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## ARTICLES

### PHARMACEUTICAL GATEKEEPERS

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#### INTRODUCTION

In an influential 1986 article, Reinier Kraakman explored the role of third party “gatekeepers” in deterring misconduct by declining to support primary wrongdoers.<sup>1</sup> Lawyers and accountants, for example, help to prevent the fraudulent issuance of securities or serious misrepresentations in financial statements by declining to provide the legal opinions or audits that are needed to close a deal.<sup>2</sup> Although Kraakman was primarily focused on wrongdoing by actors in the corporate finance sphere, the pharmaceutical marketplace provides fertile ground for the further development of a gatekeeping analysis. Few industries are characterized by such numerous and diverse potential gatekeepers, including physicians, public interest groups, insurance companies, and even patients themselves. In addition, a number of federal agencies act as gatekeepers of a different sort, wielding the power to withhold support from “wrongdoers” (to use Kraakman’s term), but do so on the basis of a statutory duty rather than out of a desire to avoid potential liability.<sup>3</sup> These agencies include the United States Patent and Trademark Office (USPTO), the Food and Drug Administration (FDA), and the Federal Trade Commission (FTC).

This Article draws inspiration from Kraakman’s framework to explore a particular and perhaps unexpected type of “wrongdoing” that is observed in the

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1. Reiner H. Kraakman, *Gatekeepers: The Anatomy of a Third-Party Enforcement Strategy*, 2 J. L. ECON. & ORG. 53 (1986).

2. *See, e.g.*, 17 C.F.R. § 229.601 (2013) (Exhibit Table) (noting that a legal opinion must be included as an exhibit for eight types of financial statements, including forms S-1 and S-3).

3. *See, e.g.*, Howard L. Dorfman et al., *Presumption of Innocence: FDA’s Authority to Regulate the Specifics of Prescription Drug Labeling and the Preemption Debate*, 61 FOOD & DRUG L.J. 585, 588 (2006) (recognizing that statutes control the FDA in the labelling of prescription drugs.)

pharmaceutical industry: the lawful sale of medicines that have little or no therapeutic effect. Previous work has described the surprising absence of substantial efficacy or advantage exhibited by many of today's most celebrated pharmaceuticals.<sup>4</sup> This lack of efficacy is all the more unexpected given the presence of myriad expert gatekeepers, both public and private, that stand watch over consumer behavior. In fact, so many gatekeepers are at work in the pharmaceutical industry that a reasonable observer might be justifiably skeptical at the assertion that the currently regulatory structure fails to adequately guard against the prevalence of ineffective medicines. A closer examination of efficacy data merely turns this skepticism to bewilderment, confirming the absence of substantial efficacy but leading the observer to wonder how such impotent drugs could have traversed so many gatekeepers' watchful eyes, evoking perhaps the image of Dr. Seuss's ineffectual bee watcher-watcher.<sup>5</sup> This Article seeks to attend to that bewilderment by explaining how the numerous well-intentioned and often well-respected gatekeepers have not been successful in fulfilling their gatekeeping duty to protect patients from minimally effective medicines.

#### I. PRIVATE PARTIES AS GATEKEEPERS

Pharmaceutical gatekeepers can be divided into two broad categories: public gatekeepers such as the FDA, which regulate drug companies directly, and private gatekeepers such as doctors, which exert varying levels of influence and control over a patient's consumption of a given drug.<sup>6</sup> This Part examines the role of the private (non-governmental) pharmaceutical gatekeepers, which fall most comfortably within Kraakman's meaning of the term. These private gatekeepers include not only doctors, who can withhold prescriptions,<sup>7</sup> but also insurance companies, which can withhold reimbursement,<sup>8</sup> advocacy organizations, which can withhold endorsements,<sup>9</sup> and consumers themselves, who can withhold purchases and thereby vote with their pocket books.<sup>10</sup>

Although these private actors can be considered gatekeepers under

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4. See Jonathan J. Darrow, *Pharmaceutical Efficacy: History and Regulation* (unpublished S.J.D. dissertation, Harvard Law School) (on file with author); Donald W. Light et al., *Institutional Corruption of Pharmaceuticals and the Consequences for Patients*, 41 J. L. MED. & ETHICS 590 (2013); see also sources cited *infra* note 108.

5. DR. SEUSS, DID I EVER TELL YOU HOW LUCKY YOU ARE? 26 (1973).

6. For the public versus private (or market) gatekeeper distinction, see Kraakman *supra* note 1, at 62.

7. See, e.g., Jessie Cheng, *An Antitrust Analysis of Product Hopping in the Pharmaceutical Industry*, 108 COLUM. L. REV. 1471, 1498 (2008) ("Physicians, acting as 'gatekeepers,' independently dictate the selection of prescription drugs for a patient's consumption.").

8. See Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 374 (2007).

9. See *id.* at 367.

10. See *id.* at 380 (noting that consumers may withhold the purchase of an expensive pharmaceutical product in favor of a less expensive one).

Kraakman's framework, they are in a sense at the fringe of his analysis, which is primarily directed at gatekeepers that can directly withhold support from the wrongdoers themselves.<sup>11</sup> In contrast, although pharmaceutical gatekeepers could be seen as potentially withholding support for drug company "wrongdoers" by refusing to prescribe or pay for a medicine, it is more natural to view them as withholding victims.<sup>12</sup> That is, these gatekeepers prevent patients from demanding the wrongdoer's products, rather than directly withholding the support needed for drug companies to make their products available on the market. This situation, where gatekeepers disrupt misconduct by withholding potential victims, is briefly alluded to by Kraakman in a footnote.<sup>13</sup> In another footnote, the possibility is raised that even victims themselves might serve as their own gatekeepers,<sup>14</sup> a fruitful point of inquiry in the present context given the ability of consumers to purchase over-the-counter drugs, to decline to purchase prescribed drugs, or to influence physician prescribing by requesting certain drugs by name. These two unique species of gatekeepers, briefly mentioned but largely undeveloped by Kraakman, are therefore especially relevant in the pharmaceutical marketplace and it is there that the discussion begins.

#### A. Physicians

One of the reasons that people find it so difficult to believe that many drugs lack substantial efficacy is that drugs are prescribed by doctors, who are often held in the highest of esteem. According to Gallup polls, doctors are the third most trusted professionals (after nurses and pharmacists), with public perception of doctor trustworthiness gradually increasing since the polls began in 1976.<sup>15</sup> This trust and esteem is not entirely misplaced. Physicians do have substantial, often highly specialized education and training. Some have extensive experience with specific medications, medical conditions, or even patients. In addition to substantial training and experience, physician gatekeepers are themselves regulated by "second-level" gatekeepers in the form of government licensing schemes, and are required to stay current via continuing medical education.<sup>16</sup> Most importantly, the vast majority of physicians likely have a sincere desire to

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11. See Kraakman *supra* note 1, at 62.

12. *Id.* at 64 n.31.

13. *Id.*

14. *Id.* at 62 n.21.

15. Jeffrey M. Jones, *Record 64% Rate Honesty, Ethics of Members of Congress Low*, GALLUP, Dec. 12, 2011, <http://www.gallup.com/poll/151460/record-rate-honesty-ethics-members-congress-low.aspx>, archived at <http://perma.cc/LR2K-76G2> ("Ratings of Honesty and Ethics of Medical Doctors and Pharmacists").

16. See Timothy Stoltzfus Jost, *Oversight of Marketing Relationships Between Physicians and the Drug and Device Industry: A Comparative Study*, 36 AM. J.L. & MED. 326, 332 (2010) (noting that continuing medical education may be a requirement to maintain licensure or specialty designation).

make decisions that are in the best interests of their patients.<sup>17</sup> These and other factors combine in the minds of the public to cast an almost deity-like aura on those in the medical profession. One physician reported literally being referred to as “Dr. God” by an admiring patient.<sup>18</sup>

Nevertheless, there are a number of reasons why physicians do not make the infallible gatekeepers that their education, training, public trust, and authority to withhold prescriptions might suggest. In some cases, doctors simply are not involved in the decision to purchase a drug, as might be the case with over-the-counter products. When doctors are involved, a number of factors may push them in the direction of prescribing a drug despite a lack of substantial therapeutic value.<sup>19</sup> Pliny lamented that in ancient Greece, “not even the physicians know their facts” about pharmaceuticals, the sale of which is “plainly a showy parade of the art, and a colossal boast of science.”<sup>20</sup> These sentiments were echoed more recently on the floor of the House of Representatives, with only slightly more restrained cynicism:

[I]t is impossible for any doctor, from his own resources, to be able to pick out the good drugs from the bad ones. Unfortunately, many doctors rely heavily and sometimes almost exclusively on detail men for information with regard to drugs . . . . Drug companies have learned that doctors respond to the same kind of emotional appeals as laymen. They are influenced by the same advertising techniques that are used by mass consumer advertising. They accept new drugs with amazing rapidity.<sup>21</sup>

In addition, patients may request a drug in general or even a particular drug, which is an intended and therefore particularly expected consequence of direct-to-consumer (DTC) advertising.<sup>22</sup> Evidence suggests that sales often increase dramatically following DTC drug advertising.<sup>23</sup> Where the drug is reasonably

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17. See *In re Gladstone*, 44 A.D.3d 777, 778 (N.Y.S.2d 2007) (noting that consideration of the patient’s best interest can be a regulatory requirement).

18. JERRY AVORN, POWERFUL MEDICINES 166 (2004).

19. See 108 CONG. REC. 19926 (Sept. 27, 1962) (statement of Rep. Celler) (quoted *infra* note 21).

20. PLINY THE ELDER, NATURAL HISTORY, Book XXIX 199 (W.H.S. Jones trans., 1963).

21. 108 CONG. REC. 19926 (Sept. 27, 1962) (statement of Rep. Celler) (internal quotations omitted).

22. See Nancy Ann Jeffrey, *A Little Knowledge . . . Doctors Are Suddenly Swamped With Patients Who Think They Know a Lot More Than They Actually Do*, WALL ST. J., Oct. 19, 1998, at R8; *Doctors Concerned by Requests for Drug Brands Seen in TV Ads*, AUSTIN AM. STATESMAN, Jan. 7, 1998, at D1; Elyse Tanouye, *Drug Ads Spur Patients to Demand More Prescriptions*, WALL ST. J., Dec. 22, 1997, at B1.

23. See Joel J. Davis, *Riskier Than We Think? The Relationship Between Risk Statement Completeness and Perceptions of Direct to Consumer Advertised Prescription Drugs*, 5 J. HEALTH COMM’N: INT’L PERSPECTIVES 349, 350 (2000) (describing “[f]ive related trends [that] help to explain how DTC advertising affects product sales.”); Milton Liebman, *Three Scenarios for Direct-to-Consumer Advertising*, 35 MED. MARKETING & MEDIA 72 (2000).

safe, as required to obtain FDA approval,<sup>24</sup> prescribing the drug for its labeled indication will satisfy the patient's demand while imposing no more than FDA-accepted levels of risk, which risk can be addressed by a brief verbal disclaimer to the patient.<sup>25</sup> The strong cultural tradition of respecting patient autonomy, even when patients wish to act against medical advice,<sup>26</sup> contributes to this tendency. In addition, doctors in the age of managed care face pressures to limit the amount of time spent with each patient.<sup>27</sup> Counseling a patient on his condition, or on appropriate non-drug treatments such as diet and exercise, can be time-consuming and might be viewed as time not particularly well spent in light of low patient compliance rates.<sup>28</sup> In contrast, once a patient has a prescription in hand, he can head out the door, satisfied that the doctor has done her job.

This is not to suggest that physicians would knowingly prescribe an ineffective drug when a substantially more effective drug is available. However, often there are simply no substantially effective drugs even in common therapeutic areas, such as depression or Alzheimer's.<sup>29</sup> In these cases, prescribing a drug can satisfy the patient, give the patient hope, and possibly even stimulate a genuine improvement caused by the placebo effect.<sup>30</sup> It can also give the doctor

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24. 21 U.S.C. § 355(d) (2013).

25. See Daniel W. Whitney, *Product Liability Issues for the Expanding OTC Drug Category*, 48 FOOD & DRUG L.J. 321, 329 (1993) (stating that the ultimate consumer must be warned in a learned intermediary situation).

26. See, e.g., *Stamford Hosp. v. Vega*, 674 A.2d 821, 831-32 (Conn. 1996) (noting the common law right to refuse medical treatment).

27. See, e.g., OHIO ELDER LAW § 13:24 (2013) (discussing time restraints on time with patients in light of Medicare coverage).

28. Sophie Desroches et al., *Interventions to Enhance Adherence to Dietary Advice for Preventing and Managing Chronic Diseases in Adults (Review)*, COCHRANE COLLABORATION, 2013 (Issue 2), at 3 (noting that non-adherence rates for medication and lifestyle changes are estimated to be between 50% and 80%).

29. C. Courtney et al., *Long-term Donepezil Treatment in 565 Patients with Alzheimer's Disease (AD2000): Randomized Double-Blind Trial*, 363(9427) LANCET 2105, 2105 (2004) (concluding that donepezil is "not cost effective, with benefits below minimally relevant thresholds"); Richard A. Hansen et al., *Efficacy and Safety of Donepezil, Galantamine, and Rivastigmine for the Treatment of Alzheimer's Disease: A Systematic Review and Meta-Analysis*, 3(2) CLIN. INTERVENTIONS IN AGING 211, 222 (2008) (finding "no clear evidence" that any of donepezil, galantamine or rivastigmine is more efficacious than the others); Irving Kirsch & Thomas J. Moore, *The Emperor's New Drugs: An Analysis of Antidepressant Medication Data Submitted to the U.S. Food and Drug Administration*, 5 PREVENTION & TREATMENT 1 (2002) (Article 23); *Petition to Ban 23 Milligram Dose of Donepezil (Aricept)*, PUB. CITIZEN, May 18, 2011, at 12, <http://www.citizen.org/documents/1950.pdf>, archived at <http://perma.cc/ZBA4-D4UJ>.

30. See, e.g., Cara Feinberg, *The Placebo Phenomenon*, HARV. MAG. 36, 38 (2013), <http://harvardmagazine.com/2013/01/the-placebo-phenomenon>, archived at <http://perma.cc/6XGH-KKR6> (describing a study where patients knew they were taking only placebos but nevertheless reported improvement "comparable to the improvement seen in trials for the best *real* IBS [irritable bowel syndrome] drugs.").

a sense of agency, even when there is little medicinally that can truly be done.<sup>31</sup> While prescribing what are essentially placebos in such circumstances may be a sensible option, or perhaps the only option, it chips away at the pristine image of today's doctors as wholly different from those of the last century, or even the last millennium. In modern times, chronocentrism<sup>32</sup> leads some to denigrate ancient healthcare workers (called "shamans," "medicine men," etc., rather than "doctors") as practicing superstitious medicine with no basis in science.<sup>33</sup> But in some cases, their treatments may have been just as effective as today's treatments.<sup>34</sup>

Adding to the problem is an absence of clearly presented and easily available efficacy data. Although drug labels are required to contain a section describing clinical trial results, this information is buried in section fourteen of the package insert,<sup>35</sup> is often written in such a way that it is difficult for doctors (let alone patients) to understand,<sup>36</sup> and is not standardized even among drugs within the same category,<sup>37</sup> making assessments of comparative efficacy difficult or impossible. The result is that even doctors do not have anything approaching adequate information regarding a drug's efficacy.

Worse, the void of non-biased information is often filled by drug company "detailers," who personally visit physicians for the primary purpose of

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31. *Id.* at 39 (introducing the idea of studying the mind of physicians as they treat patients).

32. Chronocentrism is defined as "the egotism that one's own generation is poised on the very cusp of history." TOM STANDAGE, *THE VICTORIAN INTERNET: THE REMARKABLE STORY OF THE TELEGRAPH AND THE NINETEENTH CENTURY'S ON-LINE PIONEERS* 213 (1998).

33. See DAVID EDWARD OWEN, *BRITISH OPIUM POLICY IN CHINA AND INDIA* 12 (1934) (describing tenth century Chinese opium prescriptions as "curious mixtures of shrewd empiricism and superstition"); Jerry Stannard, *Squill in Ancient and Medieval Materia Medica, With Special Reference to Its Employment for Dropsy*, 50 *BULL. N.Y. ACAD. MED.* 684, 703 (1974) (describing the medieval period as "a time in which the boundaries between science and superstition were vague").

34. See TALCOTT PARSONS, *THE SOCIAL SYSTEM* 315 (1951) ("[P]seudoscience is the functional equivalent of magic in the modern medical field."). Elsewhere Parsons explains that even "organic physician[s]" that seek to practice medicine as an empirical science nevertheless engage in "unconscious psychotherapy," a reflection that much of healing today, as always, lies not in pills but in perception, psychology and belief. See *id.* at 311.

35. See 21 C.F.R. § 201.56(d)(1) (2013).

36. See PETER TEMIN, *TAKING YOUR MEDICINE: DRUG REGULATION IN THE UNITED STATES* 9-11 (1980) ("Data on efficacy are scattered through a wide variety of medical journals that . . . are not easily understood without medical and statistical training. The extant data are, in addition, woefully incomplete so that even the trained investigator with access to a good medical library will find the pursuit of information on the comparative effectiveness of similar drugs . . . peculiarly frustrating . . . Doctors generally are not well-qualified [in statistics].").

37. See Christine H. Kim, *The Case for Preemption of Prescription Drug Failure-to-Warn Claims*, 62 *FOOD & DRUG L.J.* 399, 407 n.86 (2007) ("Congress has not specifically addressed uniformity of prescription drug labeling.").

influencing prescribing decisions.<sup>38</sup> As one medical historian notes, “[d]octors are usually unable or ill-equipped to examine the research literature. As a result, they tend to learn about new drugs from roving representatives or from advertisements . . . .”<sup>39</sup> The result of this state of affairs is unsurprising. According to *Consumer Reports*, an independent nonprofit organization, “[m]any people (including [many] physicians) think that newer drugs are better. While that’s a natural assumption to make, it’s not true. Studies consistently find that many older medicines are as good as—and in some cases better than—newer medicines.”<sup>40</sup>

The pharmaceutical pricing and payment structure provides an additional reason why doctors make imperfect gatekeepers. Physicians themselves do not pay for their patients’ drugs, so there is no direct financial disincentive to prescribe any given medicine.<sup>41</sup> Doctors also know that most patients do not bear the full costs of medications, so there is not even an indirect disincentive to prescribe (unless a doctor wants to save a faceless insurance company some expense).<sup>42</sup> Where patients do bear costs, such as with over-the-counter drugs, uninsured patients, or prescription drug co-payments, doctors may not be attuned to patients’ financial circumstances and “therefore may not think to recommend a lower cost but equally effective generic alternative.”<sup>43</sup> Not surprisingly, studies have shown that doctors generally do not consider price at the time of prescribing.<sup>44</sup> In many cases, doctors do not even know the prices of treatments.<sup>45</sup>

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38. See generally Melissa N. Hoffman, *Pharmaceutical Detailing Is Not for Everyone: Side Effects May Include Sub-optimal Prescribing Decisions, Compromised Patient Health, and Increased Prescription Drug Spending*, 33 J. LEGAL MED. 381, 386-89 (2012) (explaining several negative impacts of detailing on physician prescribing, drug cost, and patient health).

39. JACALYN DUFFIN, *HISTORY OF MEDICINE: A SCANDALOUSLY SHORT INTRODUCTION* 109 (2d ed. 2010).

40. See *Evaluating Statin Drugs to Treat: High Cholesterol and Heart Disease*, CONSUMER REPORTS HEALTH BEST BUY DRUGS 1, 21 (2012), <http://www.consumerreports.org/health/resources/pdf/best-buy-drugs/StatinUpdate-FINAL.pdf>, archived at <http://perma.cc/J29Z-MPNH> [hereinafter *Evaluating Statin Drugs to Treat*] (emphasis added).

41. See Cheng, *supra* note 7, at 1509 (“[P]hysicians who drive pharmaceutical demand are less price sensitive . . .”).

42. See Robert N. Rabec, *Health Care Fraud Under the New Medicare Part D Prescription Drug Program*, 96 J. CRIM. L. & CRIMINOLOGY 727, 742 (2006) (recognizing there is no disincentive for physicians to prescribe medications under the Medicare Part D plan).

