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## ANTICOMPETITIVE PRODUCT CHANGES IN THE PHARMACEUTICAL INDUSTRY

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When faced with a competitive threat from generic drugs, some manufacturers of brand-name pharmaceuticals have used a variety of anticompetitive tactics to maintain their sales. These techniques include settling patent challenges by paying generic manufacturers not to enter,<sup>1</sup> filing questionable patent infringement lawsuits<sup>2</sup> and frivolous “citizen’s

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1. See, e.g., *In re Ciprofloxacin Hydrochloride Antitrust Litig.* 604 F.3d 98, 102 (2d Cir. 2010); *Valley Drug Co. v. Geneva Pharm., Inc.*, 344 F.3d 1294, 1300–01 (11th Cir. 2003); *In re Cardizem CD Antitrust Litig.*, 332 F.3d 896, 902–03 (6th Cir. 2003).

2. See, e.g., *In re Neurontin Antitrust Litig.*, 2009 WL 2751029, at \*3–4 (D.N.J. Aug. 28, 2009); *In re Relafen Antitrust Litig.*, 218 F.R.D. 337, 341 (D. Mass. 2003).

petitions,”<sup>3</sup> making dubious “Orange Book” listings,<sup>4</sup> and controlling the supply of necessary ingredients.<sup>5</sup> These investments in impairing generic entry increase the returns from brand-name drugs but do not necessarily improve medicines for consumers.

Brand manufacturers also sometimes strategically redesign the brand product in anticipation of generic entry. Under the current regulatory regime, such a product reformulation prevents the generic product from being substitutable at the pharmacy counter for the redesigned brand product, and thus impairs the generic’s most cost-efficient (and only commercially feasible) means of competing. Regardless of whether the reformulated product brings any medical or other benefits to consumers—indeed, even if the reformulated product is undeniably inferior to the original brand product—the brand manufacturer’s reformulation can significantly impair consumers’ access to the far less expensive generic product.

This is the first of two articles in which we intend to address the proper antitrust treatment of pharmaceutical product reformulations that impede generic substitution. We begin this article by outlining the legal and regulatory context in which product reformulations occur, emphasizing the structural aspects of the pharmaceutical marketplace that make reformulations an effective strategy for brand manufacturers. Fundamentally, prescription pharmaceutical markets suffer from a “price disconnect”; the doctor who prescribes the product does not pay for it, and the consumer (or her insurer) who does pay does not choose the product. Thus, these markets are not founded on the consumer’s price/quality choice that, in most markets, ensures that manufacturers make only those product changes that are likely to enhance consumer welfare.

We next discuss a comprehensive database that we have assembled, which includes more than four hundred prescription pharmaceutical reformulations from 1995 through April 2009. Analysis of this data suggests that the vast majority of reformulations are not temporally linked to potential generic entry and thus are not reasonably subject to antitrust challenge. A well-crafted antitrust rule would be directed at only the subset of reformulations that are temporally linked to potential generic entry, and thus

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3. See, e.g., Gregory Glass & Erin Collins, *The Citizens Petition: For The Public Good Or Brands Behaving Badly?*, 4 J. OF GENERIC MEDICINES 87 (Jan. 2007).

4. See, e.g., *In re Neurontin Antitrust Litig.*, 2009 WL 2751029, at \*1–2; *In re Relafen Antitrust Litig.*, 218 F.R.D. at 340–41; *In re Bupirone Antitrust Litig.*, 208 F.R.D. 516, 518–20 (S.D.N.Y. 2002).

5. See, e.g., *Eli Lilly & Co. v. Am. Cyanamid Co.*, No. IP95-0536, 2001 WL 30191, at \*2–3 (S.D. Ind. Jan. 8, 2001).

would not chill the innovation that leads to the great majority of pharmaceutical reformulations.

This latter subset of reformulations in our database—those that are temporally linked to prospective generic entry—includes thirty-two that are clearly “suspect,” e.g., minor reformulations such as changes from a capsule to a tablet or vice versa; changes in chemical structure that, according to independent researchers, yielded little or no consumer value; and multiple, seriatim product reformulations. We conservatively estimate that these reformulations have impaired competition against brand products with more than \$28.1 billion in annual sales, indicating that this isolated set of product reformulations poses a significant public policy concern.<sup>6</sup> Another twenty-two reformulations involved switches to extended-release products or “combination” products in advance of generic entry for brand products with an additional \$15.8 billion in annual sales.<sup>7</sup>

After discussing the dataset, we then analyze the details of various tactics that manufacturers use in implementing reformulation strategies. In addition to physically altering the product, manufacturers often also: (1) switch promotional efforts from the original product to the reformulated product; (2) introduce the redesigned product before generic entry; or (3) withdraw the original product from the market. We examine the economic effect of each tactic, with special emphasis on identifying the particular dimension of rivalry—price competition or quality comparisons—that is affected.

Lastly, we examine two recent court decisions, involving the products TriCor<sup>8</sup> and Nexium,<sup>9</sup> that have addressed these issues, and we evaluate the extent to which the decisions effectively deal with the unique aspects of the pharmaceutical industry and with the tactics the manufacturers use. We conclude that the *Nexium* decision, which holds that reformulations can be unlawful only when the manufacturer withdraws the original product from the market, is not supportable from the perspective of either economics or law. It fails to account for the price disconnect in pharmaceutical markets, and its proposed rule would be grossly under-protective of consumers.

Our second Article will provide the results of additional detailed empirical analyses of the dataset, with the goal of identifying the manufacturer tactics that cause the most consumer harm. Guided by the

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6. See *infra* Part II, tbl.6.

7. See *infra* text following Part II, tbl.6.

8. Abbott Labs. v. Teva Pharm. USA, Inc. (*TriCor*), 432 F. Supp. 2d 408 (D. Del. 2006).

9. Walgreen Co. v. AstraZeneca Pharm. L.P. (*Nexium*), 534 F. Supp. 2d 146, 148–49 (D.D.C. 2008).

empirical analysis, that Article will conclude by offering a proposal for the proper antitrust treatment of the product-reformulation strategy. An appropriate antitrust approach must consider the unique economic characteristics of the pharmaceutical marketplace and the consequent enormous consumer welfare losses that result from impeding generic substitution. The approach must also, however, give due regard to the possibility that antitrust liability might dampen welfare-enhancing innovation; consider institutional constraints on the courts' ability to detect and remedy anticompetitive unilateral conduct; and accommodate business executives' need for usable rules to guide their product-development decisions.

## I. THE ECONOMICS OF PRODUCT REFORMULATIONS

### A. *The Regulatory Context*

Food and Drug Administration ("FDA") approval to market a prescription pharmaceutical in the United States is specific to its dosage, form, and composition.<sup>10</sup> For example, the FDA can approve the sale of a tablet containing 50 mg of the active ingredient. To change the form from a tablet to a capsule the manufacturer must obtain FDA approval. This can require a demonstration that the new product's active ingredient is absorbed into the body at the same rate as the original product,<sup>11</sup> or in the absence of such a demonstration, can require expensive new clinical studies.

Product reformulations can be socially useful.<sup>12</sup> A change in dosage form or composition might save manufacturing costs, ease the administration of medication to the patient, or increase patient compliance by reducing the dosing frequency. In some cases, the brand manufacturer may claim patent or other market exclusivity specific to the reformulated product.<sup>13</sup>

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10. 21 U.S.C. § 355(a)–(b) (2006); 21 C.F.R. § 314.50(a)(1) (2009).

11. 21 C.F.R. § 314.54(b) (2009). A manufacturer that shows that the reformulated product is equivalently absorbed is permitted to rely on the studies underlying the approval of the original product. *Id.*

12. See generally Ernest R. Berndt et al., *The Impact of Incremental Innovation in Biopharmaceuticals*, 24 PHARMACOECONOMICS 69, 71 (2006) (discussing how reformulated products can increase compliance, improve pharmacokinetics, and reduce side effects); Dennis Z. Kvesic, *Product Lifecycle Management: Marketing Strategies for the Pharmaceutical Industry*, 8 J. OF MED. MARKETING 293, 296 (2008) ("[M]ore than one-third of products launched in 2002–05 by the top 50 pharmaceutical manufacturers were reformulations.").

13. See *infra* Part II, tbl.6.

Reformulations can raise antitrust concerns because of their effect on generic substitution. Under the Hatch-Waxman Act<sup>14</sup> and state regulatory regimes, only AB-rated generic drugs may be automatically dispensed by the pharmacist without the issuing doctor's approval for substitution in lieu of the brand drug.<sup>15</sup> In order to receive an AB rating from the FDA, a generic drug must be: (1) therapeutically equivalent to its brand-name counterpart, meaning that the generic has the same active ingredient, form, dosage, strength, and safety and efficacy profile, and (2) bioequivalent to its brand-name counterpart, meaning that the generic is absorbed in the body at approximately the same rate as the brand drug.<sup>16</sup>

Without getting the doctor's approval, a pharmacist can substitute an AB-rated generic 55 mg tablet for a prescription written for "Brand X 55 mg tablet." Since the AB rating is dosage and form specific, however, a pharmacist cannot substitute, for example, a generic tablet for a prescription written for a "Brand X capsule."<sup>17</sup> Minor, medically insignificant changes to the brand product can thus prevent automatic substitution of the generic product for the brand. To achieve substitutability for the reformulated brand product, the generic manufacturer must develop the new products and then obtain FDA approval, which takes on average about eighteen months.<sup>18</sup>

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14. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 21 and 35 U.S.C.).

15. See ALLISON MASSON & ROBERT L. STEINER, FEDERAL TRADE COMM'N, *GENERIC SUBSTITUTION AND PRESCRIPTION DRUG PRICES: ECONOMIC EFFECTS OF STATE DRUG PRODUCT SELECTION LAWS* 5 (1985) [hereinafter *FTC GENERIC SUBST. REP.*].

16. See CTR. FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMIN., *APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE*, xv (29th ed. 2009) [hereinafter *Orange Book*]. Nineteen states do not specifically rely on the *Orange Book*, but still require that the generic be a pharmaceutical equivalent to the brand (same active ingredient absorption, dosage, route of administration). See *id.* at iv; Jesse Vivian, *Generic-Substitution Laws*, 33 U.S. PHARMACIST 30 (2008), [http://www.uspharmacist.com/content/t/generic\\_medications/c/9787/](http://www.uspharmacist.com/content/t/generic_medications/c/9787/).

17. The reformulation destroys the AB rating even if the tablet has the same active ingredient and is absorbed into the body at an identical rate as the capsule, and even if the brand manufacturer obtained FDA approval to market the brand tablet only by showing that the reformulated product, the capsule, was therapeutically equivalent to the original tablet. See Rebecca S. Yoshitani & Ellen S. Cooper, *Pharmaceutical Reformulation: The Growth of Life Cycle Management*, 7 HOUS. J. HEALTH L. & POL'Y 379, 398 (2007) (discussing how a brand manufacturer can sometimes get approval of reformulated product by relying on safety and efficacy data of original product).

18. See LEON SHARGEL & ISADORE KANFER, *GENERIC DRUG PRODUCT DEVELOPMENT* 366 (2004) (stating that median approval time for generics in 2004 was eighteen months); OFFICE OF INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERV., FOOD AND DRUG ADMIN.

This regulatory landscape creates an opportunity for brand manufacturers to make medically insignificant but economically crucial changes to their products. FDA regulations require generic manufacturers to notify brand manufacturers of filings requesting approval to market generic versions of branded products.<sup>19</sup> While the generic's FDA application is pending (or even before, depending on the brand manufacturer's foresight), the brand manufacturer can reformulate the product, most simply by changing the form, such as from a tablet to a capsule. FDA regulations do not require brand manufacturers to notify the generics (or the public) of these requests for reformulation, so the generics cannot anticipate and plan against them.

Manufacturers that redesign their products often also switch their promotional efforts, encouraging doctors to write prescriptions for the new formulation rather than for the original. If the manufacturer is successful in getting the prescriptions switched to the reformulated product, a manufacturer entering the market with an FDA-approved generic version of the original product will make very few sales because pharmacists will not be able to substitute the generic for the reformulated brand product, even if the two products are bioequivalent.<sup>20</sup> The generic manufacturer must first reformulate its product, and then go back to the FDA seeking approval for a generic version of the reformulated product. In the interim, the brand manufacturer may have obtained a patent on the new formulation; the generic manufacturer, even with FDA approval for the reformulated generic, will either have to challenge that patent and suffer the Hatch-Waxman Act's automatic thirty-month stay,<sup>21</sup> or wait for the patent to expire.

Importantly, neither patent law nor FDA regulations require that the reformulated brand product be superior to the original product—in terms of better medical outcomes, patient convenience, or otherwise. Patent law requires only that the applicant show that the product is useful and novel, not

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GENERIC DRUG REVIEW PROCESS 6 (June 2008) (median approval time for generics in 2006 was nearly seventeen months).

19. 21 C.F.R. §§ 314.52(a)-(a)(1), 314.95(a)-(a)(1) (2009).

20. See, e.g., Yoshitani & Cooper, *supra* note 17, at 380 ("Through reformulation, a drug company alters characteristics of a brand-name drug just enough to qualify for a new patent under patent examination procedures . . . while keeping enough characteristics the same to use previous clinical testing results for the purpose of FDA approval.").

21. Under the Hatch-Waxman Act, the FDA's approval of the generic product is automatically stayed for thirty months (unless the patent expires or a court holds the patent invalid or not infringed) if the brand manufacturer sues the generic for patent infringement within forty-five days of receipt of a notice asserting that the patent is invalid or not infringed. See 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (2006).

that it is superior in any way to existing products.<sup>22</sup> Further, the FDA requires only that the product be superior to a placebo, not to existing products.<sup>23</sup> The FDA has specifically disclaimed responsibility for determining whether reformulated brand products are better than their originals, asserting that “[t]he law does not allow the FDA to [do so].”<sup>24</sup> Consequently, “[t]he FDA does not consider whether a drug is better than others on the market before approving it.”<sup>25</sup>

As an industry insider candidly admitted, “The goal of reformulation as a means of generic defense is clear: to prevent the substitution of the branded product by generics on patent expiry.”<sup>26</sup> Brand manufacturers need not improve the product, but only change it: “it is sufficient to alter the branded product only to the extent that it is no longer the same as the product that the generic companies are using as reference for their [FDA applications]. This prevents pharmacies substituting generic product for the reformulated brand product . . . .”<sup>27</sup>

#### *B. The Economic Context*

A skeptic might ask “So what?” Can’t the market determine whether the reformulated product is superior to the original and thus prevent any harm to consumers from a product reformulation? The reformulation defeats only automatic generic *substitution*; it doesn’t prevent FDA *approval* of the generic product. Once the FDA approves the generic version of the original brand product, the generic can compete in the marketplace and doctors can prescribe it rather than the reformulated brand product. Presented with the choice, can’t consumers decide whether the reformulated brand is worth the higher price?

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22. See 35 U.S.C. § 101 (2006).

23. See 21 C.F.R. § 314.126(b)(2)–(2)(i) (2009).

24. Jeanne Whalen, *Glaxo Strategy Threatened by FDA Delays*, WALL ST. J., June 17, 2008, at B3.

25. *Id.*; see generally Stacey L. Dogan & Mark A. Lemley, *Antitrust Law and Regulatory Gaming*, 87 TEX. L. REV. 685, 709 (2009) (stating that the FDA “has neither the mandate nor the power to take competition concerns into account in approving particular pharmaceutical products”).

26. Stephen Perrett, *The Modified-Release Drug Delivery Landscape: The Commercial Perspective*, in II MODIFIED-RELEASE DRUG DELIVERY TECHNOLOGY 1, 2 (Michael J. Rathbone et al. eds., 2d ed. 2008).

27. *Id.*

### 1. Product Reformulations in Ordinary Markets

This skepticism would be justified if prescription pharmaceuticals competed in typical markets, where product reformulations usually cause few competitive problems. In most markets, a manufacturer will reformulate a product only when it is likely to lead to increased consumer welfare. Consumers compare the new product's attributes to those of existing products and buy the one that offers the best price/quality combination. With the price/quality decision effectively in the hands of the consumers who select the product and pay the price, manufacturers will make only those product changes that consumers are likely to conclude are worth the price, i.e., only those product changes that are likely to increase consumer welfare.<sup>28</sup>

Assume, for example, that Company A dominates the market for amateur photography with its Model 1 camera. Foreseeing that Company B will soon enter with a generic version of Model 1, Company A innovates by introducing Model 2, which makes minor changes to the original Model 1 camera. Such innovation certainly may harm Company B because it will not make as many sales of its generic Model 1 as it anticipated. This injury to a competitor, however, is not relevant to antitrust analysis. In fact, there is no antitrust injury because the innovation does not reduce in any way competition between Company A and Company B.

To see this, assume that the original Model 1 was sold by A for a monopoly price of \$50. With competition from B, however, the price was expected to fall to \$25. Assume that Company A then introduces Model 2, with a real innovation that makes it worth \$5 more to users than the original version. Nonetheless, even with Model 2 entering the market, Company B can compete; it simply needs to offer a price that is \$5 or more lower than the price of the new improved Model 2. The competitive result is likely the same \$25 competitive price for Model 1 that would have occurred without the innovation.<sup>29</sup> With the innovation, Company A can likely charge buyers

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28. See, e.g., PAUL A. SAMUELSON & WILLIAM D. NORDHAUS, *ECONOMICS* 80 (16th ed. 1998) (asserting that choice and utility theory are founded on "the fundamental premise that people tend to choose those goods and services they value most highly"); FTC, *TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW AND POLICY* 3 (Oct. 2003) (increased consumer welfare results from "the optimum mix of products and services in terms of price, quality, and consumer choice"), available at <http://www.ftc.gov/os/2003/10/innovationrpt.pdf>.

29. The competitive interaction between the two producers will determine the equilibrium prices in the duopoly. There is no reason to expect the competitive interaction to change as a result of the introduction of the new model.

\$30 for Model 2. Consumers therefore reap the full benefit of B's price competition because, absent that competition, the price of Model 2 would presumably have been \$55. In addition, those consumers who value A's innovation can pay the extra \$5, which is the value of the innovation, while getting a competitive price (\$25) for the non-innovative aspects of the product which now faces price competition from B. Consumers' ability to make their own price/quality decision ensures that they get both price competition and real, valuable innovations.

Note also that because B offers the original product, whether A withdraws its original product from the market is irrelevant in evaluating the benefits from the product reformulation.<sup>30</sup>

## 2. Product Reformulations in the Pharmaceutical Marketplace

Reformulations of prescription pharmaceuticals are different, however, because they can be hugely profitable to the brand manufacturer while significantly reducing consumer welfare. This divergence between the interests of manufacturers and consumers occurs because prescription pharmaceutical markets are not like other markets. Prescription pharmaceutical markets are characterized by a "price disconnect"—a doctor, rather than the consumer, decides which product will be bought, but the consumer (or her insurer), rather than the doctor, pays for the product. The result is a marketplace in which consumers do not make the price/quality choice that is the foundation of competitive markets. Pharmaceutical reformulation schemes are designed to exploit this unusual characteristic of pharmaceutical markets.

It is well established in the economics literature that markets cannot be counted on to yield welfare-enhancing outcomes when consumers do not make the price/quality choice.<sup>31</sup> With respect to the price disconnect in

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30. In the usual market, the competition between the new entrant's version of the original product and the incumbent's reformulated product is sufficient to achieve the competitive duopoly price(s). The incumbent may remove the original product from the market in order to better promote the new product, or to defer direct price competition between the same models of a product. In ordinary markets, these are all legitimate competitive activities that have little impact on the competitive outcome.

31. See, e.g., JOHN STUART MILL, PRINCIPLES OF POLITICAL ECONOMY 342 (1848) (Oxford Univ. Press 1998) ("the foundation of the *laissez-faire* principle breaks down entirely" when "[t]he person most interested is not the best judge of the matter"); *id.* at 338 (in such cases, "the supply called forth by the demand of the market will be anything but what is really required"); Kenneth J. Arrow, *Uncertainty and the Welfare Economics of Medical Care*, 53 AM. ECON. REV. 959, 967 (1963) (noting that the price disconnect results in an "extreme"

prescription pharmaceutical markets, the Federal Trade Commission (“FTC”) has noted that “[t]he basic problem is that the forces of competition do not work well in a market where the consumer who pays does not choose, and the physician who chooses does not pay. Patients have little influence in determining which products they will buy and what prices they must pay for prescriptions.”<sup>32</sup> Not having the obligation to pay, doctors are relatively

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example of a case “in which the usual assumptions of the market are to some extent contradicted” and that the disconnect forces us to “recognize the incomplete description of reality supplied by the impersonal price system”).

32. *Drug Product Selection*, Staff Report to the FTC, BUREAU OF CONSUMER PROTECTION at 2–3 (Jan. 1979) [hereinafter “FTC Staff Rep.”]; see also FTC Generic Subst. Rep., *supra* note 15, at 5 (“[T]he institutions of the prescription drug market are markedly different from those in most other product markets. For prescription drugs, it has not been the consumer who has made the choice among brands; it has been the physician.”); RONALD S. BOND & DAVID F. LEAN, FTC, SALES, PROMOTION, AND PRODUCT DIFFERENTIATION IN TWO PRESCRIPTION DRUG MARKETS 75 (1977) (“Since physicians select but do not pay for the drugs they prescribe, market forces would require physicians to consider price in their prescribing decisions only if consumers were willing and able to make informed decisions about physicians’ prescribing habits when they shopped for medical care.”); Richard Gilbert, *Holding Innovation to an Antitrust Standard*, 3 COMP. POL. INT’L 47, 66 (2007) (“[T]he objectives of the physician and his patient are not perfectly aligned [because the] doctor may be relatively insensitive to cost . . . .”); Mark A. Hurwitz & Richard E. Caves, *Persuasion or Information? Promotion and the Shares of Brand Name and Generic Pharmaceuticals*, 31 J. L. & ECON. 299, 300 (1988) (noting “prescribers’ weak incentives for selecting the lowest-price brand”); *id.* at 300 (“The physician who prescribes a drug on the basis of seller-supplied information captures no savings from selecting a cheaper generic supplier. . . so that the price elasticity of demand for the branded drug is reduced . . . .”); *id.* at 305 (“The physician has no substantial economic incentive to choose the lower-priced product, and doctors tend to be ignorant of specific drug prices[:] habit accordingly plays a strong role in the physician’s prescription practice.”); Füsün F. Gönül et al., *Promotion of Prescription Drugs and Its Impact on Physicians’ Choice Behavior*, 65 J. MARKETING 79, 79 (2001) (“[I]n the prescription drug market there is a distinct breach in the traditional buying decision process: The decision maker is the physician . . . but it is the patient who takes the drug and ends up paying . . . .”); Song Hee Hong et al., *Product-Line Extensions and Pricing Strategies of Brand-Name Drugs Facing Patent Expiration*, 11 J. MANAGED CARE PHARMACY 746, 747 (2005) (noting that, as a result of price disconnect and insurance “prescription drug markets have many characteristics that would predict price insensitivity”); Haiden A. Huskamp et al., *Generic Entry, Reformulations, and Promotion of SSRIs in the US*, 26 PHARMACOECONOMICS 603, 605 (2008) (explaining that price disconnect and insurance coverage result in prices that “well exceed marginal production costs”); Fiona M. Scott Morton, *Barriers to Entry, Brand Advertising, and Generic Entry in the US Pharmaceutical Industry*, 18 INT. J. IND. ORG. 1085, 1086–87 (2000) (noting “severe agency problems in the industry” because “[d]octors do not share in the cost of the prescriptions they write and thus do not have an incentive to consider the price of different products in making a prescription decision”); *id.* at 1087 (“[A] critical feature of the demand for prescription pharmaceuticals is that the end consumer, the patient, does not select the drug he or she will consume.”); *id.* at 1088 (“[P]hysicians are also often uninformed

price-insensitive, i.e., they select which drugs to prescribe based on factors other than price.<sup>33</sup> This results in most branded prescription pharmaceuticals—until generic entry—obtaining very substantial market power regardless of whether there are multiple branded products offering similar therapeutic results.<sup>34</sup> It is not unusual for such branded products to be sold at ten times their manufacturing costs while making sales in the hundreds of millions of dollars.<sup>35</sup>

Moreover, doctors' price insensitivity makes them particularly susceptible to "detailing"<sup>36</sup> and free samples<sup>37</sup> from brand manufacturers'

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as to the prices and availability of generics.”); F.M. Scherer, *Pricing, Profits, and Technological Progress in the Pharmaceutical Industry*, 7 J. ECON. PERSPECTIVES 97, 99 (1993) (“The combination of physician decision-making, imperfect information, and third-party payments makes drug demand stronger and less price-elastic than it might otherwise be, conferring considerable monopoly power upon the sellers of well-accepted drugs.”).

