

A Brief Response to “Drug Design Liability: Farewell to Comment k”: On the Intersection Between Patent Law and Tort Liability

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I.	Patent Law Encourages, Rather Than Inhibits, Innovation ...	560
II.	Difficulty in Pitting One Drug’s Efficacy Against Another ..	564
III.	Conclusion	565

“Drug Design Liability: Farewell to Comment k,”¹ authored by distinguished Professors James A. Henderson and Aaron Twerski, Jr., is a constructive piece of scholarship to which courts will undoubtedly turn as they render decisions on drug design liability. We agree with the article’s core conclusion that a claim that a drug is defective in its design is viable only in the rare circumstance that a drug can provide no benefit for any group of patients.² We write to respond to two relatively minor points made in the article. The first is the authors’ concern that patent law may deter drug innovation and thereby keep older, obsolete drugs on the market.³ Evidence shows, however, that patent law has facilitated an increasingly competitive pharmaceutical market. The second is the article’s suggestion

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¹James A. Henderson, Jr. & Aaron D. Twerski, *Drug Design Liability: Farewell to Comment k*, 67 BAYLOR L. REV. 522 (2015) [hereinafter “Farewell to Comment k”].

²*See id.* at 532–34.

³*See id.* at 535–36.

that one federally-approved prescription drug may, in some circumstances, provide a reasonable alternative design for another drug that treats the same condition.⁴ This position should be read consistently with the Restatement Third, allowing such comparisons only when one drug can provide no benefit to any subset of patients over another drug approved to treat the same condition.

I. PATENT LAW ENCOURAGES, RATHER THAN INHIBITS, INNOVATION

The article suggests that patent extensions on marketed drugs are anti-competitive because they “discourage the marketing of the sorts of new drugs that would tend to run the older, higher-risk, less-efficacious drugs off the market.”⁵ Evidence shows, however, that patent law encourages competition and ensures the proliferation of new designs within drug classes.

Patents protect the interests of manufacturers with first-to-market drugs, while protecting competitors that wish to create formulaically distinct drugs.⁶ Patents prevent imitation, not innovation. A patent on an existing compound prohibits rival firms from manufacturing products based on similar chemical compounds.⁷ Such imitative products, even when ultimately introduced at the end of the patent horizon, do not expand the treatment choices available to consumers; at best, they lead to cheaper, similar medications.

A reasonable alternative design to an existing drug product must, by patentability standards, be distinct from the existing drug.⁸ The patent on an existing product cannot prevent a rival firm from marketing an alternative drug, precisely because it is differentiable from the compound covered by the patent.⁹ Patents are likely to encourage rather than inhibit the emergence of alternative designs because they place sharply defined boundaries on the

⁴ See *id.* at 544–48.

⁵ *Id.* at 535–36.

⁶ See U.S. DEP’T OF JUSTICE & FED. TRADE COMM’N, TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW AND POLICY ch. 3, at 1 (2003) [hereinafter FTC Report], available at <http://www.ftc.gov/os/2003/10/innovationrpt.pdf>.

⁷ See 35 U.S.C. § 102(a) (2014); FTC Report, *supra* note 6, ch. 3 at 1–2; INNOVATION AND MARKETING IN THE PHARMACEUTICAL INDUSTRY: EMERGING PRACTICES, RESEARCH, AND POLICIES 33, 34 (Min Ding et al. eds., 7th ed. 2014) [hereinafter Innovation and Marketing].

⁸ See 35 U.S.C. § 103 (2014).

⁹ See *id.*; Innovation and Marketing, *supra* note 7, at 33, 34.

intellectual property rights associated with the existing drug. These boundaries ensure that the manufacturer of the existing drug cannot discourage rivals from developing closely adjacent designs through the threat of lengthy intellectual property disputes over amorphously defined property rights. Thus, a patent on an existing drug not only strengthens the holder’s claim on its own design, but also clarifies the right of rival firms to develop new chemical designs that enhance competition and provide consumers with more choices.

This explains why so many chemically related, yet structurally distinct, compounds can exist within a therapeutic class.¹⁰ Manufacturers have, after release of a breakthrough drug, quickly developed other distinct drugs to treat the same condition. Later drugs may build upon (and for many people improve upon) the foundation set by the former drugs. Cholesterol-reducing drugs, known as statins, are a prime example of this development.¹¹ The continued introduction of new, effective drug choices to treat depression also illustrates this point.¹² Patents (including patent extensions) associated

¹⁰See Jonathan J. Darrow, *The Patentability of Enantiomers: Implications for the Pharmaceutical Industry*, 2007 STAN. TECH. L. REV. 2, 5–11 (2007).