43. Aaron S. Kesselheim, *Think Globally, Prescribe Locally: How Rational Pharmaceutical Policy in the U.S. Can Improve Access to Essential Medicines*, 34 AM. J.L. & MED. 125, 129 (2008).

44. *Evaluating Statin Drugs to Treat*, *supra* note 40, at 21.

45. See, e.g., *Appendix 2011 Interim Meeting of the House of Delegates Reports of Reference Committees*, AM. MED. ASS’N 249, 256 (2011), <http://www.ama-assn.org/assets/meeting/2011/i11-reference-committee-reports.pdf#page=8>, archived at <http://perma.cc/92TY-86ZV> [hereinafter *Appendix 2011 Interim Meeting*] (noting that “costs of treatments are sometimes not transparent to physicians”).

Even if the issue of cost is specifically brought to their attention, some physicians shrink from their responsibility to act as prudent stewards of healthcare resources. For example, in an ongoing discussion in the American Medical Association (AMA), the Council on Ethical and Judicial Affairs recommended that the AMA adopt a policy that, where benefits of a treatment are equal, physicians should choose the less expensive alternative.<sup>46</sup> Although the recommendation by its terms was limited to circumstances where benefits were equal, some physicians nevertheless expressed concern “that making cost-conscious decisions would hamper patient care,”<sup>47</sup> and the recommendation was not adopted.<sup>48</sup> A revised version was reintroduced in 2012 and finally adopted,<sup>49</sup> but only over objections that “physicians would no longer be putting the interests of their individual patients first if they had to consider the costs of care and the impact on health care resources.”<sup>50</sup> A 1968 government task force put it thus:

Some have attempted to justify this situation [where moderate or even enormous price differences may exist between pharmaceutical products of comparable quality] by describing the physician as the patient’s expert purchasing agent. In the view of the Task Force, this concept is not valid; in most situations, a purchasing agent who purchased without consideration of both quality and price would be unworthy of trust.<sup>51</sup>

In summary, doctors make poor gatekeepers because there is little incentive for them to refrain from prescribing substantially ineffective medications, a continuous barrage of biased information flowing from drug companies and their detailers, and considerable reluctance to consider cost even where less expensive treatment options are otherwise equal. Even completely ineffective drugs can satisfy patient requests, speed patient throughput time, give patients hope, induce a placebo effect, and give doctors the satisfaction of having acted, all at no cost to the doctor, minimal cost to the insured patient, and with relatively low risk. It is truly astonishing that a drug that does almost nothing therapeutically can have

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46. Sharon P. Douglas, *Opinions of the Council on Ethical and Judicial Affairs*, AM. MED. ASS’N 85, 93 (2011), <http://www.ama-assn.org/assets/meeting/2011i/i111-ceja-reports.pdf#page=5>, archived at <http://perma.cc/MDE8-XLL8> (“When alternative courses of action offer similar likelihood and degree of benefit but require different levels of resources, [physicians should] choose the course of action requiring fewer resources.”).

47. *Appendix 2011 Interim Meeting*, *supra* note 45, at 256.

48. *Id.* (noting that the recommendation was “referred,” i.e., sent back to the committee to be redrafted).

49. See Sharon P. Douglas, *Reports of the Council on Ethical and Judicial Affairs*, AM. MED. ASS’N 141, 145 (2012), <http://134.147.247.42/han/JAMA/www.ama-assn.org/assets/meeting/2012a/a12-ceja-reports.pdf>, archived at <http://perma.cc/UGE6-449V>.

50. *Appendix 2012 Annual Meeting of the House of Delegates Reports of Reference Committees* 475, 477 (2012), <http://www.ama-assn.org/assets/meeting/2012a/a12-reference-committee-reports.pdf#page=3>, archived at <http://perma.cc/A9KJ-837N>.

51. *Task Force on Prescription Drugs: Final Report*, in MICKEY C. SMITH, *PRESCRIPTION DRUGS UNDER MEDICARE: THE LEGACY OF THE TASK FORCE ON PRESCRIPTION DRUGS* 65 (2001).

so many benefits, but this unexpected mix of benefits goes a long way toward explaining why substantially ineffective drugs are able to survive in the market.

Returning to Kraakman's framework, we find four criteria that, when present, suggest that gatekeeping is likely to be an appropriate approach to deterring undesirable behavior. They are: "(1) serious misconduct that practicable penalties cannot [directly] deter; (2) missing or inadequate private gatekeeping incentives; (3) gatekeepers who can and will prevent misconduct reliably, regardless of the preferences and market alternatives of wrongdoers; and (4) gatekeepers whom legal rules can induce to detect misconduct at reasonable cost."<sup>52</sup>

This four-part framework is offered by Kraakman as a means to determine when imposing liability on gatekeepers will be an efficient means of deterring wrongdoing, and is not meant as a tool for evaluating the adequacy of an individual gatekeeper. Nevertheless, the third criterion is useful in helping to understand why doctors are not likely to foster successful gatekeeping, namely, because they fail the third criterion's requirement that the gatekeeper "can and will prevent misconduct reliably." As discussed above, doctors' ability to prevent misconduct is impaired by the absence of clearly presented efficacy information, while their willingness to prevent misconduct is eroded by the many reasons to prescribe even drugs that lack non-placebo efficacy altogether.<sup>53</sup> That doctors "fail" the third criterion does not mean that gatekeeping cannot work as a strategy to prevent the consumption of ineffective drugs, but it does suggest that if doctors are to be gatekeepers, their ability and willingness to refrain from prescribing minimally effective medications must somehow be enhanced.

### *B. Insurance Companies*

It was stated above that the absence of cost reduces the incentive for doctors to act as effective gatekeepers. The same cannot be said of insurance companies, which do bear the financial costs of substantially ineffective drugs and therefore have an incentive to discourage their use.<sup>54</sup> Predictably, insurance companies have in fact taken steps to promote rational drug use. The most visible among these is the creation of tiered formularies, which attempt to provide a financial incentive to patients to avoid low value remedies by scaling co-payments.<sup>55</sup> One health insurer planned to pay pharmacists to convince consumers to switch to generic drugs, which by law must be "bioequivalent" but are almost always

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52. Kraakman, *supra* note 1, at 61.

53. *See supra* Part I.A.

54. *See* TOM BAKER, INSURANCE LAW AND POLICY 4 (2d ed. 2008) (discussing the "moral hazard" insurance companies face).

55. *See* Joseph J. Hylak-Reinholtz & Jay R. Naftzger, *Is It Time to Shed a "Tier" for Four-Tier Prescription Drug Formularies? Specialty Drug Tiers May Violate HIPAA's Anti-Discrimination Provisions and Statutory Goals*, 32 N. ILL. U. L. REV. 33, 41 (2011) (discussing the development of tiered formularies).

priced lower.<sup>56</sup> In light of workable solutions such as these, insurance companies may be best positioned for success as pharmaceutical gatekeepers.

In some cases, insurance companies' efforts at rational drug use have proved at least moderately successful. When combination drug BiDil (hydralazine and isosorbide) was introduced in 2005 for the treatment of heart failure, some insurance companies balked.<sup>57</sup> They stated that they would cover its two components separately, which were available as generics, but would either not cover the high-priced combination product at all or would place it in a disfavored formulary tier.<sup>58</sup> Despite a joint statement by the American Heart Association and the American College of Cardiology that either the generics or BiDil were reasonable, critics continued to condemn the insurers.<sup>59</sup> Notwithstanding this criticism, sales fell far short of their billion dollar estimates, hovering around \$15 million between 2006 and 2008.<sup>60</sup>

Nevertheless, any enthusiasm at the prospect of insurance companies acting as white knights in the fight against substantially ineffective drugs must be tempered by a dose of reality. Although tiered formularies can help to screen out expensive drugs not justified by their efficacy advantage, the alignment with efficacy is imprecise and may be both under- and over-inclusive: under-inclusive because there is little incentive to screen out cheap but ineffective drugs, and over-inclusive because exorbitantly priced drugs might be placed on a disfavored tier even if they possess respectable efficacy.

An important psychosocial factor is also at play. If an insurance company attempts to discourage the use of an ineffective drug by requiring a high copayment or withholding payment altogether, it will be viewed not as a white knight protecting the public from worthless drugs, but as a cold and greedy corporation that only wishes to prevent everyone's grandparents from obtaining the medicines that they need (or at least think that they need).<sup>61</sup> This psychological factor can be seen in the BiDil case presented above. It is no surprise, therefore, that "most payers in both the public and private sectors willingly, if complainingly, pay for whatever doctors prescribe."<sup>62</sup>

Consumer groups, such as the AARP, do not help the situation. These groups generally advocate broader insurance coverage of medicines but do not

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56. See Associated Press, *Generics May Profit Pharmacists*, 36(19) *MARKETING NEWS* 14, 14 (2002).

57. Sylvia Pagan Westphal, *Heart Medication Approved for Blacks Faces Uphill Battle—As Insurers Debate Costs and Generics Loom, BiDil Fails to Reach Needy*, *WALL ST. J.*, Oct. 16, 2006, at A1.

58. *Id.*

59. *Id.*

60. Sheldon Krinsky, *The Art of Medicine: The Short Life of a Race Drug*, 379 *LANCET* 114, 115 (2012).

61. See, e.g., Andrew Pollack, *Finding Profits, at \$28,000 a Vial*, *N.Y. TIMES*, Dec. 29, 2012, at BU1 (noting that Blue Cross Blue Shield initially refused to pay for an exorbitantly priced infantile spasm drug, but that "[a]fter a storm of publicity, the insurer backed down").

62. Jerry Avorn, *Sending Pharma Better Signals*, 309 *SCIENCE* 669, 669 (2005).

necessarily have either the inclination or expertise to discriminate in their efforts based on efficacy level.<sup>63</sup> In the international context, the absence of sensible discrimination against minimally effective drugs is exemplified by the vociferous demand for greater access to Plavix (clopidogrel) in Thailand. After public outcry, the government issued a compulsory license<sup>64</sup> notwithstanding substantial evidence that the efficacy of Plavix (clopidogrel) is no greater than that of aspirin,<sup>65</sup> while its risks may be greater.<sup>66</sup> Subsequent court proceedings in the United States echoed the lack of evidence of superior efficacy.<sup>67</sup>

Financial realities also help to explain the half-hearted efforts of insurance companies to rein in consumption of low-value drugs. Prescription drugs account for only around ten percent of total health care expenditures,<sup>68</sup> and therefore likely make up a relatively small percentage of insurance company payouts. Therefore, withholding payment for ineffective drugs that patients think they need is likely to offend many people and inflame anti-insurance-company sentiment, while saving relatively modest amounts of money. The urgency of reining in wasteful spending on substantially ineffective drugs dissipates when placed in the context of a \$100,000 hospital stay (though this may be changing as some drug prices escalate well past the \$100,000 per person per year threshold).<sup>69</sup> Insurance

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63. See Robert Pear & Robin Toner, *Medicare Plan Covering Drugs Backed by AARP*, N.Y. TIMES, Nov. 18, 2003, at A1; *What We Do*, AARP (Dec. 4, 2013, 10:21 PM), <http://www.aarp.org/about-aarp/info-2011/what-we-do.html>, archived at <http://perma.cc/K4SY-7PRD> (boasting of successful advocacy regarding improved drug coverage, but not mentioning drug efficacy).

64. *Facts and Evidences on the 10 Burning Issues Related to the Government Use of Patents on Three Patented Essential Drugs in Thailand*, THAI MINISTRY OF PUBLIC HEALTH 14–15 (Vichai Chokevivat ed., 2007), <http://apps.who.int/medicinedocs/documents/s18718en/s18718en.pdf>, archived at <http://perma.cc/34PF-DQGS>.

65. See *infra* notes 182-86 and accompanying text.

66. There is evidence that Plavix (clopidogrel) is less safe than aspirin combined with an anti-ulcer medication. See Francis K.L. Chan et al., *Clopidogrel Versus Aspirin and Esomeprazole to Prevent Recurrent Ulcer Bleeding*, 352 NEW ENG. J. MED. 238, 243 (2005) (“[A]spirin plus esomeprazole was superior to clopidogrel for the prevention of recurrent ulcer bleeding. Our observations do not support the current recommendation that clopidogrel be used for patients who have major gastrointestinal intolerance of aspirin.”).

67. See, e.g., *Soloman v. Bristol-Myers Squibb Co.*, No. 07-1102, 2009 WL 5206120, at \*3 (D.N.J. Dec. 30, 2009) (“[T]he actual findings of the CAPRIE Study were that Plavix was not proven to be significantly more effective than aspirin.”).

68. See *Financial Burden of Prescription Drugs Is Dropping, but Costs Remain a Challenge for Many Families*, RAND CORP. (Feb. 8, 2012), <http://www.rand.org/news/press/2012/02/08/index1.html>, archived at <http://perma.cc/534J-EW49> (estimating prescription drugs at 10% of total health care spending); *Health Care Costs: A Primer*, KAISER FAMILY FOUND. 1, 10 (2012), <http://www.kff.org/insurance/upload/7670-03.pdf>, archived at <http://perma.cc/XCN8-U9QC>.

69. See Pamela Jones Harbour, *The Competitive Implications of Generic Biologics*, FED. TRADE COMM’N 1, 4 (2007), <http://www.ftc.gov/speeches/harbour/070614genbio.pdf>, archived at <http://perma.cc/AZ7P-CA6B> (\$100,000 per year for Avastin (bevacizumab)); Matthew Herper, *The World’s Most Expensive Drugs*, FORBES.COM (Feb. 22, 2010), <http://www.forbes.com/2010/02/>

companies may therefore prefer to pick their battles, choosing to look the other way when it comes to a few worthless drugs in order to preserve their reputational capital for those non-drug areas where cost-cutting efforts are likely to have an even bigger impact on the bottom line, with less public push-back.

Kraakman suggests another financial dimension that can erode the effectiveness of insurance companies as gatekeepers: corruption.<sup>70</sup> Gatekeepers that can be bribed into complicity will obviously make less effective gatekeepers. This has occurred in the pharmaceutical industry where, according to *Money* magazine, “drug firms routinely offer insurers millions of dollars in discounts and cash rebates in exchange for favored places on ‘formularies[.]’”<sup>71</sup> Preferred formulary placement is a type of endorsement that can increase the volume of ineffective drugs sold. While price negotiation is a normal and expected part of a market economy, preferred formulary placement can be used to build customer loyalty and switching costs just before the patent on an older and equally effective medicine is about to expire.<sup>72</sup>

It is evident from this discussion that use of the term “bribery” is not intended to imply criminality in the legal sense, but to describe transfers of value that induce gatekeepers to be less fastidious in carrying out their gatekeeping duties, a meaning that is consistent with Kraakman’s usage.<sup>73</sup> The seriousness of such soft corruption in the pharmaceutical context was acknowledged by Congress when it enacted the Patient Protection and Affordable Care Act of 2010, which included the Physician Payment Sunshine Act (“Sunshine Act”).<sup>74</sup> The Sunshine Act requires disclosure of any “transfer of value” from drug manufacturers to physicians or teaching hospitals, although it does not prohibit such transfers.<sup>75</sup>

Industry pressure to endorse certain drugs can reach the highest levels. Richard Laing is a physician and former World Health Organization (WHO) medical officer that served as co-rapporteur<sup>76</sup> on the Expert Committee that develops the WHO’s Model List of Essential Medicines, a formulary-like document that guides drug selection and use decisions around the world. Laing reports that in his earlier work in creating an essential medicines list for use in Zimbabwe, his team “involved the industry in the process of selecting the

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19/expensive-drugs-cost-business-healthcare-rare-diseases.html, archived at <http://perma.cc/37CF-SCT4> (\$400,000 per year for Soliris (eculizumab)).

70. Kraakman, *supra* note 1, at 69-71.

71. Peter Keating, *The Right Prescription?*, MONEY, Oct. 1999, at 71.

72. See Gardiner Harris, *Prilosec’s Maker Is Switching Users to a Lookalike Pill While It Thwarts Generics*, WALL ST. J., June 6, 2002, at A1.

73. See Kraakman, *supra* note 1, at 71.

74. Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 6002, 124 Stat. 119, 689-96 (2010) (codified at 42 U.S.C. § 1320a-7h (2013)).

75. 42 U.S.C. § 1320a-7h (2013).

76. See *12th Expert Committee on the Selection and Use of Essential Medicines Meeting*, WORLD HEALTH ORG. (Apr. 15-19, 2002), <http://archives.who.int/eml/expcom/expcom12/expertmembers.htm>, archived at <http://perma.cc/KZ8T-FZVC> [hereinafter *12th Expert Committee*].

Essential Drug List.”<sup>77</sup> Naturally industry representatives had commercial incentives for advocating selection of specific drugs, and they were successful in including many ‘me-too’ drugs.”<sup>78</sup> Although the WHO Expert Committee itself has a stated policy of “taking steps to ensure scientific independence” in the drug selection process, representatives of the pharmaceutical industry were invited to provide input regarding that process,<sup>79</sup> and the policy continues to allow drug companies the opportunity to lobby for the inclusion of new drugs on the WHO list.<sup>80</sup> Members of the Expert Committee also report receiving various forms of financial support from companies such as GlaxoSmithKline, Novartis, and Pfizer.<sup>81</sup> In one case, only five of eleven experts reported no conflicts of interest.<sup>82</sup> The Committee itself has expressed some concern about the process, declaring that some applications for the inclusion of new drugs on the essential medicines list were submitted by manufacturers and may not have included all relevant data, or failed to contain critical statistical parameters such as confidence intervals.<sup>83</sup>

Even if insurers were inclined to work harder to prevent the consumption of ineffective drugs, they suffer from the same lack of information problems encountered by physicians and consumers. “It is surprisingly hard for a prescribing doctor—or even for the formulary committee of a large health care organization—to find reliable information that compares the benefits, risks, and costs of comparable drugs,”<sup>84</sup> notes Jerry Avorn, a Professor at Harvard Medical School.

### C. Consumers as Their Own Gatekeepers

Kraakman hints that “either agents for victims . . . or victims themselves . . . might usefully be viewed as gatekeepers on occasion,” but he does not develop the latter point.<sup>85</sup> In the same footnote, however, he does provide an example of

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77. Richard Laing, *Personal Reflections on 25 Years of the WHO Model List of Essential Medicines*, 23 *ESSENTIAL DRUGS MONITOR* [WORLD HEALTH ORG.] 1, 16 (2003), <http://apps.who.int/medicinedocs/pdf/s4940e/s4940e.pdf>, archived at <http://perma.cc/NR95-F3KP>.

78. *Id.*

79. *12th Expert Committee*, *supra* note 76, at 3-4.

80. *Id.* at 4; see also *The Selection and Use of Essential Medicines*, REPORT OF THE WHO EXPERT COMMITTEE, 2011, at 61, 63, [http://whqlibdoc.who.int/trs/WHO\\_TRS\\_965\\_eng.pdf](http://whqlibdoc.who.int/trs/WHO_TRS_965_eng.pdf), archived at <http://perma.cc/4W9R-EXNR> (submission of Tibotec, an international pharmaceutical company, for the inclusion of etravirine; submission by Paladin Labs Barbados, a manufacturer, for the inclusion of miltefosine).

81. WORLD HEALTH ORG., *THE SELECTION AND USE OF ESSENTIAL MEDICINES* xi-xii (2011), available at [http://whqlibdoc.who.int/trs/WHO\\_TRS\\_965\\_eng.pdf](http://whqlibdoc.who.int/trs/WHO_TRS_965_eng.pdf), archived at <http://perma.cc/SMW-9U73>.

82. *Id.*

83. *Id.* at 10.

84. AVORN, *supra* note 18, at 275.

85. Kraakman, *supra* note 1, at 62 n.21.

how an agent for a victim could act as a gatekeeper, explaining that a sophisticated lender can protect borrowers from bad purchasing decisions by withholding credit. The implicit suggestion is that the borrowers' lack of sophistication prevents them from accurately valuing the wrongdoer's product, forcing them to rely on gatekeepers. This is a similar problem to that faced by patients in the context of substantially ineffective medicines, where doctors or insurance companies are in a position analogous to that of Kraakman's lenders, in that they are more sophisticated and may be in a position to assist consumers in valuing a given drug product.