33. See, e.g., G. Michael Allan et al., *Physician Awareness of Drug Cost: A Systematic Review*, 4 PLOS MED. 1486, 1486 (2007) (explaining that studies over the last ten years consistently show that doctors “overestimated the cost of inexpensive products and underestimated the cost of expensive ones”); Michael E. Ernst et al., *Prescription Medication Costs: A Study of Physician Familiarity*, 9 ARCHIVES FAM. MED. 1002, 1004–05 (2000) (noting that “family physicians are unfamiliar with the costs of common prescription drugs,” with 89.9% of doctors underestimating the cost of brand drugs); Lillian L. Glickman et al., *Physicians’ Knowledge of Drug Costs for the Elderly*, 42 J. AM. GERIATRIC SOC’Y 992, 992 (1994) (concluding that doctors do not understand the economic implications of their prescribing habits); Gönül, *supra* note 32, at 89 (observing that “the majority of physicians either demonstrate a lack of price sensitivity or are characterized by fairly limited price sensitivity”); Joan Hoffman et al., *A Survey of Physician Knowledge of Drug Costs*, 10 J. PAIN & SYMPTOM MGMT. 432, 435 (1995) (noting that doctors underestimated the price of drugs they prescribe 65% of the time); Lucinda G. Miller & Alan Blum, *Physician Awareness of Prescription Drug Costs: A Missing Element of Drug Advertising and Promotion*, 42 J. FAM. PRACTICE 33, 35 (1993) (noting that doctors “have not shown substantial interest in the cost of medications [and] the majority of physicians could not accurately identify drug costs”); Steven Reichert et al., *Physicians’ Attitudes about Prescribing and Knowledge of the Costs of Common Medications*, 160 ARCHIVES INTERNAL MED. 2799, 2799 (2000) (concluding that doctors “were predisposed to being cost-conscious in their prescribing habits, but lacked accurate knowledge about actual costs”); William H. Shrank et al., *Physicians’ Perceived Knowledge of and Responsibility for Managing Patients’ Out-of-Pocket Costs for Prescription Drugs*, 40 ANNALS OF PHARMACOTHERAPY 1534, 1538 (2006) (explaining that doctors typically are not aware of costs and “did not feel accountable for being aware of” costs).

34. We discuss below the role of Managed Care Organizations (MCOs) in ameliorating the price-disconnect problem. See *infra* Part I.B.3.

35. See *infra* note 53.

36. “Detailing” refers to pharmaceutical representatives visiting doctors in person in order to educate them about the product and encourage them to prescribe it. It is a highly effective way of molding doctors’ prescribing decisions. See, e.g., Jerry Avorn et al., *Scientific Versus Commercial Sources of Influence on the Prescribing Behaviors of Physicians*, 73 AM.

J. MED. 4, 7 (1982) (detailing results in a “predominance of commercial rather than scientific sources of drug information”); Ernst R. Berndt et al., *Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market*, 85 AM. ECON. REV. 100, 104 (2001) (“[S]ales elasticity is largest for detailing, followed by journal pages of advertising, and is smallest for direct-to-consumer advertising.”); Mary-Margaret Chren & C. Seth Landefeld, *Physicians’ Behavior and Their Interactions with Drug Companies*, 271 J. AM. MED. ASS’N 684, 684 (1994) (“Requests by physicians that drugs be added to a hospital formulary were strongly and specifically associated with the physicians’ interactions with the companies manufacturing the drugs.”); Huskamp, *supra* note 32, at 614 (“[D]etailing does have an important effect on medication choice.”); Joel Lexchin, *Interactions Between Physicians and the Pharmaceutical Industry: What Does the Literature Say?*, 149 CAN. MED. ASS’N J. 1401, 1404 (1993) (concluding, after reviewing decades of research, that “[t]here is little doubt that detailers are effective in changing physicians’ prescribing behaviour” and that doctors who relied least on detailers were most likely to prescribe generic drugs); Nicole Lurie et al., *Pharmaceutical Representatives in Academic Medical Centers: Interaction with Faculty and Housestaff*, 5 J. GEN. INTERNAL MED. 240, 240 (1990) (“The most effective marketing technique is the use of pharmaceutical representatives . . . .”); *id.* at 242 (asserting that “contact with [detailers] is associated with changes in physicians’ prescribing practices”); John A. Rizzo, *Advertising and Competition in the Ethical Pharmaceutical Industry: The Case of Antihypertensive Drugs*, 42 J. L. & ECON. 89, 112–13 (1999) (noting that “physician prescribing behavior is substantively affected by” detailing, and it “inhibits price competition” and thus “lead[s] to higher equilibrium prices”). The sales manager of a major brand manufacturer said in an internal newsletter that, “There is a big bucket of money sitting in every [doctor’s] office. Every time you go in, you reach your hand in the bucket and grab a handful.” Thomas Ginsberg, *Sales Manager Is Fired After Comments Hit Web*, PHILA. INQUIRER, Apr. 7, 2007, at E01.

37. See, e.g., Richard F. Adair & Leah R. Holmgren, *Do Drug Samples Influence Resident Prescribing Behavior? A Randomized Trial*, 118 AM. J. MED. 881, 883 (2005) (“Resident physicians with access to drug samples in clinic were more likely to write new prescriptions for heavily advertised drugs and less likely to recommend OTC drugs than their peers[, and t]here was also a trend toward less use of inexpensive drugs.”); John M. Boltri et al., *Effect of Antihypertensive Samples on Physician Prescribing Patterns*, 34 J. FAM. MED. 729, 731 (2002) (“[T]here is an association between drug sample availability and physician prescription behavior for patients with hypertension.”); Troyen A. Brennan et al., *Health Industry Practices That Create Conflicts of Interest: A Policy Proposal for Academic Medical Centers*, 295 J. AM. MED. ASS’N 429, 431 (2006) (“The rate of drug prescriptions by physicians increases substantially after they . . . accept samples.”); Dan Brewer, *The Effect of Drug Sample Policies on Residents’ Prescribing*, 30 J. FAM. MED. 482, 486 (1998) (“[P]rescribing habits of family practice residents are associated with restricting or eliminating pharmaceutical samples.”); Lisa D. Chew et al., *A Physician Survey of the Effect of Drug Sample Availability on Physicians’ Behavior*, 15 J. GEN. INTERN. MED. 478, 482 (2000) (“[A] significant proportion of self-reported sample users subsequently would write a prescription for the more expensive sampled medication (which also differed from their preferred drug choice).”); Susan L. Coyle, *Physician-Industry Relations, Part I: Individual Physicians*, 136 ANNALS OF INTERNAL MEDICINE 396, 398 (2002) (“[O]nce a patient exhausts a free supply of medication, the physician typically writes a prescription for the same brand.”); David P. Miller et al., *The Impact of Drug Samples on Prescribing to the Uninsured*, 101 S. MED. J.

sales representatives. This reflects a notorious “agency problem”—a market defect that results from “one market participant [being] represented by an agent whose personal incentives diverge from its principal’s goals.”<sup>38</sup> Even when doctors exercise their best medical judgment on behalf of their patients,<sup>39</sup> that judgment rarely includes the intensity of price consideration that the price-paying patient herself would bring to the decision.<sup>40</sup>

Beginning in the mid-1970s, the federal and state governments acted to remedy the price disconnect and restore the price/quality choice for consumers. All fifty states and the District of Columbia enacted drug product selection (“DPS”) laws that permit or require the pharmacist to dispense a generic drug in lieu of a brand drug whenever the consumer consents.<sup>41</sup> These DPS laws are premised on the economic fact that brand manufacturers exploit the price disconnect by promoting to doctors while generic

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888, 891 (2008) (“[P]hysicians are over three times more likely to prescribe generic medications to uninsured patients when drug samples are not available . . .”).

38. IIB PHILLIP AREEDA, ET AL., *ANTITRUST LAW* ¶ 411, at 61 (3d ed. 2007); *see also* David E.M. Sappington, *Incentives in Principal-Agent Relationships*, 5 J. OF ECON. PERSP. 45, 49–52 (1991) (reviewing the literature on divergent incentives between principals and agents).

39. There is a growing concern that doctors’ “professional judgments about the welfare of the patients may be inappropriately influenced by a secondary interest – in this case, the personal gain derived from relationships with pharmaceutical companies.” David M. Studdert et al., *Financial Conflicts of Interest in Physicians’ Relationships with the Pharmaceutical Industry—Self-Regulation in the Shadow of Federal Prosecution*, 351 NEW ENG. J. MED. 1891, 1891 (2004). Studies show that “even [a] small gift[] is a powerful influence on people’s behavior. Individuals receiving gifts are often unable to remain objective; they reweigh information and choices in light of the gift.” Brennan, *supra* note 37, at 431.

40. *See supra* note 33; *see also* William T. Robinson et al., *First-Mover Advantages from Pioneering New Markets: A Survey of Empirical Evidence*, 9 REV. INDUS. ORG. 1, 5 (1994) (“Market share leadership was *not* driven by the pioneer’s superior product quality or lower prices . . . ,” but was driven by “physician preference for the established and familiar pioneering brand names.”) (emphasis in original); Lexchin, *supra* note 36, at 1404 (noting that detailers caused significant percentages of doctors to adopt “the commercial view of a product rather than the scientific view . . . .”); Chren & Landefeld, *supra* note 36, at 689 (finding “a strong and specific association between the [prescribing] behavior and the physicians’ interactions with drug companies, independent of the merits of the companies’ products”).

41. *See, e.g.*, Norman V. Carroll et al., *The Effects of Differences in State Drug Product Selection Laws on Pharmacists’ Substitution Behavior*, 25 MED. CARE 1069, 1069 (1987) (“Over the past 15 years all 50 states have amended or enacted legislation to enable pharmacists to engage in drug product selection (DPS).”); NAT’L ASS’N OF BOARDS OF PHARMACY, *SURVEY OF PHARMACY LAW* (2009), *available at* <http://www.nyschp.org/associations/8780/files/FINAL%20survey%20with%20letter.pdf>. Approximately 28% of states require the pharmacist to substitute a generic when one is available; about 78% of states require the pharmacist to obtain the patient’s consent before substituting a generic. *Id.*

manufacturers are unable to do so economically. Generics instead compete by offering low prices to pharmacies.<sup>42</sup> An FTC report concluded:

Since physicians are an unlikely force behind a switch to lower-cost brands after the patent period has expired, an erosion of the patent-conferred monopoly must depend on others who have both the power and the incentive to respond to lower prices. That is the role envisioned for the drug product selection laws: to transfer some of this power to pharmacists. Consumers are the ones most interested in a lower price, and pharmacists must respond to consumer demand because of direct competition with other pharmacies on prescription prices.<sup>43</sup>

DPS laws “shift the choice of [product] for most prescriptions from the physician to the pharmacist.”<sup>44</sup> The FTC noted, “the laws foster price competition by allowing the only principals who have financial incentives to make price comparisons—the pharmacist and the patient—to select drug products on the basis of price.”<sup>45</sup> Pharmacies have such an incentive because they generally make greater margins on generic rather than branded drugs.<sup>46</sup>

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42. Competition among generic sellers is on the basis of price. With multiple generic sellers, the price approaches marginal cost. *See infra* note 53. We discuss further below the “externality” problem that generic sellers face related to promotion.

43. FTC Generic Subst. Rep., *supra* note 15, at 7. The FDA and FTC worked together to develop a Model Drug Product Selection Act for State legislatures to enact. *See* FTC Staff Rep., *supra* note 32 at 273. The FTC and FDA were “committed to facilitating drug product selection [i.e., generic substitution],” and believed that “effective drug product selection laws will work to stimulate price competition in a multi-source prescription drug market.” *Id.* at 291–92. The FDA developed a list of therapeutically equivalent drugs, today called the Orange Book (*supra* note 16) in order to “increase[] consumer awareness of less expensive [generic drugs],” with the goal of “stimulat[ing] greater consumer demand for less expensive [generics] and physicians and pharmacists should be influenced to respond to that demand by prescribing and dispensing such less expensive drug products.” Therapeutically Equivalent Drugs; Availability of List, 45 Fed. Reg. 72,582, 75,583 (Oct. 31, 1980). The list helped make drugs products “sufficiently interchangeable so that price can be a major factor in their selection.” OFFICE OF TECH. ASSESSMENT, DRUG BIOEQUIVALENCE at 57 (1974), *available at* <http://www.fas.org/ota/reports/7401.pdf>.

44. FTC Generic Subst. Rep., *supra* note 15, at 1.

45. *Id.*

46. *See, e.g.,* Richard E. Caves et al., *Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry*, in BROOKINGS PAPERS ON ECON. ACTIVITY, MICROECONOMICS: 1991 at 6 (Martin Neil Bailey & Clifford Winston eds., 1991) (noting that generics “tend to yield higher gross margins to pharmacists, so that both pharmacist and consumer share an interest in substituting generic products where possible”); Stuart O. Schweitzer & William S. Commanor, *Controlling Pharmaceutical Prices and Expenditures*, in CHANGING THE U.S.

Although pharmacy retailers' margins are relatively greater for generics, intense retail competition in this sector drives them to pass on large savings to consumers on generics.<sup>47</sup>

Unlike brand manufacturers, generic manufacturers cannot profitably exploit the price disconnect by detailing doctors. Detailing is very expensive and generally is not economically feasible once generics are available. If multiple generics of a product are or will soon be available, a manufacturer cannot profitably promote a generic product to doctors because a pharmacist could easily substitute some other manufacturer's generic version of the same drug. Thus, if one generic seller promotes the product to doctors, other generic sellers can free ride on that promotion by having lower costs and offering prices below the promoting seller's cost.<sup>48</sup> For the same reason, brand manufacturers typically also stop detailing and otherwise promoting the brand product once generic versions are available.<sup>49</sup> This post-generic-entry free-riding makes active promotion of the product by anyone – brand and generic manufacturers alike – economically infeasible. Unable to exploit the price disconnect by detailing doctors, generic manufacturers make sales by offering low prices to pharmacies – the entities that use low retail prices to encourage consumers to substitute the generic for the brand.<sup>50</sup>

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HEALTH CARE SYSTEM 165 (Ronald M. Anderson et al. eds., 3d ed. 2007) (noting that retailer margins are greater on generics than brands).

47. Net profit margins for pharmacy retailers rarely exceed 2.5% of revenue. See SEC EDGAR Reports for SIC 5912 (1989–2008).

48. Generic sellers typically do not promote their products to doctors even during the six-month Hatch-Waxman exclusivity period. See 21 U.S.C. §355(j)(5)(B)(iv)(I–II) (2006) (providing 180 days for generic “first-filer” under certain circumstances). Promotion is a capital good whose impact extends beyond the six-month period. Subsequent entry by multiple generics, and the resulting low prices, render uneconomic the first generic's promotion efforts even during the exclusivity period.

49. See, e.g., Caves et al., *supra* note 46, at 39 (noting that brand firms curtail most promotion before generic entry).

50. Generic entry typically does not prompt the brand manufacturer to lower its price. Instead, it continues to exploit the price disconnect by pursuing a “harvest strategy,” keeping its price at the monopoly level and making far fewer sales to a small group of brand-loyal buyers (inelastic demanders). See, e.g., Claude E. Barfield & Mark A. Groombridge, *Parallel Trade In The Pharmaceutical Industry: Implications for Innovation, Consumer Welfare, and Health Policy*, 10 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 185, 242 (1999); Jayanta Bhattacharya & William B. Vogt, *A Simple Model of Price Dynamics*, 46 J.L. & ECON. 599, 602 (2003); Daniel Goldberg, *Cornering the Market in a Post 9/11 World: The Future of Horizontal Restraints*, 36 J. MARSHALL L. REV. 557, 570 (2003); Henry G. Grabowski & John N. Vernon, *Brand Loyalty, Entry, and Price Competition in Pharmaceuticals After the 1984 Drug Act*, 35 J.L. & ECON. 331, 339–40 (1992); CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE

When the generic substitution system works as intended, the availability of a generic alternative effectively puts the price/quality choice back in consumers' hands. The doctor, price insensitive and conditioned by years of brand promotion, may continue to write prescriptions for the brand product. But pursuant to the DPS laws, the pharmacist, absent the consumer's disapproval, can substitute the less expensive generic. When a generic is automatically substitutable at the pharmacy counter, the price/quality decision is back in the hands of economic decision makers who take account of prices: the pharmacist who makes greater margins on generics suggests them to consumers, and consumers can choose the lower-priced generic or decide that the value of the brand justifies a higher price or higher insurance co-payment.<sup>51</sup>

This restoration of the price/quality choice for consumers results in much lower prices for prescription drugs. The first generic typically enters the market at a price at least 30% below that of the brand.<sup>52</sup> The price discount grows—often to 80% or more—as more generics enter, and generics rapidly take the vast majority of unit sales.<sup>53</sup> Consumers get an opportunity for significant savings.

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PHARMACEUTICAL INDUSTRY [hereinafter CBO Study] 29–30 (1998). *But see* Hong et al., *supra* note 32, at 751–52 (asserting that brand manufacturers often raise original product's price, not in order to harvest inelastic demanders, but in order to make the reformulated product more attractive). Several courts have mistakenly implied that generic entry may reduce consumer welfare by causing the brand to raise its price. *See, e.g., In re Tamoxifen Citrate Antitrust Litig.*, 429 F.3d 370, 393 & n. 23 (2d Cir. 2005); *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 363 F. Supp. 2d 514, 522 (E.D.N.Y. 2005). These implications are wrong; generic entry causes a dramatic reduction in the average price of the molecule (brand plus generic), despite the brand's harvesting strategy. *See, e.g., CBO Study, supra*, at 31–32.

51. While the AB-rated generic is therapeutically equivalent to the branded product, other “quality” dimensions may make the branded drug preferable. For example, the size, color, or markings of the branded product may help ease compliance with the dosing regimen for patients who take many drugs.

52. *See, e.g., Caves et al., supra* note 46, at 60 (noting that first generic typically enters at 40% discount to brand, and more entrants drive discounts even further).

53. *See, e.g., David Reiffen & Michael R. Ward, Generic Drug Industry Dynamics*, 87 REV. ECON. & STAT. 37, 38 (2005) (stating that multiple generics drive price to near marginal cost); Atanu Saha et al., *Generic Competition in the US Pharmaceutical Industry*, 13 INT. J. ECON. BUS. 15, 28, 31 (2006) (explaining that, in the blockbuster drug market, multiple generics result in a 60% discount and gain nearly an 80% share two years after entry); *Generic Competition and Drug Prices*, (April 2006), available at <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm129385.htm> (asserting that with multiple generics, “the average generic price falls to 20% of the branded price and lower”); Steven N. Wiggins & Robert Maness, *Price Competition In Pharmaceuticals: The Case of*

These consumer savings would not come at the expense of any patent or FDA exclusivities that protect the original brand product. If the FDA approves the marketing of a generic product, it is legally entitled to enter the market and be substituted for the branded original product.<sup>54</sup>

Note that the critical factor necessary to give consumers the price/quality decision is the ability to substitute without the approval of the doctor. If the pharmacist cannot substitute the generic for the brand, the consumer must buy the higher-priced brand unless the doctor rewrites the prescription. Most consumers would be unaware of the value of having the doctor rewrite the script and would be reluctant to challenge the doctor's drug choice.

As we have discussed, it is the consumer's ability to make the price/quality decision that, in ordinary markets, ensures that manufacturers will make only those product changes that are likely to increase consumer welfare. Preventing generic substitution prevents consumers from making the price/quality decision as between the generic and brand. So, by preventing substitutability, the brand manufacturer severs the connection between product reformulations and presumed increases in consumer welfare.

Preventing substitutability is exactly what many pharmaceutical product reformulations do.<sup>55</sup> A medically insignificant redesign of the brand product that prevents the generic from getting an AB rating destroys substitutability, significantly impairing the generic rival's only commercially viable means of competing. Also, unlike in other markets, a brand manufacturer's design change automatically invokes a regulatory barrier to entry, with any generic firm unable to compete for all of the relevant sales unless it begins the FDA approval process anew. Frequently a generic manufacturer that successfully reformulates its generic product to match the reformulated brand product then faces a statutory thirty-month stay of entry.<sup>56</sup>

Thus, as compared to the usual market, the pharmaceutical marketplace increases both the opportunity and incentive for brand manufacturers to redesign their products with an anticompetitive effect. A reformulated

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*Anti-Infectives*, 42 *ECON. INQUIRY* 247, 250–51 (2004) (finding that a large number of generics can drive price to less than 10% of pre-generic brand price).

54. *Illinois Tool Works, Inc. v. Grip-Pak, Inc.*, 906 F.2d 679, 684 (Fed. Cir. 1990). Absent a preliminary injunction, even a generic that enters at risk (i.e., while the brand's patent infringement claim is pending against it) has a "right to compete." *Id.*

55. See Dogan & Lemley, *supra* note 25, at 715 (Reformulations "exploit[] the product-approval process precisely because of its exclusionary effects . . .").

56. See 21 U.S.C. § 355(j)(2)(A)(vii)(IV); *supra* text accompanying note 21; see also *Geneva Pharm. Tech Corp., Inc. v. Barr Lab. Inc.*, 386 F.3d 485, 499 (2d Cir. 2004) (noting high barriers to generic entry). See *infra* Part II, tbl.6 for the frequency with which brand manufacturers claim market exclusivity for the reformulated product.

product will impair generic competition even if the reformulation provides no medical or other benefits to consumers as compared to the original product; the reformulated product need only be different from – not better than – the original product. By redesigning the product, the brand manufacturer prevents the generic from being AB-rated to the redesigned product, impairs the generic manufacturer's only viable means of competing for all sales, and thus prevents consumers from making the price/quality choice at the pharmacy counter.

Contrast the innovation scenario in the pharmaceutical marketplace to the typical one we addressed above regarding cameras. Assume Brand A is selling for \$2 per tablet, and that Generic A has filed an Abbreviated New Drug Application ("ANDA")<sup>57</sup> for an AB-rated version. Brand A successfully innovates with a capsule, Brand B, which is easier to swallow and has an additional value of 50¢ to consumers. If the market were like that for cameras or most other products, competition between the Generic A and Brand B would drive the competitive price of the original product (both branded and generic) to, say, \$1 per unit, with Brand B charging \$1.50 for its capsule (reflecting the incremental value of its innovation). With the price/quality choice in consumers' hands, all consumers would benefit from the price competition generated by the generic's entry, and those consumers who value the innovation would benefit from it. In the pharmaceutical marketplace, however, competition does not follow this paradigm. Through a product change scheme, Brand B can significantly impair the competition from Generic A, and the vast majority of consumers will continue to pay the monopoly price of \$2.50. Consumers now reap no benefits from competition or from innovation. Thus, proper economic analyses of the competitive impact of product changes are very different in the pharmaceutical industry than in more typical industries.