¹¹After Merck broke into the cholesterol-reducing drug market by patenting Mevacor in 1979 and receiving FDA approval in 1987, Merck kept its dominance by releasing Zocor in 1992. Other manufacturers rushed to develop even better anti-cholesterol drugs. For example, Pfizer introduced Lipitor in 1996, which became the top-selling anti-cholesterol drug. There are now seven structurally distinct statin drugs approved by the FDA for treating high cholesterol (Lipitor, Lescol, Altoprev, Livalo, Pravachol, Zocor, and Crestor). See *Evaluating Statin Drugs to Treat: High Cholesterol and Heart Disease Comparing Effectiveness, Safety, and Price*, CONSUMERREPORTS BEST BUY DRUGS 2, 5, <https://www.consumerreports.org/health/resources/pdf/best-buy-drugs/StatinsUpdate-FINAL.pdf> (last updated Mar. 2014). There are also four distinct combination drugs on the market that contain both a statin and another lipid lowering drug. See *id.* at 5.

¹²There are seven selective serotonin reuptake inhibitors (SSRIs) currently available to treat depression anxiety, and other mood disorders. *Selective Serotonin Reuptake Inhibitors (SSRIs) Information*, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm283587.htm> (last updated Dec. 23, 2014). This does not take into account the other types of anti-depressant drugs available on the market (i.e., serotonin-norepinephrine reuptake inhibitors (SNRIs), serotonin modulators and stimulators (SMSs), serotonin antagonist and reuptake inhibitors (SARIs), and others). See, e.g., Melissa Healy, *FDA Approves a New Antidepressant: Brintellix*, L.A. TIMES, Sept. 30, 2013, <http://www.latimes.com/science/sciencenow/la-sci-fda-approval-antidepressant-20130930-story.html> (discussing agency approval of a novel SMS that will interact with the brain in different ways than SSRIs to ease depression); Randy A. Sansone & Lori A. Sansone, *Serotonin Norepinephrine Reuptake Inhibitors: A Pharmacological Comparison*, INNOVATIONS IN CLINICAL NEUROSCIENCE, Mar.–Apr. 2014, at 37, 37–38, available at <http://>

with each drug in no way limit innovation and consumer choice within these therapeutic classes.

Pharmaceutical markets have actually become significantly *more* competitive, not less, in recent decades. A study of 72 drug classes found that the median time taken for a second branded drug to follow a breakthrough drug in a drug class fell from 10.2 years in the 1970s to a mere 1.2 years by the late 1990s.¹³ Indeed, the speed of entry was quicker not just for the first competing entrants but for subsequent competitors as well. The median time from the first follow-on drug to the second fell from 4.2 years in the 1970s to just 1.7 years in the 1990s.¹⁴ While the third follow-on drug entered the market in a median 3.7 years in the 1970s, that time fell to less than a year in the 1990s.¹⁵ Patent protection accorded the breakthrough drug has done little to hinder competition from rival, chemically distinct branded drugs, within the same class.

Many “follow-on” drugs are as efficacious as their predecessors. More than half of all drug classes had at least one follow-on drug that the FDA assigned a priority review designation,¹⁶ a status accorded to drugs that “treat serious conditions and provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions compared to available therapies.”¹⁷ This continued innovation is exemplified by the FDA’s assignment of priority review to an investigational drug developed by Sanofi for patients with high cholesterol in January 2015.¹⁸ AstraZeneca’s patent rights to the blockbuster drug,

www.ncbi.nlm.nih.gov/pmc/articles/PMC4008300/ (examining the pharmacological differences of five FDA-approved SNRIs that may ultimately relate to clinical nuances in patient care); *see also* *Drugs to Treat Major Depressive Disorder*, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/safety/medwatch/safetyinformation/ucm409855.htm> (last updated Aug. 15, 2014) (exploring available medications).

¹³ See Joseph A. DiMasi & Cherie Paquette, *The Economics of Follow-on Drug Research and Development*, 22 PHARMACOECONOMICS 1, 5 fig.2 (2004).

¹⁴ *Id.* at 8 tbl.3.

¹⁵ *Id.*

¹⁶ *Id.* at 8.

