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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,[1] filing questionable patent infringement lawsuits[2] 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,"[3] making dubious "Orange Book" listings,[4] and controlling the supply of necessary ingredients.[5] 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* Buspirone 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.[6] 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.[7]

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[8] and Nexium,[9] 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

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.[10] 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,[11] or in the absence of such a demonstration, can require expensive new clinical studies.

Product reformulations can be socially useful.[12] 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.[13]

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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[14] 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.[15] 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.[16]

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."[17] 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.[18]

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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/.

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.

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