### 3. The Role of Managed Care Organizations

We have emphasized the price disconnect between doctors who decide which drugs to use and consumers who must pay. But a significant part of the cost of pharmaceuticals is covered for most consumers by Managed Care Organizations ("MCOs").<sup>58</sup> Unlike the consumer/patient, MCOs have the

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57. An ANDA is an Abbreviated New Drug Application that a manufacturer files with the FDA to seek approval to market a generic version of a branded pharmaceutical. *See* 21 U.S.C. § 355(j) (2006).

58. For purposes of this analysis, we intend the term "MCO" to encompass any organization that provides insurance or other coverage for all or part of a consumer's

ability and incentive to acquire expertise concerning the therapeutic efficacy of alternative pharmaceuticals, and can use differential co-payment requirements to encourage the patient to influence the doctor's prescribing decisions. Alternatively, MCOs that have contractual arrangements with doctors can attempt to directly influence their prescribing. Formularies that provide differential co-payments reflect MCOs' efforts to reduce drug costs by influencing patients' and doctors' choices.

It would seem that MCOs have an opportunity to substantially reduce the cost of reimbursing prescription medicines by countering brand-drug reformulations that impair generic competition. For example, the MCOs could refuse to pay for reformulated products or could relegate them to a disadvantaged place on the formulary, causing patients to question the pharmacist or the doctor as to the high cost of reformulated products. MCOs also could inform doctors of the reason for such disadvantaged treatment of the reformulated product. We address here in a preliminary fashion some of the possible structural impediments and manufacturer tactics that have prevented MCOs from defeating anticompetitive reformulations.

First, we start with the *fact* that MCOs have not defeated these reformulations. The data cited below for the examples of Hytrin, Wellbutrin, Celexa, TriCor, and Nexium<sup>59</sup> demonstrate that MCOs have not in fact prevented these reformulations from significantly impairing price competition from generics. Despite MCOs' theoretical ability to use disadvantaged formulary placement and other tactics to defeat anticompetitive product reformulations, they have not done so. Truly competitive prices have generally occurred in this industry only with the introduction of generics, which manufacturers market to retail pharmacies based on price.

Several structural impediments may be preventing MCOs from defeating anticompetitive product reformulations. First of all, insured consumers face only a part of the cost of prescriptions. This results in a classic "moral hazard" problem,<sup>60</sup> whereby consumers do not perceive the true cost of their

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prescription pharmaceuticals, including pharmacy benefit managers, indemnity insurance providers, etc.

59. See *infra* notes 127–128, 91–95, 118–120, 160–171, 191–199 and accompanying text.

60. Arrow, *supra* note 31, at 961–62. The moral hazard problem refers to situations in which the cost of actions is not fully borne by the decision maker. In the health insurance context, when patients face a "subsidized" cost of a particular medical service, they consider the "price" to be the cost to them. As a consequence, the consumer will over-consume the service. See, e.g., *id.* at 961–62.

decisions. The cost to themselves being masked, consumers tend to press their employers or other sponsors to include more rather than less-generous prescription coverage. Operationally, this translates into MCOs implementing less stringent controls on physician prescribing. This is exemplified by MCOs typically paying for and giving equal formulary treatment to branded pharmaceuticals in crowded therapeutic categories even when there are no meaningful medical differences among the products. Other things equal, consumers prefer that MCOs pay for, without requiring large co-payments, the prescriptions that their doctors write. Absent the imprimatur of the FDA that two drugs are therapeutically equivalent (AB-rated), we simply do not observe payors, whether consumer or MCO, influencing doctor prescribing to a degree sufficient to drive prices down to levels achieved by generic competition.

In the context of reformulated products of particular antitrust concern—those introduced to the market before the entry of the generic<sup>61</sup>—it is especially unlikely that an MCO would discourage the writing of prescriptions for the reformulated product. The generic is not yet available, and the brand manufacturer usually prices the original and reformulated products at par, or even with a slight discount for the reformulated product. On entry of the generic, the MCOs then face the problem of getting consumers to switch back to a product from which their doctors already switched them away.

An individual MCO also likely faces a significant free-rider problem. An individual MCO will incur costs to discourage the writing of prescriptions for the new product. These costs include the loss of goodwill from consumers who prefer broad coverage, as well as the out-of-pocket costs of monitoring reformulation schemes, requiring physician committees to compare the original and new products, and implementing plans to discourage doctors from writing prescriptions for the new product. Except in the rare instance in which the prescribing doctor is employed exclusively by the MCO, consumers covered by an individual MCO usually represent only a small fraction of a doctor's patients.<sup>62</sup> To the extent that an individual MCO is successful in discouraging the doctor from writing scripts for the new product, the costs incurred by that MCO will benefit its competitors. Thus,

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61. See *infra* at Part II tbl.2.

62. See Russell Jackson, *Practice Guidelines, Physician Groups, and Drug Formularies*, 3 J. MANAGED CARE PHARM. 489, 489 (1997) (explaining that many physicians have contracts with up to twenty MCOs). Kaiser Permanente is an example of an MCO that, by virtue of directly employing the doctors and implementing stringent formulary controls, may be able to defeat anticompetitive reformulations.

the private benefits to the MCO are significantly less than the social benefits from changing doctor behavior, reducing the individual MCO's incentive to incur costs trying to influence doctor prescribing.

Moreover, doctors usually are not responsive to the efforts of an individual MCO to change their prescribing habits. A doctor is influenced most effectively when the collective pressures on her reach a tipping point—that is, when MCOs collectively representing a sufficient percentage of her patients discourage her from writing scripts for the reformulated product. An individual MCO's success in discouraging doctors from writing scripts for the new product is therefore dependent on the action of its competitors. Paradoxically, those competitors' incentive is to do nothing and instead free-ride on others' efforts.

We also believe that these structural impediments to effective MCO action are compounded by brand manufacturer tactics that exploit “agency” problems between MCOs and their sponsors/payors (e.g., employers and unions). The financial interests of MCOs and the payors for which they manage prescription plans can diverge in important ways. If the payor-MCO contract provides that the MCO retains all or a percentage of the rebates that brand manufacturers pay for favorable formulary placement, the brand manufacturer may be able to avoid disadvantaged formulary placement by paying rebates to the MCO on the reformulated product and terminating rebates on the original product.

We are exploring these and other issues further in our second article. What we know at this point is that structural and manufacturer-imposed impediments in fact prevent the typical MCO from deterring anticompetitive product reformulations.

## II. AN EMPIRICAL OVERVIEW OF PHARMACEUTICAL PRODUCT CHANGES

To date, analyses of pharmaceutical product changes have proceeded without any detailed empirical examination of their scope, nature, or magnitude. To remedy this, we have assembled a database of prescription pharmaceutical product changes from 1995 through April 2009. Using the FDA's Monthly Original and New Drug Application approval reports,<sup>63</sup> we identified those changes that the FDA classified as “New ester, new salt or

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63. See FDA Drug Approval Reports (2009), available at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Reports.ReportsMenu>.

other noncovalent derivative,”<sup>64</sup> “New Formulation,” or “New Combination” and designated as NDA Chemical Type “2,” “3,” or “4.”<sup>65</sup> The Monthly Drug Approvals reports provided the dates on which the FDA approved the reformulated products, and the Orange Book provided the date of approval for the original products. The Orange Book also provided the FDA approval date for the generic version of the original brand product.<sup>66</sup> We used the earliest approval date (whether tentative or final) for a given molecule and form.<sup>67</sup>

We excluded the following:

1. “Orphan drugs,” because of the presumption that they serve a limited market and that the potential harm from impaired generic entry is correspondingly limited.<sup>68</sup>

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64. This and the following terms in the text are defined and further discussed *infra* notes 71, 72 and accompanying text.

65. By focusing solely on the type 2, 3, and 4 New Drug Application approvals, the dataset does not include Supplemental New Drug Application approvals. We therefore excluded from the dataset all “New Dosage” reformulations, most of which are filed as Supplemental New Drug Applications. Additionally, the dataset does not include New Indications (which are approvals by the FDA to market the drug to treat additional disease states other than the one for which the drug had previously been approved). Approvals for New Indications usually do not by themselves create any impediment to AB-rated substitution.

66. For New Combinations, we used the generic approval date for the product nearest in time to the approval of the combination. An exception occurred when there was a combination of two previously marketed brand drugs by two different manufacturers where both had a relevant generic approval date; in that case, we used the generic approval date for the prior product of the manufacturer of the combination product.

67. The FDA apparently deletes the tentative approval date from the Orange Book when the generic receives final approval. Note that the approval dates, both for the branded and generic products, do not necessarily reflect actual market launch dates. Also note that when a generic entrant seeks FDA approval to market its product before the expiration of patents that protect the brand product, the generic manufacturer must provide notice to the brand manufacturer. The notice generally precedes the tentative or final approval by at least 12 months. Those notices, however, are not publicly available for the entire study period, so the dates of those notices are not included in our database.

68. See Orphan Drug Act, Pub. L. 97-414, 1(b)(4), 96 Stat. 2049, 2049 (1983) (explaining that “so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss”). Even some orphan drugs have been the subject of generic-impairment strategies. For example, Provigil (modafinil) was approved as an orphan

2. Drugs that had numerous brand and generic manufacturers, because the original molecule for these drugs typically had been introduced long before 1990 and had numerous brand and generic forms introduced before our study period (examples are levothyroxine sodium, compazine, hydroxocobalamin, progesterone, insulin products, and oral contraceptives).

3. Drugs with numerous active ingredients (e.g., M.V.I. Adult), because determining the potential predecessor drug or drugs would have required an unduly complicated methodology with little gain to our analysis.

4. Over-the-Counter products. Products that were introduced as OTC products are excluded; products that were initially prescription, but subsequently were approved as OTC were included if a form change involving a prescription strength version occurred during the study period.

Our first effort was to categorize each reformulation by type of change. In determining the type of product change, we compared the new form to the original approved version of the drug molecule. Where the manufacturer introduced a second new form of the same molecule, we also compared that second new form to the original product (rather than to the first reformulated product).<sup>69</sup> Where there was a change to a new salt or an enantiomer of a

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drug, yet it achieved significant sales (\$846 million in 2008). Top 200 Branded Drugs By Retail Dollars, <http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard/drugtopics/192009/597083/article.pdf> (last visited May 13, 2010). Its manufacturer, Cephalon, reformulated Provigil and obtained approval for Nuvigil (armodafanil), which is an enantiomer of Provigil. *See infra* note 78. Nevertheless, we excluded Provigil from the dataset because it was approved as an orphan drug.

69. In determining which generic product to consider as being a potential threat to the brand product, we focused only on the approval date of the first generic version of the first brand version of the product (except when dealing with New Salts, in which case, for all new forms of those products, we focused on the approval date of the first generic version of the New Salt). In certain cases in which there was more than one form change, however, the original brand product had either been discontinued or the brand manufacturer had moved all of its promotional efforts to one of the follow-on products, rendering the original form the subordinate product. Thus, the generic approval for the original form may not be any significant threat driving subsequent formulation changes, but, instead, generic approval of one of the follow-on formulations is the true threat. As a result, our analysis is likely underinclusive of instances in which the formulation change may have been part of a generic-impairment strategy. A prime example is TriCor. *See generally* Abbott Labs. v. Teva Pharm. USA, Inc., 432 F. Supp. 2d 408 (D. Del. 2006). TriCor was originally approved in 1998 as a capsule product, and Abbott got approval for TriCor tablets in September 2001. *Id.* at 415–16. Abbott then discontinued the capsule. *Id.* at 416. The FDA granted tentative approval for a generic TriCor capsule in February 2002. *Id.* Abbott then obtained approval for a new tablet

prior approved product,<sup>70</sup> we compared the change against the first version of the salt or enantiomer.

These are the basic types of reformulations in our database:

New Forms. “New form” changes consist of reformulations from an original form, such as a capsule, tablet, injectable, solution, suspension, or syrup to another form, including those already mentioned as well as extended-release capsules or tablets, orally dissolving (“OD”) tablets, and chewable tablets.

Enantiomers. Each isomer<sup>71</sup> of a chiral molecule<sup>72</sup> is an “enantiomer,” with the left-handed isomer often designated as the “S” enantiomer and the right-handed isomer often designated as the “R” enantiomer. Sometimes manufacturers switch from a chemical compound that is an equal mixture of each enantiomer, only one of which contains the active ingredient, to a compound that includes only the enantiomer that contains the active ingredient (an example here is the switch from Prilosec to Nexium, discussed at length *infra*). The FDA has approved enantiomer reformulations as either New Forms (e.g., Lexapro, which is an enantiomer of Celexa), or as a New Salt, New Ester, or other Non-covalent Derivative (e.g., Nexium, which is an enantiomer of Prilosec).<sup>73</sup>

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form in December 2004, which is two years after the tentative approval of the generic TriCor capsule. Abbott again discontinued the predecessor form, the first tablet. *Id.* at 416–17. Under the rules we apply in the dataset, the second TriCor tablet is not considered to be in the “Generic Window,” see *infra* tbl.3, because it was approved more than two years after the tentative approval for generic TriCor capsules. The second TriCor tablet, however, was approved only a few months before the generic approval for the first TriCor tablet, which occurred in March 2005. *Id.* at 417. The TriCor example demonstrates that the key question is whether the formulation change is within the Generic Window that threatens the brand manufacturer’s dominant brand form. In the case of TriCor, each formulation change would be suspect because each formulation change was undertaken within the Generic Window threatening the dominant predecessor formulation. Under our methodology, however, the second formulation change for TriCor was not considered to be within the Generic Window because it was approved more than three years after approval of the generic for the original TriCor formulation. Our methodology thus may understate the number of reformulations that are of antitrust concern.

70. For an explanation, see *infra* notes 71–73 and accompanying text.

71. Isomers are compounds that share the same molecular formula but have different structural formulas. PAUL B. KELTER, ET AL., CHEMISTRY, THE PRACTICAL SCIENCE 498 (2008).

72. “Chiral” molecules are molecules that are mirror images of one another, but that cannot be superimposed on one another (such as right and left hands). *Id.* at 525.

73. For enantiomers and new salts, we determined the appropriate predecessor drug by reviewing documents provided on the FDA website for the new drug. Where that information was insufficient, we reviewed information on the brand manufacturer’s website, including press releases or other information devoted to the new product.

New Salts. Some manufacturers make changes to molecules that are already on the market, which result in new esters, new salts, or other non-covalent derivatives (hereafter “new salts”).<sup>74</sup> Such alterations can occur, for example, by adding or removing chemical compounds that affect acids, bases, or other aspects of the molecule. For example, in 1995 the FDA approved Smithkline’s Coreg, the active ingredient of which is Carvedilol. Smithkline created a new salt of Carvedilol, Carvedilol Phosphate, which the FDA approved in 2006 as Coreg CR, an extended-release version of Coreg.

Combination Products. Manufacturers sometimes produce “combination” products that combine in one form two or more pharmaceutical compositions that previously were marketed separately. An example of this is Caduet, which is a combination of two Pfizer products, Norvasc and Lipitor.

In addition to categorizing the product changes by type, we also identified the product changes that were at least potentially made in response to imminent generic competition. For each product change, we cataloged the dates on which the FDA approved the reformulated product and gave tentative or final approval, if any, to the generic version of the original brand product. We paid special attention to those product changes in which the reformulated brand product was approved in the period of time from three years before FDA approval of the generic to one year after approval of the generic. We refer to this four-year span as the “Generic Window.”

We are interested in product reformulations accomplished three years or less before generic approval because the average time from the generic’s filing of an ANDA to FDA tentative approval is about eighteen months, and we included an additional eighteen months of leeway to account for those many instances in which the brand manufacturer can reasonably anticipate the filing of ANDAs before they are actually filed. We include a one-year period after FDA approval of the generic to account for those instances in which the brand manufacturer tried but failed to get FDA approval of the reformulated product before the generic was approved. For purposes of

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74. With one exception, we did not include in the database any products that the FDA characterized as a “New Molecular Entity” (“NME”). The one exception is Clarinex, which is a metabolite that the FDA approved as an NME. Clarinex’s active ingredient is Desloratadine, which is the metabolite created in the human body from ingestion of the prodrug Loratadine, which was sold under the brand name Claritin. Despite the FDA’s characterization of it as an NME, we think that the Claritin/Clarinex reformulation is the type of product change that merits inclusion in the dataset. The FDA approved at least one other metabolite during our study period—Soriatane (Acitretin), which is a metabolite of Tegison (Etretinate)—and characterized it as a new salt.

drawing tentative conclusions about the nature and order of magnitude of potential anticompetitive concerns raised by pharmaceutical reformulations, we hypothesize that reformulations made within the Generic Window were potentially part of a manufacturer's strategy to impair generic competition.

We emphasize that we have not used the dataset to determine whether any particular reformulation was in fact (or was not) part of a generic-impairment strategy. The dataset, in its current form, allows only very broad conclusions about the types and relative timing of reformulations that should be the subject of further, more detailed analysis.<sup>75</sup> It permits a rough "first cut" of the data that gives an overall view of the playing field.

Table 1 summarizes the results of our categorizations of the reformulations and whether they occurred within the Generic Window:

TABLE 1: TOTAL PRODUCT CHANGES			
	Within Generic Window*	Outside Generic Window**	Total
New Form***	53	267	320
Enantiomer	3	5	8
New Salt	4	16	20
Combo	21	56	77
<b>Total</b>	81	344	425
This table is calculated based on the Category column compared to the Generic Window Calculation column in the database. All calculations exclude the New Molecular Entity "NME" category. There are two Metabolite entries that are being included in the New Salt category for calculation purposes.			
* The calculation for "Within Generic Window" is based on the Generic Window Calculation equaling 3 years or less before generics and 0-1 years after generics and excludes any new reformulations undertaken by a manufacturer other than the manufacturer of the original form of the molecule or the new salt.			

75. In our second article, we will include data regarding actual generic entry dates; detailed sales data for the original product (brand and generic), the reformulated product, and other products in the therapeutic category; and data on promotion expenditures for the original and the reformulated brand product.

\*\* The calculation for "Outside Generic Window" includes all values excluding 3 years or less before generics and 0-1 years after generics. This calculation includes 69 products with No Generic Entry and 24 products with Potential Generic Entry. "Potential Generic Entry" is defined as products that could potentially fall within the generic window depending upon generic approval in the future and calculated based on a Brand Approval Date of April 2006 forward.

\*\*\* The New Form category calculation includes Cipro XR, which for purposes of calculating the Generic Window would be 1 or more years after generics, but it is being included within the Generic Window because while it was 4 years from tentative approval, it was 14 months before final approval of generic entry.

Note that of the total 425 product changes within the study period, only 81 occurred within the Generic Window. This should give comfort to those who worry that subjecting pharmaceutical product changes to antitrust scrutiny would unduly chill innovation. The vast majority of the product reformulations appear not to be even temporally linked to the manufacturer's concern about imminent generic competition.<sup>76</sup> Accordingly, a reasonable antitrust rule can avoid chilling the great majority of these innovations by simply targeting only those reformulations that are temporally linked to imminent generic entry.

Within the group of "new form" product changes, certain types of changes are likely to be of least therapeutic value to consumers and therefore of most antitrust concern. Table 2 below identifies changes from a capsule to another pill form (i.e., a tablet, OD tablet, or chewable tablet), or from a tablet to another pill form (i.e., a capsule, OD tablet, or chewable tablet). The data include five such reformulations, shown in "Group One" in Table 2, within the Generic Window.<sup>77</sup>

76. We again emphasize that this dataset and our methodology are designed only to produce generalizations about broad types of reformulations. It is quite possible that reformulations that are outside the Generic Window (as we have defined it for this broad analysis) were in fact part of an overall scheme to impair generic substitution.

77. We were surprised by the relatively small number of pill-to-pill switches within the Generic Window (5 within the Generic Window, and 35 outside the Generic Window). Investigation revealed several explanations. *First*, some of the switches outside the Generic Window appear to have been made for legitimate medical reasons. An example is the capsule-to-capsule switch from Invirase to Fortovase. In 1995, Hoffman LaRoche obtained approval for Invirase (Saqinavir Mesylate) as a treatment for HIV in a hard capsule formulation. *See* Invirase and Fortovase, AIDS Community Research Initiative of America, Fall 2003 / Winter 2004, <http://www.aegis.com/pubs/cra/2003/CR030911.html> (last visited May 18, 2010). In 1997, after significant clinical experience, Hoffman LaRoche introduced Fortovase (Saqinavir Mesylate) which has a higher dose than Invirase and has a soft gel capsule formulation that delivers more of the active ingredient. *Id.* Due to side effects from the higher

At the other end of the spectrum, shown in “Group Three,” are changes from a tablet or a capsule to a substantially different form or route of administration, such as an injectable or syrup. We think these reformulations are least likely to be part of a generic-impairment strategy, and are instead more likely to be legitimate efforts to round out a product line to encompass all specialty or “niche” uses for the product.

Lying between these extremes are form changes from a tablet or capsule to an extended-release capsule or tablet. These form changes permit consumers to take a pill only once a day rather than multiple times a day (or twice a day rather than three or more times a day). These reformulated products may be more convenient for consumers and may also provide a therapeutic benefit by improving the patient’s compliance with the drug regimen. But the brand manufacturer may strategically time the introduction of these extended-release products to impair generic competition. The data include twelve such reformulations, shown in “Group Two,” within the Generic Window.

TABLE 2: SELECTED “NEW FORM” PRODUCT CHANGES			
	Within Generic Window	Outside Generic Window	Total
<b>Group 1</b>			
Capsule to tablet or OD tablet/chewtab	2	16	18

dose, however, Fortovase has not been as successful as Invirase. *Id.* As of 2009, no generic has been approved for Saquinavir Mesylate.

*Second*, the majority of pill-to-pill reformulations outside the Generic Window occurred within four or five years after approval of the product’s original formulation. This raises the prospect that the switches were timed to coincide with the termination of the five-year New Chemical Entity exclusivity. *See* 21 U.S.C. § 355(c)(3)(E)(ii). Brand manufacturers can gain an additional period of practical exclusivity, beyond the NCE exclusivity, by launching a reformulated product at that time: knowing that the brand manufacturer may reformulate, a generic manufacturer may delay filing an ANDA in order to match the reformulated brand. Thus, these reformulations may well have been part of a subtle generic impairment strategy, but, under our methodology, they would not fall within the Generic Window.

All of this may be of mostly historic significance. Of the 40 pill-to-pill reformulations in our database, only five (Abilify, Altace, Aricept ODT, Risperdal, and TriCor) occurred after 2002. Increasing public scrutiny of medically insignificant reformulations may account for this substantial decrease in pill-to-pill changes.