¹⁷ Office of New Drugs, *Manual of Policies and Procedures Center for Drug Evaluation and Research*, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffPoliciesandProcedures/ucm082000.pdf> (effective date June 25, 2013).

¹⁸ *Regeneron Pharms., Inc., Regeneron and Sanofi Announce Praluent™ (alirocumab) Biologics License Application has Been Accepted for Priority Review by US FDA*, REGENERON (Jan. 26, 2015), <http://newsroom.regeneron.com/releasedetail.cfm?releaseid=892747>.

Crestor, until 2016¹⁹ did not stop other manufacturers from researching and investing in other, novel options for lowering cholesterol.

“Newer,” however, does not necessarily mean “better” for all patients. While continued innovation increases choices, many first-to-market drugs in a therapeutic class remain the standard of care years after their patents expire and other drugs enter the market. For example, Coumadin (Warfarin), the anti-coagulant approved in 1954, still largely remains the gold standard for most patients for the treatment for preventing dangerous blood clots even though many other drugs have entered into the market such as Pradaxa, Xaralto, and Eliquis.²⁰

Mounting competition has resulted not only in the emergence of alternative chemical designs but in manufacturers of branded drugs continuing research and development even after a drug is approved and marketed. Post-marketing research studies, commonly referred to as Phase IV trials, examine the effectiveness of the drug in real-world conditions and across various cross-sections of the population.²¹ They also help document potential side-effects in long-term use and in interactions with other combinations of drugs, leading to significantly improved safety warnings and more informed prescriptions.²² Between 1976 and 1989, pharmaceutical firms spent between 3.2% and 5.0% of their total research and development budgets on Phase IV clinical trials.²³ By 2013, the

¹⁹ See *In re Rosuvastatin Calcium Patent Litig.*, 703 F.3d 511 (Fed. Cir. 2012) (affirming validity of AstraZeneca’s patent); Jessica Hodgson, *AstraZeneca Settles Suit, Protecting Crestor*, WALL ST. J., Mar. 25, 2013, <http://www.wsj.com/articles/SB10001424127887324789504578381871497235276>.

²⁰ *Warfarin: Still the Gold Standard*, REPERTOIRE MAGAZINE (May 2014), <http://www.repertoiremag.com/warfarin-still-the-gold-standard.html>; see also John Fauber & Coulter Jones, *New Anticoagulant Drugs Provide Stroke Prevention With Dose of Danger*, J. SENTINEL, Aug. 1, 2015, <http://www.jsonline.com/watchdog/watchdogreports/new-anticoagulant-drugs-provide-stroke-prevention-with-dose-of-danger-b99545719z1-320303991.html> (comparing risks, benefits, and cost of warfarin to new blood thinning drugs).

²¹ See Viraj Suvarna, *Phase IV of Drug Development*, PERSP. IN CLINICAL RES., Apr.–June 2010, at 57, 57–59.

²² See *id.* at 59.

²³ *Pharmaceutical R&D: Costs, Risks and Rewards*, U.S. CONGRESS OFFICE OF TECHNOLOGY ASSESSMENT, 44, tbl.2–3 (1993), available at http://govinfo.library.unt.edu/ota/Ota_1/DATA/1993/9336.PDF.

percentage of R&D devoted to Phase IV trials had increased substantially to 14.7%.²⁴

II. DIFFICULTY IN PITTING ONE DRUG'S EFFICACY AGAINST ANOTHER

We agree with the article's conclusion that it is not proper for courts to compare the design of a drug that the FDA approved after a lengthy and expensive review process to a hypothetical reasonable "alternative" design developed for the purpose of litigation.²⁵ The article's unqualified statement that a plaintiff could propose a reasonable alternative design based on another, possibly newer, FDA-approved drug by arguing that the drug would provide the same benefits with fewer risks²⁶ is, however, problematic.

Professors Henderson and Twerski soundly observe that the Restatement Third generally precludes design liability with respect to prescription drugs.²⁷ Such liability is inappropriate "even if it would be unacceptably risky to prescribe [a drug] for a clear majority of patients in need of the type of therapeutic benefit the drug provides."²⁸ The alternative is a tort system that would encourage pharmaceutical manufacturers to remove from the market drugs that may offer the only effective treatment option for certain groups of patients. For this reason, tort law requires manufacturers to address known drug risks by adequately warning healthcare professionals of them, not altering the chemical composition that defines a drug.²⁹ As the article recognizes, "[a]nyone proposing a change in the molecular structure of an already-approved drug must present the proposed altered molecule to the FDA for approval, thus initiating the

²⁴Pharmaceutical Manufacturers Association of America, *PhRMA Annual Membership Survey* tbl.4 (2015), http://www.phrma.org/sites/default/files/pdf/2015-phrma_profile_membershi_p_results.pdf.