Notwithstanding a relative lack of sophistication, it is not immediately obvious why patients cannot adequately serve as their own gatekeepers. Like all market participants, patients have a natural incentive to act in their own best interests, which in the present context means consuming medicines that possess the greatest efficacy (and do the least harm). Truth-in-labeling laws have been on the books for over 100 years, and now include required disclosures of clinical trial information. The Internet has dramatically increased patient access to drug information, providing relatively easy access to professional drug labels,<sup>86</sup> medical journal articles,<sup>87</sup> and critical reviews.<sup>88</sup> Patients intent on investigating have the ability to uncover substantial, if far from complete, information on drug efficacy, just as the author of this Article has done.

There are a plethora of reasons, however, why patients fail to screen out ineffective drugs. If efficacy information is challenging for physicians to understand, it is all the more so for laypersons. Information about efficacy is not only presented in tiny font that is buried deep within the lengthy package insert in a section labeled "clinical trials" rather than "efficacy," but is also generally described in impenetrable jargon that requires a simultaneous understanding of medicine, clinical trial practice, chemistry, statistics, and law. In the case of drugs that are consumed infrequently, patient demand for efficacy information may be inelastically low for the same reason that consumer demand is price inelastic for infrequent purchases: the transaction costs of obtaining information are high relative to the frequency of consumption. Pharmaceuticals and other health-related products are literally textbook examples of "credence goods"—products whose attributes are hidden, unknown, or difficult to discern, such as where information-acquisition costs cannot be justified.<sup>89</sup> Demand for efficacy information is also inelastically low both because the risk will generally be acceptably low due to FDA requirements for approval, and because financial

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86. See *Drugs@FDA*, FDA (Dec. 5, 2013, 10:33 PM), <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>, archived at <http://perma.cc/ZLJ2-QG8E>.

87. See, e.g., *BMJ*, BRIT. MED. J. (Dec. 5, 2013, 10:34 PM), <http://www.bmj.com/>, archived at <http://perma.cc/W7AX-T9F2> (providing freely available full-text articles).

88. See, e.g., *Consumer Reports Health Best Buy Drugs*, CONSUMERREPORTS.ORG (Dec. 5, 2013, 10:35 PM), <http://www.consumerreports.org/health/best-buy-drugs/index.htm>, archived at <http://perma.cc/6LHG-X8KZ>.

89. GEOFFREY PAUL LANTOS, *CONSUMER BEHAVIOR IN ACTION: REAL-LIFE APPLICATIONS FOR MARKETING MANAGERS* 81-82 (2010).

cost may often be unnaturally low due to insurance, triggering a type of moral hazard. Patients might rationally conclude that they may as well consume a drug without bothering to investigate efficacy information, because there is little reason not to. These are among the many reasons that consumers have been characterized by the Ninth Circuit as “helpless because [they are] uninformed [about drugs]”<sup>90</sup> and assumed by the Supreme Court to be “unable to protect themselves in this field [of pharmaceuticals].”<sup>91</sup>

#### D. Consumer Organizations and Academics

If the absence of expertise and information is a problem, an obvious gatekeeping solution is to involve a third party that has sufficient expertise and that can translate and simplify the relevant information into a usable form. This is, more or less, the function performed by Kraakman’s lawyers and accountants, who take complex information and convey its material aspects to others in the form of legal opinions and audit letters. Although practicing physicians and insurance companies may not adequately perform this function, as discussed above, they are not the only candidates for the role. In fact, the market has produced a number of third-party information brokers who can and do take complex pharmaceutical efficacy information and translate it into a form that can be more easily understood. These entities include Consumers Union, Public Citizen, and a host of academic authors, among others.<sup>92</sup>

Founded in 1936, Consumers Union is an independent, nonprofit organization<sup>93</sup> that is best known for its widely-respected *Consumer Reports* magazine. Its philosophy involves “empower[ing] consumers to protect themselves” by providing “a reliable source of information they [can] depend on to help them distinguish hype from fact and good products from bad ones,”<sup>94</sup> an orientation that makes Consumers Union an attractive potential gatekeeper in the pharmaceutical marketplace where hype and substantially ineffective products are

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90. *Alberty Food Prods. Co. v. United States*, 185 F.2d 321, 325 (9th Cir. 1950).

91. *Kordel v. United States*, 335 U.S. 345, 349 (1948).

92. In France, for example, an independent organization known as the *Association Mieux Prescrire* provides a monthly journal addressing drug efficacy and related issues. An international edition is also published regularly in English. See *Who We Are*, PRESCRIRE IN ENGLISH (Dec. 5, 2013, 10:54 PM), <http://english.prescrire.org/en/82/169/0/0/About.aspx>, archived at <http://perma.cc/WRG5-4TDC>. Other notable providers of high-quality efficacy information directed at medical professionals include *The Medical Letter* and *The Cochrane Collaboration*, non-profit organizations that each advocate for evidence-based decision making. See *About Us*, THE MEDICAL LETTER ONLINE (Dec. 5, 2013, 10:54 PM), <http://secure.medicalletter.org/about>, archived at <http://perma.cc/A4HJ-VVBQ>; *About Us*, THE COCHRANE COLLABORATION (Dec. 5, 2013, 10:55 PM), <http://www.cochrane.org/about-us> archived at <http://perma.cc/S53N-3WKU>.

93. *About Us*, CONSUMERSUNION (Dec. 5, 2013, 10:57 PM), <http://www.consumersunion.org/about/>, archived at <http://perma.cc/LL95-MHHQ>.

94. *Id.*

commonplace. Since 2004,<sup>95</sup> Consumers Union has applied this philosophy in the pharmaceuticals marketplace by issuing a series of reports collectively entitled Consumer Reports Best Buy Drugs, which now covers more than 600 drugs that are used to treat more than fifty conditions.<sup>96</sup> For example, its report on insomnia notes that heavily advertised prescription treatments such as Lunesta (eszopiclone) and Ambien (zolpidem) are effective, but not necessarily any more effective than much older and less expensive drugs that are available over the counter, such as Nytol (diphenhydramine) or Benadryl (diphenhydramine).<sup>97</sup> They may also not be any more effective than much older prescription medicines called benzodiazepines, and may be *less* effective than non-drug treatments such as relaxation techniques.<sup>98</sup>

Other individuals or groups have similarly acted as information brokers, seeking to translate complex drug efficacy information into usable form. Public Citizen, the public interest organization founded by consumer activist Ralph Nader, has been assessing drug efficacy since 1971.<sup>99</sup> Its 1981 book, *Pills that Don't Work: A Consumer's and Doctor's Guide to over 600 Prescription Drugs the Lack Evidence of Effectiveness*,<sup>100</sup> describes the large number of prescription drugs that were still being prescribed years after an FDA-contracted report<sup>101</sup> had concluded that they lacked evidence of effectiveness.<sup>102</sup> More recently, it has petitioned the FDA to remove from the market certain drugs that lack effectiveness, such as Aricept (donepezil), which according to the petition was approved by the FDA division director over objections from both the FDA's statistical and medical reviewers.<sup>103</sup> A host of academic commentators have

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95. Press Release, *New Public Education Campaign Helps Consumers Save on Medicines*, CONSUMERSUNION (Dec. 9, 2004), <http://www.consumersunion.org/news/new-public-education-campaign-helps-consumers-save-on-medicines/>, archived at <http://perma.cc/GBD3-ASLQ>.

96. *Drugs A-Z*, CONSUMERSREPORTS.ORG (Dec. 5, 2013, 11:04 PM), <http://www.consumerreports.org/health/drugs-a-z/best-buy-drugs/index-by-condition.htm>, archived at <http://perma.cc/Z33R-PXNX>.

97. *Evaluating Newer Sleeping Pills Used to Treat: Insomnia*, CONSUMER REPORTS HEALTH BEST BUY DRUGS 1, 3 (2012), <http://www.consumerreports.org/health/resources/pdf/best-buy-drugs/InsomniaUpdate-FINAL-July2008.pdf>, archived at <http://perma.cc/WLU5-7TGN>.

98. *Id.* at 7, 9-10; see generally Donald W. Light, *Effectiveness and Efficiency Under Competition: The Cochrane Test*, 303 BRIT. MED. J. 1253, 1253 (1991) (questioning the value of drugs and other expensive treatments when compared to non-medical treatments such as participating in prayer, owning a pet, or bed rest).

99. *Drug Projects*, PUB. CITIZEN (Dec. 5, 2013, 11:23 PM), <http://www.citizen.org/Page.aspx?pid=4374>, archived at <http://perma.cc/7D32-VXVW>.

100. SIDNEY M. WOLFE ET AL., *PILLS THAT DON'T WORK: A CONSUMER'S AND DOCTOR'S GUIDE TO OVER 600 PRESCRIPTION DRUGS THAT LACK EVIDENCE OF EFFECTIVENESS* (1981).

101. *Drug Effectiveness Study: Final Report to the Commissioner of Food and Drugs, Food and Drug Administration, from the Division of Medical Sciences National Research Council* (1969).

102. WOLFE ET AL., *supra* note 100, at 4.

103. *Petition to Ban 23 Milligram Dose of Donepezil (Aricept)*, *supra* note 29, at 12.

similarly voiced their concerns with the absence of meaningful drug efficacy. Irving Kirsch, the Associate Director of the Program on Placebo Studies at Harvard Medical School,<sup>104</sup> exposed the surprisingly weak data supporting the efficacy of the depression medications in his book *The Emperor's New Drugs*.<sup>105</sup> Joanna Moncrieff, a medical doctor and faculty member at University College London,<sup>106</sup> wrote a similarly critical book entitled *The Myth of the Chemical Cure: A Critique of Psychiatric Drug Treatment*.<sup>107</sup> Dozens of others academic commentators as well as several investigative journalists have repeatedly explained the lack of robustness in the medicine cabinet, often critiquing some aspect of drug efficacy along the way.<sup>108</sup>

Despite the substantial volume of commentary and informational aids provided by consumer organizations and others, these third parties make poor

104. *Harvard Catalysts Profiles: Irving Kirsch, Ph.D.*, HARV. CATALYST (Dec. 5, 2013, 11:30 PM), <http://connects.catalyst.harvard.edu/profiles/profile/person/96221>, archived at <http://perma.cc/7YH5-3VND>.

105. IRVING KIRSCH, *THE EMPEROR'S NEW DRUGS: EXPLODING THE ANTIDEPRESSANT MYTH* (2010).

106. *Dr. Joanna Moncrieff*, UNIV. COLL. LONDON (Dec. 5, 2013, 11:31 PM), <https://iris.ucl.ac.uk/research/personal?upi=JMMON33>, archived at <http://perma.cc/VE3X-TNU9>.

107. JOANNA MONCREIFF, *THE MYTH OF THE CHEMICAL CURE: A CRITIQUE OF PSYCHIATRIC DRUG TREATMENT* (2009).

108. *See, e.g.*, JOHN ABRAMSON, *OVERDOSED AMERICA: THE BROKEN PROMISE OF AMERICAN MEDICINE* (2008) (physician academic); MARCIA ANGELL, *THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT* (2004) (physician academic); AVORN, *supra* note 18 (physician academic); SHANNON BROWNLEE, *OVERTREATED* (2007) (journalist); JAY S. COHEN, *OVERDOSE: THE CASE AGAINST THE DRUG COMPANIES* (2001) (physician academic); BEN GOLDACRE, *BAD PHARMA: HOW DRUG COMPANIES MISLEAD DOCTORS AND HARM PATIENTS* (2012) (physician academic); KATHARINE GREIDER, *THE BIG FIX: HOW THE PHARMACEUTICAL INDUSTRY RIPS OFF AMERICAN CONSUMERS* (2003) (journalist); HEINZ KOHLER, *CAUTION: SNAKE OIL! HOW STATISTICAL THINKING CAN HELP US EXPOSE MISINFORMATION ABOUT OUR HEALTH* (2009) (academic statistician); RAY MOYNIHAN & ALAN CASSELS, *SELLING SICKNESS: HOW THE WORLD'S BIGGEST PHARMACEUTICAL COMPANIES ARE TURNING US ALL INTO PATIENTS* (2005) (journalist and policy researcher); MELODY PETERSEN, *OUR DAILY MEDS* (2008) (journalist); TIMOTHY SCOTT, *AMERICA FOOLED: THE TRUTH ABOUT ANTIDEPRESSANTS, ANTIPSYCHOTICS AND HOW WE'VE BEEN DECEIVED* (2006) (psychology professor); *THE RISKS OF PRESCRIPTION DRUGS* (Donald W. Light ed., 2010) (academic bioethicist); *see also* HAROLD AARON, *GOOD HEALTH AND BAD MEDICINE* (1940); STUART CHASE & F.J. SCHLINK, *YOUR MONEY'S WORTH: A STUDY IN THE WASTE OF THE CONSUMER'S DOLLAR* (1928) (chapters VII and VIII); JAMES COOK, *REMEDIES AND RACKETS: THE TRUTH ABOUT PATENT MEDICINES TODAY* (1958); PETER MORELL, *POISONS, POTIONS & PROFITS* (1937); MILTON SILVERMAN & PHILIP R. LEE, *PILLS, PROFITS, AND POLITICS* (1974); WOLFE ET AL., *supra* note 100; JAMES HARVEY YOUNG, *THE TOADSTOOL MILLIONAIRES* (1961); AMERICAN MEDICAL ASSOCIATION, *NOSTRUMS AND QUACKERY* (1911); BRITISH MEDICAL ASSOCIATION, *SECRET REMEDIES: WHAT THEY COST AND WHAT THEY CONTAIN* (1909); CONSUMER'S UNION, *THE MEDICINE SHOW: SOME PLAIN TRUTHS ABOUT POPULAR REMEDIES FOR COMMON AILMENTS* (1961) (six editions from 1961-1989).

gatekeepers because their messages are simply drowned out by the far more voluminous and accessible messages of the drug industry.<sup>109</sup> Moncreiff's book, for example, sold just over 4,500 copies during the three years following its publication.<sup>110</sup> Thus, unlike Kraakman's missing audit letter, which causes fraudulent securities transactions to collapse before they occur,<sup>111</sup> the lack of endorsement or even the well-articulated criticism of a drug product by a consumer organization or physician-academic does not have the same dramatic effect. While every television viewer is inundated with endless advertisements for the latest prescription drug, only a tiny minority of those will read a critical book. Similarly, when this author has described Consumer Reports' *Best Buy Drugs* series at academic presentations, audience members consistently report being unaware of the publications, with rare exception. Moreover, direct-to-consumer advertising is just the tip of the promotional iceberg. There is an extensive literature documenting the ability of pharmaceutical companies to proselytize to physicians,<sup>112</sup> influence legislators and the FDA,<sup>113</sup> and disseminate studies or information of questionable quality.<sup>114</sup>

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109. See, e.g., Donald W. Light, *Bearing the Risks of Prescription Drugs*, in *THE RISKS OF PRESCRIPTION DRUGS* 9 (Donald W. Light ed., 2010) (“[P]hysicians . . . do not use independent sources like *The Medical Letter* . . . . Instead, they get their information from friendly, generous sales reps . . .”).

110. Email from Joanna Moncreiff to Jonathan J. Darrow, Dec. 6, 2012 (on file with author).

111. Kraakman, *supra* note 1, at 58.

112. See, e.g., Murthy v. Abbott Labs., 847 F. Supp. 2d 958, 972 n.5 (S.D. Tex. 2012) (collecting studies regarding the influence of industry gifts on prescribing decisions); Susan Chimonas & Jerome P. Kassirer, *No More Free Drug Samples?*, 6 PLOS MED. 1000074 (2009); JEROME P. KASSIRER, *ON THE TAKE: HOW MEDICINE'S COMPLICITY WITH BIG BUSINESS CAN ENDANGER YOUR HEALTH* (2004); David Korn, *Conflicts of Interest in Biomedical Research*, 284 J. AM. MED. ASS'N 2234, 2235 (2000) (noting the “deep and extensive financial entanglements that may exist between medical school researchers (and often their parent institutions) and industry”).

113. See, e.g., M. Asif Ismail, *A Record Year for the Pharmaceutical Lobby in '07: Washington's Largest Lobby Racks Up Another Banner Year on Capitol Hill*, CENTER FOR PUB. INTEGRITY, June 24, 2008, <http://www.publicintegrity.org/2008/06/24/5779/record-year-pharmaceutical-lobby-07>, archived at <http://perma.cc/4LD4-NAGN>; Daniel P. Carpenter, *The Political Economy of FDA Drug Review: Processing, Politics, and Lessons for Policy*, 23 HEALTH AFF. 52, 53 (2004) (“FDA drug review is an exercise in learning shaped by organized interests.”); Robert Pear, *Drug Companies Increase Spending to Lobby Congress and Governments*, N.Y. TIMES, May 31, 2003, at 33 (reporting \$150 million in lobbying expenses by PhRMA alone).

114. See, e.g., David H. Freedman, *Lies, Damned Lies, and Medical Science*, ATLANTIC, Nov. 2010, at 76; John P.A. Ioannidis, *Why Most Published Research Findings Are False*, 2 PLOS MED. 0020124 (2005); see also Michael Kelley et al., *Evidence Based Public Health: A Review of the Experience of the National Institute of Health and Clinical Excellence (NICE) of Developing Public Health Guidance in England*, 71 SOC. SCI. & MED. 1056, 1058 (2010) (noting that even the best “trials are always flawed in various ways”).

*E. Expert Bodies and the Drug Effectiveness Review Project*

If the gatekeeping ability of doctors and patients is impaired by too little accessible data while the measured reports of consumer groups or academics are drowned out by too much promotional material, a possible solution is to engage a disinterested and adequately funded expert body that could delve into the data to determine which drugs are meaningfully effective and which are not. Like consumer organizations and academics, these entities could use their expertise to translate complex efficacy information into an understandable form. Unlike nonprofit consumer organizations, however, an expert body could be endowed by the government with the authority to influence policy.

The Agency for Healthcare Research and Quality (AHRQ)<sup>115</sup> is, like the FDA, one of the twelve agencies under the umbrella of the Department of Health and Human Services, and works with an annual budget of about \$400 million.<sup>116</sup> Its mission is “to improve the quality, safety, efficiency, and effectiveness of health care for all Americans” by helping people to make more informed decisions.<sup>117</sup> Its mission is therefore quite broad and not limited to pharmaceutical efficacy. Nevertheless one of its principal activities involves the funding of eleven “evidence-based practice centers” that gather and examine existing evidence related to healthcare.<sup>118</sup> One of these, the Pacific Northwest Evidence-Based Practice Center, administers the Drug Effectiveness Review Project (DERP)<sup>119</sup> which, though not funded by AHRQ,<sup>120</sup> has produced and continues to update lengthy and detailed reports that synthesize available evidence of drug effectiveness.

The lengthy, professional-grade DERP reports are divided into a number of therapeutic categories such as allergy drugs, cardiovascular drugs, dermatologic

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115. Another initiative, the Patient-Centered Outcomes Research Institute (PCORI), was authorized by the Patient Protection and Affordable Care Act of 2010, but has a focus much broader than drug efficacy and so far has not devoted substantial resources to the efficacy of prescription drugs. See *Patient-Centered Outcomes Research Institute: National Priorities for Research and Research Agenda*, PCORI BOARD OF GOVERNORS, May 21, 2012, <http://www.pcori.org/assets/PCORI-National-Priorities-and-Research-Agenda-2012-05-21-FINAL.pdf>, archived at <http://perma.cc/BVH6-CL9N> (listing ten priority areas for comparative effectiveness research: prevention, acute care, care coordination, chronic disease care, palliative care, patient engagement, safety, overuse, information technology infrastructure, and impact of new technology).

116. *AHRQ at a Glance*, AGENCY FOR HEALTHCARE RESEARCH & QUALITY (Dec. 6, 2013, 7:55 AM), <http://www.ahrq.gov/about/ataglance.htm>, archived at <http://perma.cc/8VF7-3FZ9>.

117. *Id.*

118. *Pacific Northwest Evidence-Based Practice Center*, OR. HEALTH & SCI. UNIV. (Dec. 6, 2013, 7:57 AM), <http://www.ohsu.edu/xd/research/centers-institutes/evidence-based-practice-center/>, archived at <http://perma.cc/ZJH4-3WZ9>.

119. See generally Marian S. McDonagh et al., *Methods for the Drug Effectiveness Review Project*, 12 BMC MED. RES. METHODOLOGY 1 (2012).