Tablet to capsule or OD tablet/ chewtab	3	19	22
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<b>Group 2</b>			
Capsule to extended release capsule or tablet	3	3	6
Tablet to extended release tablet or capsule	9	21	30
<b>Group 3</b>			
Capsule to injectable or injectable IV	1	5	6
Tablet to injectable or injectable IV	3	7	10
Capsule to solution/suspension/syrup	5	13	18
Tablet to solution/suspension/syrup	3	27	30
Injectable to injectable	5	11	16
Injectable to non-injectable	4	17	21
Other or Unknown Forms *	16	102	118
<b>Total**</b>	54	241	295
<p>This table is calculated based on selecting New Form in the Category column, then New Form Product Changes by Category, and comparing to the Generic Window Calculation column in the database. Any new reformulations undertaken by a manufacturer other than the manufacturer of the original form of the molecule are excluded when calculating within the Generic Window.</p>			
<p>For purposes of this table, "Outside Generic Window" includes those products with no generic entry.</p>			
<p>* Other or Unknown Forms includes all other form changes not already represented in the table and 14 "unknown" form changes for which we were unable to determine the original form from the FDA data.</p>			
<p>** The Total of 295 products is different from the Total of 320 from the New Form Category in the <i>Total Product Changes Table</i> because (1) Lodine XL's form change is from Capsules and Tablets to Extended Release Tablet, and therefore is being counted twice under Group 2 above; (2) when calculating Within Generic Window, there are 7 products within the New Form category excluded due to different manufacturers for those products; (3) there are a total of 19 products that are classified as Potential Generic Entry, which are not included in the calculations of this table. "Potential Generic Entry" is defined by products that could potentially fall within the generic window depending upon generic approval in the future and calculated based on a Brand Approval Date of April 2009 forward.</p>			

The switching of a product to an extended-release version is most likely to be of antitrust concern when the switch is one in a series of product changes involving the same pharmaceutical composition. For example, the manufacturer may switch the product from a capsule, to a tablet, to a twice-daily tablet, and to a once-daily tablet. The heightened competitive concern is that, to the extent the once-daily version of the product truly provides a benefit in customer convenience or even therapeutic effect, the manufacturer may be intentionally delaying the introduction of the once-daily version as part of a long-term strategy to impair generic competition by employing as many product changes as possible.<sup>78</sup>

Table 3 below collects each pharmaceutical composition for which the manufacturer made more than two product changes during the study period, with at least one of the changes within a Generic Window. We have screened out those instances that appear to be legitimate efforts to round out a product line (e.g., switches from a tablet to an injectable or a solution), leaving only those instances that are potentially efforts to switch the entire market from, say, a tablet, to a capsule, then to an extended release capsule. The products listed in “Group One” include at least one switch to an extended release product, while those listed in “Group Two” do not. The data show that a significant portion of suspect multiple-product switches include at least one switch to an extended-release product, raising the possibility that the

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78. See, e.g., Maribel Rios, *The Outsourcing Advantages in Formulation Development*, PHARM. TECH. 38, 40 (Jan. 2005) (“In some cases . . . innovator companies will go to market with a new drug in a three-times-a-day formulation, intentionally holding back a twice- or once-a-day formulation to use against generic competition later on.”). The same concern also can arise with other types of product changes. For example, Cephalon, Inc., the maker of the wakefulness-promoting drug Provigil, was preparing to launch a reformulated version of the drug, Nuvigil, in 2005. Cephalon claims that Nuvigil is superior to Provigil in that it provides a longer duration of effect. In late 2005, however, Cephalon was able to thwart the then-impending entry of generic Provigil by paying the generic manufacturers to withdraw their challenges to the Provigil patent, with the generics agreeing not to enter until 2012. Press Release, FTC, *FTC Sues Cephalon, Inc. for Unlawfully Blocking Sale of Lower-Cost Generic Versions of Branded Drug Until 2012* (Feb. 13, 2008), available at <http://www.ftc.gov/opa/2008/02/ceph.shtm>. So Cephalon delayed the launch of Nuvigil until 2009, telling investors that it would switch almost all of the market from Provigil to Nuvigil before the generics entered in 2012: “if we do our job right . . . the PROVIGIL number in 2012 that will be genericized will be very, very small. So we do not expect a big business to be lost by that generic erosion at that time.” Cephalon, Inc., Q4 2008 Earnings Call Transcript, available at <http://seekingalpha.com/article/120423-cephalon-inc-94-2008-earnings-call-transcript?page=-1>. Cephalon’s “objective number one” is “to make PROVIGIL as small as we possibly can.” *Id.* In that pursuit, Cephalon Executive Vice President Bob Roche stated that “my team has some tremendously creative, and I believe effective plans to ensure that just that happens.” *Id.*

technology was available earlier in the product life-cycle but the manufacturer intentionally withheld it from the market as part of a generic-impairment strategy.

TABLE 3: PRODUCTS WITH MULTIPLE SWITCHES				
Product	Total Switches	Switches Within Generic Window	Switches Outside Generic Window	Extended Release Reformulations
<b>Group 1</b>				
Amoxicillin / Amoxicillin; Clavulanate Potassium (Amoxil (3) and Augmentin (5))	8	2	6	1
Azithromycin / Azithromycin Dihydrate, Trovafloxacin Mesylate (Zithromax)	8	1	7	1
Bupropion Hydrochloride (Wellbutrin, Zyban)	3	1	2	3
Desloratadine / Loratadine (Claritin/Clarinet)	9	1	8	3
Fexofenadine Hydrochloride / Fexofenadine Hydrochloride; Pseudoephedrine Hydrochloride (Allegra)	5	1	4	1
Levetiracetam (Keppra)	3	2	1	1
<b>Group 2</b>				
Abacavir Sulfate / Lamivudine (Epivir/Combivir, Epzicom, Trizivir, Ziagen) (Epivir Family)	6	1	5	0
Amlodipine Besylate (Norvasc)	5	3	2	0
Brimonidine Tartrate / Brimonidine Tartrate; Timolol Maleate (Alphagan)	4	1	3	0
Budesonide / Budesonide; Formoterol Fumarate Dihydrate (Rhinocort, Pulmicort, Symbicort)	5	1	4	0

Citalopram Hydrobromide / Escitalopram Oxalate (Celexa/Lexapro)	3	1	2	0
Esomeprazole Sodium / Esomeprazole Magnesium /Omeprazole Magnesium (Nexium/Prilosec)	4	3	1	0
Fenofibrate / Choline Fenofibrate (TriCor/Trilipix)	3	1	2	0
Fluticasone Furoate / Fluticasone Propionate (Flovent, Flonase, Advair)	7	2	5	0
Leuprolide Acetate (Lupron)	3	3	0	0
Risperidone (Risperdal)	3	1	2	0
Sumatriptan / Sumatriptan Succinate / Sumatriptan Succinate; Naproxen Sodium (Imitrex, Treximet)	3	1	2	0
Terbinafine Hydrochloride (Lamisil)	4	1	3	0
<b>Total</b>	86	27	59	10
This table is calculated by searching the database by the Active Ingredient(s) column, then excluding any non-applicable Brand Names, then reviewing the Generic Window Calculation.				
For purposes of this table, "Outside Generic Window" includes those products with no generic entry.				

The next type of reformulation involves a change to the chemical composition itself, i.e., enantiomers, metabolites, and new salts. As shown in Table 1 above, seven such reformulations were made during the Generic Window. Of course, these changes could theoretically have brought real benefits for consumers, either in improved therapeutic efficacy or reduced side effects, etc. In order to see whether these changes might be of antitrust concern, we searched for any reliable studies that had questioned whether the reformulated product had in fact yielded such consumer benefits. As summarized in Table 4 below, we found such studies for five of the seven chemical changes within the Generic Window. In every instance, we also found studies asserting that the reformulated product does deliver consumer benefits. Our purpose is not to resolve these factual disputes, but only to identify those reformulations that may warrant antitrust scrutiny.

TABLE 4: CHEMICAL CHANGES		
Reformulated (Original) Product	Studies Questioning Benefits	Source
Clarinox (Claritin)	Clarinox is “probably not superior to Claritin”	European Agency for the Evaluation of Medical Products*
Coreg CR (Coreg)	No greater compliance with extended release; worse side effects in elderly patients	Manufacturer-sponsored double-blind study**
Kapidex (Prevacid)	Kapidex does “not have a significant, clinically meaningful therapeutic advantage in terms of effectiveness, safety, and clinical outcomes”	Tricare***
Lexapro (Celexa)	Manufacturer did not disclose negative clinical trial results	U.S. Department of Justice****
Nexium (Prilosec)	Doctors “should be embarrassed if you prescribe Nexium,” and “Nexium is a game that is being played on the people who pay for drugs.”	Administrator, Center for Medicare & Medicaid Services*****
Nimbex (Tracrium)	N/A	N/A
Valtrex (twice daily) (Zovinox - 5 times daily)	N/A	N/A
<p>*See Maryann Napoli, <i>Clarinox: The Latest Overpriced, Knock-Off Allergy Drug</i>, Healthfacts, May 2002, available at, <a href="http://findarticles.com/p/articles/mi_m0815/is_2002_May/ai_85500239/">http://findarticles.com/p/articles/mi_m0815/is_2002_May/ai_85500239/</a>. The dean of the University of Arizona College of Medicine called the manufacturer’s claims of superiority “hocus-pocus.” See Rita Rubin, <i>Claritin to go OTC Next Spring, Clarinox to Replace It</i>, USA Today, Apr. 22, 2002 available at, <a href="http://www.usatoday.com/news/health/drugs/2002-04-23-claritin.htm">http://www.usatoday.com/news/health/drugs/2002-04-23-claritin.htm</a></p>		
<p>**Study No. CCS-2005-001, Results of A Multicenter, Randomized, Double Blind, Double Dummy, Parallel Group Study to Compare Effects of Coreg CR and Coreg IR on Left Ventricular End Systolic Volume Index in Subjects with Stable Chronic Heart Failure (The COMPARE Trial) (10/7/08)</p>		
<p>***Study available at, <a href="http://www.tricare.mil/pharmacy/BAP/30%20July%202009%20BAP%20Background%20Information%20final.pdf">http://www.tricare.mil/pharmacy/BAP/30%20July%202009%20BAP%20Background%20Information%20final.pdf</a></p>		

\*\*\*\*See Barry Meier & Benedict Carey, *Drug Maker Is Accused of Fraud*, NY Times, Feb. 25, 2009 at B1. Although the alleged fraud does not relate directly to comparative studies of Celexa and Lexapro, the general allegation that the manufacturer has withheld adverse studies has prompted us to include Lexapro on the list of drugs that may warrant further inquiry.

\*\*\*\*\*Robert Pear, *U.S. Limiting Costs of Drugs For Medicine*, N.Y. Times, Apr. 21, 2003 at A1; *see also* AstraZeneca Clinical Trial studies nos. 172 and 174 (studies comparing equal doses of Prilosec and Nexium showed no superiority for Nexium).

The last type of reformulation is a “combination” product. Combination products can be welfare enhancing by assuring that patients take the proper dosages of complementary products and simplifying patients’ pill-taking routines. When one or more of the complementary products faces imminent generic competition, however, the reformulation can raise consumers’ cost of the combination as compared to the cost of the separate brand product and the entering generic. If the combination product is launched before the generic enters, doctors are likely to focus on the convenience benefits and to not even be aware that a generic of one of the complementary products is in the offing. As we show in detail below,<sup>79</sup> even after generic entry doctors who have become accustomed to prescribing the combination product are unlikely to switch back to prescribing the complementary products separately in order to take advantage of the newly available lower prices. And, of course, the price disconnect works against doctors taking account of the price effects of their prescribing choice in any event.

We will address the economics of combination products in more detail in our second article. Those economics may vary depending on whether the combined products are both still patent-protected when they are combined, or whether one is on-patent and the other a generic.<sup>80</sup> Table 5A below shows the number of combinations that were launched within the Generic Window, categorizing them by whether they were brand+brand or brand+generic (as well as a few other varieties) and by their approval dates. The data show that the majority of combinations fuse a brand and generic. Table 5B below

79. *See infra* Part III.

80. For example, the fusing of two brand products suggests positive value of the brand name of the product facing the generic entry: doctors and consumers have knowledge and familiarity with the entry-facing brand product. Unlike a brand+brand combination, a generic+brand combination cannot be promoted as a combination of the two brand products. In addition, the combination of two brand products can bring to bear the promotional and detailing specializations of two brand manufacturers.

shows the products that were the most frequently combined with other products to make combinations during the period.

<b>TABLE 5A: COMBINATION PRODUCTS</b>			
<b>Type of Combination</b>	<b>1995 - 2002</b>	<b>2003 - Apr. 2009</b>	<b>Total</b>
Brand/Brand	13	11	24
Brand/Generic	24	18	42
Brand/New	2	2	4
Generic/Generic	0	1	1
Generic/New	2	1	3
New/New	2	1	3
<b>Total</b>	<b>43</b>	<b>34</b>	<b>77</b>
This table is calculated by identifying the Reformulation Approval Date for products in the Combination Category.			
A Brand/Brand combination is one that combines two or more brand products.			
A Brand/Generic combination is one that combines at least one brand product and one generic product.			
The Generic/Generic is a combination of two generic drugs.			
The "New" combinations are either Brand, Generic, or New drugs that are combined with another active ingredient that had not been marketed separately previously.			

<b>TABLE 5B: COMBINATION PRODUCTS</b>			
<b>Most Popular Partners</b>	<b>1995 - 2002</b>	<b>2003 - Apr. 2009</b>	<b>Total</b>
Glucophage	3	3	6
Hydrochlorothiazide	8	4	12
Norvasc	1	3	4
<b>Total</b>	<b>12</b>	<b>10</b>	<b>22</b>

This overview of the dataset reveals four clearly identifiable types of product changes that are most likely to be of antitrust concern. These include product changes, within the Generic Window, involving a form change from a capsule to a tablet/OD tablet/chewtab; a form change from a tablet to a capsule/OD tablet/chewtab; chemical changes with questionable consumer benefits; and multiple switches. As listed below in Table 6, these four categories account for only 32 of the total 425 product changes in the database; the great majority of product changes are outside the Generic

Window or otherwise unlikely to be of great antitrust concern. Consequently, a reasonable antitrust rule is very unlikely to chill innovation with respect to this large group of products.

But the comfort drawn from that observation necessarily raises the converse issue: Is the number of product changes of potential antitrust concern so small that the issue is really of no significant public importance? Table 6 answers that question. For each product in one of the four categories of potential concern, we collected data regarding the annual sales of the original branded product in the year before the FDA approved the reformulated product. We also determined whether the manufacturer claimed some form of exclusivity (whether based in patent law or FDA regulations) for the reformulated product. A claim of exclusivity would protect the relevant sales from generic competition for multiple years, ranging from thirty months of exclusivity under the Hatch-Waxman Act stay provisions, to three years for a claim of certain FDA exclusivities, to ten years or more of exclusivity for the successful assertion of patent rights.

<b>TABLE 6: ANNUAL SALES BEFORE REFORMULATION (SELECTED PRODUCTS WITHIN GENERIC WINDOW)</b>					
<b>Product</b>	<b>New Dosage Form/ Strength</b>	<b>Original Form/ Strength</b>	<b>Approval Date (of Reform- ulation)</b>	<b>Annual Sales (for Original Brand Year Before Reformulation Approval Date)</b>	<b>Exclusivity</b>
<b>Type of Change:</b> Capsule to tablet or OD tablet/ chewtab					
Prozac	10, 20 mg Tablet	10, 20, 40, 60 mg Capsule	3/9/1999	\$1,942,001,000	No
TriCor	54, 160 mg Tablet	67, 134, 200 mg Capsule	9/4/2001	\$158,741,000	Yes
<b>Type of Change:</b> Tablet to capsule or OD tablet/ chewtab					
Buspar	5, 7.5, 10, 15 mg Capsule	5, 10, 15, 30 mg Tablet	12/20/2000	\$231,416,000	Yes
Pepcid RPD	20, 40 mg Tablet Orally Disintegrating	20, 40 mg Tablets	5/28/1998	Not Available	Yes
Remeron Soltab	15, 30, 45 mg Tablet Orally Disintegrating	Remeron Regular 15, 30, 45 mg Tablets	1/12/2001	\$266,707,000	Yes

Type of Change: Chemical Changes					
Clarinet	5 mg Tablet	Claritin	12/21/2001	\$1,667,347,000	Yes
Coreg CR	10, 20, 40, 80 mg Capsule	Coreg 3.125, 6.25, 12.5, 25 mg Tablet	10/20/2006	\$846,802,000	Yes
Kapidex	30, 60 mg Capsule Delayed Release	Prevacid	1/30/2009	\$3,295,465,000	Yes
Lexapro	5, 10, 20 mg Tablet	Celexa 10, 20, 40, 60 mg Tablet	8/14/2002	\$1,139,686,000	Yes
Nexium / Nexium IV	20, 40 mg Capsule Delayed Release; 20, 40 mg Injectable	Prilosec	2/20/2001	\$4,102,195,000	Yes
Nimbex	2, 10 mg injectable	Tracrium Preservative Free 10 mg Injectable	12/15/1995	Not Available	Yes
Valtrex	500 mg, 1gm Tablet	Zovirax Injectable and other forms	6/23/1995	Not Available	Yes
Type of Change: Multiple Switches					
Advair HFA	Aerosol Metered inhalation: 0.045mg/inh;EQ 0.021mg base; 0.115mg/inh;EQ 0.021mg base/inh; 0.23mg/inh;EQ 0.021mg; base/inh	Advair Diskus	6/8/2006	\$2,830,047,000	Yes
Allegra D 24 Hour	180, 240 mg Tablet Extended Release	Allegra 60 mg Capsule	10/19/2004	\$1,449,846,000	Yes
Alphagan P	.15% Solution	Alphagan .2% Solution	3/16/2001	\$159,631,000	Yes

Augmentin ES 600	Powder Oral Suspension 600MG/5ML; EQ 42.9MG BASE/5ML	Augmentin 500, 500 mg; EQ 125mg base	6/22/2001	\$1,584,397,000	No
Augmentin XR <sup>(1)</sup>	Extended Release Tablet 1gm; EQ 62.5mg base	Augmentin 500, 500 mg; EQ 125mg base	9/25/2002	Excluded	No
Azor <sup>(2)</sup>	5/20, 5/40, 10/20, 10/40 mg Tablet	Norvasc and Benicar	9/26/2007	\$312,791,000	Yes
Caduet <sup>(3)</sup>	5/10, 5/20, 5/40, 5/80, 10/10, 10/20, 10/40, 10/80, 2.5/10, 2.5/20, 2.540 mg Tablet	Norvasc and Lipitor	1/30/2004	\$1,820,452,000	Yes
Epzicom <sup>(4)</sup>	Tablet EQ 600mg base;300mg	Epivir and Ziagen	8/2/2004	\$225,776,000	Yes
Exforge <sup>(5)</sup>	5/160, 10/160, 5/320, 10/320 mg Tablet	Norvasc and Diovan	6/20/2007	\$972,055,000	Yes
Flovent HFA <sup>(6)</sup>	Aerosol Metered inhalation 0.22mg/inh, 0.11mg/inh, 0.44mg/inh	Cutivate ointment	5/14/2004	Not available	Yes
Keppra	500 mg Injectable/IV	Keppra Tablet, 250, 500, 750 mg	7/31/2006	\$379,564,000	Yes
Keppra XR <sup>(7)</sup>	500, 750 mg Tablet, Extended Release	Keppra Tablet, 250, 500, 750 mg	9/12/2008	Excluded	Yes
Lamisil <sup>(8)</sup>	Oral Granule EQ 125mg base/packet And EQ 187.5mg base/packet	1% Cream	9/28/2007	Not available	No

Lupron Depot / Lupron Depot 3 / Lupron Depot 4	Injectable 22.5mg /vial; Injectable 11.25mg/vial; Injectable 30mg/vial	Lupron injectable 4/9/85	12/22/1995 3/7/1997 5/30/1997	Not available	Yes
Nexium	20, 40 mg Suspension Delayed Release	Nexium 20, 40 mg Capsule Delayed Release	3/31/2005	\$2,963,518,000	No
Risperdal Consta	12.5, 25, 37.5, 50 mg Injectable, Intramuscular	Risperdal Tablet 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg	10/29/2003	\$1,343,318,000	Yes
Symbicort <sup>(9)</sup>	Metered inhalation Spray 0.08mg/inh;0.04 5mg/inh And 0.16mg/inh;0.04 5mg/inh	Rhinocort & Formoterol Fumarate Dihydrate	7/21/2006	Excluded	Yes
Treximet <sup>(10)</sup>	Tablet 500mg;EQ 85mg base	Imitrex and Naproxen Sodium	4/15/2008	Not available	Yes
Zmax <sup>(11)</sup>	Oral Suspension Extended Release 2gm/Bottle	Zithromax 250 mg Capsule	6/10/2005	\$330,200,000	No
Zyban <sup>(12)</sup>	Extended Release Tablet, 100 mg, 150 mg	Wellbutrin 50, 75, 100 mg tablets	5/14/1997	\$102,000,000	Yes
<b>Total</b>				<b>\$28,123,955,000</b>	
This table is calculated by selecting the appropriate Category and New Form Product Changes by Category or Products with Multiple Switches columns in the database, excluding any products due to different manufacturers, then reviewing the Generic Window Calculation.					

The Annual Sales Data for this table comes from The Top 200 Brand-Name Drugs by Retail Sales reports issued annually. The reports available from 1994 - 1997 did not list sales data. The sales data available from 1998 contains only the Top 20 Leading Prescriptions by Dollar Sales - Through All Channels as published in the 1998 Annual Report of Retail Pharmacies, Chain Drug Review (Aug. 31, 1998). The Annual Sales Data is calculated based on the Original Form of the reformulated product the year prior to the Approval Date of Reformulation.

Exclusivities include New Drug Form, New Combinations, New Chemical Entity, New Product, and any patents listed specific to the new formulation. New Indications, Miscellaneous Exclusivities (relating to information in the label), and the addition of Pediatric Exclusivity associated with patents are excluded.

Among the products listed under Multiple Switches, there are 6 Combination products, including Azor, Caduet, Epzicom, Exforge, Symbicort, and Treximet.

(1). Augmentin sales are counted under Augmentin ES 600.

(2). The 2006 sales data includes \$312,791,000 for Benicar, but excludes Norvasc sales because Norvasc is counted under Caduet.

(3). The 2003 sales data includes \$1,820,452,000 for Norvasc. Lipitor sales are not included because there is no generic approval for Lipitor.

(4). The 2003 sales data is for Epivir. Ziagen is not listed on the Top 200 Brand-Name Drugs by Retail Dollars in 2003.

(5). The 2006 sales data includes \$972,055,000 for Diovan. Norvasc sales are counted under Caduet.

(6). Cutivate is not listed in the Top 200 Brand-Name Drugs by Retail Dollars in 2003. Flonase, the immediate predecessor reformulation, had sales of \$889,893,000 in 2003, but it is excluded because it is not the original form of the product.

(7). Keppra sales are counted under the Keppra injectable formulation.

(8). Lamisil is not listed in the Top 200 Brand-Name Drugs by Retail Dollars in 2006. Lamisil Oral had 2006 sales of \$613,006,000, but it is excluded because it is not the original form of the product.

(9). Rhinocort is not listed in the Top 200 Brand-Name Drugs by Retail Dollars in 2005. Rhinocort Aqua had 2005 sales data of \$296,463,000, but it is excluded because it is not the original form of the product. The original formulation, Rhinocort aerosol, was not on the market in 2005; to be conservative, sales of its successor are not included.

(10). Imitrex is not listed in the Top 200 Brand-Name Drugs by Retail Dollars in 2007. Imitrex Oral had 2007 sales of \$950,585,000, but it is excluded because it is not the original form of the product.

(11). The 2004 sales data includes \$330,200,000 for Zithromax. It is not clear whether this is for the capsule or tablet form of Zithromax. Also listed on The Top 200 Brand-Name Drugs by Retail Dollars in 2004 are Zithromax Z-pak with \$1,070,535,000 annual sales and Zithromax Suspension with \$289,444,000 annual sales, which are excluded because they are not the original form of the product.

(12). The 1996 sales data includes \$102,000,000 for Wellbutrin. *See* Intelligent Polymers Limited, Registration Statement (Form F-1), at 28 (Sept. 17, 1997).

The total annual pre-generic sales for these products for which we currently have data was \$28.1 billion. Given that unimpaired generic competition typically garners 85% of unit sales at price discounts of 80% or more,<sup>81</sup> impairing generic competition on more than \$28 billion in commerce is clearly a matter of public concern.<sup>82</sup>

There are also seven pill-to-extended-release pill reformulations and fifteen combination reformulations that were not otherwise included in the four most-suspect categories. We have pre-generic approval annual sales data for fourteen of these twenty-two reformulations, totaling \$15.8 billion. Combined, these categories and the four most suspect categories account for more than \$43.9 billion in brand sales that may be inefficiently shielded from generic competition.