²⁵See Farewell to Comment k, *supra* note 1, at 544–45.

²⁶See *id.*

²⁷See *id.* at 532–34.

²⁸*Id.* at 532–33.

²⁹See *Mutual Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2475 (2013) (recognizing that the only way for a manufacturer to ameliorate the drug's "risk-utility" profile is to alter its warnings to avoid an unreasonable risk of harm from hidden dangers or from foreseeable uses and thus a state's design-defect cause of action imposed a duty on a manufacturer to alter its product warnings).

selfsame review that is required for a new drug.”³⁰ “For good reason,” the authors explain, “courts are incapable of administering such a test,” which would require replication of the FDA process.³¹

The article leaves open the door, however, for plaintiffs to assert that an FDA-approved drug provides a reasonable alternative design, claiming that another drug that is on the market would provide the same benefits with fewer risks.³² In that situation, the article observes, a court is not placed in the position of stepping into the shoes of the FDA to guess whether the agency would approve the proposed alternative drug.³³

The reasonable alternative design standard, however, should not allow plaintiffs’ lawyers to pit the risks and benefits of one FDA-approved drug against another. Each drug has a specific risk-benefit profile.³⁴ It is often unpredictable which of several alternative drugs to treat a condition will work best for a particular patient.³⁵ Learned healthcare providers, who know a patient’s medical history and condition, can work with a patient to make this assessment. An older drug may well turn out to be more effective or otherwise preferable for a particular individual than a newer one.

Under the Restatement Third, if an existing drug could be more effective for any subset of patients than another FDA-approved option, it should remain available and not subject to design liability.³⁶ The article is consistent with this point, but could be misread by courts to more broadly support design liability claims based on comparisons between different FDA-approved drugs used to treat the same condition.

III. CONCLUSION

Two greatly respected scholars, Professors Henderson and Twerski, have continued their perceptive perspectives on tort law. Our two issues with the article are minor, but important. In bidding farewell to Comment k,

³⁰ See Farewell to Comment k, *supra* note 1, at 544–45.

³¹ *Id.* at 544.

³² *Id.* at 545–46.

³³ See *id.* (finding that in such circumstances “the court would not be required to replicate the administrative approval process and the case would presumably be adjudicable”).

³⁴ Barry R. Furrow, *Enterprise Liability for Bad Outcomes from Drug Therapy: The Doctor, the Hospital, the Pharmacy, and the Drug Firm*, 44 *DRAKE L. REV.* 377, 427 (1996).

³⁵ See, e.g., *Find the Best Medications for Rheumatoid Arthritis*, CONSUMERREPORTS, <http://www.healthline.com/health/consumer-reports-rheumatoid-arthritis> (last visited Oct. 4, 2015).

³⁶ See RESTATEMENT (THIRD) OF TORTS: PRODS. LIAB. § 6(c) (AM. LAW INST. 1998).

the article forays from tort law into patent law, viewing the latter as deterring innovation rather than demanding it.³⁷ Evidence suggests, however, that patent law has led to an increasingly competitive marketplace where manufacturers are seeking to produce new and more effective drugs, even as drugs on the market may remain the best option for certain patients.³⁸

The article also wisely rejects the viability of drug design defect claims that rely on a reasonable alternative design that only the FDA could approve.³⁹ In leaving the door open to design defect claims comparing the risks and benefits of one FDA-approved drug to another, it is essential to return to principles of the Restatement Third. Under its reasoning, an older drug may be considered defective in design only if a newer approved drug renders risks of the older drug unsuitable for prescribing the older drug to any class of patients.⁴⁰ Otherwise, the liability system would provide an incentive for manufacturers to remove drugs from the market that certain patients find effective simply because newer products may have greater benefits, or less risk, for a larger group of patients.

³⁷ See Farewell to Comment k, *supra* note 1, at 534–37.

³⁸ See Innovation and Marketing, *supra* note 7, at 35.

³⁹ See Farewell to Comment k, *supra* note 1, at 544–46.

⁴⁰ See RESTATEMENT (THIRD) OF TORTS: PRODS. LIAB. § 6(c) (AM. LAW INST. 1998).