120. E-mail from Kathryn Clark, Administrative Coordinator, Drug Effectiveness Review Project, to Jonathan J. Darrow (Jan. 2, 2013) (on file with author).

drugs, etc.,<sup>121</sup> and seem to have had some impact. Most visibly, the reports provide much of the information and analysis on which the Consumer Reports *Best Buy Drugs* series is based.<sup>122</sup> Less visible is the direct but difficult to quantify impact on policymakers. DERP is funded by eleven nonprofit state Medicaid agencies (as well as the Canadian Office of Health Technology Assessment),<sup>123</sup> and has gone through three rounds of such funding since its inception in 2003.<sup>124</sup> Organizers at DERP assert that the impact of the reports is reflected in the decisions of these Medicaid organizations to continue to provide funding to DERP, though not all have done so.<sup>125</sup>

Although DERP provides reports that are high quality, unbiased, comprehensive, up-to-date, and publicly available, the ability of DERP to act as a gatekeeper should not be overstated. If few people have heard of *Best Buy Drugs*, fewer still have engaged in careful study of any of the DERP reports, so direct impact on patients and physicians may be modest at best. Moreover, awareness of the DERP reports is not the only challenge; a presentation at the 2011 AHRQ annual conference listed “[i]nitial prescriber resistance [to change]” as an obstacle that frustrates evidence-based prescribing.<sup>126</sup> Indirect impact via Medicaid coverage decisions seems more likely, but specific changes in policy causally related to DERP’s efforts are difficult to ascertain. Given that Medicaid prescription drug spending constitutes only around 6% of overall U.S. prescription drug spending,<sup>127</sup> the impact on medicine use may be modest.

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121. *Final Documents*, OR. HEALTH & SCI. UNIV. (Dec. 6, 2013, 8:03 AM), <http://derp.ohsu.edu/about/final-document-display.cfm>.

122. *Best Medicines for Less*, CONSUMER REPORTS 27, 28 (2008), <http://www.consumerreports.org/health/resources/pdf/best-buy-drugs/CR-Jan-2008-Article-Best-Medicines.pdf>, archived at <http://perma.cc/9MH3-MFBQ>.

123. Although the Pacific Northwest Center for Evidence-Based Policy is supported by the AHRQ, DERP does not appear to receive any direct funding from that agency.

124. *See About DERP*, OR. HEALTH & SCI. UNIV. (Dec. 6, 2013, 8:10 AM), <http://www.ohsu.edu/xd/research/centers-institutes/evidence-based-policy-center/derp/about/index.cfm>, archived at <http://perma.cc/R25R-34M8> (founding 2003); McDonagh et al., *supra* note 119, at 3 fig.1 (listing the states that provide funding).

125. McDonagh et al., *supra* note 119, at 10 (suggesting that impact is “reflected by the ongoing financial support of the constituent organizations”).

126. Siri Childs, *Washington's Prescription Drug Program: Using Systematic Reviews to Make Policy Decisions in the Effort to Contain Prescription Drug Expenditures*, AHRQ 2011 ANN. CONF., Sept. 20, 2011, at slide 7, [http://www.ahrq.gov/legacy/about/annualconf11/bar-cohen\\_childs\\_qaseem/childs.htm](http://www.ahrq.gov/legacy/about/annualconf11/bar-cohen_childs_qaseem/childs.htm), archived at <http://perma.cc/KSF4-2V9A>.

127. *See* Katrice Bridges Copeland, *Enforcing Integrity*, 87 IND. L.J. 1033, 1072 n.264 (2012) (noting that prescription drugs spending by Medicaid exceeded \$20 billion in 2010); *Top U.S. Pharmaceutical Products by Spending*, IMS HEALTH 1, 1 (2013), <http://tinyurl.com/ca7lmfm>, archived at <http://perma.cc/4NGY-FYGT> (reporting total prescription drug spending in the U.S. in 2010 as \$308.6 billion).

*F. Expert Bodies and the UK Model: NICE*

The United States is of course not alone when it comes to the need for the rational use of medicines. One of the AHRQ's foreign analogues, the United Kingdom's National Institute for Health and Care Excellence (NICE), is notable for the widespread attention it has received. Founded in 1999, NICE is an independent, government-funded expert body that evaluates new drugs and other treatments for evidence of effectiveness.<sup>128</sup> The expertise of its 270 staff members<sup>129</sup> is supplemented by four external collaborating centers<sup>130</sup> as well as the input of patient groups, healthcare organizations, pharmaceutical companies, clinicians, and other stakeholders.<sup>131</sup> Databases such as MEDLINE, CINAHL, and Cochrane are consulted for evidence. Once draft guidelines are developed, they are made available for external review by stakeholders, providing transparency and peer review, before final guidelines are issued.<sup>132</sup>

One might expect that NICE's focused expertise, broad input, transparency, government endorsement, and relative neutrality should earn its guidelines far more respect than what is accorded the advertisements and other promotional efforts of drug makers, whose interests in a market-based economy are obvious. In the view of much of the public, however, this is not the case. Instead of revering expert bodies for their help in screening out substantially ineffective drugs, NICE has been condemned as an arbiter of death,<sup>133</sup> a state of affairs that no doubt elicits exuberant jollity from drug manufacturers whose products do not even meet the very generous and flexible standard applied by NICE.<sup>134</sup> In effect, NICE and other similar organizations face a public relations conundrum not unlike that of insurance companies: if they decline to endorse a drug because it fails to meet even minimally relevant efficacy thresholds, they are reviled by the public.<sup>135</sup> Likely aware of this concern, the United Kingdom tipped the balance in favor of coverage by requiring the UK National Health Service (NHS) to pay

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128. See Robert Steinbrook, *Saying No Isn't NICE: The Travails of Britain's National Institute for Health and Clinical Excellence*, 359 NEW ENG. J. MED. 1977, 1977 (2008).

129. *Id.* at 1979.

130. Jennifer Hill et al., *A Summary of the Methods that the National Clinical Guideline Centre Uses to Produce Clinical Guidelines for the National Institute for Health and Clinical Excellence*, 154 ANNALS OF INTERNAL MED. 752, 752 (2011).

131. *Id.* at 753.

132. *Id.* at 756.

133. See, e.g., Peter Singer, *Why We Must Ration Health Care*, N.Y. TIMES, July 19, 2009, at MM38 (noting criticism that "NICE regularly hands down death sentences to gravely ill patients" (internal quotes omitted)).

134. Michael D. Rawlins & Anthony J. Culyer, *National Institute for Clinical Excellence and Its Value Judgments*, 329 BRIT. MED. J. 224, 224 (2004) (noting that there is no "absolute threshold" of cost effectiveness beyond which a drug will be automatically rejected).

135. See Steinbrook, *supra* note 128, at 1977; Ed Silverman, *UK's NICE Loses Decision-Making Powers*, PHARMALOT, Nov. 2, 2010, <http://www.pharmalot.com/2010/11/uks-nice-loses-decision-making-powers/>, archived at <http://perma.cc/GS49-5NKU>.

for medicines that are endorsed by NICE, while allowing (but not requiring) the NHS to pay for medicines that do not receive NICE endorsement.<sup>136</sup> Even this was not enough. In 2010, reports circulated that the government would bow to public pressure and further reduce NICE's power.<sup>137</sup>

The public's condemnation of the negative evaluations by NICE is understandable, but misguided. It is arguably true, as the criticism often asserts, that placing a value on even a few weeks or months of extra life is not the place of government.<sup>138</sup> However, among the 21% of interventions that are not recommended by NICE<sup>139</sup> are drugs that have such little benefit that it would be unsurprising if further, more thorough and unbiased study showed them to be completely ineffective. The decision by NICE to not recommend certain Alzheimer's drugs in mild cases of the disease, for example, was harshly criticized<sup>140</sup> and vigorously opposed by industry,<sup>141</sup> notwithstanding reputable evidence that efficacy was "below minimally relevant thresholds."<sup>142</sup> Similarly, the decision by NICE to refrain from recommending Avastin (bevacizumab) in 2010 was characterized as a betrayal because the drug "can prolong the lives of breast . . . cancer patients,"<sup>143</sup> but in 2011 the FDA recommended removal of Avastin's (bevacizumab's) breast cancer indication because, according to the

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136. Andrew Dillon, Executive Director of NICE, *Presentation at the Massachusetts Institute of Technology*, Nov. 5, 2009; see also Corinna Sorenson et al., *National Institute for Health and Clinical Excellence (NICE): How Does It Work and What Are the Implications for the U.S.?*, NAT'L PHARM. COUNCIL 1, 9 (2008); *How Nice Is Nice: A Conversation with Tony Culyer*, HASTINGS CENTER, <http://healthcarecostmonitor.thehastingscenter.org/admin/how-nice-is-nice-a-conversation-with-anthony-culyer/>, archived at <http://perma.cc/NMX4-ATYN> (last visited July 10, 2014) ("NICE cannot ban anything. It issues guidance . . ."); E-mail from Andrew Dillon to Jonathan J. Darrow (Dec. 9, 2012) (on file with author).

137. Sarah Boseley, *NICE to Lose Powers to Decide on New Drugs*, GUARDIAN [UK], Oct. 29, 2010, <http://www.guardian.co.uk/politics/2010/oct/29/nice-to-lose-new-drug-power>, archived at <http://perma.cc/V2DR-UBG3>.

138. See, e.g., David Catron, *Obamacare Could Kill You*, AM. SPECTATOR, Jan. 15, 2009, <http://spectator.org/archives/2009/01/15/obamacare-could-kill-you>, archived at <http://perma.cc/KML2-WGAZ>.

139. *Technology Appraisal Recommendation Summary*, NAT'L INST. FOR HEALTH & CARE EXCELLENCE, [www.nice.org.uk/newsroom/nicestatistics/TADecisionsRecommendationSummary.jsp](http://www.nice.org.uk/newsroom/nicestatistics/TADecisionsRecommendationSummary.jsp) (last visited July 10, 2014).

140. *NICE Accused of Ageism*, DOCTOR, Mar. 22, 2005, at 5.

141. *Independent Nurse: NICE Will Not Change Alzheimer's Advice*, GEN. PRACTITIONER, June 26, 2009, at 11.

142. Sarah Houlton, *Aricept Takes a Blow*, PHARM. EXEC., Aug. 2004, at 20 (quoting the Lancet study; internal quotes omitted).

143. Daniel Martin, *Betrayal of 20,000 Cancer Patients: Rationing Body Rejects Ten Drugs (Allowed in Europe) that Could Have Extended Lives*, DAILYMAIL, Mar. 15, 2010, <http://www.dailymail.co.uk/health/article-1257944/NICE-rejects-cancer-drugs-extended-patients-lives.html>, archived at <http://perma.cc/WEW4-VGXY>.

FDA, “the drug has not been shown to be safe and effective for that use,”<sup>144</sup> thus vindicating the NICE decision.

Oddly, public skepticism of expert, transparent bodies that methodically evaluate evidence and welcome input from a broad array of stakeholders is greater than its skepticism of self-interested pharmaceutical companies. Whether this reflects the triumph of irrational optimism over considered thought, a general distrust of government interference, or the power of advertising and promotion, the result is that expert bodies such as NICE make only somewhat effective gatekeepers. Because victims view these bodies as barriers to a chance at health, however small, rather than guardians against fraud and substantially ineffective medicines, such bodies can be of only limited effectiveness as gatekeepers.

## II. THE GATEKEEPER ACHILLES HEEL: DRUG EFFICACY HEURISTICS

The absence of efficacy information combined with the difficulties faced in evaluating efficacy through use can lead to the use of heuristics when evaluating efficacy.<sup>145</sup> Although patients may be most susceptible to these heuristics, even experts such as physicians and members of insurance company formulary committees are not immune from their influence. Underlying them are a number of cognitive biases,<sup>146</sup> and so alluring can they be that the term “halo” will be used in order to convey the almost mystical aura of value that they engender. The halos described below are the Achilles heel of the gatekeepers’ mission, distracting patients from acting as their own gatekeepers and causing push-back by patients and others when more rational or better informed gatekeepers try to perform their gatekeeping role.

### A. *The Patent Halo*

Most new drugs are patented and thereby able to benefit from a “patent halo,” the perception or assumption that patented items are of higher value than unpatented ones simply because they are patented.<sup>147</sup> According to one

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144. FDA News Release, *FDA Begins Process to Remove Breast Cancer Indication from Avastin Label: Drug Not Shown to Be Safe and Effective in Breast Cancer Patients*, FDA (Dec. 16, 2010), <http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm237172.htm>, archived at <http://perma.cc/9FUG-XCDY>.

145. Cf. Christine Jolls et al., *A Behavioral Approach to Law and Economics*, 50 STAN. L. REV. 1471, 1477 (1998) (“To deal with limited brain power and time, we use mental shortcuts and rules of thumb.”).

146. Although in a similar vein to the heuristics and biases characterized by psychologists, most of the halos do not align especially well with them. See *generally* HEURISTICS AND BIASES: THE PSYCHOLOGY OF INTUITIVE JUDGMENT (Thomas Gilovich et al. eds., 2002); RICHARD H. THALER & CASS R. SUNSTEIN, *NUDGE: IMPROVING DECISIONS ABOUT HEALTH, WEALTH, AND HAPPINESS* 17-39 (2008) (discussing biases related to anchoring, availability, representativeness, optimism, losses versus gains, the status quo, and framing); Amos Tversky & Daniel Kahneman, *Judgment Under Uncertainty: Heuristics and Biases*, 185 SCIENCE 1124 (1974).

147. Evidence of this can be found in the acknowledged jury bias in favor of patentees. See

commentator, a patent “appears to consumers and investors as clear proof of superiority, the government’s version of a Good Housekeeping Seal of Approval.”<sup>148</sup> Donald Chisum, the author of the leading patent treatise, noted how this dynamic has been regarded as particularly important in the pharmaceutical industry:

Early decisions established a higher standard of proof of the utility of inventions claimed to have value in the treatment of human disease. These decisions reasoned that issuance of a patent gave the drug or other medical invention an ‘appearance of authenticity,’ an ‘oblique imprimatur of the Government’ that might be used to mislead and deceive the consuming public.<sup>149</sup>

The Supreme Court has also long acknowledged the assumption of respect accorded to patented products,<sup>150</sup> and numerous commentators have noted the public’s admiration and respect for patents in general,<sup>151</sup> no doubt spurred along by the romantic image of the brilliant independent inventor creating breakthrough products in his garage.<sup>152</sup> Pharmaceutical companies have sometimes quite

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John R. Allison & Mark A. Lemley, *Empirical Evidence on the Validity of Litigated Patents*, 26 AIPLA Q.J. 185, 251 (1998) (conducting an eight year empirical study of patent validity determinations and concluding that “juries are extremely favorable to patentees”); Kimberly A. Moore, *Judges, Juries, and Patent Cases—An Empirical Peek Inside the Black Box*, 99 MICH. L. REV. 365, 408 (2000) (“Juries find for the patent holder more often on validity, infringement, and willfulness issues . . . .”); see also *Thompson v. Haight*, 23 F. Cas. 1040, 1041 (S.D.N.Y. 1826) (“The most frivolous and useless alterations in articles in common use are denominated improvements, and made pretexts for increasing their prices, while all complaint and remonstrance are effectually resisted by an exhibition of the great seal.”); Anthony Baldo, *Juries Love the Patent Holder*, FORBES, June 17, 1985, at 147 (quoting Pennie & Edmonds attorney John Kidd: “Juries believe in the patent system more than judges do.”).

148. Andrew B. Dzeguze, *The Devil in the Details: A Critique of KSR’s Unwarranted Reinterpretation of “Person Having Ordinary Skill,”* 10 COLUM. SCI. & TECH. L. REV. 1, 6 (2009).

149. DONALD S. CHISUM, CHISUM ON PATENTS § 4.04[2] (2009); see also *Isenstead v. Watson*, 157 F. Supp. 7, 9 (D.D.C. 1957) (“While the granting of a patent does not legally constitute a certificate that the medicine to which it relates is a good medicine and will cure the disease or successfully make the test which it was intended to do, nevertheless, the granting of such a patent gives a kind of official imprimatur to the medicine in question on which as a moral matter some members of the public are likely to rely.”).

150. *Reckendorfer v. Faber*, 92 U.S. 347, 351 (1875) (referring to the “prima facie respect arising from . . . government approval [i.e., arising from the patent]”); see also C.O. Marshall, *Comparative Utility as a Requisite to Patentability*, 550 J. PAT. OFF. SOC’Y 550, 553 (1919) (The prestige of the patent “has a distinct and immense money value to the public . . . .”) (internal quotation omitted).

151. See sources cited *supra* note 147.

152. See generally Jessica Silbey, *The Mythical Beginnings of Intellectual Property*, 15 GEO. MASON L. REV. 319 (2008).

sensibly leveraged the patent halo as part of their efforts to increase sales.<sup>153</sup> As explained *infra*, there is no basis in patent doctrine to justify such a patent halo, since patents may be obtained on inventions that have lower value than existing products.<sup>154</sup>

The practice of implying that a government mark should be recognized as a symbol of drug efficacy is neither recent, nor limited to patents. More than 100 years ago, the British Medical Association noted that pharmaceutical advertisers “took to inserting in their advertisements phrases intended to suggest that the Inland Revenue stamp upon their packages implied some sort of Government guarantee of the efficacy of the remedy.”<sup>155</sup> The stamp was in fact merely connected to the collection of taxes, but the government nevertheless eventually felt compelled to correct the public’s misimpression, altering the stamp such that it bore the cautionary disclaimer: “This stamp implies no Government guarantee.”<sup>156</sup>

### B. The FDA Approval Halo

Patients falsely assume that if the FDA approved a drug, it must be very effective. A recent study by researchers at Dartmouth Medical School surveyed 2944 adults to assess their understanding of the meaning of FDA approval.<sup>157</sup> The researchers found nearly four in ten people believed, mistakenly, that the FDA only approves drugs that are “extremely effective.”<sup>158</sup> One in four respondents erroneously believed that the FDA would not approve drugs with serious side effects, and the same proportion that only “extremely effective” drugs could be advertised.<sup>159</sup> As the researchers pointed out, none of these statements is true.<sup>160</sup> Others have pointed out the common misimpression that FDA approval of a new

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153. Explicit promotion of patent status is more often seen in non-prescription medications, such as sunscreen. *See, e.g., Transformational Ideas*, JOHNSON & JOHNSON (Dec. 6, 2013, 9:47 AM), <http://www.jnj.com/connect/about-jnj/company-history/healthcare-innovations?pageNo=2>, archived at <http://perma.cc/EV7Q-XLLH> (boasting that “NEUTROGENA® and AVEENO® brands now use a patented advanced sun protection system”). However, in light of frequent news coverage of drug “patent cliffs” and the like, the public can reasonably infer that advertised medicines are probably patented. *See, e.g., Jessica Hogdson, Big Pharma Tries to Look Past “Patent Cliff,”* WALL ST. J., Oct. 24, 2012, <http://online.wsj.com/article/SB10001424052970203897404578076173187345806.html>.

154. *See infra* Part III.A.

155. BRITISH MEDICAL ASSOCIATION, SECRET REMEDIES: WHAT THEY COST AND WHAT THEY CONTAIN 184 (1909), available at [https://archive.org/stream/secretremedieswh00brit/secretremedieswh00brit\\_djvu.txt](https://archive.org/stream/secretremedieswh00brit/secretremedieswh00brit_djvu.txt), archived at <http://perma.cc/65WA-N2QY>.

156. *Id.*

157. Lisa M. Schwartz & Steven Woloshin, *Communicating Uncertainties about Prescription Drugs to the Public: A National Randomized Trial*, 171 ARCH. INTERNAL MED. 1463 (2011).

158. *Id.* at 1465.

159. *Id.*

160. *Id.* (“Fifty-six percent held at least 1 of the foregoing misconceptions.”).

drug in a given therapeutic category means that the drug must be better than pre-existing drugs.<sup>161</sup> Again, this is a popular view that is nevertheless without firm moorings to any statute. The overall message of these findings and observations is that FDA approval confers a halo of efficacy that is not warranted.