Finally, as noted in the introduction and explored in detail in Section IV below, one court has suggested that the only product changes of antitrust concern are those in which the manufacturer switched products and then also entirely withdrew the original product from the market. Table 7 includes sales data for those reformulations for which the manufacturer discontinued the original formulation within three years prior to or two years after actual market entry by the generic.

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81. *See supra* note 47.

82. We have not tried to calculate the actual lost consumer welfare, because each individual reformulation scheme succeeded in impairing generic competition to a different degree. For example, the attempted switch from Remeron tablets to OD tablets was a flop, and the switch from Claritin to Clarinex was only partially successful. In many other cases, the reformulation scheme was highly effective in impairing generic competition. Whatever the specifics of individual reformulations, it is clear that, overall, a significant amount of commerce is being affected by these reformulations.

**TABLE 7 - WITHDRAWN PRODUCTS  
(SELECTED PRODUCTS WITHIN GENERIC WINDOW)**

<b>Product</b>	<b>New Dosage Form/Strength</b>	<b>Original Form/Strength Discontinued</b>	<b>Approval Date (of Reformulation)</b>	<b>Annual Sales (Year Before Reformulation Approval Date)</b>	<b>Actual Generic Entry Date*</b>	<b>Discontinued Date for Original Formulation</b>
TriCor	54, 160 mg Tablet	67, 134, 200 mg Capsule	9/4/2001	\$158,741,000	2/26/2002	Mar-03
Versed <sup>(1)</sup>	2 mg Syrup	1, 5 mg Injectable	10/15/1998	\$1,335,600,000	6/22/2000	May-02
Zmax <sup>(2)</sup>	Oral Suspension Extended Release 2gm/Bottle	Zithroma x 250 mg Capsule	6/10/2005	\$330,200,000	11/14/2005	Mar-04
<b>Total</b>				<b>\$1,824,541,000</b>		
The Annual Sales Data for TriCor and Zmax for this table comes from The Top 200 Brand-Name Drugs by Retail Sales report issued annually.						
Included in this chart are those reformulations for which there was generic approval within the generic window, there was actual generic entry for the original form and the original form was discontinued. The "discontinued date" was the date the FDA listed as the date of discontinuance. It is likely that the last date of sale by the manufacturer occurred some time prior to the date the FDA listed. The relevant comparison of the date of discontinuance is to the date of actual generic entry. We define the window in this circumstance as being discontinuance three years prior and two years after actual generic entry. We chose two years after generic entry to account for the period in which the distribution pipeline is depleted after the manufacturer's last date of sale.						
* "Actual Generic Entry Date" was obtained from First Data Bank.						
(1). This number represents global Versed sales in 1999 reported by Roche in its annual report as 840,000,000 Swiss Francs, based upon a conversion rate of 1 Swiss Franc per 1.59 U.S. dollars (a rate reported for exchange on January 1, 2000 on www.xe.com). See 1999 Roche Annual Report, at 17.						
(2). The 2004 sales data reflects \$330,200,000 for Zithromax. It is not clear whether this is for the capsule or tablet form of Zithromax. Also listed on The Top 200 Brand-Name Drugs by Retail Dollars in 2004 are Zithromax Z-pak with \$1,070,535,000 annual sales and Zithromax Suspension with \$289,444,000 annual sales, which are not included in the calculation for this table.						

These reformulations-plus-withdrawals involve pre-generic annual sales of only \$1.8 billion, about 6% of the sales of the products identified in Table 6 above.<sup>83</sup> The data thus show that this exceedingly narrow category of reformulation-plus-withdrawal represents only a small fraction of the reformulations that are likely of significant competitive concern. An antitrust rule that limited liability to this very narrow category of changes would need an especially strong rationale to support the many false negatives that it would yield.

### III. THE MECHANICS OF EXCLUSION

The welfare effect of a product reformulation depends on two basic factors: (1) the number of prescriptions that the incumbent switches from the original product to the new; and (2) the change in value to consumers of the new product relative to the original. In this Article we address the first of these factors and assume, for purposes of the analysis in this section, that the original and new formulations are of roughly equal value to consumers.<sup>84</sup>

Given that generic versions of the original product are priced substantially below the original brand product, more switching of prescriptions from the original product to the new results (other things equal) in greater welfare loss. Brand manufacturers employ several tactics to increase the number of prescriptions switched from the original product to the new, and thereby increase their profits at the expense of consumer welfare.

The most basic tactic is for the brand manufacturer to cause the sales force to stop detailing the original product, discourage doctors from writing prescriptions for it, and start writing them for the new product. The manufacturer switches the market from the original product to the new by using the customer lists, marketing know-how, and product expertise that it built up through years of detailing the original. Brand manufacturers often refer to this tactic of detailing against their own products as “cannibalizing,” and we will also use that term. Even when the generic version of the original

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83. Our focus on product discontinuations was limited to situations in which the original product was completely discontinued, as opposed to situations in which only one or a few of the original doses were discontinued. Additionally, we excluded from consideration situations in which the original manufacturer discontinued the product and a new formulation was later marketed by a different manufacturer.

84. Our forthcoming second article will address how to weigh any decreases or increases in value of the new product against the adverse price effects of impairing generic competition.

product is available on the market, cannibalizing can result in substantial switching to the new product because the generic firms lack the incentive to have—and therefore do not maintain—sales forces, and doctors are relatively insensitive to the substantially lower prices offered by the generics.

Another tactic is for the brand manufacturer to start the cannibalizing before the generic is even available on the market. Manufacturers often accomplish the switch twelve to eighteen months before the generic version of the original product is expected to enter. Price competition between the reformulated product and the generic original product, which is muted by the price disconnect even when a generic is available, is nearly completely eliminated by this tactic. Detailers encourage doctors to prescribe the new product rather than the original, and the doctors have no price reason whatever to decline to switch—the low-price generic is not yet available in the market.

This pre-generic entry tactic can be even more effective if the brand manufacturer not only cannibalizes sales from the original brand product but stops selling it altogether. By withdrawing the original brand product from the market before the generic becomes available, the manufacturer requires doctors who want to continue prescribing that particular chemical entity to prescribe the new brand product. They cannot prescribe the original product, and have the prescriptions filled, until the generic enters.

We discuss each of these tactics below, giving a detailed description and an example of its use in one of the many product reformulations in recent years.

#### *A. Product Cannibalizing*

Mechanics: The basic tactic that brand manufacturers use in order to influence doctors to switch prescriptions to the new product is a change in the use of their sales forces and other advertising. Brand manufacturers that are reformulating in order to impair generic competition typically instruct their detailers to stop encouraging doctors to write prescriptions for the original product and to instead write them for the new product. Sometimes the new marketing extols the virtues of the new product while remaining silent about the original; other times the marketing compares the new product favorably to the original or even makes negative references to the original. The brand manufacturers also stop all other promotion of the original

product—such as medical journal ads and direct-to-consumer advertising—and focus all of their sales efforts on the new product.<sup>85</sup>

When the brand manufacturer stops detailing and promoting the original product, no competitor has both the incentive and ability to do so; doctors receive an entirely one-sided presentation as to the comparative qualities of the original and new products. Manufacturers of other brand products in the therapeutic category have sales forces but no incentive to promote a generic competitor's product. Manufacturers of generic versions of the original product cannot detail it because they typically do not have large sales forces and, in any event, have insufficient incentive because other manufacturers could free-ride on their sales efforts.<sup>86</sup>

Markets can work only when the consumer makes an informed choice among products, weighing both price and quality. The brand manufacturer's tactic of switching its promotional efforts from the original to the new formulation has significant consequences for consumer welfare. Detailing is the single most effective means of providing doctors with information as to the comparative quality of pharmaceuticals,<sup>87</sup> and brand manufacturers typically spend large proportions of their enormous marketing budgets on detailing and other promotion to doctors.<sup>88</sup> Cannibalizing eliminates the most

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85. See, e.g., Hong et al., *supra* note 32, at 753 (“In this market environment, the owner of the brand is able to shift demand from the original brand to the line extension by promotion of the line-extension brand to physicians, including the use of product sampling to physicians.”); Huskamp, *supra* note 32, at 612 (“[M]anufacturers have an incentive to shift demand for the original formulation of a brand drug that will soon lose patent protection onto a reformulation of the drug.”); Morton, *supra* note 32, at 1088 (“[A]dvertising is the instrument with which innovator firms can create switching costs and move future demand from the generic to the branded product.”); Andrew Parece et al., *Your Patent is About to Expire: What Now?*, PharmExec.com (Nov. 1, 2004) (describing reformulation as “[t]ransferring brand equity (and prescriptions) to a follow-on product”), available at <http://pharmexec.findpharma.com/pharmexec/article/articleDetail.jsp?id=136706>.

86. See *supra* notes 48–50 and accompanying text; see also John Lucas & Paul Burgess, *When Form Equals Substance: The Value of Form Screening and Product Life-Cycle Management*, PHARMAVOICE 54, 56–57 (Feb. 2004) (Reformulation destroys substitutability and “[c]ompetitors must therefore rely on their own marketing and salesforce to successfully market their alternative drug form.”); Richard Daly & Mick Kolassa, *Start Earlier, Sell More, Sell Longer*, in PHARM. EXEC. SUPP. HANDBOOK 18 (March 2004) (“Cannibalization is best if it’s kept in the family[;] a company can compete against itself and win.”).

87. See *supra* note 36.

88. See, e.g., Julie M. Donohue et al., *Effects of Pharmaceutical Promotion on Adherence to the Treatment Guidelines for Depression*, 42 MED. CARE 1176, 1181 (2004) (“The bulk of antidepressant promotional spending has been aimed at physician detailing.”); Hurwitz, *supra* note 32, at 302 (“For many research-based firms the promotion budget can be twice to four times as large as the budget for research and development, with sales promotion

important source of doctor information on an essential dimension of competition—the doctor’s quality comparison between the original and reformulated products.

This near-elimination of the quality dimension of competition takes on added importance because it occurs in a context in which the other dimension of competition – price – is already muted. This is seen most clearly by recalling the state of competition when there is generic competition without a reformulation of the branded product. Absent a reformulation, generic entry elicits fair competition in both the price and quality dimensions. As noted in detail above, generic competition reconnects the consumption decision and the payment obligation – the consumer, rather than her price-insensitive doctor, decides whether to consume the brand rather than the generic product. Consequently, price competition is restored. As to the quality comparison, FDA regulations mandate that the generic product be bioequivalent and therapeutically equivalent to the branded product, so there is a regulatory guarantee of equal quality as between the original brand product and its generic equivalents.

The brand manufacturer’s introduction of a reformulated product alters this competitive state. If the brand firm continues to detail both the original and new products with equal vigor, competition in the quality dimension is maintained. But the reformulation of the product mutes price competition. If the doctor writes the prescription for the new product, it faces no price competition from the generic. In deciding whether to prescribe the original or the new product, the doctor may be aware that a low-cost generic is available for the original product, but, as noted in detail above, doctors are notoriously price-insensitive. This context illuminates the effect of the brand manufacturer’s cannibalizing. With price competition already muted by the introduction of the reformulated product, cannibalizing now exacerbates the

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running 20 to 30 percent of sales.”); *id.* (“Almost 70 percent of the pharmaceutical industry’s promotional budget is spent on personal promotion, known as ‘detailing.’”); Huskamp, *supra* note 32, at 605 (“almost 60% of the combined promotional expenditures are aimed at physicians”); Morton, *supra* note 32, at 1087 (“[I]nnovator pharmaceutical firms do a great deal of advertising which is primarily directed at the physicians who decide which drugs a patient will use.”); *id.* at 1088 (“Pharmaceutical firms spend as much on promotion of brands (much of it directed at physicians) as on R&D.”); *Prescription Drugs and Mass Media Advertising*, NAT’L INST. FOR HEALTH CARE MGMT 5 (Sept. 2000), available at <http://nihcm.org/~nihcmor/pdf/DTCbrief.pdf> (in 1999, brand manufacturers spent 83% of their marketing budgets on detailing and free samples); Brennan, *supra*, note 37, at 430 (“Approximately 90% of the \$21 billion marketing budget of the pharmaceutical industry continues to be directed at physicians, despite a dramatic increase in direct-to-consumer advertising.”).

-muted price competition by almost entirely eliminating quality competition between the original and reformulated products.

Table 8 below summarizes the effect on price competition and quality comparisons in the various scenarios. The scenarios we have addressed thus far are depicted in Row 1 (generic competition without a product reformulation); Row 2 (generic competition with equal detailing of the original and new products); and Row 3 (generic competition with cannibalizing).

TABLE 8: EFFECTS ON PRICE AND QUALITY COMPETITION		
	Price Competition	Quality Comparison
1. No Reformulation	Yes	Yes
2. Generic Available/Equal Detailing	Muted	Yes
3. Generic Available/Cannibalizing	Muted	Nearly Eliminated
4. Generic Not Available/Cannibalizing	Nearly Eliminated	Nearly Eliminated
5. Generic Not Available/Product Withdrawn	Nearly Eliminated	Eliminated/Nearly Eliminated

**Example of Cannibalizing:** Cannibalizing, and the importance of the timing of the cannibalizing, are shown in the launches of GlaxoSmithKline's ("GSK") Wellbutrin products and King Pharmaceutical's ("King") Altace.

GSK's predecessor, Burroughs-Wellcome, first marketed Wellbutrin in December 1985 as the first NDRI (norepinephrine/dopamine reuptake inhibitor) anti-depressive.<sup>89</sup> GSK initially marketed the product in an immediate-release version, Wellbutrin IR, which was taken 3-4 times daily.<sup>90</sup>

89. See Daniel M. Perrine et al., *A Short, One-Pot Synthesis of Bupropion (Zyban, Wellbutrin)*, 77 J. CHEMICAL EDUC. 1479 (2000), available at <http://jchemed.chem.wisc.edu/Journal/Issues/2000/Nov/plussub/v77n11/p1479.pdf>. NDRIs are differentiated in side effects from SSRIs (selective serotonin reuptake inhibitors, e.g., Prozac) and SNRIs (serotonin and norepinephrine reuptake inhibitors, e.g., Effexor). *Id.*

90. Maurizio Fava et al., *15 Years of Clinical Experience with Bupropion HCl: From Bupropion to Bupropion SR to Bupropion XL*, 7 THE PRIMARY CARE COMPANION TO THE J. OF CLINICAL PSYCHOL. 106-07 (2005).

Wellbutrin IR was a successful product, with sales reaching \$102 million by 1996.<sup>91</sup>

Anticipating the eventual entry of a generic IR product, in October 1996 GSK obtained FDA approval of a sustained-release version of Wellbutrin, Wellbutrin SR, which was taken only twice daily. Years in advance of the entry of generic Wellbutrin IR in December 1999, GSK shifted its detailing and other promotion of Wellbutrin IR to the SR product. The cannibalizing worked: by the first quarter 2000, more than 85% of Wellbutrin prescriptions were for the SR product, and only 5% of the total prescriptions were filled with the generic IR product.

GSK reformulated and cannibalized again, but this time did not get enough of a head start against the generics and was less successful in switching the market to the reformulated product. Beginning in 1999, generic firms filed ANDAs for an SR version of Wellbutrin,<sup>92</sup> were eventually found not to have infringed GSK's SR patent, and entered the market with generic Wellbutrin SR in January 2004.<sup>93</sup> Meanwhile, in October 2001 GSK had obtained an exclusive license to Biovail's technology to make a once-a-day extended-release version of Wellbutrin, Wellbutrin XL. GSK entered the market with Wellbutrin XL in August 2003, only five months before the entry of the generic SR.

In anticipation of the XL launch, GSK substantially reduced the promotion of its SR product, and with the entry Wellbutrin XL nearly eliminated it.<sup>94</sup> GSK switched essentially all of its detailing efforts to Wellbutrin XL and conducted a substantial direct-to-consumer advertising campaign focused on the once-a-day reformulation. The cannibalizing,

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91. See Intelligent Polymers Ltd., Registration Under the Securities Act of 1933 (Form F-1) (Sept. 17, 1997) at 28, [http://edgar.brand.edgar-online.com/DisplayFilingInfo.aspx?Type=HTML&text=%2526lt%253bNEAR%252f4%2526gt%253b\(%22B.S.%22%2C%22CHEM%22\)&FilingID=1550614&ppu=%2FpeopleFilingResults.aspx%3FPersonID%3D2241026%26PersonName%3DB.S.%2520CHEM](http://edgar.brand.edgar-online.com/DisplayFilingInfo.aspx?Type=HTML&text=%2526lt%253bNEAR%252f4%2526gt%253b(%22B.S.%22%2C%22CHEM%22)&FilingID=1550614&ppu=%2FpeopleFilingResults.aspx%3FPersonID%3D2241026%26PersonName%3DB.S.%2520CHEM).

92. See *In re Wellbutrin SR/Zyban Antitrust Litig.*, 281 F. Supp. 2d 751, 755 (E.D. Pa. 2003).

93. In September 2003, the court of appeals overturned a decision that Andrx's generics did not infringe GSK's patents. See *Glaxo Wellcome, Inc. v. Andrx Pharmaceuticals, Inc.*, 344 F.3d 1226, 1233–34 (Fed. Cir. 2003). In January 2004, however, the appellate court upheld the district court's finding that Impax's generic Wellbutrin SR did not infringe. See *Glaxo Wellcome Inc. v. Impax Laboratories, Inc.*, 356 F.3d 1348, 1356 (Fed. Cir. 2004).

94. In the fourth quarter 2003, Wellbutrin SR had less than 5% of the total detailing expenditures, less than 4% of the sampling for Wellbutrin, and none of the professional journal ads. By the fourth quarter 2004, the SR product accounted for only 1% of the Wellbutrin detailing and sampling efforts. See generally IMS Health, Inc., Wellbutrin SR Data Report (Unpublished Report Compiled for Authors) (2009) (on file with the author).

however, was not as successful as in the IR-to-SR switch. Wellbutrin XL captured 40% of new Wellbutrin prescriptions by the month before the entry of generic SR, 55% by the sixth month after generic entry, and about 75% by the end of 2006.<sup>95</sup>

The consequences of the brand manufacturer's failure to cannibalize before generic entry are exemplified by the launch of King's ACE Inhibitor, Altace. Altace capsules came to market in 1991,<sup>96</sup> reaching annual sales of \$646 million by 2007.<sup>97</sup>

Anticipating eventual entry of a generic capsule product, King got approval for a tablet version of Altace on February 28, 2007.<sup>98</sup> But King, which was enmeshed in patent litigation against the generics,<sup>99</sup> mistimed the launch and did not bring the Altace tablets to market until February 2008.<sup>100</sup> In the interim, a generic had won the patent case and entered in December 2007.<sup>101</sup> Having failed to beat the generic to market, King's cannibalization

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95. The Wellbutrin saga continues; beginning in late 2004, a number of manufacturers sought FDA approval for a generic version of Wellbutrin XL, claiming non-infringement and invalidity of the Biovail patent. A court enjoined generic entry until resolution of the patent case, and to date no generic version of Wellbutrin XL has entered the market.

96. *See* *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293, 1298 (Fed. Cir. 2007). King sold Altace under a license from Aventis. *See id.* at 1294.

97. *See* Press Release, King Pharm., Year-End and Fourth-Quarter 2008 Financial Results (Feb. 2009), available at [http://www.kingpharm.com/Investors/News\\_Document.cfm?news\\_item\\_id=506&attachment\\_filename=02-26-20094QEarningsReleaseCompleteFinal&attachment\\_file\\_type=pdf](http://www.kingpharm.com/Investors/News_Document.cfm?news_item_id=506&attachment_filename=02-26-20094QEarningsReleaseCompleteFinal&attachment_file_type=pdf) (last visited September 16, 2009) (describing Altace sales for year end 2007 and 2008).

98. *See* Press Release, King Pharm., FDA Approval of Altace Tablet formulation, available at, [http://www.kingpharm.com/Investors/News\\_Details.cfm?news\\_item\\_id=418](http://www.kingpharm.com/Investors/News_Details.cfm?news_item_id=418) (last visited Sept. 16, 2009) (announcing FDA approval of tablet February 2007).

99. *Id.*; *see also* *Aventis Pharm.*, 499 F.3d at 1298–99 (describing litigation with Lupin over Altace).

100. *Id.*; *see also* Press Release, King Pharm., Altace Tablets Launch, available at [http://www.kingpharm.com/Investors/News\\_Details.cfm?news\\_item\\_id=462](http://www.kingpharm.com/Investors/News_Details.cfm?news_item_id=462) (last visited Sept. 16, 2009) (announcing launch of Altace tablets in February 2008).

101. *See* Press Release, King Pharm., First Quarter 2008 Financial Results, available at [http://www.kingpharm.com/Investors/News\\_Details.cfm?news\\_item\\_id=467](http://www.kingpharm.com/Investors/News_Details.cfm?news_item_id=467) (last visited September 16, 2009) (announcing generic entry for Altace capsules in December 2007). King was under FTC scrutiny at the time, in connection with an exclusion payment it had made to one of the generic litigants. *See* King Pharm., Quarterly Report (Form 10-Q), at 18 (May 9, 2006) (disclosing FTC inquiry in connection with dismissal of infringement suit against Cobalt).

effort was a dismal failure, with Altace sales plummeting from \$646 million in 2007 to \$166 million in 2008.<sup>102</sup>

*B. Cannibalizing Before Generic Entry*

Mechanics: As these examples illustrate, the brand manufacturer can increase the switch rate, and thereby increase the consumer welfare losses, by accomplishing the switch from the original to the new product long before a generic version of the original product enters. Many brand manufacturers launch their reformulated products twelve to eighteen months (or more) before the expected entry of generic versions of the original product. If generic entry is expected to occur at the expiration of a patent, the manufacturer knows the exact date of likely generic entry and can plan accordingly.<sup>103</sup> If the brand product is the subject of ongoing patent litigation, the manufacturer can make an educated estimate of the likely generic entry date.

By reformulating the product and cannibalizing it long before the expected onset of generic competition for the original product, the brand manufacturer adds the near-elimination of price competition<sup>104</sup> to the near-elimination of quality competition. The manufacturer's detailers extol the virtues of the new product, and they do so when no one is promoting the original and when doctors do not have a generic alternative available and do not know that one may be on the way. Doctors are presented a choice between two branded products, usually offered at the same price (sometimes even with a slightly lower price for the new product), often with an uncontested message that the new product is better. The generic version of the original product being unavailable, consumers have no choices at all. As demonstrated in Row 4 of Table 8 above, this tactic—cannibalizing before generic entry—nearly eliminates both price competition and quality competition as between the original and new products.

Of course, once the generic version of the original product enters the market, doctors theoretically could prescribe the original product, which

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102. See Press Release, King Pharm., Year-End and Fourth-Quarter 2008 Financial Results, available at [http://www.kingpharm.com/Investors/News\\_Details.cfm?news\\_item\\_id=506](http://www.kingpharm.com/Investors/News_Details.cfm?news_item_id=506) (last visited Sept. 19, 2009).

103. See 21 U.S.C. §§ 355(j)(2)(A)(vii), 355(j)(2)(B)(iii) (2006) (requiring generics to notify brand of intent to market upon patent expiration).

104. This tactic does not altogether eliminate price competition because some MCOs may not put the reformulated product in a preferred position on the formulary, and some consumers may be savvy enough to ask their doctors to prescribe the generic once it becomes available.

would then allow the consumer to choose a lower-priced generic alternative. Those doctors who had previously begun writing prescriptions for the new product could reswitch and start writing them for the original product again. Substantial evidence shows, however, that most doctors simply will not reswitch.

