's Acquisition of Novazyme Pharmaceuticals Inc. 2–3 (Jan. 14, 2004), *available at* http://www.ftc.gov/os/2004/01/harbourgenzymestmt.pdf.

321. Muris Statement, *supra* note 2, at 18.

322. *Id.* at 8–9.

323. *Id.* at 9–10.

324. The Pharming product had been abandoned by the time of the merger, and the Synpac program was suspended in early 2002 because "manufacturing problems were preventing production on a scale sufficient for commercialization." *Id.* at 9.

325. Press Release, U.S. Food and Drug Admin., FDA Approves First Treatment for Pompe Disease (Apr. 28, 2006), *available at* http://www.fda.gov/bbs/topics/NEWS/2006/NEW01365.html. Amicus Therapeutics currently has a compound, AT2220, in Phase I trials for the treatment of the disease. Amicus Therapeutics, AT2220 for Pompe Disease, http://amicustherapeutics.com/pipeline/at2220.asp (last visited Oct. 2, 2007).

such firms in determining market concentration. The agency's refusal to challenge the merger thus is consistent with my conclusion that there was no significant concentration among firms reasonably likely to reach the market.

The merging firms also could have offered a strong efficiency defense under my test. The parties offered merger-specific benefits that made it more likely that one firm would reach the market (and reach it faster). This was particularly important because there was no treatment for a fatal disease, one that, as a type of lysosomal storage disorder ("LSD"), presented exceedingly difficult challenges.[326]

Additionally, the firms could offer a Schumpeterian defense. Novazyme was "a small research company" with "approximately 80 employees," "no sales revenue,"[327] and "less than $10 million in total assets."[328] It "had no products in clinical trials, and no clinical-scale or commercial-scale manufacturing facilities."[329] The merger was necessary for Novazyme to survive the regulatory process.

Finally, an ex post analysis of the market shows that the lack of merger challenge did not prevent Genzyme's Myozyme from reaching the market in 2006.[330]

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The chart below synthesizes these cases.

326. *See supra* notes 176-81 and accompanying text.

327. Muris Statement, *supra* note 2, at 8.

328. *See* Chester, *supra* note 316, at 1.

329. Wald & Feinstein, *supra* note 179, at 2.

330. *See supra* note 325 and accompanying text.

| | Date of Challenge | Product | Pre-merger Treatment | Stage of Review | Other Parties | Current Market |
|---|---|---|---|---|---|---|
| Genzyme – Novazyme | Jan. 2004 *(No challenge)* | Pompe disease | None | Novazyme: preclinical<br>Genzyme: II/III | No | Genzyme (approved Apr. 2006) |
| Glaxo Wellcome – Smith Kline Beecham | Dec. 2000 | Prophylactic herpes vaccine | Glaxo's suppressive herpes drug | GW: II<br>SKB: III | No | No vaccine<br>Suppressive treatment (GSK) & Novartis) |
| Pfizer – Warner-Lambert | June 2000 | EGFR inhibitors for solid cancerous | No EGFR inhibitors | Pfizer: II<br>WL: I | Astra Zeneca: III<br>Imclone: III | Imclone, OSI, Amgen |
| Ciba-Geigy – Sandoz | Mar. 1997 | Gene therapy | None | CG: preclinical<br>Sandoz: II/III | Systemix: I/II | None |
| Baxter – Immuno | Mar. 1997 | Fibrin sealants | Homemade fibrin sealants | Baxter: II/III<br>Immuno: II or III | Vitex: II | Baxter market leader |
| Upjohn – Pharmacia | Feb. 1996 | Topoisomerase I inhibitors for colorectal cancer | Chemotherapy combination | Upjohn: II/III<br>Pharmacia: II | No | Amgen, Genentech, Imclone/BMS, Pfizer, Roche, Sanofi-Synthelabo |
| Glaxo – Wellcome | June 1995 | Noninjectable migraine treatment | Glaxo's injectable Imitrex | Glaxo: II/III<br>Wellcome: III | No | Glaxo 56%<br>Merck >10%<br>Pfizer >10%<br>Zeneca >10% |
| AHP – American Cyanamid | Nov. 1994 | Rotavirus vaccine | None | AHP: II/III<br>Cyanamid: preclinical | Virus Research Institute: preclinical | Merck (approved Feb. 2006) |
| Roche – Genentech | Nov. 1990 | CD4-based drugs for HIV/AIDS | None | Genentech: I<br>Roche: preclinical | Biogen: I/II | No CD4-based drugs (Related Roche drug) (approved Mar. 2003) |

Challenges to mergers in pharmaceutical innovation markets are most effective when the merging firms are the only companies in advanced clinical trials. This was the case in four of the FTC's challenges to mergers: (1) Glaxo and Wellcome, (2) Upjohn and Pharmacia, (3) GlaxoWellcome and SmithKline Beecham, and (4) Baxter and Immuno. In a fifth correct decision, the FTC decided not to challenge the merger between Genzyme and Novazyme.

But the lack of an analysis similar to the Merger Guidelines and the neglect of the stage of FDA review led to unnecessary (and even counterproductive) challenges in four of the nine mergers: (1) Roche and Genentech, (2) AHP and Cyanamid, (3) Ciba-Geigy and Sandoz, and (4) Pfizer and Warner-Lambert. By fleshing out the FTC's current ad hoc analysis, my test promises to increase confidence in a justifiable and beneficial innovation-markets framework.

## CONCLUSION

The concept of innovation markets has been much maligned. This Article has shown that, for pharmaceutical mergers, the characteristics of the industry rebut most of the criticisms. It also offers a partial resolution of the longstanding debate between Schumpeter and Arrow about the market structure most conducive to innovation. An analysis of product innovation, technological opportunity, and appropriability demonstrates the importance of size and (especially) competition in the industry. And the showing of competition's significance confirms the propriety of enforcement in pharmaceutical innovation markets.

On a practical level, the Article offers the first comprehensive framework that can be applied to innovation-market analysis. The framework improves the current analysis by considering not only the number of firms in R&D, but also the stage of FDA review. Given the significant hurdles facing firms in pharmaceutical development and the wildly varying odds of success at each of the stages, it no longer is appropriate to neglect this factor. Firms in preclinical development should not be considered part of the relevant market, and the most imminent harm is presented by merging firms in Phase III. The new test also creates new defenses based on entry, efficiencies, and lack of size.

Finally, the Article offers the first empirical analysis of all the challenged innovation-market cases in the pharmaceutical industry. It ventures far beyond the FTC allegations that, until now, have constituted the record upon which discussion has taken place. And it concludes that the FTC was only correct in approximately half of the challenged cases.

Applying the economic studies to the pharmaceutical industry demonstrates the important role to be played by innovation markets. But these markets need a better framework. The test I offer in this Article is

more comprehensive, predictable, and rooted in industry realities. In short, it is a more powerful foundation for innovation-markets analysis.