The fact that FDA approval suggests efficacy levels that are not warranted has not stopped businesses from using, or trying to use, the “imprimatur”<sup>162</sup> of FDA approval to their advantage. Internet pharmacies prominently boast that their products are “FDA-approved,”<sup>163</sup> while direct-to-consumer television advertisements for individual drugs often include the phrase “FDA approved” in a way that suggests a certification of value.<sup>164</sup> The biotechnology industry has welcomed the possibility of formal review by the FDA because the “FDA Seal of Approval” would be beneficial for marketing purposes.<sup>165</sup> The FDA “seal of legitimation” has been used for decades, thus conditioning generations of consumers to misunderstand the meaning of FDA approval in a way that favors sales.<sup>166</sup>

The significance of the FDA approval halo to the pharmaceutical industry is confirmed by the particularly interesting and unusual case of *Mutual Pharmaceutical Co. v. IVAX Pharmaceuticals*, in which Mutual claimed that IVAX was implicitly promoting its anti-malaria products as FDA-approved when in fact they were not.<sup>167</sup> The drug in question, quinine sulfate, was never FDA approved because it has been used for hundreds of years to treat malaria and was therefore “grandfathered” under the 1938 Federal Food, Drug and Cosmetic Act.<sup>168</sup> In 1998, the FDA restricted quinine products to prescription-only status on the basis of safety concerns, triggering the requirement that any further sale would require a New Drug Application (NDA).<sup>169</sup> Mutual filed an NDA and obtained FDA approval in 2005,<sup>170</sup> but IVAX and others did not, instead continuing to sell their quinine sulfate through channels that implied FDA approval.<sup>171</sup> The court found that IVAX’s representations were likely false or

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161. See, e.g., PAMELA ARMSTRONG, *SURVIVING HEALTHCARE* 270 (2004).

162. *Mutual Pharm. Co. v. Ivax Pharms., Inc.*, 459 F. Supp. 2d 925, 941 (C.D. Cal. 2006).

163. *Id.* at 942.

164. See, e.g., *CommercialsUSA, Lipitor Medication 2010 Commercial*, YOUTUBE (Jan. 4, 2011), <http://www.youtube.com/watch?v=ogyC9rEjxDM>; *theBESTforYourNeeds, Lyrica TV Commercial, 'Terry,'* YOUTUBE (Jul. 26, 2013), <http://www.youtube.com/watch?v=UO6H9i8T--k>.

165. HENRY I. MILLER & GREGORY P. CONKO, *THE FRANKENFOOD MYTH* 122 (2004).

166. See DANIEL CARPENTER, *REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA* 177 (2010).

167. *Mutual Pharm. Co. v. Ivax Pharms., Inc.*, 459 F. Supp. 2d 925, 931 (C.D. Cal. 2006).

168. See Clark G. Sullivan, *Grandfathered Drugs: What's Behind the Huge Price Increases?*, ARNALL GOLDEN GREGORY LLP (June 1, 2011), <http://www.lexology.com/library/detail.aspx?g=804cf4f9-83f6-431e-b4f2-6775d3909b8d>, archived at <http://perma.cc/GRS7-FR64>.

169. 21 C.F.R. § 310.547 (1998).

170. *Mutual Pharm. Co.*, 459 F. Supp. 2d at 929.

171. *Id.* at 940.

misleading, and issued a preliminary injunction.<sup>172</sup>

However, this is not to suggest that FDA approval means nothing. As United States Senator Dodd recently stated, “[t]hroughout the world, the FDA seal of approval—the words ‘FDA Approved’—has stood as the gold standard for safety and quality.”<sup>173</sup> The FDA does act to ensure that manufacturing practices are up to par and that purity standards are met, for example. But these aspects of quality appear to be unjustifiably extended in the minds of a substantial proportion of consumers to assumptions about efficacy (and safety) that are not warranted. FDA oversight is therefore a double-edged sword. On the one hand, the FDA works to protect the public by assuring minimum levels of safety and quality. In this respect, the creation of the FDA has made the public safer and less likely to be duped than it was prior to the Pure Food and Drug Act of 1906. At the same time, however, FDA approval is often misunderstood to certify efficacy levels that are simply not part of its statutory mandate. This gives the patients a false sense of security that counter-intuitively increases the public’s vulnerability. Whether the negative impacts of substituting “FDA approved” for *caveat emptor* exceed the benefits of FDA oversight is a subject ripe for future research.

### C. *The Novelty Halo*

There is an acknowledged bias in favor of new products and against old ones,<sup>174</sup> what has sometimes been referred to as “the cult of the new.”<sup>175</sup> “Just a simple count of the number of times you have heard the phrase ‘new and improved’ should indicate the size of the consumer appetite for new and supposedly better products[,]” offers a sales management textbook.<sup>176</sup> Use of the novelty halo to sell medical treatments goes back at least as far as Pliny (23-79 A.D.), who chronicles the successful tactics of physicians who achieved fame by “reversing the treatment” of their predecessors and “swe[eping] away all received doctrines.”<sup>177</sup> As if he lived today, when every new drug is a breakthrough

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172. *Id.* at 946.

173. 151 CONG. REC. 7952 (Apr. 27, 2005) (statement of Sen. Dodd).

174. C.S. Lewis characterized this bias as “chronological snobbery.” C.S. LEWIS, *THE CASE FOR CHRIST* 38 (1973); *see also* AVORN, *supra* note 18, at 273 (“In fact many new drugs are *not* better than already available alternatives.”).

175. Trent Hamm, *The Cult of the New*, CHRISTIAN SCI. MONITOR (Mar. 9, 2010), <http://www.csmonitor.com/Business/The-Simple-Dollar/2010/0309/The-Cult-of-the-New>, *archived at* <http://perma.cc/8J2K-FQ5X>.

176. ROBERT D. HISRICH & RALPH W. JACKSON, *SELLING AND SALES MANAGEMENT* 7 (1993); *see also* T.C. DOYLE, *The Lure of New and Improved*, CRN (July 13, 2005, 5:00 PM), <http://www.crn.com/blogs-op-ed/the-daily-doyle/164903978/the-lure-of-the-new-and-improved.htm>, *archived at* <http://perma.cc/4XJD-QR7P> (“Since the days of the Gillette Safety Razor, Americans have been tempted by two words that have proved nearly impossible to resist: ‘new’ and ‘improved.’”). *See generally* RICHARD S. TEDLOW, *NEW AND IMPROVED: THE STORY OF MASS MARKETING IN AMERICA* (1996).

177. PLINY THE ELDER, *supra* note 20, at 187.

welcomed by an uncritical populace, Pliny wrote: “Medicine changes every day, being furbished up again and again, and we are swept along on the puffs of the clever brains of Greece.”<sup>178</sup> A distant echo of Pliny, the *Consumer Reports* publication cited earlier confirms that the novelty bias continues its effect today, sweeping within its influence both laypersons and those in the medical profession itself: “Many people (including many physicians) also believe that newer drugs are always or almost always better . . . .”<sup>179</sup>

#### D. The Expert Halo

Patients assume that if a drug is prescribed by a physician, who is presumed to be knowledgeable about drug efficacy, the drug chosen by this expert must be the most effective drug available. In some cases, the expert halo is combined with the novelty halo. As one commentator mistakenly asserts, “the marketplace virtually demands that a new drug must be more effective than already established competitors if physicians are to prescribe it.”<sup>180</sup> A review of top-selling drugs suggests otherwise. For example, the twelfth best-selling drug of 2012 was Plavix (clopidogrel),<sup>181</sup> a blood thinner, more than \$5 billion of which was prescribed by doctors in that year alone.<sup>182</sup> Doctors prescribed this massive volume of Plavix (clopidogrel) even though the FDA repeatedly warned as early as 1998 of the lack of Plavix’s (clopidogrel’s) superior efficacy over time-tested aspirin, noting that Sanofi’s “claims that suggest Plavix has been ‘proven’ to be more effective than aspirin are misleading because they are not based on substantial evidence.”<sup>183</sup> The FDA again warned against Sanofi’s misleading and unsubstantiated overstatements of efficacy in 2001,<sup>184</sup> and a study published in

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178. *Id.* at 189.

179. *Evaluating Statin Drugs to Treat*, *supra* note 40, at 16.

180. JAY S. COHEN, MAKE YOUR MEDICINE SAFE: HOW TO PREVENT SIDE EFFECTS FROM THE DRUGS YOU TAKE 479 (1998).

181. John D. Carroll, *The 15 Best-Selling Drugs of 2012*, FIERCE PHARMA (Oct. 9, 2012), <http://www.fiercepharma.com/special-reports/15-best-selling-drugs-2012>, *archived at* <http://perma.cc/EZ8K-M29B>.

182. *Plavix*, FIERCE PHARMA (Oct. 9, 2012), <http://www.fiercepharma.com/special-reports/Plavix>, *archived at* <http://perma.cc/KW3-BXCG>.

183. Letter from Janet Norden, Regulatory Review Officer, Div. of Drug Mktg., Adver. and Comm’ns, to Gregory M. Torre, Senior Director, Drug Regulatory Affairs, Sanofi Pharms. (Dec. 18, 1998) (on file with the FDA), <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM166391.pdf>, *archived at* <http://perma.cc/E99M-37MC>.

184. Letter from Andrew S.T. Haffer, Regulatory Review Officer, Div. of Drug Mktg., Adver., and Comm’ns, to Kenneth Palmer, Associate Director, Drug Regulatory Affairs, Sanofi-Synthelabo Inc. (May 9, 2001) (on file with the FDA), <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM166467.pdf>, *archived at* <http://perma.cc/LH23-D2VS>.

the Lancet in 2006 concluded that “the combination of clopidogrel plus aspirin was not significantly more effective than aspirin alone in reducing the rate of myocardial infarction, stroke, or death from cardiovascular causes.”<sup>185</sup> Today, Plavix’s (clopidogrel’s) own labeling continues to acknowledge a “Lack of Established Benefit of Plavix plus Aspirin in Patients with Multiple Risk Factors or Established Vascular Disease.”<sup>186</sup> The statement is made in the context of a study of 15,603 patients, presumably large enough to detect a meaningful efficacy difference if one exists. Moreover, the aforementioned lack of established benefit is in relation not to aspirin, but to placebo.

### *E. The Prescription Halo*

Patients and others may assume that prescription products are more powerful than over-the-counter (OTC) products because the dispensing of prescription drugs is regulated by the government. Once again, the assumption of greater efficacy is not necessarily true. Most new OTC drugs today were initially sold as prescription products. Frequently cited examples include pain medicines like Advil (ibuprofen) and Tylenol (acetaminophen) and heartburn medicine Zantac (ranitidine),<sup>187</sup> but one could also add allergy medicines Zyrtec (cetirizine) and Claritin (loratadine), morning-after pill Plan B (levonorgestrel), heartburn medicine Prilosec (omeprazole), and antifungal Monistat (miconazole),<sup>188</sup> among many others. More generally, a drug’s prescription status often has more to do with the amount of time since its entry on the market or with its safety profile than with efficacy. Nevertheless, consumers may misinterpret frequent advertising statements that drugs are “available by prescription”<sup>189</sup> to mean that the drug is very potent, when by law prescription status means only that “because of its toxicity or other potentiality for harmful effect . . . [a drug] is not safe for use except under the supervision of a practitioner licensed by law.”<sup>190</sup>

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185. Deepak L. Bhatt et al., *Clopidogrel and Aspirin Versus Aspirin Alone for the Prevention of Atherothrombotic Events*, 354 NEW ENG. J. MED. 1706, 1714 (2006).

186. *Drug Label for Plavix (clopidogrel bisulfate)*, § 14.3 *Lack of Established Benefit of Plavix plus Aspirin in Patients with Multiple Risk Factors or Established Vascular Disease*, Full Prescribing Information, Plavix (Dec. 2011) (revised Sept. 2013), § 14.3, [http://packageinserts.bms.com/pi/pi\\_plavix.pdf](http://packageinserts.bms.com/pi/pi_plavix.pdf), archived at <http://perma.cc/TJ75-YAXG>.

187. F.M. Scherer, *The Pharmaceutical Industry*, in HANDBOOK OF HEALTH ECONOMICS 1300 (2000).

188. *Prescription to Over-the-Counter (OTC) Switch List*, FDA, <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm106378.htm>, archived at <http://perma.cc/9S54-ZZGU> (last visited July 10, 2014).

189. See, e.g., *Humira Ad, May 13, 2012*, <http://www.youtube.com/watch?v=hII7iSulmGc> (last visited Feb. 4, 2013) (“By prescription only.”); *LUNESTA® (eszopiclone) Sleeping Pill Commercial ad - USA (real one)*, <http://www.youtube.com/watch?v=vu0rXFhsM8w> (last visited July 10, 2014) (“Available by prescription only.”).

190. 21 U.S.C. § 353(b)(1)(A) (2013).

*F. The Premium Price Halo*

It was noted above that credence goods, including many pharmaceuticals, are those goods whose utility is difficult for consumers to ascertain even after consumption.<sup>191</sup> Another economic concept relevant to the consideration of drug products is embodied by the concept of Veblen goods, which are those goods for which desirability counter-intuitively *increases* as price increases, based on the signaling value of price. Veblen goods can, perhaps, be distinguished in that the high price of a Veblen good is generally associated with high social status, luxury, or exclusivity, whereas high drug prices are more likely to be perceived as implying effectiveness or quality.<sup>192</sup> The signaling value of the high price, however, is shared in common.

Economists have long acknowledged the practice of relying on price as a proxy for value.<sup>193</sup> In a seminal 1945 article, Stanford economist Tibor Scitovszky explained that the perceived relationship between price and value might not be irrational, because if buyers do not find prices justified, sellers would eventually have to lower them.<sup>194</sup> Scitovszky cautioned, however, that the relationship may break down where goods are complex or where new products are frequently introduced to replace old ones,<sup>195</sup> the precise scenario faced with drugs where chemical formulae and clinical trial data are incomprehensible to the ordinary consumer and where dozens of new drugs are introduced each year.

Marketers evidently believe that a premium price can increase sales even with simple products whose characteristics can be directly and immediately perceived. Michelob, for example, once sold its beer using the slogan, “Michelob, America’s highest-priced beer!”<sup>196</sup> More generally, retailers across the spectrum of product categories can readily be observed to use a two-price system: the “regular” price, to signal value, and the “sale” price,<sup>197</sup> both sometimes prominently marked upon

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191. Michael R. Darby & Edi Karni, *Free Competition and the Optimal Amount of Fraud*, 16 J. L. & ECON. 67-88 (1973); FRANCISCO CABRILLO & SEAN FITZPATRICK, *THE ECONOMICS OF COURTS AND LITIGATION* 159 (2008).

192. See Giovanni Mastrobuoni et al., *Price as a Signal of Product Quality: Some Experimental Evidence* 1 (Working Paper Feb. 2013), [http://www.tetenov.com/wine\\_tastings.pdf](http://www.tetenov.com/wine_tastings.pdf), archived at <http://perma.cc/ZU8S-ZP3P> (distinguishing the signaling effect of price from its “status” effect). Mastrobuoni et al. also report that young/inexperienced consumers may be more greatly influenced by the price signal. *Id.* at 4; see also Akshay R. Rao & Kent B. Monroe, *Causes and Consequences of Price Premiums*, 69 J. BUS. 511, 511 (1996) (noting that “poorly informed consumers may rely on a ‘You get what you pay for’ decision rule”).

193. See Akshay R. Rao & Kent B. Monroe, *The Moderating Effect of Prior Knowledge on Cue Utilization in Product Evaluations*, 15 J. CONSUMER RES. 253, 254 (1988) (“[I]ntegrative reviews of this research stream indicate a positive price-perceived quality relationship.”).

194. Tibor Scitovszky, *Some Consequences of the Habit of Judging Quality by Price*, 12 REV. ECON. STUD. 100, 100-01 (1944-45).

195. *Id.* at 101.

196. *Id.* at 100.

197. *Id.* at 101. The two-priced system can be commonly observed in: automobile dealerships,

the product.

Like other sellers, pharmaceutical companies have sometimes deliberately priced their products higher than a competitor's product regardless of comparative efficacy, in order to convey an impression of superiority. For example, in *Our Daily Meds*, Melanie Peterson describes Glaxo's strategy of pricing newcomer Zantac (ranitidine) at a substantial premium over incumbent Tagamet (cimetidine).<sup>198</sup> The two products both fall within the category of drugs known as H2 blockers, as reflected in their similar generic names, and research at the time showed them to be both safe and equally effective in the treatment of ulcers.<sup>199</sup> Nevertheless, the new drug was priced as much as 50% higher than Tagamet (cimetidine), a move described by Peterson as "like that of an underweight boxer trying to fool the prizefighter with his swagger."<sup>200</sup> Within three years, the demand of a credulous public allowed Zantac (ranitidine) to surpass Tagamet (cimetidine) in sales.<sup>201</sup> Even more disconcerting is that, although in this case the two drugs were nearly equivalent in efficacy, nothing prevents the use of such a pricing strategy even where the new drug is *inferior* in efficacy.

Such pricing strategies reflect the notion, articulated by historian Barbara Tuchman in the 1970s, that "a patient's sense of therapeutic value is in proportion to expense."<sup>202</sup> Tuchman was speaking of the powdered pearls, emeralds, and other rare treatments that were prescribed to victims of the plague during the 1300s, but she recognized that the perception of high price as a value proxy is "not unknown to modern medicine."<sup>203</sup> Indeed, the signaling value of high price may reflect an underlying universal human tendency. According to a commentator on the drug trade in ancient Rome, "[a] cheap concoction to them signified a bad one, and hence physicians and druggists were advised to add harmless spices, perfumes and suchlike to common, effective, and inexpensive bases in order to convince their rich customers that here was something really worth having."<sup>204</sup> Pliny himself railed against "the stupid convictions of certain

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where the manufacturer's suggested retail price (MSRP) is rarely the price paid; supermarkets, where "customer loyalty cards" allow consumers to pay less than the "regular" price, the pharmaceutical industry, where the average wholesale price (AWP) "[does] not reflect the physicians' actual acquisition cost, or anything close to it." *In re Pharm. Indus. Avg. Wholesale Price Litig.*, 582 F.3d 156, 160 (1st Cir. 2009).

198. See PETERSEN, *supra* note 108, at 137.

199. John Feely & Kenneth G. Wormsley, *H2 Receptor Antagonists: Cimetidine and Ranitidine*, 286 BRIT. MED. J. 695, 697 (1983) (stating that both drugs were "equally effective").

200. See PETERSEN, *supra* note 108, at 137.

201. See *id.* at 138.

202. BARBARA WERTHEIM TUCHMAN, *A DISTANT MIRROR: THE CALAMITOUS 14TH CENTURY* 107 (1979).

203. *Id.* at 106-07.

204. Vivian Nutton, *The Drug Trade in Antiquity*, 78 J. ROYAL SOC'Y MED. 138, 142 (1985); see also LAURENCE M. V. TOTELIN, *HIPPOCRATIC RECIPES: ORAL AND WRITTEN TRANSMISSION OF PHARMACOLOGICAL KNOWLEDGE IN FIFTH- AND FOURTH-CENTURY GREECE* 259-60 (2009)

people who consider nothing beneficial unless it is costly.”<sup>205</sup> More than 1000 years later in an entirely different medical culture, Chinese writer Hsu Ta-ch’un wrote accusingly, in 1757, that “stupid people believe that expensive drugs must be good drugs, while cheap drugs are supposed to be inferior[.]”<sup>206</sup> Even if people today are more intelligent or better informed than those of centuries past, a hypothesis itself pregnant with doubt, the allure of high price and its potential to distort perceptions of value should not be underestimated.

### G. *The Unrealistic Optimism Halo*

Absent efficacy data, patients may significantly overestimate the likelihood of therapeutic value in the spirit of blind optimism. In an influential paper, Neil Weinstein of Rutgers University reported study findings demonstrating that people “tend to believe that they are more likely than their peers to experience positive events and less likely to experience negative events.”<sup>207</sup> The relevance of this optimism bias in the health sector has been noted.<sup>208</sup> In the 1950s, Harvard sociologist Talcott Parsons discussed the “optimistic bias” that pervades medical treatment, often taking the form of an irrational belief in efficacy, and closely tied to the “physician’s so frequent insistence that his patients should have ‘confidence’ in him.”<sup>209</sup> It is plausible, furthermore, that such optimism bias could synergistically combine with pharmaceutical company claims of theoretical “subpopulations” to inflate any expected therapeutic benefit beyond reason. That is, because of the tendency to overestimate one’s chances of experiencing positive events, patients may tend to believe that they are more likely to fall within the favored theoretical subpopulation than is objectively probable,<sup>210</sup> assuming *arguendo* that such subpopulations exist.