For example, in one recent product reformulation, Abbott Laboratories (“Abbott”) and Fournier Industrie et Sante (“Fournier”) switched their TriCor cholesterol drug from a once-daily tablet that had to be taken with a meal to a once-daily tablet that could be taken without a meal. Fournier estimated that the entire benefit to be gained from the new product would derive from eliminating generic substitutability rather than from any improvement in the product (and hence an increased share of sales within the therapeutic category). Fournier’s internal document stated: “The 145 mg, no food effect formulation replaces existing products and will therefore not have an expansive effect [on sales] on its own. However, it will have a substantial benefit in avoiding losses of sales due to generics . . . .”<sup>105</sup> Fournier emphasized the importance of launching the new formulation before the generics of the original version entered. By cannibalizing before the generic entered, Fournier estimated it would sell more than ten times as many TriCor tablets than if the reformulated product competed head-to-head with the generic with simultaneous market entry.<sup>106</sup>

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105. Transcript of Testimony at 994-95, *Teva Pharmaceuticals USA, Inc. et al. v. Abbott Laboratories et al.*, No. 02-1512 (D. Del.), (Nov. 17, 2008) (on file with author).

106. *Id.* at 815-16, 994-95.

Other manufacturers have reached similar conclusions. We are aware, for example, of a brand manufacturer that estimated that its post-generic-entry sales would be three times greater if it launched a once-daily version of its product two years before entering generic versions of its twice-daily product.<sup>107</sup> Another domestic manufacturer concluded that launching its reformulated product well before the anticipated generic entry would be a “dream world”; launching it after the generic entered would be a “Total Disaster.”<sup>108</sup> Another manufacturer acknowledged that, from a medical standpoint, its reformulation was “a gimmick” and that switching the market before generic entry was the “cardinal” determinant of success.<sup>109</sup> Independent industry analysts in the U.S. confirm that a reformulated product’s chances for success are directly tied to how far in advance of generic entry it is launched.<sup>110</sup>

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107. A protective order prevents us from discussing the details of this estimate and identifying the product.

108. *Meijer, Inc. v. Barr Pharm., Inc.*, 572 F. Supp. 2d 38, 42–43 (D.D.C. 2008) (quoting Plaintiff’s Motion Ex. 19 at 3).

109. A protective order prevents us from identifying this product or its manufacturer.

110. *See, e.g., Perrett, supra* note 26, at 3 (“It is essential that the brand holder switch their patients to the new formulation prior to generic launch . . . .”); Rita Rubin, *Claritin Going OTC Next Spring, Will Heir be Prescription For Success?*, USA TODAY, Apr. 22, 2002, at 11D, available at <http://www.usatoday.com/news/health/drugs/2002-04-23-claritin.htm>. The article concluded:

Independent industry analyst Hemant Shah of Warren, N.J., says, ‘Clarinet will never achieve the level of Claritin sales.’ Shah says Clarinet would have had a better chance if it had been approved a year or a year-and-a-half earlier, giving Schering-Plough more time to switch allergy sufferers before Claritin’s patent expired.

*Id.*; *see also* Lewis Krauskopf, *King Says Cobalt plans to launch generic Altace*, REUTERS, Nov. 11, 2007, available at <http://www.reuters.com/article/health-SP/idUSN1142025320071112> (quoting an industry analyst who said “[t]he potential imminent launch of generic Altace compromises . . . King’s strategy to switch Altace from capsule formulation to tablet”); W. Murray Spruill & Michelle L. Cunningham, *Strategies for Extending the Life of Patents*, BIOPHARMINTERNATIONAL.COM (Mar. 1, 2005), available at <http://biopharminternational.findpharma.com/biopharm/article/articleDetail.jsp?id=150834> (“[C]ompanies should consider seeking patent protection for new formulations, new methods of use, and potential combination products even before launching the original product. Such strategies must be developed before patent expiration and prior to imminent market entry of generic competitors.”).

This comports with the European Commission's Final Report in its pharmaceutical sector inquiry,<sup>111</sup> which concluded "it is of utmost importance for the originator company to bring the follow-on product on the market before the first product effectively loses exclusivity."<sup>112</sup> Whether the reformulated product beats the generic to the market is "crucial for the market success of both originator companies and generic companies."<sup>113</sup> Documents that the Commission obtained from the manufacturers confirm our conclusion:

- "If [generics] come together with or prior to [second generation product] the switch rate is dramatically reduced. [ . . . ] Once [generics] come in it becomes more difficult to get switches from [old original product]."<sup>114</sup>
- "If the prescriber is prepared to accept this Innovator argument [that the reformulated product is "better and similarly cost effective"] and switch prescribing, he is unlikely to go back subsequently to the first generation product when a generic is available. If the second generation product appears after patent expiry of the original product, then the pricing climate will be different. The generic will have caused the market price to fall, and thus the switch to the newer product will likely incur a cost penalty to the physician budget, something he is likely to resist unless the second generation is a compellingly better product. This is seldom if ever the case."<sup>115</sup>
- "[E]ach patient that is not switched quickly enough to [our second generation product] is forever lost to the generics. Once the patient is switched to [our second generation product] the physician does not have to, cannot and will not switch him to a generic, and what is more important: the pharmacist cannot substitute!!"<sup>116</sup>

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111. EUROPEAN COMMISSION, FINAL REPORT (8 July 2009), [http://www.europa-nu.nl/id/vi6wcj7amsx3/pharmaceutical\\_sector\\_inquiry\\_final?start\\_006\\_00c=10](http://www.europa-nu.nl/id/vi6wcj7amsx3/pharmaceutical_sector_inquiry_final?start_006_00c=10) (follow "Open document as PDF" hyperlink).

112. *Id.* at 356.

113. *Id.* at 361.

114. *Id.* at 359.

115. *Id.* at 360.

116. *Id.*

- “It will be very difficult to launch [the reformulated product] successfully” if the brand did not beat the generic to market.<sup>117</sup>

Several factors may contribute to this phenomenon. *First*, patients and third-party payers may resist a switch from a generic to a higher-priced brand, whereas they may not resist, at least not as strongly, a failure to switch from a higher-priced brand to a generic. When the reformulated product is introduced before the entry of the generic, detailers will have encouraged doctors to switch to the new product while consumers and payers are relatively passive to such switching. Moreover, the generic firms have no detailers to encourage the doctors to switch from the new product back to the original. *Second*, doctors may be reluctant to authorize a second switch of the patient’s medication within a relatively short period of time. If the generic of the original product becomes available only after entry of the reformulated product, the patient will have recently switched from the branded original product to the branded new product, and the doctor may be reluctant to then switch the patient back to the original.

Example of Pre-Generic Cannibalizing: From 2000 to 2002, Forest Laboratories nearly doubled the sales of its antidepressant, Celexa, from 10,680 units to 19,787 units.<sup>118</sup> Celexa contained a mixture of the S-enantiomer and R-enantiomer of citalopram, with the active agent being the S-enantiomer. Facing expected generic competition in December 2004, Forest reformulated the product to contain only the S-enantiomer and branded the new product as Lexapro.<sup>119</sup> When Lexapro entered in August 2002, Forest cannibalized Celexa’s sales, reducing its detailing and other promotion of Celexa from \$92.7 million the year before Lexapro’s launch to \$3.5 million the year after, while spending \$140.6 million annually on Lexapro.<sup>120</sup>

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117. *Id.* at 362.

118. *See, e.g.*, Top 200 Brand-Name Drugs by Units Reports 2000, <http://drugtopics.modernmedicine.com/drugtopics/pharmacy+facts+%26+figures/top-200-brand-name-drugs-by-prescription-in-2000/articlestandard/article/detail/104549?contextcategoryid=7604> (last visited May 18, 2010); Top 200 Brand-Name Drugs By Units Reports 2002, <http://drugtopics.modernmedicine.com/drugtopics/pharmacy+facts+%26+figures/top-200-brand-name-drugs-by-prescription-in-2002/articlestandard/article/detail/104564?contextcategoryid=7604> (last visited May 18, 2010).

119. *See* HOWARD SOLOMAN, FOREST LABORATORIES ANNUAL REPORT: LETTER TO OUR SHAREHOLDERS 11 (2005), *available at* [http://media.corporate-ir.net/media\\_files/irol/83/83198/reports/2005/LetterToShareholders.pdf](http://media.corporate-ir.net/media_files/irol/83/83198/reports/2005/LetterToShareholders.pdf).

120. *See id.* at 7; *see also* Huskamp, *supra* note 32, at 610 (“[P]romotional detailing expenditures had virtually stopped [for Celexa] by the time of generic entry.”).

The result was to reverse Celexa's earlier sales trend, nearly halving its sales from 19,787 units in 2002 to 10,242 units in 2004.<sup>121</sup> The previous sales growth now went to Lexapro, which sold 22,392 units in 2004 and grew to 26,098 in 2006.<sup>122</sup>

Consequently, generic Celexa, which entered in December 2004, had achieved sales of only 11,986 units by 2006, less than 31% of the molecule (Celexa/Lexapro/generic) unit sales.<sup>123</sup> Absent the impairment of generic competition, and absent Forest's reformulation and pre-generic-entry cannibalizing, the generics could reasonably have garnered 85% of those sales.<sup>124</sup>

### C. *Withdrawal of the Original Product*

Reformulating the product and cannibalizing before generic entry nearly eliminates price competition, and very substantially reduces—but does not entirely eliminate—quality competition between the original and reformulated products. The most important sources of marketing of the original product—detailing, sampling, medical journal ads, and direct-to-consumer advertising—are eliminated, but doctors may still receive comparative information through academic studies and symposia, and specialists may conduct their own comparisons by analyzing the competing products' labels.

In a few instances (three according to Table 7 above), brand manufacturers have not only reformulated and cannibalized the original product, but have stopped making it available for sale. Any doctor who concluded that the original product was superior, or that any improvement in the reformulated product was not worth the disruption of switching the patient's medication, is deprived of the option to continue prescribing the

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121. See, e.g., Top 200 Brand-Name Drugs by Units Reports 2004, <http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard//drugtopics/102005/150068/article.pdf> (last visited May 18, 2010).

122. *Id.* Top 200 Brand-Name Drugs By United Reports 2006, <http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard//drugtopics/092007/407649/article.pdf> (last visited May 18, 2010).

123. *Id.* Some industry observers believe Forest gave up too many sales to the generics by not switching the market as quickly as it could have. See, e.g., Perrett, *supra* note 26, at 7 ("This launch was not as successful as it might have been . . . due to Forest's failure to switch patients quickly enough from Celexa to Lexapro before generic Celexa entered the U.S. market . . .").

124. See *supra* note 53.

original product.<sup>125</sup> The new product is likely to be the closest therapeutic substitute for the original, and so is likely to garner almost all of the scripts that were previously written for the original product. This tactic is expected to cause only an incremental loss in consumer welfare because the principal source of quality competition is detailing and advertising, not academic journals and self-help.<sup>126</sup>

This tactic entirely eliminates the doctor's ability to make a quality-based choice between the original and new brand products during the period before the generic enters. Once the generic enters, the doctor can again begin to prescribe the original product, but, as noted above, few doctors will in fact reswitch their prescribing. The competition-impairing attributes of this tactic are reflected in Row 5 of Table 8 above.

Example of Product Withdrawal: Abbott's Hytrin, originally developed to treat high blood pressure, became successful when it was approved for treatment of benign prostatic hyperplasia (enlarged prostate), reaching sales of \$500 million in the U.S. in 1995.<sup>127</sup> In anticipation of generic entry, Abbott reformulated Hytrin in 1994 from a tablet to a capsule. It entered with Hytrin capsules in 1995 and stopped selling its tablets to the retail market. By the time the first generic tablet received final FDA approval on December 31, 1998, Abbott had annual sales of \$540 million, having converted

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125. More precisely, the doctor could prescribe the original product, but the patient could not get the prescription filled.

126. The manufacturer's draining of the supply pipeline in this manner could also have a small effect on price competition with respect to "refill" prescriptions. Some maintenance medications (those taken for chronic conditions) are written for 90-day supplies, with several refills permitted before a new prescription is required. If the manufacturer does not drain the supply pipeline before entry of the generic original product, and a pharmacy has sufficient inventory, pharmacists can continue filling these "refill" prescriptions with the branded original product until the generic original product becomes available, and thereafter fill them with the generic. If the manufacturer drains the supply pipeline, however, pharmacies soon have no more branded original product available. In this circumstance, a pharmacist presented with the refill prescription must call the doctor to ask how the script should be filled, and will almost always be told to dispense the branded new product. In this respect, the product-withdrawal tactic reinforces the negative effect on price competition by preventing pharmacists from trying to "bridge the time gap" by continuing to fill long-term refill prescriptions with the branded original product until the generic becomes available. It seems clear, however, that the principal effect of the tactic is to prevent quality comparisons between the original product and the branded new product.

127. See Sheryl Gay Stolberg & Jeff Gerth, *Keeping Down the Competition: How Companies Stall Generics and Keep Themselves Healthy*, N.Y. TIMES, Jul. 23, 2000, at 1. Hytrin is not included in our dataset because the reformulated product was approved before 1995.

essentially all of its sales from tablets to capsules.<sup>128</sup> The generic tablets did not even enter the market until 2001.<sup>129</sup>

In August 1999, the first generic received tentative FDA approval for the tablet version.<sup>130</sup> Abbott reacted by paying the generics \$6.5 million per month to stay out of the market pending resolution of the parties' dispute as to the validity of Abbott's patents.<sup>131</sup> The generics ultimately won the patent litigation and then entered in August 1999.<sup>132</sup> By the end of 2000, the generics had garnered 63% of Hytrin prescriptions.<sup>133</sup>

#### IV. EARLY COURT ANALYSIS OF PHARMACEUTICAL PRODUCT REFORMULATIONS

Two cases, both of which were decided on motions to dismiss the complaints, have recently addressed product reformulations in the pharmaceutical industry. Because both of those decisions discuss two important cases that arose in other industries, we begin with them.

##### A. *Microsoft*

The en banc court of appeals in *United States v. Microsoft Corp.*<sup>134</sup> adopted the "rule of reason" approach to Section 2 liability for product changes.<sup>135</sup> The government asserted that three of Microsoft's design

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128. See *In re Terazosin Hydrochloride Antitrust Litig.*, 352 F. Supp. 2d 1279, 1287, 1289 (S.D. Fla. 2005).

129. *Id.* at 1289.

130. *Id.* Abbott successfully fought off much potential generic entry by serially invoking the Hatch-Waxman thirty-month stay provision. See *id.* at 1288–89. Its executives forgot, however, to sue Geneva with respect to its ANDA for a capsule version of Hytrin, and Geneva got final FDA approval for the capsule version in March 1998. *Id.* at 1289.

131. *Id.* at 1291.

132. *Id.* at 1290, 1291.

133. Compare Janice Zoeller, *The Top 200 Drugs*, AM. DRUGGIST, Feb. 1999, at 47 (Hytrin 1998 units sales: 8,292,000), with *Top 200 Generic Drugs By Prescription in 2000*, DRUG TOPICS (Jan. 1, 2001), available at <http://drugtopics.modernmedicine.com/drugtopics/article/articleDetail.jsp?id=104549> (generic Hytrin units: 5,245,000).

134. 253 F.3d 34 (D.C. Cir. 2001) (en banc).

135. This approach, which is similar to the rule of reason analysis in Section 1 cases, proceeds through a series of steps:

First, to be condemned as exclusionary, a monopolist's act must have an "anticompetitive effect." That is, it must harm the competitive *process* and thereby harm consumers. . . .

changes were exclusionary under Section 2.<sup>136</sup> Writing after a full trial, the court of appeals noted that “courts are properly very skeptical” of claims that design changes have harmed competition.<sup>137</sup> But the court then refused to create a safe harbor from antitrust scrutiny, holding that “[j]udicial deference to product innovation, however, does not mean that a monopolist’s product design decisions are per se lawful.”<sup>138</sup>

Microsoft aggressively urged the court to adopt a more lenient (for the monopolist) standard, arguing, for example, that “design changes that improve a product cannot violate Section 2.”<sup>139</sup> The court rejected that contention, holding that product design changes are subject to a

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Second, the plaintiff, on whom the burden of proof of course rests, must demonstrate that the monopolist’s conduct indeed has the requisite anticompetitive effect. . . .

Third, if a plaintiff successfully establishes a *prima facie* case under § 2 by demonstrating anticompetitive effect, then the monopolist may proffer a “procompetitive justification” for its conduct. If the monopolist asserts a procompetitive justification . . . then the burden shifts back to the plaintiff to rebut that claim.

Fourth, if the monopolist’s procompetitive justification stands un rebutted, then the plaintiff must demonstrate that the anticompetitive harm of the conduct outweighs the procompetitive benefit. . . .

253 F.3d at 58–59 (citations omitted); *see also* III PHILLIP AREEDA & HERBERT HOVENKAMP, ANTITRUST LAW ¶ 651a, at 72 (2d ed. 2002) (Conduct is exclusionary if it is “reasonably capable of . . . prolonging monopoly power” and does “not benefit consumers at all” or is “unnecessary for the particular consumer benefits” or “produce[s] harms disproportionate to the resulting benefits.”).

136. 253 F.3d at 64–65.

137. *Id.* at 65.

138. *Id.* In an earlier, related decision, *United States v. Microsoft Corp.*, 147 F.3d 935 (D.C. Cir. 1998), the government asserted that Microsoft had violated the terms of a prior consent decree by creating a technological integration between its operating software and its Internet browser. *Microsoft*, 147 F.3d at 940. The court declined to weigh the alleged benefits of the integration against its anticompetitive effects, holding that Microsoft need only ascribe “facially plausible benefits” to the integration. *Id.* at 950. The court held that “[t]he question is not whether the integration is a *net* plus but merely whether there is a plausible claim that it brings some advantage.” *Id.* (emphasis in original). The court was careful to note, however, that this test was required by the terms of the consent decree, not by antitrust law. *See id.* at 950 n.14. Judge Wald rejected adoption of a “plausible benefit” standard, instead asserting that “[t]he courts are certainly capable of determining whether a particular integration offers any synergistic benefit at all and whether these benefits are minimal, significant, or great.” *Id.* at 959 n.3 (Wald, J., concurring in part and dissenting in part).

139. *See* Reply Brief of Defendant-Appellant at 27, *United States v. Microsoft Corp.*, 253 F.3d 34 (D.C. Cir. 2001) (No. 00-5212).

straightforward application of the rule of reason.<sup>140</sup> The government met its initial burden by proving that all three of the design changes were anticompetitive because they reduced the usage share of rival browsers, thereby protecting Microsoft's operating system monopoly.<sup>141</sup> The burden then shifted to Microsoft to establish a business justification for the design changes, and although Microsoft made "some general claims regarding the benefits" of two of the design changes, "it neither specific[d] nor substantiate[d] those claims."<sup>142</sup> Because the government made out a prima facie case of harm to competition, and Microsoft failed to substantiate its alleged procompetitive justifications, those two design changes were unlawfully exclusionary under Section 2.<sup>143</sup>

As to the third design change, Microsoft demonstrated "valid technical reasons" for the change – that "it was necessary" to design the product as it had.<sup>144</sup> The government did not rebut the proffered justification, or show that the anticompetitive effect of the design change outweighed its procompetitive benefits, so Microsoft was not liable for the third change.<sup>145</sup>

#### B. Berkey Photo

In *Berkey Photo, Inc. v. Eastman Kodak Co.*,<sup>146</sup> the plaintiff-competitor asserted that Kodak unlawfully used its monopoly in film to make sales of cameras and film-processing services.<sup>147</sup> Kodak designed its new 110 camera so that it could be used only with the new Kodacolor II film, and, for a period of eighteen months, Kodak made Kodacolor II film only for the 110 camera.<sup>148</sup> Plaintiff asserted, inter alia, that by linking together the 110 camera and the widely advertised Kodacolor II film, Kodak made camera

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140. Other courts have similarly applied the rule of reason to allegations of exclusionary product design changes. See, e.g., *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1382–83 (Fed. Cir. 1998) (holding the jury was entitled to reject proffered procompetitive justifications as pretextual); *Caldera Inc. v. Microsoft Corp.*, 72 F. Supp. 2d 1295, 1313 (D. Utah 1999) (holding that court must consider effects on competitors and consumers and whether product was improved); *In re IBM Peripheral EDP Devices Antitrust Litig.*, 481 F. Supp. 965, 1003 (N.D. Cal. 1979) (stating that factfinder must consider effects of design on competitors).

141. 253 F.2d at 65.

142. *Id.* at 66.

143. *Id.* at 67.

144. *Id.*

145. *Id.*

146. 603 F.2d 263 (2d Cir. 1979).

147. *Id.* at 278.

148. *Id.* at 286.

sales at plaintiff's expense.<sup>149</sup> Writing after a full trial on the merits, the *Berkey Photo* court rejected that contention, noting that the evidence showed that Kodacolor II film was inferior to its predecessor, Kodacolor X, in some respects and superior in others.<sup>150</sup> The court held that the market was able to determine the product's relative superiority "so long as the free choice of consumers is preserved."<sup>151</sup>

*Berkey Photo* considered a market in which consumers made the price/quality choice. In such a market, said the court, whether the price/quality proposition offered by a reformulated product is superior to that offered by the original product is properly "inferred from the reaction of the market."<sup>152</sup> When consumers make the price/quality choice, the market will reflect "whether there is sufficient demand for a particular product to make its production worthwhile . . . ."<sup>153</sup>

Notably, the court emphasized that its analysis applied only "so long as the free choice of consumers is preserved . . . ."<sup>154</sup> For example, even in a market in which consumers otherwise make the price/quality choice, Kodak arguably prevented free consumer choice by restricting the use of the new Kodacolor II film to its own camera for the first eighteen months after entry.<sup>155</sup> Given the "head start" for the Kodak camera, a consumer's decision to buy the Kodak camera might not reflect a decision that it was superior to competing cameras, but merely that it was the only camera that was compatible with the film that the consumer desired.<sup>156</sup> Plaintiff *Berkey* failed, however, to produce evidence that it was injured by the arguable violation.<sup>157</sup>

Thus, *Berkey Photo* does not assert that consumers make free price/quality choices and therefore product reformulations are competitively benign; it instead asserts that *if* consumers make such choices a product reformulation will be benign.

We now address the two recent cases in the pharmaceutical industry.

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149. *Id.*

150. *Id.* at 286–87.

151. *Id.* at 287 ("[I]t is of no importance that a judge or jury may later regard them as inferior, so long as that success was not based on any form of coercion.").

152. *Id.*

153. *Id.*

154. *Id.*

155. *Id.* at 288. Similarly, markets cannot produce increased consumer welfare when consumers' choices are coerced. *See id.* at 287.

156. *Id.* at 288.

157. *Id.*

*C. TriCor*

In a case that is simply known as “*TriCor*,”<sup>158</sup> Abbott and Fournier<sup>159</sup> implemented a product reformulation scheme that featured two product redesigns, pre-generic entry cannibalizing, withdrawal of the original products, and other generic-impairing conduct. Abbott sold TriCor as a 200 mg capsule, reaching annual sales of \$200 million by August 2001.<sup>160</sup> Anticipating generic entry, Abbott applied for FDA approval of a 160 mg tablet version.<sup>161</sup> When generic manufacturer Teva filed an ANDA for the original capsule versions, Abbott responded by filing a patent infringement suit which gave it an automatic thirty-month stay on generic entry.<sup>162</sup> Before Teva could enter, Abbott got quick approval for the 160 mg tablets by proving that they were bioequivalent to the already approved 200 mg capsules.<sup>163</sup>

Abbott introduced the tablets in September 2001, immediately began cannibalizing the 200 mg capsule sales, and altogether withdrew the capsules from the market.<sup>164</sup> Abbott also took actions to interfere with insurance coverage for generic TriCor and bought back inventory of the original product held by retailers.<sup>165</sup> By the time Teva obtained final FDA approval for its 200 mg capsules in March 2002, Abbott had already succeeded in switching nearly all TriCor capsule prescriptions to TriCor tablet prescriptions.<sup>166</sup> Abbott’s sales of 200 mg capsules in the third quarter of 2001 were over \$68 million, and its sales in the first quarter of 2002 were only \$2 million, while its 160 mg tablet sales were over \$80 million in that quarter. Teva never received more than 2% of combined capsule and tablet TriCor unit sales.

When Teva filed an ANDA for 160 mg tablets in June 2001, Abbott again sued and again obtained an automatic thirty-month stay.<sup>167</sup> Abbott withdrew the lawsuit on the eve of trial in May 2005, and Teva received final

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158. Abbott Labs. v. Teva Pharm. USA, Inc., 432 F. Supp. 2d 408 (D. Del. 2006).

159. For convenience, we hereafter refer to Abbott and Fournier collectively as “Abbott.”

160. Amended Complaint at ¶ 40, CVS Pharmacy, Inc., *In re TriCor Direct Purchaser Antitrust Litig.* (CVS Complaint), 432 F. Supp. 2d 408 (D. Del. 2006) (No. 05-340-KAJ).

161. *TriCor*, 432 F. Supp. 2d at 416.

162. *Id.*; see also CVS Complaint, at ¶¶ 67–70.

163. *TriCor*, 432 F. Supp. 2d at 416; see also CVS Complaint, at ¶¶ 67–70.

164. *TriCor*, 432 F. Supp. 2d at 416.

165. *Id.* at 416.

166. CVS Complaint, at ¶¶ 53–57.

167. *TriCor*, 432 F. Supp. 2d at 417.

FDA approval to market the 160 mg tablets.<sup>168</sup> By then, however, Abbott had received quick approval to sell 145 mg TriCor tablets, again by showing that they were bioequivalent to the 200 mg capsules.<sup>169</sup> Upon launch of the 145 mg tablets in November 2004, Abbott again cannibalized the existing TriCor sales and withdrew the 160 mg tablets from the market.<sup>170</sup> Informed by its prior experience in unsuccessfully trying to sell its 160 mg capsules, Teva chose not to market its 160 mg generic TriCor tablets.<sup>171</sup> In 2007, Abbott had TriCor sales of \$1.3 billion.

Plaintiff purchasers of TriCor asserted that Abbott serially reformulated the product “not to improve the product but simply to prevent generic formulations from becoming AB-rated for substitution with TriCor.”<sup>172</sup> Denying Abbott’s motion to dismiss the complaints, the *TriCor* court gave two separate reasons for concluding that Abbott’s conduct was potentially unlawful under the rule of reason. The district court judge first held that, “[t]he nature of the pharmaceutical drug market, as described in Plaintiffs’ allegations, persuades me that the rule of reason approach should be applied here . . . .”<sup>173</sup> Plaintiffs’ allegations included a description of the price “disconnect” discussed above – that doctors, not consumers, select which product to buy.<sup>174</sup> The market cannot determine which product is superior when the patient pays but does not choose, and the doctor chooses but does not pay.<sup>175</sup>

The *TriCor* court also noted that Abbott had removed the original product from the market.<sup>176</sup> Discussing *Berkey Photo*, the *TriCor* court commented that “the fact that consumers bought Kodak’s new products instead of those of its competitors accurately reflected the value of the new products ‘so long as the free choice of the consumers [was] preserved.’”<sup>177</sup> In contrast, Abbott “prevented [consumer] choice by removing the old

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168. *Id.*

169. *Id.* at 418. The FDA also approved a change to the “dosage and administration” portion of Abbott’s product label to delete the statement that the drug should be taken with food. *Id.*

170. *Id.*

171. Because it could not achieve sales through AB-rated pharmacy substitution, Teva entered with a branded product, Lofibra. *Id.* at 416.

172. *Id.* at 415.

173. *Id.* at 422.

174. CVS Complaint, at ¶¶ 10–18.

175. *Id.*

176. *TriCor*, 432 F. Supp. 2d 408, 423 (D. Del. 2006).

177. *Id.* at 421 (quoting *Berkey Photo, Inc. v. Eastman Kodak Co.*, 603 F.2d 263, 287 (2d Cir. 1979)).

formulations from the market while introducing new formulations.”<sup>178</sup> The court concluded that this conduct also justified “an inquiry into the effect of Defendants’ formulation changes, following the rule of reason approach.”<sup>179</sup>

Seizing on the second of the court’s two rationales, some commentators have argued that *TriCor* permits rule of reason analysis of pharmaceutical reformulations only when the brand manufacturer removes the original product from the market.<sup>180</sup> For three reasons, we think this misreads the decision:

First, as noted, the plain language of the opinion says that antitrust scrutiny is justified by *each* of (1) the “nature of the pharmaceutical drug market, as described in Plaintiffs’ allegations” and (2) the withdrawal of the product.<sup>181</sup> The court did not state or imply that such analysis was required by only the second rationale or by a combination of the two. Instead, the court held that “the allegations of product removal . . . , like the allegations related to the product changes themselves, support Plaintiffs’ antitrust claims.”<sup>182</sup>

Second, the opinion’s principal focus was whether Abbott’s conduct had impaired generic substitution, not whether Abbott had withdrawn the original products. For example, the court expressly noted that the generics “have not been prevented from marketing the formulations that were the subject of their ANDAs, i.e., the old *TriCor* formulations.”<sup>183</sup> But while Teva and Impax (another generic manufacturer) were free to market a generic of the original product, the product change destroyed the AB-rated substitutability with the reformulated product:

Here, while Teva and Impax may be able to market their own branded versions of the old *TriCor* formulations, they cannot provide generic substitutes for the current *TriCor* formulation, which is alleged to be their cost-efficient means of competing in the pharmaceutical drug market. That

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178. *Id.* at 422.

179. *Id.*

180. See Alan Devlin, *Exclusionary Strategies in the Hatch-Waxman Context*, 2007 MICH. ST. L. REV. 631, 660–61 (2007); see also Jessie Cheng, Note, *An Antitrust Analysis of Product Hopping in the Pharmaceutical Industry*, 108 COLUM. L. REV. 1471, 1501–02 (2008).

181. *TriCor*, 432 F. Supp. 2d at 422.

182. *Id.* at 424.

183. *Id.* at 423.

opportunity has allegedly been prevented entirely by Defendants' allegedly manipulative and unjustifiable formulation changes.<sup>184</sup>

The court concluded that "[s]uch a restriction on competition [the destruction of substitutability with the reformulated product], if proven, is sufficient to support an antitrust claim in this case."<sup>185</sup> Having taken note of "the nature of the pharmaceutical drug market, as described in Plaintiffs' allegations," the court concluded that generic substitutability was essential to rivals' "cost-efficient means of competing in the pharmaceutical drug market."<sup>186</sup> Abbott's destruction of this substitutability through reformulating the product—not the withdrawal of the original product—was the focus of the court's analysis and was "sufficient to support an antitrust claim."<sup>187</sup> The court removed any doubt on this by characterizing the product withdrawals as mere "[a]ctions [t]aken to [s]upport the [f]ormulation [c]hanges."<sup>188</sup>

Third, the court should not be read to have made the relevant "consumer choice" hinge on removal of the original product from the market, because such a holding would have been highly problematic. We show why in the next section.

#### *D. Nexium*

The court in *Nexium*<sup>189</sup> granted defendants' motion to dismiss complaints alleging that AstraZeneca's product-switch scheme violated Section 2.<sup>190</sup> In order to put the court's decision in context, we review the plaintiffs' allegations in detail.

Prilosec, a proton pump inhibitor used to treat acid reflux and related conditions, was the top-selling drug in the world in 1999, with U.S. sales of more than \$4 billion.<sup>191</sup> The patent on the active ingredient in Prilosec was slated to expire in October 2001, and AstraZeneca responded to this imminent threat by making a small change in Prilosec's chemical

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184. *Id.*

185. *Id.* at 422.

186. *Id.* at 423.

187. *Id.*

188. *Id.* at 423–24.

189. *Walgreen Co. v. AstraZeneca Pharm. L.P. (Nexium)*, 534 F. Supp. 2d 146 (D.D.C. 2008).

190. *Id.* at 147.

191. *Id.* at 148.

composition, branding the reformulated product as Nexium, and then implementing a pre-generic-entry cannibalization.<sup>192</sup>

Plaintiffs' Complaints alleged that the reformulation brought no benefits of any kind to consumers; it "created no efficiency gains or increases in consumer welfare."<sup>193</sup> Specifically, the clinical studies comparing 20mg of Nexium to 20mg of Prilosec showed no superiority of Nexium.<sup>194</sup> A few studies showed a slight clinical advantage for a double dose (40mg) of Nexium versus 20mg of Prilosec, but the Complaints alleged that any therapeutic gain for the double dose of Nexium is no more than the gain routinely shown for a double dose of Prilosec; that any gains result solely from the increased dosage; and that AstraZeneca knew there is such a dose-response relationship for all proton pump inhibitors.<sup>195</sup>

Beginning in March 2001, eighteen months before the expected entry of generic Prilosec, AstraZeneca began cannibalizing Prilosec, and its force of 6000 detailers stopped detailing Prilosec, pushed Nexium, and compared Prilosec unfavorably to Nexium.<sup>196</sup> Over those eighteen months, AstraZeneca reduced Prilosec's annual unit sales from 29.6 million to 19.6 million, while increasing Nexium's from zero to 13.4 million.<sup>197</sup>

After generic Prilosec entered in December 2002, AstraZeneca caused MCOs to stop providing reimbursement to consumers for purchases of Prilosec (whether branded or generic). Taking advantage of MCO policies that end coverage for prescription pharmaceuticals when an over-the-counter version becomes available, AstraZeneca introduced Prilosec OTC in September 2003.<sup>198</sup> Many MCOs stopped providing coverage for generic Prilosec, and the combined sales of branded and generic prescription Prilosec declined from 15.9 million units in 2003 to less than 8.4 million units in

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192. *Id.* at 148–49. The active ingredient in Prilosec, omeprazole, is a racemic mixture, which means it is an equal-parts mixture of an S-enantiomer and R-enantiomer. Omeprazole, whether the mixture or either enantiomer alone, is only a prodrug, i.e., the compound itself is inactive, and the active drug is formed only after it is ingested into the body. The active drug, cyclic sulfonamide, is not a chiral compound, so there is no reason to believe that a dose of one enantiomer of omeprazole would interact with the body's proton pumps any differently than would an equal dose of the mixture. AstraZeneca's redesigned drug, Nexium, is simply the S-enantiomer of omeprazole, i.e., esomeprazole. *Id.* at 148–49.

193. First Amended Complaint and Demand for Jury Trial (Walgreen Complaint) at 40, Walgreen Co. v. AstraZeneca Pharm. L.P., 534 F. Supp. 2d 146 (D.D.C. 2008) (No. 1:06-cv-02084-RWR).

194. *Id.* at 26.

195. *Id.* at 30.

196. *Id.* at 32–33.

197. *Id.* at 21–22.

198. *Id.* at 36.

2005.<sup>199</sup> This occurred despite the fact that AstraZeneca's price for OTC Prilosec was more than twice that of generic Prilosec.<sup>200</sup>

The Complaints alleged that, absent the reformulation, cannibalization, and interference with MCO reimbursement, generic Prilosec would have gained at least 85% of the unit sales.<sup>201</sup> As a result of AstraZeneca's conduct, however, the generics made only 25% of unit sales, with the difference costing consumers more than \$1 billion annually.<sup>202</sup>

Free Consumer Choice

Granting AstraZeneca's motion to dismiss the Complaints, the *Nexium* court found dispositive that AstraZeneca had not altogether withdrawn branded Prilosec from the market. The court asserted that, by introducing Nexium and not withdrawing Prilosec, AstraZeneca had "added choices" and therefore could not be liable.<sup>203</sup>

The court's pithy analysis would have made sense in ordinary markets, where the addition of another product alternative can be expected to lead to an increase in consumer welfare. Consumers who can make the price/quality choice will switch from existing products to the newly added product only if the combination of quality and price of the new product is superior to that of existing products. Only those consumers who think the price/quality offering of the new product is superior will buy it, leading to increased consumer welfare.

As noted in detail above, however, consumers in prescription pharmaceutical markets do not make the price/quality choice unless and until they can substitute a generic drug for prescriptions written for the brand. Increasing the number of branded pharmaceuticals on the market does not change that fact.

Marketing another branded product can increase consumer welfare, *all other things equal*, if the new product is an improvement over existing

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199. *Id.* at 38.

200. *Id.* at 38–39. This is another example of an agency problem. The price of generic Prilosec was half that of Prilosec OTC, but by enforcing a policy of not reimbursing for a generic product when an OTC version is available, the cost to the MCO of either choice is zero. See Holly M. Spencer, *The Rx-To-OTC Switch of Claritin, Allegra, and Zyrtec: An Unprecedented FDA Response to Petitioners and the Protection of Public Health*, 51 AM. U. L. REV. 999, 1001–02 (2002) (“[A]n Rx-To-OTC switch would save the provider millions of dollars in prescription costs and co-payments, a savings which will, necessarily, become the consumer's expense”).

201. Walgreen Complaint, *supra* note 193, at 38–39.

202. *Id.* at 22, 38–39.

203. Walgreen Co. v. AstraZeneca Pharm. L.P. (*Nexium*), 534 F. Supp. 2d 146, 151 (D.D.C. 2008).

products. For example, assume that a new brand Product B has features that each of one hundred consumers values at an additional \$5 as compared to existing brand Product A; that the manufacturer offers Products A and B at the same price; and that doctors switch the prescriptions for all one hundred consumers from Product A to Product B. All other things equal, this would result in an increase in consumer welfare of \$500.

The problem, however, is that all other things are not equal. As detailed above, the manufacturer's introduction of Product B and cannibalizing of Product A can have the effect of impairing price competition from the generic version of Product A. In such a case, the introduction of Product B, although delivering a \$5 value in improvements, also impairs the ability of consumers to weigh the price and quality of brand Product B against the price and quality of the generic version of Product A.<sup>204</sup> Assume that, in a world in which consumers could make that price/quality choice, all one hundred of them would choose the generic version of Product A, at a \$20 discount compared to Product B. In that case, the introduction of Product B and cannibalizing of Product A will have resulted in a \$1,500 net loss in consumer surplus. In short, the reformulation and cannibalizing of Product A eliminates consumers' ability to make the appropriate price/quality comparisons and, consequently, can result in substantial losses in consumer welfare.

The court in *Nexium* reached the conclusion it did by denying that prescription pharmaceutical markets are any different from ordinary markets. The court asserted that, "[n]ew products are not capable of affecting competitors' market share unless consumers prefer the new product."<sup>205</sup> This denies the fact that, absent generic competition, consumers in these markets do not make the price/quality choice. The court asserted that by introducing another brand product "AstraZeneca added choices,"<sup>206</sup> but ignored the fact that this addition did not result in any consumer gaining the ability to make

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204. In *Nexium*, the effect on consumer welfare was even worse than in this example because the Complaints alleged, and the sales data confirmed, that Nexium was not an improvement over Prilosec. Walgreen Complaint, *supra* note 193, at 40.

205. *Nexium*, 534 F. Supp. 2d at 151. The court's statement appears to be an ideological assertion that the market outcome necessarily reflects the free and unfettered choices of consumers; the court's statement was not a conclusion that the facts showed that the market reflects the price/quality choices of consumers. In using the term "free consumer choice," the court sometimes identified patients as the "consumers," *id.* at 151, and sometimes identified doctors as the "consumers." *Id.* at 152. Nowhere did the court address the key marketplace fact—that patients have the payment obligation while doctors make the product selection.

206. *Id.* at 151.

the relevant price/quality choice. In asserting that “there is no allegation that AstraZeneca eliminated any consumer choices,”<sup>207</sup> the court ignored the Complaints’ detailed allegations that the reformulation and cannibalizing of branded Prilosec impaired the only competition that would have provided the relevant price/quality choice – i.e., competition provided by generic Prilosec.

The court’s ideological assertion that the introduction and promotion of a new prescription pharmaceutical will “affect[] competitor’s market share . . . [only if] consumers prefer the new product” is hard to square with the facts (and with plaintiffs’ detailed allegations). Economists have known for more than three decades that the price disconnect in these markets prevents consumers from making the price/quality choice that would reveal whether “consumers prefer the new product.”<sup>208</sup> Indeed, the court’s assertion seems to deny the economic foundation of fifty state DPS statutes, the federal regulatory regime for introducing generic drugs, and the generic-encouraging provisions of the Hatch-Waxman Act.<sup>209</sup> If consumers made the price/quality choice, special legislation to permit and encourage generic substitution would not be necessary.<sup>210</sup>

Take, for example, the GERD/heartburn therapeutic category in which Prilosec and Nexium compete. That category features competition among five branded products, all of which treat essentially the same conditions and do so equally effectively—they are all essentially “me-too” versions of Prilosec.<sup>211</sup> Yet, as shown in the price discounts that occur when these

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207. *Id.*

208. *Id.*

209. *See supra* notes 41–47 and accompanying text (showing that these provisions were intended to remedy the price disconnect).

210. These state and federal regimes are important because they both reflect the truth about the industry economics (especially the existence of the price disconnect) and embody substantial and clear governmental policies about the proper response to those economics. Both the economic truth and the governmental judgment about how to respond to it should help inform a proper antitrust standard for pharmaceutical reformulations. *See generally* C. Scott Hemphill, *Paying for Delay: Pharmaceutical Patent Settlement as a Regulatory Design Problem*, 81 N.Y.U. L. REV. 1553, 1560–62 (2006); Michael A. Carrier, *Unsettling Drug Patent Settlements: A Framework for Presumptive Illegality*, 108 MICH. L. REV. 37, 38–39 (2009).

211. *See, e.g., Comparing Health Care Choices: Gastroesophageal Reflux Disease (GERD)*, AHRQ Pub. No. 06-EHC003-A (Dec. 2005), available at <http://effectivehealthcare.ahrq.gov/repfiles/consumer.gastro.pdf> (“Studies show that, overall, each PPI works about as well as another for relieving symptoms.”); Stanley Ip et al., U.S. DEP’T OF HEALTH & HUMAN SERVS., *Comparative Effectiveness of Management Strategies for Gastroesophageal Reflux Disease* 35 (2005), available at <http://effectivehealthcare.ahrq.gov/reports/final.cfm> (finding no comparative differences in effectiveness of equal doses of omeprazole, esomeprazole, lansoprazole, pantoprazole, and

branded products face generic competition, the brands are sold at 10 times their marginal costs. A marketplace with five close functional substitutes could not yield margins anywhere near that magnitude if consumers made the relevant price/quality choices.

Similarly, as shown in detail above,<sup>212</sup> a reformulated product that beats the generic to the market will make sales three to ten times greater than one that does not. Again, these data are completely inconsistent with the *Nexium* court's assertion that the outcomes in prescription pharmaceutical markets, absent generic substitutability, reflect the price/quality decisions of consumers.

The *Nexium* court's rationale is insupportable. It is nevertheless worthwhile to ask whether there is any basis to give definitive antitrust significance to the manufacturer's (a) reformulating, cannibalizing, and withdrawing the original product from the market, as opposed to (b) only reformulating and cannibalizing it. We know of no such basis.

In several respects, cannibalizing a product is similar to removing it from the market. First, neither activity is the type of conduct that ordinarily results in antitrust liability. In ordinary markets—absent the price disconnect that makes prescription pharmaceutical markets different – even a monopolist is generally free to cannibalize its existing products and to withdraw them from the market altogether.<sup>213</sup>

Second, neither cannibalizing a product nor withdrawing it from the market prevents the FDA from approving the generic of the original product or prevents doctors from writing prescriptions for it. Both cannibalizing a product and withdrawing it affect only the likelihood that doctors will in fact write prescriptions for the original product once the generic has become available. Both activities have that effect only because of the price disconnect that exists in these markets.

Removing the original product from the market has two competitive effects that cannibalizing it does not. As summarized in Table 8 above, removing the original product eliminates quality competition between the

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rabeprazole). See generally MARCIA ANGELL, THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT 74–93 (2004) (explaining “me-too” drugs, and using PPIs as an example).

212. See *supra* notes 90–124 and accompanying text.

213. See, e.g., *Cont'l Paper Bag v. E. Paper Bag*, 210 U.S. 405, 429 (1908) (stating that patentee generally has no obligation to market a patented product because “it is the privilege of any owner of property to use or not use it”); *In re Indep. Serv. Orgs. Antitrust Litig.*, 203 F.3d 1322, 1326 (Fed. Cir. 2000) (asserting that patentee is generally immunized from antitrust liability for refusal to license or use patent).

original and the reformulated brand products. Importantly, however, this effect on quality competition occurs for only a limited period of time—from the date of the withdrawal of the original brand product until the entry of the generic original product. Once the generic is approved, doctors can write prescriptions for it, and have those prescriptions filled, whether or not the original brand product has been withdrawn.

The real competitive concern is not the effect of the removal on quality competition between the original and reformulated products, but on price competition between the brand and generic versions of the molecule. The removal of the original brand product before the entry of the generic increases the number of prescriptions that will be written for the reformulated brand product, rather than for the original brand product, when the generic enters. Importantly, this competitive effect is not different in kind from the competitive effect of the manufacturer's cannibalization of the original brand product. The anticompetitive effect of both activities is to increase the percentage of pre-generic-entry scripts that are written for the reformulated brand – i.e., to increase the success of the manufacturer's pre-generic switching. In these price-disconnected markets, the generics generally can never win back those scripts. The anticompetitive effect of both types of conduct is the same; the *degree* of consumer harm from withdrawal of the original brand is marginally worse.

Some may argue that the pre-generic entry removal of the original product, unlike mere cannibalizing, “forces” physicians who want to prescribe the molecule to write the prescription for the reformulated product. The reality, however, is that the removal does not “force” the physician to *continue* writing scripts for the reformulated product once the generic enters. Again, the key point is that, in terms of the effect on generic competition, the difference between removing the original product and cannibalizing it is simply the number of scripts that the manufacturer will have successfully switched to the reformulated product before the generic enters. This is a difference of degree, not kind.

This reality is confirmed by the facts of *TriCor* and *Nexium*. Absent any impairment of generic competition, we would expect that, several years after generic entry, generics would be making approximately 85% of unit sales of the molecule.<sup>214</sup> In *TriCor*, the brand manufacturers reformulated the product, cannibalized it, entirely removed it from the market, interfered with the generics' insurance coverage, and drained the supply chain of the original product. Several years after generic entry, the generics were making only 2%

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214. See *supra* note 53.

of unit sales.<sup>215</sup> In *Nexium*, the manufacturer reformulated the product, cannibalized it, did not remove it from the market, and interfered with the generics' insurance coverage. Several years after generic entry, the generics had captured only 7.4 million annual unit sales, or roughly 25% of Prilosec's pre-reformulation sales of 29.6 million units.<sup>216</sup> The generics' sales likely would have been much less in the absence of extraordinary, well-publicized efforts by federal officials and others to alert doctors to the fact that "[y]ou should be embarrassed if you prescribe Nexium," because it increases costs with no medical benefits" to consumers.<sup>217</sup>

It seems plain that two types of conduct, of the same nature and with the same kind of anticompetitive effect, should not be accorded dispositively different antitrust treatment when each of them maintains the incumbent's shares (98% for TriCor, and 75% for Nexium) very substantially above the 15% level that would have resulted from unimpaired generic competition.

#### 1. The "Elimination" of Consumer Choice

The *Nexium* court also seemed to hold that antitrust liability attaches only when the monopolist's conduct altogether eliminates a rival's competition, not merely impairs it. The court quoted the correct rule that Section 2 liability arises not only when the defendant's conduct "prevents . . . rivals from competing," but also when it "impairs their opportunities to do so effectively."<sup>218</sup> But the court then focused solely on whether AstraZeneca's conduct altogether prevented FDA approval of the generic, rather than whether that conduct interfered with the effective distribution of the generic, i.e., its substitutability. The court held that plaintiffs failed to state a claim because AstraZeneca's scheme did not "effectively eliminate[]" consumers' ability to purchase generic Prilosec.<sup>219</sup>

The court distinguished *Microsoft*, asserting that the product design changes there had "effectively eliminated the customers' choice of internet

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215. See *infra* note 226.