The placebo effect is perhaps the most tangible indication that irrational patient optimism regarding drug efficacy exists. As one team of researchers pointed out, placebos by definition do not produce any therapeutic effect; it is the meaning mistakenly ascribed to them that leads to the so-called “placebo

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(arguing that Hippocratic recipes were “based on luxury and exotic ingredients,” while those during subsequent centuries were even more expensive and complex).

205. PLINY THE ELDER, *supra* note 20, at 201.

206. HSU TA-CH’UN, I-HSUEH YUAN LIU LUN [FORGOTTEN TRADITIONS OF ANCIENT CHINESE MEDICINE] 179 (Paul U. Unschuld trans., 1990) (1757).

207. Neil D. Weinstein, *Unrealistic Optimism About Future Life Events*, 39(5) J. PERSONALITY & SOC. PSYCH. 806, 818 (1980); *see also* Neil D. Weinstein, *Unrealistic Optimism About Susceptibility to Health Problems: Conclusions from a Community-Wide Sample*, 10 J. BEHAV. MED. 481 (1987).

208. *See, e.g.*, Kathrin Milbury et al., *Treatment-Related Optimism Protects Quality of Life in a Phase II Clinical Trial for Metastatic Renal Cell Carcinoma*, 42 ANNALS OF BEHAV. MED. 313, 315 (2011).

209. PARSONS, *supra* note 34, at 315.

210. *See* Light, *supra* note 109, at 8 (noting that drug executives and marketers “have developed some of the most elaborate institutions of hope and magic in modern culture”).

effect.”<sup>211</sup> In a study cited by those researchers, patients received either aspirin or placebo, each of which was labeled either as branded or unbranded, creating four possible combinations.<sup>212</sup> The percent of headaches reported by patients to be substantially improved following treatment was revealing: unbranded placebo (74%); branded placebo (78%); unbranded aspirin (86%); and branded aspirin (89%).<sup>213</sup> The slight outperformance of both branded categories over their unbranded counterparts suggests that some form of optimism is playing a role in outcomes, even where no placebo is involved. This inference is buttressed by the only modestly larger difference (about 10%) between placebo and aspirin, across both branded and unbranded categories, which suggests that the large majority of any therapeutic benefit in the case of aspirin and headache pain is created by optimism (i.e., placebo effect) rather than by the chemical agent.

#### H. *The Last Resort Halo*

Desperate patients will try anything, from risky or unproven experimental therapies,<sup>214</sup> to traveling abroad to obtain medical treatment that is criminalized in the United States,<sup>215</sup> to submitting themselves to the care of those whose only product or service is unadulterated fraud.<sup>216</sup> The unifying theme of patient actions such as these is the strong desire to believe that a treatment exists combined with the knowledge that there may be little or nothing to lose by trying.<sup>217</sup> In a statement to Congress in 1911, President Taft urged legislators to better protect the public from “the raising of false hopes of speedy cures,” asserting that “[t]here are none so credulous as sufferers from disease.”<sup>218</sup> If the desire to

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211. Daniel E. Moerman & Wayne B. Jonas, *Deconstructing the Placebo Effect and Finding the Meaning Response*, 136 ANNALS OF INTERNAL MED. 471, 472 (2002).

212. A. Branthwaite & P. Cooper, *Analgesic Effects of Branding in Treatment of Headaches*, 282 BRIT. MED. J. 1576 (1981).

213. *Id.* at 1577, Table 2 (percentage figures reflect the sum of the categories: “a lot better”; “quite a lot better”; “considerably better”; and “completely better”).

214. *See, e.g.*, Nancy M.P. King & Gail Henderson, *Treatments of Last Resort: Informed Consent and the Diffusion of New Technology*, 42 MERCER L. REV. 1007 (1991).

215. *See* I. Glenn Cohen, *Circumvention Tourism*, 97 CORNELL L. REV. 1309, 1398 (2012) (addressing the question of whether countries that criminalize certain medical treatment should condone travel to other countries for the purpose of circumventing the domestic prohibition, and generally arguing that they should not).

216. *See, e.g.*, Press Release, *San Fernando Valley Doctor Convicted of Selling Bogus Cancer Cure to Christians Across the Nation*, FDA (Sept. 27, 2011), <http://www.fda.gov/ICECI/CriminalInvestigations/ucm273777.htm>, archived at <http://perma.cc/HJ2W-HJ64> (describing a doctor who was convicted of peddling a treatment that could purportedly cure cancer, multiple sclerosis, Alzheimer’s, diabetes, and other diseases, and for which she charged up to \$150,000 per six-month treatment program).

217. *See* King & Henderson, *supra* note 214, at 1011.

218. Message from the President of the United States, 62 CONG. REC. 2380 (June 21, 1911) (Document No. 75).

believe, against evidence, that a “miracle cure” exists creates an unwarranted efficacy halo even where the product in question has been criminalized or adjudged worthless by an expert government body such as the FDA, it is easy to imagine what occurs when the counterweight of FDA disapproval is replaced with FDA approval and negative evidence is replaced with equivocal or confusing evidence. In these cases, the desire to believe that a treatment is meaningfully effective can predominate even where the medical condition in question is of only moderate or minimal severity.

### *I. Halo Convergence and Human Perception*

Each halo might alone be sufficient to convince even educated and circumspect patients to believe in the efficacy of a substantially ineffective remedy. Halos are rarely found alone, however. Instead they generally converge to create an overwhelming impression of efficacy that is stubbornly difficult to dislodge even when the evidence is uncontroverted and clear. When a consumer compares a heavily advertised, new, patented, FDA-approved, and very expensive product that is prescribed by his trusted physician, to a much cheaper, older, over-the-counter product, the tendency to believe that the expensive new product is better can be irresistible. If it were not better, one might reason, how could it be the third (or fifth, or eleventh) best-selling drug in the world? As with movies and other forms of popular culture, wide awareness and success of a product can itself lead to greater success, constituting a type of cumulative product advantage.<sup>219</sup>

Study results have confirmed the triumph of halo convergence over actual product efficacy. One study of the Canadian pharmaceutical market, for example, revealed that 80% of the increase in drug spending between 1996 and 2003 resulted from consumer use of “new, patented drug products that did not offer substantial improvements on less expensive alternatives available before 1990.”<sup>220</sup> Similarly, an independent French organization examined 998 new medicinal products and indications from the period 1990–2011 and concluded that only fifteen offered “a real advance” and of those fifteen, only two were breakthroughs (“bravo,” to use the organization’s own language).<sup>221</sup>

Patients, therefore, make poor gatekeepers due to a confluence of factors. Kraakman’s analysis provides a starting point for understanding this

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219. Cf. Derek De Solla Price, *A General Theory of Bibliometric and Other Cumulative Advantage Processes*, 27 J. AM. SOC’Y INFO. SCI. 292, 292 (1976) (noting the benefits of cumulative advantage to income, academic publication success, citation success, and journal prominence).

220. See Steven G. Morgan et al., “Breakthrough” Drugs and Growth in Expenditure on Prescription Drugs in Canada, 331 BRIT. MED. J. 815, 815 (2005).

221. *New Drugs and Indications in 2011: France Is Better Focused on Patients’ Interests After the Mediator Scandal, But Stagnation Elsewhere*, 21 LA REVUE PRESCRIRE 106, 107 (Apr. 2012) (table) (translating 32 LA REVUE PRESCRIRE 134 (Feb. 2012)) [hereinafter *New Drugs and Indications in 2011*].

phenomenon, suggesting that primary deterrence will fail where actors lack sufficient information or expertise to make appropriate decisions in their own self-interest.<sup>222</sup> Yet while a lack of expertise and capacity is certainly a factor for patients in the complex environment of pharmaceutical products, it only begins to explain the inadequacy of patients as gatekeepers. The proxies for efficacy discussed above, which can take on greater importance in the absence of information, take the theory a great deal further, explaining not only why consumers fail to screen out ineffective drugs, but why they may tend to affirmatively demand them.

### III. REGULATORS AS GATEKEEPERS

The lack of efficacy exhibited by many drugs is surprising in light of the highly regulated nature of pharmaceutical products themselves, with substantial involvement by government agencies or actors from the time a drug is first patented to when it is advertised to when patients or others bring suit for physical or economic harms. This Part examines how ineffective drugs are able to slip through the hands of government gatekeepers, not as a consequence of incompetence, inadequate resources, or failure of attention to duty, but despite general compliance with all legal requirements at every stage.

It should be noted that government actors do not seem to be what Kraakman had in mind in his discussion of gatekeepers, which he limits to *private* third-parties that can prevent misconduct by withholding support.<sup>223</sup> He specifically distinguishes direct enforcement against wrongdoers from the enlistment of those wrongdoers' "associates and market contacts" in an effort to indirectly discourage undesirable behavior.<sup>224</sup> In addition, Kraakman is most interested in gatekeepers who are motivated by liability, and to some extent reputational harm, rather than statutory duty.<sup>225</sup>

Nevertheless, government actors are gatekeepers in several important senses that are consistent with Kraakman's framework. Most importantly, they are able to disrupt misconduct by withholding support, such as when the United States Patent and Trademark Office declines to grant a patent on a new molecular entity that might form the basis of a new drug. Moreover, much of the enforcement by government agencies that will be discussed is *ex ante*, serving to prevent wrongdoing by limiting access to the market rather than punishing conduct after the fact. This characteristic is consistent with the ordinary meaning of the word "gatekeeping," that is, controlling access.<sup>226</sup>

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222. Kraakman, *supra* note 1, at 56.

223. Kraakman's classification of "public" and "market" gatekeepers is not to the contrary, since by "public" Kraakman merely means those private gatekeepers who are motivated by liability rather than private incentives such as the fear of reputation loss. *See id.* at 62.

224. *Id.* at 53.

225. *Id.* at 53-54 & n.3, 60 (gatekeeper liability); *id.* at 61 & n.20 (reputational harm).

226. *Gatekeeper Definition*, OXFORD DICTIONARIES, <http://oxforddictionaries.com/definition/english/gatekeeper>, archived at <http://perma.cc/K5CP-2NTX> (last visited July 10, 2014) ("a person

It is also important to clarify what it is that these government gatekeepers are guarding against. Kraakman describes the deterrence of “misconduct” or “wrongdoing,”<sup>227</sup> and his examples reveal a focus on gatekeepers who can withhold support for misconduct that is criminal or at least obviously pernicious: doctors and pharmacists, as guardians against drug abuse;<sup>228</sup> sellers of firearms who must obtain export licenses to deter actions by foreign enemies;<sup>229</sup> social hosts that restrain the actions of their intoxicated guests;<sup>230</sup> and auditors that prevent securities fraud.<sup>231</sup> Although this type of wrongdoing could occur in the context of pharmaceutical efficacy, such as where a drug company fraudulently falsifies clinical trial data to obtain FDA approval, the “wrongdoing” that is the focus of the present discussion is ordinarily much more subtle, involving the induced but voluntary transfer of vast amounts of wealth to companies whose products in reality are worth little or nothing. It is “wrongdoing” in a systems-based sense, akin to Lawrence Lessig’s concern with the institutional corruption of politicians.<sup>232</sup>

Voluntary transactions, of course, are the essence of a market-based economy, and it is not suggested that limitations should be placed on an individual’s right to pay a high price for a small gain in health. The concern is that the absence of clearly communicated efficacy information is causing doctors, patients, and others to demand drugs that they never would ask for if they understood just how ineffective these drugs are. Kraakman does mention such gatekeepers against “soft” wrongs, such as his reference to lenders that protect unsophisticated borrowers from bad investments by refusing to lend.<sup>233</sup> The USPTO and the FDA are like Kraakman’s lenders in that they can effectively prevent consumption of bad drugs by unsophisticated doctors and patients. Another government agency, the FTC, acts as a gatekeeper by policing misleading promotional activities. It is explained below why none of these agencies is an adequate gatekeeper, and why they may ironically be making the problem worse.

#### *A. The U.S. Patent and Trademark Office*

Few drugs are developed if they are not covered by strong patent protection.<sup>234</sup> In the United States, patents are granted by the United States Patent

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or thing that controls access to something”).

227. Kraakman, *supra* note 1, at 53.

228. *Id.* at 54 n.3.

229. *Id.* at 64.

230. *Id.*

231. *Id.* at 58.

232. See, e.g., Lawrence Lessig, *What Everybody Knows and What Too Few Accept*, 123 HARV. L. REV. 104, 106-07 (2009).

233. Kraakman, *supra* note 1, at 62 n.23.

234. Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503, 513 (2009) (“[I]t is well known that pharmaceutical companies generally refuse to

and Trademark Office, thereby casting this organization into the role of potential gatekeeper against ineffective drugs. The USPTO is a sensible gatekeeper not only because it can withhold patent protection from undeserving products, but because patent doctrine straightforwardly specifies that an invention cannot be patented unless it is “useful.”<sup>235</sup> This utility requirement traces its roots at least as far back as the United States Constitution, which provides that patents may be granted in order “to Promote the Progress of Science and useful Arts,”<sup>236</sup> and patents are therefore traditionally conceived of as temporary rewards for contributing useful inventions to society.

Any optimism that patent law’s utility requirement could screen out ineffective drugs by negating patentability, however, can be quickly dispelled. The bar for patentable utility is so low that almost any invention will meet it.<sup>237</sup> Even an invention that could be “used” to mislead customers has been held patentable.<sup>238</sup> Patentable utility has thus appropriately been described as de minimis standard<sup>239</sup> and it has been noted that even inventions that have no proven use in the real world can meet it.<sup>240</sup> Reflecting this almost inconsequentially low threshold is the USPTO’s cautionary statement to would-be inventors that an alleged utility “of a complex invention as landfill” would not be sufficient.<sup>241</sup>

The rationale for a minimal utility standard in patent law seems to be that the market is the best judge of an invention’s worth. In the landmark opinion of *Lowell v. Lewis*, Justice Story rejected the view that an invention must be better than—or even as good as—the existing state of the art, stating that “whether it [the invention] be more or less useful [than existing products] is a circumstance very material to the interests of the patentee, but of no importance to the public. If it be not extensively useful, it will silently sink into contempt

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develop new drugs unless they have strong patent protection over them.”).

235. 35 U.S.C. § 101 (2013).

236. U.S. CONST. art I, § 8, cl. 8.

237. See Kathleen N. McKereghan, *The NonObviousness of Inventions: In Search of a Functional Standard*, 66 WASH. L. REV. 1061, 1077 n.94 (1991) (“[T]he utility requirement has long had a very low threshold.”); see generally GERALD R. FERRERA ET AL., *CYBERLAW: TEXT AND CASES* 179-80 (3d ed. 2012) (providing examples of arguably frivolous or banal utilities that have nevertheless been found sufficient for patentability purposes).

238. See, e.g., *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1368 (Fed. Cir. 1999).

239. See Joseph P. Pieroni, *The Patentability of Expressed Sequence Tags*, 9 FED. CIR. B.J. 401, 405 (2000) (“The utility requirement is usually considered a very low hurdle, a de minimis [sic] standard.”).

240. See Robert P. Merges, *Commercial Success and Patent Standards: Economic Perspectives on Innovation*, 76 CAL. L. REV. 803, 812 (1988) (“Today, a patent will not be withheld even though the invention works only in an experimental setting, and has no proven use in the field or factory.”).

241. Utility Examination Guidelines, 66 Fed. Reg. 1098 (Jan. 5, 2001).

and disregard.”<sup>242</sup> While this may be true of the water pumps at issue in *Lowell*, where the invention’s utility was easily understandable by laypersons, it may be less true with complex pharmaceutical inventions (and other credence goods) where even medical experts cannot articulate or even agree on the degree to which a drug has improved a given patient’s condition. Justice Story could not have had in mind the modern pharmaceuticals marketplace, where consumers spend billions of dollars on products that scarcely merit the label “extensively useful.” During the patent period at least, these products rarely sink into contempt and disregard on the basis of a lack of meaningful efficacy.

Another possible gatekeeping lever at the hands of the USPTO is the non-obviousness standard, another requirement for patentability.<sup>243</sup> Previous physician-commentators have advocated elevating this standard, thereby preventing the patentability of “one-atom changes” to existing molecules that result in supposedly-innovative new molecular entities.<sup>244</sup> Non-obviousness, however, is a very rough proxy for efficacy that focuses on the technical difficulty<sup>245</sup> of creating the invention, and not on its therapeutic value. It is entirely possible that a new drug with decidedly unimpressive efficacy might meet even an elevated non-obvious standard.<sup>246</sup> Celebrex (celecoxib), Vioxx (rofecoxib), and the other COX-2 inhibitors are good examples. These drugs resulted from years of research and development<sup>247</sup> that culminated in 1998 in the market entry of Celebrex (celecoxib), a type of supposed “super aspirin”<sup>248</sup> that selectively inhibits only one of two cyclooxygenase (COX) enzymes. The structures of the COX-2 drugs depart markedly from those of ibuprofen, aspirin and other previous non-steroidal anti-inflammatories (NSAIDs), the larger class to which COX-2 inhibitors belong.<sup>249</sup> As the first in its class, Celebrex

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242. *Lowell v. Lewis*, 15 F. Cas. 1018, 1019 (D. Mass. 1817).

243. 35 U.S.C. § 103 (2013).

244. Avorn, *supra* note 62, at 669; *see also* MARCIA ANGELL, *THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT* (2004) (describing the ways in which drug companies make similar drugs in the same therapeutic class appear to differ in efficacy, even when they likely do not, with particular attention to the statins).

245. *See* Merges, *supra* note 240, at 812 (“[N]onobviousness attempts to measure . . . the *technical accomplishment* reflected in an invention.”).

246. Also problematic is the fact that an elevated obviousness standard could prevent the patentability of technically obvious drugs that exhibit exceptionally high efficacy, either because the technical challenge involved in creating them is small or even because they have already been described in the literature without recognition of their therapeutic value. *See* Roin, *supra* note 234, at 536-37.

247. *See, e.g., Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 918 (Fed. Cir. 2004) (noting that Rochester scientists filed a patent application in 1992 related to this research).

248. *Pfizer Settles College’s Lawsuit over Development of Celebrex*, N.Y. TIMES, May 1, 2012, at B2.

249. Susan K. Paulson & Timothy J. Maziasz, *Role of Preclinical Metabolism and Pharmacokinetics in the Development of Celecoxib*, in *APPLICATIONS OF PHARMACOKINETIC: PRINCIPLES IN DRUG DEVELOPMENT* 405 (Rajesh Krishna ed., 2004).

(celecoxib) very likely deserved to be judged non-obvious by the USPTO, and even the manufacturer's praise of its own drug as a "scientific breakthrough"<sup>250</sup> was deserved. The manufacturer's adjacent claim that Celebrex (celecoxib) delivers "powerful" relief,<sup>251</sup> however, was less deserved. The expensive, new, innovative, patented, FDA-approved drug provided no greater pain relief than any other NSAID, nor did its sponsor claim that it could do so.<sup>252</sup> The government-funded Oregon Evidence-based Practice Center concluded bluntly that "COX-2 selective NSAIDs and nonselective NSAIDs did not clearly differ in efficacy for pain relief, based on many good-quality, published trials."<sup>253</sup> Thus, the two principal tools that the USPTO might use to screen out ineffective drugs are simply not up to the task.

Even if one were inclined to raise the utility or non-obvious standards, which has been recommended as appropriate where the pace of invention is fast,<sup>254</sup> it is no simple matter to discern the efficacy of a drug. As a primarily technical agency with expertise in invention but not in the clinical trials that produce evidence of efficacy, the Patent and Trademark Office is poorly positioned to evaluate questions of efficacy in the context of complex health policy considerations.<sup>255</sup> Following concerns over a lack of drug efficacy expressed by Congress<sup>256</sup> and the President<sup>257</sup> in 1962, a provision was enacted into law that requires the FDA, if requested by the USPTO, to provide technical assistance with respect to the patenting of a new drug product.<sup>258</sup> As codified and amended at 21 U.S.C. § 372(d), this provision now reads:

The Secretary [of Health and Human Services] is authorized and directed, upon request from the Under Secretary of Commerce for

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250. See, e.g., Celebrex Print Advertisement, EBONY, Feb. 2001, at 105 ("Celebrex is a scientific breakthrough . . .").