216. Walgreen Complaint, *supra* note 193, at 22, 38–39.

217. See Robert Pear, *U.S. Limiting Costs of Drugs For Medicare*, N.Y. TIMES, Apr. 21, 2003, at A1 (quoting Thomas Scully, former Administrator of the Center for Medicare and Medicaid Services, in an address to the American Medical Association).

218. Walgreen Co. v. AstraZeneca Pharm. L.P. (*Nexium*), 534 F. Supp. 2d 146, 150 (D.D.C. 2008) (citing III PHILLIP E. AREEDA & HERBERT HOVENKAMP, ANTITRUST LAW ¶ 650a at 67 (2d ed. 2002)).

219. 534 F. Supp. 2d at 151; see also *id.* (no "elimination of choice"); *id.* (conduct did not "eliminate[] any consumer choices").

browsers.”<sup>220</sup> The facts show, however, that both Microsoft’s own pre-design-change, unbundled operating system and its competitors’ browsers remained available for sale. Microsoft did not withdraw the prior operating systems from the market,<sup>221</sup> and the millions of users of Windows 95 were free to choose a rival browser.<sup>222</sup> The product changes in *Microsoft* were unlawful not because they entirely eliminated rivals’ products—they didn’t—but because they “significantly reduc[ed] usage of rivals’ products.”<sup>223</sup> AstraZeneca’s conduct was alleged to have reduced its rivals’ usage shares from 85% to 25%, an impairment every bit as severe as that at issue in *Microsoft*.

The *Nexium* court relied on *TriCor*,<sup>224</sup> but the defendants’ conduct there did not eliminate any consumer choices in the sense in which the *Nexium* court uses that term. The FDA approved Teva’s generic *TriCor*,<sup>225</sup> and it garnered a 2% market share.<sup>226</sup> Indeed, *TriCor* emphasized that liability hinges not on elimination of rivals’ products, but on impairment of their “cost-efficient means of competing.”<sup>227</sup>

The *Nexium* court also relied on *Berkey Photo* which, as noted above, reasoned that product reformulations cannot reduce consumer welfare if

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220. *Id.* (citing *United States v. Microsoft*, 253 F.3d 34, 64–65 (D.C. Cir. 2001)).

221. *See United States v. Microsoft*, 84 F. Supp. 2d 9, 21, 26–27 (D.D.C. 1999). In fact, Microsoft did not stop supporting Windows 95 until December 31, 2001. *See Windows Life-Cycle Policy*, <http://www.microsoft.com/windows/lifecycle/default.mspx> (last visited May 13, 2010). The *Nexium* court cited “[*United States v. Microsoft*, 253 F.3d 34, (D.C. Cir. 2001)] at 64–65” for the proposition that Microsoft’s conduct had “effectively eliminated the customers’ choice of internet browsers.” *Nexium*, 534 F. Supp. 2d at 151. But on the pages cited by *Nexium*, the Court of Appeals *rejects* Microsoft’s contention that its conduct was lawful because “Netscape is not completely blocked from distributing its product.” *Microsoft*, 253 F.3d at 64. Liability was properly found because “although Microsoft did not bar its rivals from all means of distribution, it did bar them from the cost-efficient ones.” *Id.*

222. The *Nexium* court lost track of the fact that prescription drugs are consumables that can be effectively withdrawn from the market by the manufacturer’s not selling any more of them; in contrast, Windows 95 would have remained installed and usable by millions of customers even if Microsoft had stopped supporting it (which it did not).

223. *Microsoft*, 253 F.3d. at 65; *see also id.* (“reducing rival browsers’ usage share”); *id.* (“reduces rivals’ usage share”).

224. *Nexium*, 534 F. Supp. 2d at 151.

225. *See Abbott Labs. v. Teva Pharms. USA, Inc.*, 432 F. Supp. 2d 408, 416 (D. Del. 2006).

226. Transcript of Testimony at 534–35, *Teva Pharmaceuticals USA, Inc. et al. v. Abbott Laboratories et al.*, No. 02-1512 (D. Del. Nov. 12, 2008) (on file with author).

227. 432 F. Supp. 2d at 423.

consumers make the price/quality choice.<sup>228</sup> A straightforward application of *Berkey Photo* to AstraZeneca's conduct would seem to have required the denial of its motion to dismiss the Complaints. Plaintiffs alleged four circumstances that prevented consumers from making the price/quality choice: (1) the price disconnect; (2) AstraZeneca's "head start" in converting the market to the reformulated product – the very circumstance that *Berkey Photo* itself said could impair free consumer choice even absent a price disconnect;<sup>229</sup> (3) the absence of insurance coverage for generic Prilosec; and (4) AstraZeneca's misrepresentations to consumers and doctors that Nexium is superior to Prilosec.<sup>230</sup> The *Nexium* court did not address any of the first

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228. See *Nexium*, 534 F. Supp. 2d at 151 (citing *Berkey Photo, Inc. v. Eastman Kodak Co.*, 603 F.2d 263, 287 (2d Cir. 1979)). The *Nexium* court cited the Areeda/Hovenkamp treatise for the proposition that "all product innovation should be lawful in the absence of bundling . . . ." *Nexium*, 534 F. Supp. 2d at 152 (quoting IIIA PHILLIP E. AREEDA & HERBERT HOVENKAMP, ANTITRUST LAW ¶ 781e, at 271 (2d ed. 2002)). The court appears not to have realized that the treatise's invocation of "bundling" is a reference to "technological tying," i.e., the monopolist's strategic redesign of the product in order to impair competition from complementary products. See IIIB PHILLIP AREEDA & HERBERT HOVENKAMP, ANTITRUST LAW ¶ 776, at 299 (Microsoft's technological integration of its Internet Explorer with Windows was a "bundling strategy"); *id.* ¶ 777a, at 301 (redesigning a product in order to impair competition from rivals' complementary products is a "bundling strategy"). Pharmaceutical redesigns are analogues, if not examples, of such conduct. See I HERBERT HOVENKAMP, MARK D. JANIS & MARK A. LEMLEY, IP AND ANTITRUST § 12.5, at 12–47 (1st ed. Supp. 2007) (stating that pharmaceutical product changes should be analyzed "[u]nder the analysis we offer in section 12.3e3," which addresses technological "bundling" designed to impair competition from complementary products).

229. See 603 F.2d at 288 (Kodak arguably interfered with consumer choice by making new film available only for its own camera for 18 months). Note that *Berkey Photo* held that such a head start could prevent markets from increasing consumer welfare even in markets in which consumers otherwise make the price/quality choice. We showed above the overwhelmingly distortive effects of such a head start in prescription pharmaceutical markets, where consumers (absent generic substitutability) do not make such choices.

230. Relying on authority addressing otherwise competitive markets, the *Nexium* court held that misrepresentations to doctors should be considered to have a de minimis effect on competition because the market would correct them. 534 F. Supp. 2d at 152. The court ignored the fact that markets can overcome false and deceptive advertising only to the extent that rivals have the means of countermending it. See, e.g., *Nat'l Ass'n of Pharm. Mfrs., Inc. v. Ayerst Labs.*, 850 F.2d 904, 916 (2d Cir. 1988) (listing one factor in determining whether misleading advertising has anticompetitive effects as whether it is "readily susceptible to neutralization or other offset by rivals"); IIIA PHILLIP AREEDA & HERBERT HOVENKAMP, ANTITRUST LAW ¶ 782b at 275 (2d ed. 2002) ("[M]isrepresentations and organized deception by a dominant firm may have §2 implications when used against a nascent firm just as it is entering the market. Such a firm has no established customer base and typically lacks the resources to answer the dominant firm's deception effectively."). As noted in detail above, in pharmaceutical product reformulations, no competing manufacturer has the incentive or

three sets of allegations and, as to the fourth, considered only whether the conduct was independently actionable rather than whether it in fact impaired the “free consumer choice” on which *Berkey Photo* is founded.

Ultimately, the court rested entirely on its counter-factual assertion that brand products can garner sales in pharmaceutical markets only if consumers prefer them on a price/quality basis. The court implied that antitrust liability might have been appropriate if AstraZeneca had withdrawn brand Prilosec from the market, but the court gave no indication of how many fewer generic sales, if any, this might have caused. Nor did the court provide any reason why any such incremental adverse effect—reducing generic sales from 85% to, say 2%—should result in antitrust liability when the reduction from 85% to 25% did not.

## 2. The Profit Sacrifice Test

The *Nexium* plaintiffs also asserted that AstraZeneca’s conduct was unlawful under the much more permissive (for the monopolist) “profit sacrifice” test. Many cases indicate that such allegations are sufficient to state a claim under Section 2.<sup>231</sup> The district court did not address this allegation, but it merits exploration here.

The rule of reason asks whether the benefits of the design change to consumers are greater than the losses to consumers. The profit sacrifice test asks whether the benefits of the design change to the monopolist (i.e., additional sales and profits), absent the effect of maintaining the monopoly, are greater than the costs to the monopolist. The profit sacrifice test is, in essence, an economic test for determining whether the monopolist’s sole

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means to countermand a brand manufacturer’s deceptive campaign against its own original product. The *Nexium* court also noted that the de minimis presumption applies unless the misrepresentations were “made to buyers without knowledge of the subject matter,” and implied that doctors are the “buyers” of pharmaceuticals and are knowledgeable of the subject matter. 534 F. Supp. 2d at 152. Doctors are not the buyers of the products and, being price insensitive, lack the incentive to overcome the misrepresentations.

231. See, e.g., *Ne. Tel. Co. v. AT&T*, 651 F.2d 76, 94–95 (2d Cir. 1981) (holding that properly instructed jury could reasonably find that monopolist designed product in order to impede competition); *Response of Carolina, Inc. v. Leasco Response, Inc.*, 537 F.2d 1307, 1330 (5th Cir. 1976) (holding that technological tying cases are “limited to those instances where the technological factor tying the hardware to the software has been designed for the purpose of tying the products, rather than to achieve some technologically beneficial result”); *ILC Periph. Leas. Corp. v. IBM*, 458 F. Supp. 423, 439–41 (N.D. Cal. 1978) (no liability where “there was no evidence that IBM was sacrificing present profits with the expectation of recouping its losses with subsequent price increases”).

motive was to impair competition. If a profit-maximizing firm engages in conduct that would not be economically rational (i.e., increase profits) absent a reduction in competition, then it can be inferred that the firm was aware of and motivated solely to achieve that reduction.<sup>232</sup>

Professors Ordover and Willig explored the application of the profit sacrifice test to product design changes.<sup>233</sup> They note that even the “technological superiority” of the new product does not prevent a finding of exclusionary conduct:

[T]he technological superiority of a new system does not preclude a finding of predatory product innovation. . . . Under this standard, a new system is immune from a finding of predation if and only if the value to consumers of the new system relative to the preexisting system is greater than the required development costs.<sup>234</sup>

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232. See, e.g., *Verizon Commc'ns, Inc. v. Law Offices of Curtis V. Trinko, LLP*, 540 U.S. 398, 408 (2004) (finding that evidence in *Aspen Skiing* reflected “a willingness to forsake short-term profits to achieve an anticompetitive end”); *Aspen Skiing Co. v. Aspen Highlands Skiing Co.*, 472 U.S. 585, 610–11 (1985) (finding that the defendant “was willing to sacrifice short-run benefits and consumer goodwill in exchange for a perceived long-run impact on its smaller rival”); *Covad Commc'ns v. Bell Atlantic Corp.*, 398 F.3d 666, 676 (D.C. Cir. 2005) (predatory practice “is one in which a firm sacrifices short-term profits in order to drive out of the market or otherwise discipline a competitor”); *IIIB AREEDA & HOVENKAMP*, *supra* note 228, ¶ 773e at 253 (A refusal to deal is unlawful if it is irrational in the sense that the defendant sacrificed an opportunity to make a profitable sale only because of the adverse impact the refusal would have on a rival.).

233. Janusz A. Ordover & Robert D. Willig, *An Economic Definition of Predation: Pricing and Product Innovation*, 91 YALE L.J. 8, 22 (1981); see also A. Douglas Melamed, *Exclusionary Conduct Under the Antitrust Laws: Balancing, Sacrifice, and Refusals to Deal*, 20 BERKELEY TECH. L.J. 1247, 1256–57 (2005) (discussing virtues of the profit sacrifice test); Gregory J. Werden, *Identifying Exclusionary Conduct Under Section 2: The ‘No Economic Sense’ Test*, 73 ANTITRUST L.J. 413, 422–25 (2006) (discussing “no economic sense” test). But see Daniel A. Crane, *Mixed Bundling, Profit Sacrifice, and Consumer Welfare*, 55 EMORY L.J. 423, 450–53 (2006) (criticizing sacrifice test as too difficult to apply); Gilbert, *supra* note 32, at 72–73 (criticizing sacrifice test as both over- and under-inclusive).

234. Ordover & Willig, *supra* note 233, at 49; see also *Spirit Airlines, Inc. v. Northwest Airlines, Inc.*, 431 F.3d 917, 953 (6th Cir. 2005) (Moore, J., concurring) (noting that predation claims are based on the theory that “an incumbent seeks to retain monopolist control in the future by ceasing to engage in economically rational behavior in the present in an effort to drive potential rivals from the market”); ROBERT H. BORK, *THE ANTITRUST PARADOX: A POLICY AT WAR WITH ITSELF* 144 (1978) (stating that sacrifice test is used to identify business practices that “would not be considered profit maximizing except for the expectation either that (1) rivals will be driven from the market, leaving the predator with a

The *Nexium* plaintiffs alleged that the product redesign scheme was profitable for AstraZeneca only because the change had the effect of impairing generic competition. The Complaints alleged that AstraZeneca made no additional sales or profits with Nexium, as compared to Prilosec, except those it made by impairing generic competition. Specifically, the Complaints alleged that, in 2000 (the year before Nexium entered) AstraZeneca had U.S. sales of 29.6 million units of Prilosec. In 2002 (the first full year after Nexium's entry), it had U.S. sales of 33 million units of Prilosec and Nexium combined, an 11.4% increase.<sup>235</sup> In that period, however, the number of prescriptions written in the U.S. for the relevant conditions increased over 30%—a rate of increase twice that of Prilosec/Nexium.<sup>236</sup> Thus, the development and marketing of Nexium caused AstraZeneca to lose sales (except those it kept by impairing generic competition).<sup>237</sup> This empirical allegation comports with Plaintiffs' allegations that the design change brought no consumer benefits.<sup>238</sup>

The Complaints also alleged that AstraZeneca incurred very substantial R&D and marketing costs to switch to a product with fewer sales.<sup>239</sup> Accordingly, the strategy was profitable only because of its effect of impairing competition from generic Prilosec. Discovery undoubtedly would have revealed complications and subtleties, but, on its face, this seems like a viable allegation that the conduct flunked the profit sacrifice test.<sup>240</sup>

## V. CONCLUSION

Product reformulations in prescription pharmaceutical markets raise significant issues of public concern. The price disconnect in these markets often prevents prices from reaching competitive levels until generic

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market share sufficient to command monopoly profits, or (2) rivals will be chastened sufficiently to abandon competitive behavior the predator finds inconvenient or threatening”).

235. Walgreen Complaint, *supra* note 193, at 22

236. *Id.*

237. *Id.* For example, the sales of Prevacid, a very similar PPI, increased 17% during the same period. *See* Top 200 Reports by Units, 1999–2003.

238. Indeed, the Complaints quoted a public statement from the manufacturer's former chief executive that, based only on its medical merits, Nexium “would not have been developed.” Walgreen Complaint, *supra* note 193 at 23.

239. *Id.*

240. Plaintiffs' allegations, made without the benefit of discovery, were based on an ex-post analysis of the sales that Nexium actually achieved. A proper profit-sacrifice analysis, made with the benefit of discovery, proceeds ex ante, i.e., is based on defendant's projected sales and profits.

substitutability reconnects the price/quality choice for consumers. By law, this substitutability and its consequent price competition depend on the technological congruence between the brand and generic products. The brand manufacturer can destroy this congruence with a strategy of redesigning its product.

Our data suggest that the great majority of pharmaceutical reformulations are temporally unrelated to imminent generic entry and thus are unlikely to be part of a generic-impairment scheme. A sensible antitrust rule designed to thwart such schemes will not chill these reformulations.

The data also show that there are thirty-two reformulations that are temporally linked to imminent generic entry and that offer seemingly little therapeutic benefit for consumers, including redesigns from one form of a pill to another or one enantiomer to another, and multiple switches. There are another twenty-two reformulations to extended-release or combination products that may offer some convenience (and thus possibly some increased compliance) for those consumers who can afford them, but can cause substantially reduced compliance for those consumers who cannot afford them and can prevent consumers from choosing a lower price in lieu of increased convenience.<sup>241</sup> A workable antitrust rule must be powerful enough to deter welfare-reducing reformulations but subtle enough to appropriately deal with reformulations that can bring both some modest gains in medical benefit and some significant impairment of price competition. The stakes for consumers are enormously high, with annual losses of up to \$2 billion per anticompetitive reformulation.

Some early antitrust analyses of pharmaceutical reformulations have looked for an easy answer in the false talisman of whether the original product was withdrawn from the market. In otherwise price-competitive markets – i.e., markets that do not suffer from a price disconnect – withdrawal of the original product can in some circumstances interfere with the consumer's price/quality choice and thus negate the inference that the

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241. It is well documented that the high price of prescriptions causes many consumers to either not purchase the product at all or to take less than they should (skip pills or split pills). See, e.g., Claudia L. Schur et al., *Lack of Prescription Coverage Among the Under 65: A Symptom of Underinsurance*, Issue Brief, The Commonwealth Fund Task Force on the Future of Health Ins., at 2–3 (Feb. 2004), [http://www.commonwealthfund.org/usr\\_doc/Schur\\_under65.pdf](http://www.commonwealthfund.org/usr_doc/Schur_under65.pdf); PRESCRIPTION DRUGS: A VITAL COMPONENT OF HEALTHCARE 4, GEORGETOWN UNIV. CTR. ON AGING & SOC. (Sept. 2002); *Higher Out-Of-Pocket Costs Cause Massive Non-Compliance in the Use of Prescription Drugs, and This is Likely to Grow*, 2 HEALTH CARE NEWS 1, 2–3 (Dec. 6, 2002); T. Rice & K. Matsuoka, *The Impact of Cost-Sharing On Appropriate Utilization and Health Status: A Review of the Literature On Seniors*, 61 MED. CARE RESEARCH & REV. 415, 427–28 (2004); Shrank, *supra* note 33, at 1534.

product change has increased consumer welfare. In prescription pharmaceutical markets, the price disconnect exists whether or not the original product is withdrawn. Without AB-rated generic substitutability, the absence of consumers' price/quality choice is endemic in prescription pharmaceutical markets, and thus the inference of increased consumer welfare from product changes is negated regardless of whether the original brand product is withdrawn. Our examples show that redesigning and cannibalizing the original product can cause massive consumer welfare losses, reducing generics' market shares, and increasing brand manufacturers' shares by sixty points or more. Withdrawal of the original product merely increases losses that are already massive, and it thus likely cannot demark welfare-enhancing from welfare-reducing reformulations.

*Microsoft* subjected product changes to traditional rule of reason analysis, while *Berkey Photo* effectively granted them an antitrust safe harbor. The *Nexium* district court tried to reconcile the two decisions by asserting that the original product was withdrawn in *Microsoft* but was not in *Berkey Photo*. That proposed distinction fails not only on the economics, but also on the facts—Microsoft did not (and could not) withdraw the prior versions of Windows.

An analysis of the facts and economics of *Microsoft*, however, does yield some important insights. The strong network effects in *Microsoft* increased the importance of compatibility between Microsoft's operating system and the rivals' browsers. This "premium on compatibility" allowed "a dominant firm . . . [to] exclude rivals anticompetitively by engineering incompatibilities between the dominant product and the product offered by rivals."<sup>242</sup> In markets with significant network externalities, compatibility may be "a key to market success."<sup>243</sup> Consequently, the premium on compatibility "increas[ed] both the incentive and the opportunities" for anticompetitive product redesigns.<sup>244</sup> For generic pharmaceuticals, compatibility with the branded product is *the* key to market success, and the incentives and opportunities for welfare-reducing reformulations are consequently even greater.

The strong network effects, together with Microsoft's large installed base, gave it a significant advantage over rivals whose product consumers might have otherwise preferred on a price/quality basis.<sup>245</sup> Netscape's web

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242. IIIB AREEDA & HOVENKAMP, *supra* note 228, ¶ 776b, at 296.

243. *Id.*

244. *Id.*

245. *Id.* at 298.

browsers threatened Microsoft with the possibility that web-based applications would offer compatibility among alternative operating systems and thereby assist in overcoming Microsoft's installed base and network-effects advantages. If those advantages were overcome, consumers "could base their purchasing decisions on factors such as price or quality."<sup>246</sup> Microsoft's exclusionary conduct consisted of actions, including product redesigns, intended to "keep this switch from being deployed."<sup>247</sup>

In prescription pharmaceutical markets, the price disconnect (like the network effects in *Microsoft*) prevents consumers from making the relevant price/quality choice. And the generic substitution laws of fifty states (like the development of OS-independent applications in *Microsoft*) promises to put that choice back in consumers' hands. As in *Microsoft*,<sup>248</sup> the economic features of prescription pharmaceutical markets preclude application of indiscriminate, overly-broad antitrust safe harbors.

The price disconnect in prescription pharmaceutical markets also highlights the shortcomings in analyses that treat these markets as competitive and, correspondingly, treat generic substitutability as some sort of special, supra-competitive novelty that should be safeguarded, if at all, by regulation rather than antitrust law.<sup>249</sup> The reverse is true: the need for consumers to get a prescription from their doctors—a permission slip to buy a product—makes prescription pharmaceutical markets non-competitive, with each of many close functional substitutes making hundreds of millions or billions of dollars in sales with up to 90% gross margins. Generic substitutability restores the normal price/quality choice to consumers and drives prices down closer to competitive levels.

Critics say that generics that are hindered by pharmaceutical reformulations are merely trying to "free-ride" on the innovation efforts of brand manufacturers. Again, this has matters exactly backwards. If generics are granted final approval by the FDA, they by definition are not free-riding on the brand's efforts in any meaningful economic sense. The original brand product has already enjoyed whatever patent or FDA-exclusivity reward that

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246. *Id.*

247. *Id.*

248. *See id.* ¶ 776a, at 288 (advocating "more aggressive [antitrust] treatment" for network markets where product compatibility is important for rival success).

249. *See, e.g.,* Guy V. Amoresano, *Branded Drug Reformulation: the Next Brand vs. Generic Antitrust Battleground*, 62 FOOD & DRUG L.J. 249, 255–56 (2007); *see also* Jessie Cheng, Note, *An Antitrust Analysis of Product Hopping In the Pharmaceutical Industry*, 108 COLUM. L. REV. 1471, 1501–02 (2008).

society has granted it. Consumers have already paid (handsomely) for the reward that the brand manufacturer enjoyed.

Product redesign schemes are efforts by brand manufacturers to parlay consumers' prior investments in the original product – the installed base of sales for which consumers already paid – into a continued monopoly that would not exist absent the very price disconnect that generic substitutability is intended to overcome. This is clearly seen in the data and other evidence showing that sales of the reformulated product are critically dependent on whether it beats the generic to market. Without a significant head start, reformulated products competing head-to-head with the generic of the original product would often make little more sales than the original brand product would have made. But the price disconnect and the installed base of scripts written for the original brand product allow the brand manufacturer to switch the market from the original to the reformulated product before the generic can enter. This economic phenomenon must be a significant concern of a fact-based antitrust approach to pharmaceutical reformulations.

Guided by further, detailed mining of our database, and by additional data and analysis, we hope to advocate such an approach in our next paper on this issue.