251. See *id.* ("Celebrex . . . delivers powerful 24-hour relief of your osteoarthritis pain and inflammation.").

252. See *id.*

253. Roger Chou et al., *Comparative Effectiveness and Safety of Analgesics for Osteoarthritis*, OREGON EVIDENCE-BASED PRACTICE CENTER 1, 3 (2006), <http://effectivehealthcare.ahrq.gov/repFiles/AnalgesicsFinal.pdf>, archived at <http://perma.cc/ZS36-W8K4>.

254. Edmond W. Kitch, *Graham v. John Deere Co.: New Standards for Patents*, 1966 SUP. CT. REV. 293, 305 (citing an 1826 judicial opinion for the proposition that a higher utility standard is more appropriate the faster the rate of innovation.).

255. For example, a single drug may prove effective in treating multiple conditions or in certain subsets of the population; side effects must be weighed against benefits; statistical aspects of clinical trials may be intricate or subject to surreptitious manipulation.

256. See S. Rep. No. 87-1744 (1962), reprinted in 1962 U.S.C.C.A.N. 2884, 2900.

257. Letter from Pres. John F. Kennedy to Sen. Eastland on Pending Legislation Relating to Drug Mktg. (Apr. 11, 1962), <http://www.presidency.ucsb.edu/ws/?pid=8596>, archived at <http://perma.cc/EH3X-4Q2K>.

258. Drug Amendments of 1962, Pub. L. No. 87-781, § 308, 52 Stat. 780, 796 (1962) (codified as amended at 21 U.S.C. § 372(d) (2013)).

Intellectual Property and Director of the United States Patent and Trademark Office, to furnish full and complete information with respect to such questions relating to drugs as the Director may submit concerning any patent application. The Secretary is further authorized, upon receipt of any such request, to conduct or cause to be conducted, such research as may be required.<sup>259</sup>

The stated purpose of § 372(d), as described in the accompanying 1962 Senate Report, was unambiguously to reduce the number of patents issued on therapeutically questionable drugs: “Presumably, if the Patent Office, which has no physicians or pharmacologists on its staff, is able to secure information from HEW [i.e., from the FDA<sup>260</sup>] on the therapeutic properties of drugs—which it is now able to obtain only with the consent of the patent applicant—fewer patents may be issued.”<sup>261</sup> However, the USPTO appears to have rarely, if ever, requested information pursuant to this authority. Only three cases, all from the now-defunct Court of Customs and Patent Appeals, cite § 372(d): the first notes that the USPTO did not exercise its authority under the provision;<sup>262</sup> the second cites § 372(d) only to explain that the USPTO hypothetically could consider, as an aid when deciding the question of utility, the FDA’s determination that a drug is “totally unsafe in all circumstances,” a determination that the court found was not present in the case at bar;<sup>263</sup> and, the third cites the provision, in dissent and in a footnote, to further the dissent’s argument that the USPTO rather than other agencies is ultimately responsible for determining patentability.<sup>264</sup> One commentator interpreted these cases as rebuffing the USPTO’s attempts to exercise its authority under § 372(d),<sup>265</sup> though the cases themselves suggest that only publicly available information was used and that no information was “furnished” by the FDA in the collaborative sense suggested by the statute.<sup>266</sup>

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259. 21 U.S.C. § 372(d) (2013).

260. “HEW” refers to the Department of Health Education and Welfare, predecessor to the Department of Health and Human Services, the Department to which the FDA belongs.

261. S. Rep. No. 87-1744 (1962), reprinted in 1962 U.S.C.C.A.N. 2884, 2900; see also *id.* at 2888 (noting that the proposed bill “would help to insure that patents are promptly issued for those developments in the drug field that are true inventions which the patent system is designed to reward.”); *id.* at 2897 (noting that the proposed bill would “assure consideration of therapeutic effectiveness in the granting of patents for drugs that are modifications of other drugs”).

262. *In re Sichert*, 566 F.2d 1154, 1159 (C.C.P.A. 1977).

263. *In re Anthony*, 414 F.2d 1383, 1398-99 (C.C.P.A. 1969). The court ultimately held the drug to possess sufficient utility. *Id.* at 1399. The court also collected cases addressing the relationship of safety to utility with respect to drugs. *Id.* at 1394-95 nn.10-12.

264. *In re Hartop*, 311 F.2d 249, 264 (C.C.P.A. 1962) (Worley, C.J., dissenting).

265. C. Leon Kim, *The Utility Requirement for Patenting Therapeutic Inventions*, 24 BUFF. L. REV. 595, 596 (1975) (“The [Patent and Trademark] Office’s assumption of such power [under § 372(d)], however, was vehemently opposed by the CCPA.”).

266. See, e.g., *In re Anthony*, 414 F.2d at 1391 (noting that the examiner relied upon articles appearing in the *New York Times* and the *Washington Daily News*); see also *Patent Law Revision*:

Moreover, even if the USPTO was to consistently supplement its own expertise by exercising its right under § 372(d), the evidence needed to ascertain a drug's true efficacy in humans is not usually available at the time of patenting, which occurs relatively early in the research and development process. The assistance that the FDA would be able to provide would therefore be limited. In summary, the USPTO cannot act as an effective gatekeeper because the utility and non-obviousness doctrines are not up to the task, because the agency lacks appropriate health-related expertise, and because the USPTO "gate" is too far upstream in the drug development process.

### B. *The U.S. Food and Drug Administration*

The FDA is perhaps the most obvious gatekeeper given its statutory duty to decline approval of any drug for which "there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have."<sup>267</sup> A careful reading of this statutory provision, however, reveals that there is no requirement that a drug possess any particular level of efficacy. So long as a drug company does not "purport or . . . represent" the drug to have greater efficacy than it actually has, the drug can be approved.<sup>268</sup> As a result, the efficacy of approved drugs ranges from near 100% in the case of certain contraceptives, antibiotics, and vaccines, to near 0% in the case of certain Alzheimer's medications, depression medications, and cancer medications. Like judicial attitudes toward patent law's *de minimis* utility standard, the prevailing view of the FDA's similarly *de minimis* efficacy requirement appears to be that the market is the best judge of a drug's worth. In other words, although the FDA is a gatekeeper against absolutely worthless drugs, "the market"—whatever entities or individuals that comprises—is erroneously assumed to be a good gatekeeper against almost-but-not-quite worthless drugs.

The FDA approval scheme, then, continues by and large to embrace the philosophy of *caveat emptor* with respect to any non-zero level of drug efficacy. Yet, at the same time the phrase "FDA approved" is used in advertisements, and perceived by the public, as if it were a guarantee that a drug has some meaningful level of efficacy.<sup>269</sup> Either of these approaches might have merit. One might take

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*Hearing Before the Subcomm. on Patents, Trademarks, and Copyrights of the Senate Comm. on the Judiciary*, 93d Cong. 292 (1973) (statement of Pharm. Mfr.'s Ass'n) ("In our view, 21 U.S.C. 372(d) [sic] is an acceptable provision by which the Patent Office may seek the advice of other government scientists in particular instances without significant adverse consequences to the public or to the patent applicant. 21 U.S.C. 372(d) was enacted in 1962 as an alternative to a proposal which would have in effect conditioned the patent grant upon a determination by a separate federal agency of greater therapeutic effect. A patentability requirement of this nature was wisely rejected by Congress.")

267. 21 U.S.C. § 355(d) (2013) ("[H]e shall issue an order refusing to approve the application.") (emphasis added).

268. *Id.* § 355.

269. See Jonathan J. Darrow, *Pharmaceutical Efficacy: The Illusory Legal Standard*, 70

the more traditional approach and reasonably argue that consumers (and their physicians) should take responsibility themselves for guarding against ineffective remedies, following the principle of *caveat emptor*. Alternately, one might more liberally argue that the FDA should be given the responsibility to protect the public from ineffective remedies. The current system, however, combines these two approaches in the most unfortunate way possible, with patients and physicians assuming that the FDA has vetted drugs for meaningful levels of effectiveness, while the FDA in fact leaves this discerning task to those same patients and physicians, fully compliant with its statutory duties. In this way FDA oversight ironically may make the efficacy problem worse, creating unjustified perceptions of government approval that can induce market players to let down their guard.

This is not to say that the FDA is always ineffective as a gatekeeper of efficacy. Not only does the FDA have the power to reject entirely fraudulent remedies, it also administers a statutory framework that provides incentives that are roughly—perhaps very roughly—scaled to a drug’s likely level of efficacy. The Federal Food, Drug, and Cosmetic Act (FDCA) provides three years of exclusivity for new indications of existing medicines.<sup>270</sup> Because doctors can legally prescribe FDA-approved drugs for unapproved indications, the marginal gains in real-world efficacy brought about by a new indication approval are likely to be small. New molecular entities (NMEs), by contrast, are assumed to be a rough proxy for increased innovativeness and thus, indirectly, efficacy levels. The FDCA offers five years of exclusivity for such NMEs (or four years, if patent invalidity or noninfringement is alleged).<sup>271</sup> Under the Orphan Drug Act, seven years of market exclusivity may be granted for drugs that treat rare diseases or conditions.<sup>272</sup> The rationale, recorded in the corresponding session law, is that there may be no adequate drugs at all for these conditions “because so few individuals are affected” that pharmaceutical companies might not be expected to even attempt development of such drugs.<sup>273</sup> If no drugs are currently available to treat an orphan disease, it could be reasoned, the efficacy gains of a new medication are likely to be larger than if drugs are already available. Unfortunately, even in this category products all too often disappoint. An analysis by a French nonprofit drug evaluation organization found that “[n]one of the 6 orphan drugs examined by *Prescrire* in 2011 represented a real breakthrough.”<sup>274</sup> Biologics, whose theorized impressive gains in efficacy have

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WASH. & LEE L. REV. 2073, 2122 (2013) (explaining that efficacy that is meaningful to a patient is often labeled “clinical efficacy” by physicians, but that by law clinical efficacy means only efficacy, of any amount, in humans).

270. *Id.* § 355(c)(3)(E)(iii) & (j)(5)(F)(iii).

271. *Id.* § 355(c)(3)(E)(ii) & (j)(5)(F)(ii). A thirty-month stay provision effectively extends these four- or five-year periods to seven and one-half years, if a patent infringement suit is timely commenced. *Id.*

272. *Id.* § 360cc(a).

273. Orphan Drug Act, Pub. L. No. 97-414, § 1(b), 96 Stat. 2049 (1983).

274. *New Drugs and Indications in 2011*, *supra* note 221, at 108.

so far proven largely elusive, may be granted twelve years of exclusivity under a 2009 law.<sup>275</sup>

The role of this scaled incentive regime on efficiently eliciting effective drugs may be deserving of further study, but is too large and complex an issue to be adequately explored here.<sup>276</sup> Suffice it to say that these scaled incentives are at best a very rough proxy for efficacy. Simply because a drug can be categorized as an NME or a biologic, or purportedly treats an orphan disease, does not necessarily say anything at all about its absolute (or even relative) level of efficacy.

#### IV. POST-HOC GATEKEEPING: ADMINISTRATIVE AND COURT-MEDIATED ENFORCEMENT

If overstatement of drug efficacy were truly a problem, it might be expected that government regulators and other interested parties would seek legal redress. In this regard, the record does not disappoint. A number of lawsuits have been brought by individuals, competitors, and insurance companies alleging fraud against drug companies for their inflated claims of efficacy. Government regulators, notably the FDA, have also acted via administrative channels to temper exaggerated drug efficacy claims. For various reasons explored below, the majority of these efforts have either failed or been only partially effective in preventing misleading information from reaching both consumers and the medical community.

##### *A. Enforcement Actions by the FDA*

The regulation of drug advertising is shared between the FTC, which regulates advertising for over-the-counter products,<sup>277</sup> and the FDA, which regulates the advertising of prescription drugs as well as labeling for both prescription and over-the-counter products.<sup>278</sup> Although the FTC has taken frequent action against overstatements of efficacy in the dietary supplements sector,<sup>279</sup> litigation by FTC against overstatements of efficacy for over-the-

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275. Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, 124 Stat. 119 (2010).

276. *See generally* Eisenberg, *supra* note 8, at 387 (concluding that the FDA plays an important role in innovation policy).

277. *See* Anne V. Maher & Leslie Fair, *The FTC's Regulation of Advertising*, 65 FOOD & DRUG L.J. 589 (2010). The FTC's enforcement authority with respect to OTC drugs originates in Sections 5, 12 and 15 of the Federal Trade Commission Act. *See* Francis B. Palumbo & C. Daniel Mullins, *The Development of Direct-to-Consumer Prescription Drug Advertising Regulation*, 57 FOOD & DRUG L.J. 423, 427 (2002).

278. *See* DePriest v. AstraZeneca Pharms., 351 S.W.3d 168, 177 n.9 (Ark. 2009); Memorandum of Understanding Between the FTC and the FDA, 36 Fed. Reg. 18,539 (Sept. 16, 1971).

279. 279. *See, e.g.*, FTC v. Cent. Coast Nutraceuticals, Inc., No. 10C-4931 (N.D. Ill. Jan. 9, 2012) (stipulated order) (acai berry supplements); FTC v. CVS Pharmacy, Inc., No. CA-09-420

counter drugs has been sparse,<sup>280</sup> and as just mentioned, the FDA rather than the FTC regulates advertising of prescription drugs.

The FDA's authority derives from the Federal Food, Drug, and Cosmetic Act, which allows the FDA to take action against any drug that is "misbranded."<sup>281</sup> Misbranding includes not only "labeling [that] is false or misleading in any particular"<sup>282</sup> but also television advertisements for prescription drugs that contain untrue statements regarding "side effects, contraindications, and effectiveness."<sup>283</sup>

Pursuant to these provisions, the FDA rebukes drug companies with regularity for their overzealous claims of efficacy. A television advertisement for Amgen's Enbrel (etanercept) for example, resulted in a warning letter from the FDA that noted that the advertisement's description of the drug as a "BREAKTHROUGH," combined with other attributes of the advertisement, implied efficacy beyond what had been proven.<sup>284</sup> Despite the "overwhelming impression conveyed by the TV ad . . . that Enbrel completely clears skin with psoriasis," no evidence supported this claim.<sup>285</sup> To the contrary, the FDA offered its opinion that "Enbrel is not a breakthrough therapy for moderate to severe plaque psoriasis because it does not offer any documented material difference that offers a significant advantage over other drugs already available . . ."<sup>286</sup>

In another case, G.D. Searle & Co. received a warning letter for distributing promotional materials for Celebrex (celecoxib) that, according to the FDA,

(D.R.I. final order Sept. 9, 2009) (AirShield, a purported treatment for colds and influenza); FTC v. Airborne Health, Inc., No. CV-08-05300 (C.D. Cal. final order Sept. 5, 2008) (Airborne, a purported cold preventative); *In re* Vital Basics, Inc., 137 F.T.C. 254 (2004) (Focus Factor, a purported enhancer of concentration); FTC v. Rexall Sundown, Inc., Civ. No. 00-706-CIV (S.D. Fla. Mar. 11, 2003) (Cellasene, a purported anti-cellulite dietary supplement); *see also* Laurel A. Price, *Advertising and Unfair Competition: Federal Enforcement*, ST056 ALI-ABA 541 (2012) (collecting cases).

280. *See* Press Release, *FTC's Cutler Says OTC Drug Manufacturers Must Have High Advertising Standards*, FTC (Oct. 23, 1990), <http://www.ftc.gov/opa/predawn/F93/bjc-otc-a1.htm>, archived at <http://perma.cc/L2ZS-XXNC> (noting enforcement "sweeps" against unsubstantiated claims in the 1970s); *see also* Final Order, *In re* Novartis Corp. et al., 127 F.T.C. 580, 674 (May 13, 1999) (company may not make unsubstantiated claims of superior efficacy of analgesic products); *Am. Home Prods. v. FTC*, 695 F.2d 681, 683 (3d Cir. 1983) (Anacin (400 mg aspirin plus 32.5 mg caffeine)); *In re* Thompson Med. Co., 104 F.T.C. 648 (F.T.C. Nov. 23, 1984), *aff'd*, *Thompson Med. Co. v. FTC*, 479 U.S. 1086 (1986) (Aspercreme).

281. 21 U.S.C. § 352 (2013).

282. *Id.* § 352(a).

283. *Id.* § 352(n); *see also* 21 C.F.R. § 202.1(e)(6) (2013) ("Advertisements that are false, lacking in fair balance, or otherwise misleading.").

284. Letter from Thomas W. Abrams, FDA, to Kevin W. Sharer, Chairman and Chief Exec. Officer, Amgen Inc. (Feb. 18, 2005), <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLettersToPharmaceuticalCompanies/ucm055677.pdf>, archived at <http://perma.cc/HJ4F-36AS> (Enbrel).

285. *Id.* at 4.

286. *Id.*

claimed superiority over not only Vioxx (rofecoxib), but also “all analgesic and anti-inflammatory therapies for the management of [arthritis].”<sup>287</sup> In fact, Searle had not demonstrated that Celebrex (celecoxib) was any better than other NSAIDs, such as aspirin, Advil (ibuprofen), or Vioxx (rofecoxib).<sup>288</sup> But these promotional materials along with other forms of promotion had already had their effect: How many members of the public today understand that Advil (ibuprofen) and Celebrex (celecoxib) have approximately the same level of efficacy in relieving pain? The \$35 billion<sup>289</sup> that Celebrex (celecoxib) has earned Pfizer suggests that far too many patients—and doctors—have not reviewed the relevant literature do not understand that the drugs are approximately equivalent in efficacy.

Despite diligent efforts by the FDA’s Office of Prescription Drug Promotion (OPDP, formerly the Division of Drug Marketing and Advertising, or DDMAC), a tide of information indicating or implying greater efficacy than is present continues to reach consumers. In part, this is due to the sheer magnitude of violations. OPDP issued twenty-eight enforcement letters in 2012,<sup>290</sup> thirty-one in 2011,<sup>291</sup> fifty-one in 2010,<sup>292</sup> and forty in 2009.<sup>293</sup> By way of context, the FDA

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287. Letter from Spencer Salis, FDA, to Jerome M. Prah, Assoc. Dir. Reg. Aff., G.D. Searle & Co., at 3 (Oct. 6, 1999) [hereinafter Spencer Salis Letter], <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM166210.pdf>, *archived at* <http://perma.cc/5ACH-PLMF>.

288. *Id.* (“[T]his global superiority claim has not been demonstrated by substantial evidence.”). In fact, the statements of superiority criticized by the FDA did not directly assert superior *efficacy*, a subtlety that may well have been lost on the recipients of the information. *See id.*

289. Wendy Kaufman, *Pfizer Settles Suit Involving Celebrex*, NAT’L PUB. RADIO (May 2, 2012), <http://www.npr.org/2012/05/02/151832691/pfizer-settles-suit-involving-celebrex>, *archived at* <http://perma.cc/SMH8-T468>.

290. *Warning Letters 2012*, FDA Dec. 6, 2013, 11:54 AM), <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm289143.htm>, *archived at* <http://perma.cc/Q7HV-7NU8>.

291. *Warning Letters 2011*, FDA (Dec. 6, 2013, 11:53 AM), <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm238583.htm>, *archived at* <http://perma.cc/72T9-43PW> (many of these letters are untitled letters, which nevertheless warn against violations of the FDCA).

292. *Warning Letters 2010*, FDA (Dec. 6, 2013, 11:50 AM), <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm197224.htm>, *archived at* <http://perma.cc/MH78-PRWU>.

293. *Warning Letters 2009*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm055773.htm>, *archived at* <http://perma.cc/75TG-TWM8> (last visited July 10, 2014).

approved only thirty-nine new molecular entities in 2012,<sup>294</sup> thirty in 2011,<sup>295</sup> twenty-one in 2010, and twenty-six in 2009.<sup>296</sup> This means that, on average, there was more than one enforcement letter for every one new molecular entity approval.

FIGURE 1: ENFORCEMENT LETTERS AND NME APPROVALS, 2009-2012

	NME Approvals	Enforcement Letters
2012	39	28
2011	30	31
2010	21	51
2009	26	40
<b>TOTAL</b>	<b>116</b>	<b>150</b>

As noted above, post hoc enforcement letters are a second-best solution because, by the time they are received and acted upon, the public has already been exposed to misinformation.<sup>297</sup> To counteract this shortcoming, the FDA in 2007 was empowered by statute to require that any advertising and promotional materials be submitted to the FDA for review at least forty-five days prior to dissemination.<sup>298</sup> Funding for this program, however, was then withheld.<sup>299</sup> The FDA finally promulgated draft guidance in 2012,<sup>300</sup> but it has not yet been

294. *New Molecular Entity Approvals for 2012*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm336115.htm>, archived at <http://perma.cc/Y5VT-24T5> (last visited July 10, 2014).

295. *New Molecular Entity Approvals for 2011*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm285554.htm>, archived at <http://perma.cc/HHH9-TM8M> (last visited July 10, 2014).

296. *NMEs Approved by CDER*, FDA 1, 1 (2010), <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM242695.pdf>, archived at <http://perma.cc/GZM3-3N6Q> (also providing data for 2008 (24 NMEs), 2007 (18 NMEs), and 2006 (22 NMEs)).

297. *Cf. Upjohn Co. v. Finch*, 422 F.2d 944, 953 (6th Cir. 1970) (quoting congressional testimony of the Commissioner of the New York Department of Health regarding the impact of drug efficacy legislation: “Long before governmental authorities are in a position to prove the illegality of these [advertising] practices and get the cumbersome legal machinery into motion and remove the drug from the market, grave harm has been done . . .”).

298. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(d)(2), 121 Stat. 939 (2007) (codified at 21 U.S.C. § 353b (2013)); *see also* 21 C.F.R. § 314.550 (2013) (requiring promotional materials to be submitted 30 days in advance of dissemination, in the case of drugs subject to accelerated approval); 21 C.F.R. § 601.45 (2013) (stating 30-day period for biologics subject to accelerated approval).

299. Gary C. Messplay & Colleen Heisey, *FDAAA Ad Program Stumbles: DTC PreReview Program Fails to Launch*, CONTRACT PHARMA: FDA WATCH, Mar. 2008, at 18.

300. *See Guidance for Industry Direct-to-Consumer Television Advertisements: FDAAA DTC Television Ad Pre-Dissemination Review Program*, FDA (2012), <http://www.fda.gov/downloads/>

finalized. The results are predictable: the FDA website notes that the agency “see[s] many ads at about the same time the public sees them.”<sup>301</sup> The public (including doctors) therefore continues to be subjected to misleading efficacy information until corrective action is taken. Even if implemented in its current form, the guidance would only require submission for six categories of advertisements, in light of the FDA’s limited resources.<sup>302</sup>

Even corrected or technically compliant advertisements may nevertheless convey an impression of effectiveness that is not warranted. For example, a Celebrex (celecoxib) advertisement aimed at physicians states that “[w]ith all the experience that you and thousands of other physicians just like you have with the proven efficacy and benefit of superior safety of Celebrex, why wouldn’t you want to prescribe Celebrex?”<sup>303</sup> By strategically inserting the word “efficacy” among the words “proven,” “benefit,” and “superior,” viewers are left with the impression that the efficacy of Celebrex (celecoxib) is superior, even though this was not stated. The effect is reminiscent of the legal canon of *noscitur a sociis*, which “counsels that a word is given more precise content by the neighboring words with which it is associated.”<sup>304</sup> In this case, however, the tendency of an audience to consider context has been used to mislead.

Pharmaceutical companies have little incentive to refrain from testing the limits of what they can claim or imply in advertisements. Although the FDA can and has taken action even against advertisements that only subtly overstate efficacy by the “totality of [the] presentation,” warning letters themselves carry no penalties and generally request only that the recipient desist.<sup>305</sup> Legislation in

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Drugs/.../Guidances/UCM295554.pdf, archived at <http://perma.cc/49P5-4GDK>.

301. *Prescription Drug Advertising: Questions and Answers*, FDA (Dec. 6, 2013, 11:35 AM), <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/UCM076768.htm>, archived at <http://perma.cc/MR4C-6UA3> (“[T]he public may see ads that violate the law before we can stop the ad from appearing . . .”).

302. *Guidance for Industry Direct-to-Consumer Television Advertisements—FDAAA DTC Television Ad Pre-Dissemination Review Program*, FDA 1, 2 (2012), <http://www.fda.gov/downloads/Drugs/.../Guidances/UCM295554.pdf>, archived at <http://perma.cc/5Q7K-DUGS> (The categories are: (1) the initial TV ad for a new prescription drug; (2) certain ads for drugs subject to REMS; (3) ads for Schedule II drugs; (4) ads following certain label updates pertaining to safety; (5) certain ads aired subsequent to the receipt of warning letters; and (6) those ads specifically identified by the FDA as subject to pre-review).

303. Spencer Salis Letter, *supra* note 287, at 3.

304. *Freeman v. Quicken Loans, Inc.*, 132 S. Ct. 2034, 2042 (2012) (quoting *United States v. Williams*, 553 U.S. 285, 294 (2008)).

305. *See, e.g.*, Letter from Roberta T. Szydlo & Lisa M. Hubbard, FDA, to Randy Russell, Asst. Dir. Reg. Aff., Alcon Res., Ltd., Nov. 13, 2012, <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM328637.pdf>, archived at <http://perma.cc/ZV7T-B78J> (Patanase); *see also* David C. Vladeck, *The Difficult Case of Direct-to-Consumer Drug Advertising*, 41 LOY. L.A. L. REV. 259, 273 (2007) (“The FDA has no statutory authority to impose civil penalties for misleading ads, and the only real sanction it has (apart from

2007 empowered the FDA to impose civil penalties of up to \$250,000 for direct-to-consumer advertising that is false or misleading,<sup>306</sup> but only following a formal administrative hearing.<sup>307</sup> Given the significant resources required for such a hearing, it is not surprising that no reported cases indicate that such penalties have ever been imposed.<sup>308</sup> Even if a penalty were imposed, the statute allows reduction in dollar amounts based on a number of factors, including: subsequent, voluntary remedial action that is undertaken; whether the advertisement had been reviewed by qualified medical, regulatory, and legal reviewers prior to its dissemination; and whether the person promptly ceased distribution of the advertisement.<sup>309</sup> Even if the maximum amount were imposed, a rational drug company might still opt for inflating efficacy claims. A blockbuster drug that earns \$1 billion per year translates into more than \$2.7 million per day. If an overstatement of efficacy can increase sales by 10%, a \$250,000 penalty is less than one day's additional revenue.

### *B. Lawsuits by Consumers Alleging Fraud*

In theory, consumer fraud actions might also serve as a check against false or misleading claims of efficacy. Consumers and non-profit public interest organizations, however, have often encountered significant legal barriers when attempting to bring these claims. In one case, a group of consumers sought class action status in a suit against Johnson & Johnson for running advertisements that allegedly included misleading claims of superiority of Johnson & Johnson's Pepcid (famotidine) product over Tagamet (cimetidine). The plaintiffs were likely emboldened by a then-recent holding in the Southern District of New York that had enjoined the advertisements in question.<sup>310</sup> Despite this favorable precedent, the New Jersey trial court denied class certification, noting that although common questions of law and fact existed with respect to the allegedly misleading nature of the advertisements,<sup>311</sup> individual questions regarding

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bringing a misbranding action in court) is to issue public warning letters . . .”).

306. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(d)(4), 121 Stat. 823 (2007) (codified at 21 U.S.C. § 333(g) (2013)). Criminal penalties may also be imposed. 21 U.S.C. § 333(a) (2013); *see also Guidance for Industry Direct-to-Consumer Television Advertisements—FDAAA DTC Television Ad Pre-Dissemination Review Program*, FDA 1, 7-8 (2012), <http://www.fda.gov/downloads/Drugs/.../Guidances/UCM295554.pdf>, archived at <http://perma.cc/H8E9-53G6>.

307. 21 U.S.C. § 333(g)(2) (2013).

308. A search of the Westlaw ALLCASES and JLR databases on November 21, 2012 for the search string “21 U.S.C. s 333(g)” produced 1 result and 4 results, respectively, but none indicated that a penalty had been imposed. Searches of the Federal Register and the FDA’s website were similarly non-responsive.

309. 21 U.S.C. § 333(g)(3) (2013).

310. *SmithKline Beecham Consumer Healthcare, L.P. v. Johnson & Johnson-Merck Consumer Pharms. Co.*, 906 F. Supp. 178, 183-86, 188 (S.D.N.Y. 1995).

311. *Gross v. Johnson & Johnson-Merck Consumer Pharms. Co.*, 696 A.2d 793, 795 (N.J.

reliance on those advertisements predominated.<sup>312</sup>

The inability to bring a class action suit makes private enforcement by consumers much less cost effective, and therefore much less likely to occur.<sup>313</sup> In contrast to drug product liability litigation, where serious drug-related injury or death can lead to very large jury awards, the economic losses occasioned by misleading advertising are likely to be relatively small with respect to any one consumer, perhaps on the order of hundreds of dollars. This minimal amount is not enough to motivate most consumers to bring suit. In addition, although total economic losses may aggregate to millions or billions of dollars when one considers the entire consumer population for a given pharmaceutical product, the inability to aggregate the claims associated with those losses into a single lawsuit means that it will not be financially attractive for attorneys to undertake representation.

The inability to obtain class certification is only one of a number of challenges that consumers face in attempting to bring a successful fraud claim. Several of these challenges are illustrated in a 2003 New Jersey case, in which a state consumer advocacy group brought a fraud claim against Schering-Plough and two of its advertising agencies, alleging that the allergy medicine Claritin (loratadine) had been portrayed as more effective than it actually was.<sup>314</sup> The advertisement in question told consumers that “you . . . can lead a normal nearly symptom-free life again.”<sup>315</sup> The New Jersey appeals court dismissed the action not because Claritin (loratadine) was in fact as effective as claimed, nor because the plaintiffs did not suffer a loss. Instead, the court provided three primary reasons for dismissing the action for failure to state a claim. First, it found the statement that assured patients that they could “lead a normal nearly symptom-free life again” was “not [a] statement[] of fact” but was instead “mere puffing” and as such not actionable.<sup>316</sup> Second, the court found the statement not actionable because the advertisement was subject to FDA oversight.<sup>317</sup> Third, the

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Super. Ct. Law Div. 1997).

312. *Id.* at 799. One legal commentator has described an emerging presumption against class certification and argued that this presumption creates a regulatory gap for potentially harmful drugs. See Young K. Lee, *Beyond Gatekeeping: Class Certification, Legal Oversight, and the Promotion of Scientific Research in “Immature” Pharmaceutical Torts*, 105 COLUM. L. REV. 1905 (2005).

313. Joseph J. Leghorn, *Defending an Emerging Threat: Consumer Fraud Class Action Suits in Pharmaceutical and Medical Device Products-Based Litigation*, 61 FOOD & DRUG L.J. 519, 530 (2006) (“In most instances, a consumer fraud action brought by one or more individual plaintiffs will not present an economically attractive proposition to the plaintiffs’ bar.”). Leghorn was speaking primarily about failure-to-warn claims, where harm to the health of a single plaintiff, and therefore damages, can be relatively high. With efficacy fraud claims, in contrast, the economic incentive would be even smaller.

314. N.J. Citizen Action v. Schering-Plough Corp., 842 A.2d 174, 176 (N.J. Super. Ct. App. Div. 2003).

315. *Id.* at 177.

316. *Id.*

317. *Id.*

court noted that in any event plaintiffs could not prove that their purchases were caused by the allegedly fraudulent statement, because Claritin was available only by prescription.<sup>318</sup> As such, the presence of the doctor as a “learned intermediary”<sup>319</sup> in the distribution chain broke the causal link between the alleged wrongdoing and the harm suffered.<sup>320</sup>

*Schering-Plough* is troubling for at least three reasons. First, the court failed to consider the nature of pharmaceutical products as both Veblen-like goods (to the extent that desirability rises as price rises)<sup>321</sup> and simultaneously as credence goods (goods for which consumers cannot ascertain value even after consumption).<sup>322</sup> With goods that exhibit both of these characteristics, “mere puffery” combined with elevated prices may have a greater impact than with ordinary goods, because there is little else on which to base value. It also ignores the obvious and measurable impact that advertising has on aggregate purchases. It is notable that the court specifically rejected the “fraud on the market” theory, often used in securities fraud litigation, as inappropriate in context of drug litigation.<sup>323</sup>

Second, in relieving the defendant of liability based on FDA oversight authority, the court apparently did not consider the possibility that the FDA might not have the resources to exercise that authority in all cases that merit such oversight. The court also failed to give sufficient weight to the fact that private litigants may bring suit alongside state and federal agencies in an analogous context where the consumer interest is implicated, namely, antitrust. In fact, United States antitrust law provides an incentive for private litigation in the form of treble damages awards,<sup>324</sup> based in part on the premise that private suits improve compliance with the law by harnessing the aggregated power of “private Attorneys General.”<sup>325</sup> Even in the pharmaceuticals context, the Supreme Court has affirmed the right of private citizens to bring drug products liability claims based on state failure-to-warn laws, notwithstanding the FDA’s substantial

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318. *Id.* at 177-78.

319. See Richard B. Goetz & Karen R. Growdon, *A Defense of the Learned Intermediary Doctrine*, 63 FOOD & DRUG L.J. 421 (2008) (defending the learned intermediary doctrine); but see Heather Harrell, *Direct-to-Consumer Advertising of Prescription Pharmaceuticals, the Learned Intermediary Doctrine, and Fiduciary Duties*, 8 IND. HEALTH L. REV. 69 (2011) (critiquing the learned intermediary doctrine).

320. *Id.*

321. See Jeremy N. Sheff, *Veblen Brands*, 96 MINN. L. REV. 769, 795-97 (2012) (describing Veblen goods as luxurious and signals of social status).

322. See Omari Scott Simmons, *Taking the Blue Pill: The Imponderable Impact of Executive Compensation Reform*, 62 SMU L. REV. 299, 318 (2009).

323. N.J. Citizen Action v. Schering-Plough Corp., 842 A.2d 174, 178 (N.J. Super. Ct. App. Div. 2003).

324. 15 U.S.C. § 15(a) (2013).

325. *Mitsubishi Motors Corp. v. Soler Chrysler-Plymouth, Inc.*, 473 U.S. 614, 654 (1985) (Stevens, J., dissenting).

oversight of the warnings that appear on drug labels.<sup>326</sup>

*Schering-Plough* is also troubling for a third reason: Rejecting the plaintiff's claim based on the involvement of a physician immunizes a vast swath of potential wrongdoing from consumer suits. This is because, by definition, physicians (or other prescribers) will necessarily be involved in any lawful purchase by a lay consumer of prescription drugs.<sup>327</sup> If the presence of these prescribers is viewed as breaking the causal link between the advertising and the taking by patients of a medication, fraud cannot be established because causation is a necessary element of a fraud action. Even if plaintiffs were to put forth data showing a correlation between increased advertisements and increased drug sales, courts have repeatedly stated that such evidence would be insufficient to establish causation.<sup>328</sup> Because prescription drugs are the most advertised and most costly class of drugs, the largest economic losses will arise far more often in this context than in the context of non-prescription drugs. Unfortunately, *Schering-Plough* is not alone in dismissing fraud actions that allege misrepresentation of drug efficacy.<sup>329</sup>

### C. *Lawsuits by Insurers Alleging Fraud*

Third-party payers, such as insurance companies, generally have greater institutional capacity to bring legal action based on fraudulent overstatements of efficacy. One might therefore expect that such relatively sophisticated third-party payers would enjoy a larger measure of success in bringing suit. In fact, analogous cases by payers have not only failed, but have done so at very early stages of the proceedings. As with the consumer lawsuits discussed above, the pharmaceutical manufacturer's shield from liability derives from the presence of physicians, who break the causal link.

In *Southern Illinois Laborers' and Employers Health and Welfare Fund v.*

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326. See *Wyeth v. Levine*, 555 U.S. 555 (2009).

327. See 21 U.S.C. § 353(b) (2013).

328. *In re Neurontin Mktg. & Sales Practices Litig.*, 677 F. Supp. 2d 479, 494 (D. Mass. 2010) (“[T]rial courts have almost uniformly held that in a misrepresentation action involving fraudulent marketing of direct claims to doctors, a plaintiff TPP [third party payor] or class . . . cannot rely on aggregate or statistical proof.”).

329. See, e.g., *Cooper v. Bristol-Myers Squibb Co.*, No. 07-885, 2009 WL 5206130, at \*9 (D.N.J. Dec. 30, 2009) (noting evidence that called into question claims of the superior efficacy of Plavix (clopidogrel) over aspirin, but dismissing the case because the plaintiff had “fail[ed] to identify any specific advertisements he viewed, how he was misled by these advertisements, [or] how these advertisements affected his prescription for Plavix”); *S. Ill. Laborers' & Emp'rs Health & Welfare Fund v. Pfizer, Inc.*, No. 08-5175, 2009 WL 3151807, at \*5-6 (S.D.N.Y. Sept. 30, 2009) (dismissing a class action suit alleging the fraudulent overstatement of the efficacy of Lipitor (atorvastatin) on the ground that plaintiffs failed to adequately allege causation and therefore they lacked standing); *but cf.* *In re Warfarin Sodium Antitrust Litig.*, 391 F.3d 516, 521-22 (3d Cir. 2004) (approving \$44.5 million class action settlement following allegations that DuPont falsely claimed Coumadin (warfarin) was more effective than Barr's generic warfarin).

*Pfizer*, for example, a putative nationwide class of eleven third-party payers brought suit against Pfizer alleging that it had overstated the efficacy of its cholesterol-lowering drug Lipitor (atorvastatin), by promoting its use in patient groups in which Pfizer allegedly knew the drug would not be effective.<sup>330</sup> The payers alleged that they had sustained “economic loss as a result of paying [on behalf of their beneficiaries] for Lipitor instead of cheaper, safer, and equally effective courses of treatment.”<sup>331</sup> The court dismissed claims brought under the federal Racketeer Influenced and Corrupt Organizations Act (RICO)<sup>332</sup> on the ground that the plaintiffs lacked standing; standing under RICO can be established only by showing that the RICO violation caused the injury.<sup>333</sup> Although plaintiffs alleged that Pfizer made misrepresentations to both physicians and Pharmacy Benefit Decision Makers (PBDMs), the plaintiffs did not specifically allege that the physicians or PBDMs relied on those representations in making their decisions to prescribe Lipitor (atorvastatin) or include it on a formulary, respectively. State law claims brought under the consumer protection laws of Ohio, Texas, and New Jersey were also dismissed because plaintiffs were not “consumers” as required to bring suit under those laws.<sup>334</sup> Other courts have dismissed efficacy fraud cases on similar reasoning.<sup>335</sup>

#### *D. Lawsuits by State Attorneys General Alleging Fraud*

State governments have also actively sought to protect their citizens from the economic harms that result from fraudulent overstatements of drug efficacy, but have encountered significant roadblocks. In 2011, the Attorney General of Michigan sought to recover up to the \$20 million that the state had spent on Vioxx (rofecoxib) via its Medicaid program, arguing that it would not have spent that amount had Merck not made exaggerated efficacy (and safety) claims.<sup>336</sup> The

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330. *S. Ill. Laborers' & Emp'rs Health & Welfare Fund*, 2009 WL 3151807, at \*1.

331. *Id.* at \*5.

332. Organized Crime Control Act of 1970, Pub. L. No. 91-452, 84 Stat. 941, 941–48 (1970) (codified as amended at 18 U.S.C. §§ 1961-1968 (2013)).

333. *S. Ill. Laborers' & Emp'rs Health & Welfare Fund*, 2009 WL 3151807, at \*4.

334. *Id.* at \*8-10.

335. See, e.g., *In re Bextra & Celebrex Mktg., Sales Practices & Prod. Liab. Litig.*, No. 05–CV–01699, 2012 WL 3154957, at \*8 (N.D. Cal. Aug. 2, 2012); *In re Yasmin & Yaz (Drospirenone) Mktg., Sales Practices & Prods. Liab. Litig.*, Nos. 3:09-md-02100-DRH-PMF, 3:0-cv-20071-DRH-PMF, 2010 WL 3119499, at \*7-8 (S.D. Ill. Aug. 5, 2010); *Pa. Emp. Benefit Trust Fund v. Zeneca, Inc.*, 710 F. Supp. 2d 458, 480 (D. Del. 2010) (dismissing claims based on allegation that Zeneca had falsely portrayed Nexium (esomeprazole) as superior to Prilosec (omeprazole), because plaintiff third party payers failed to allege reliance on the allegedly false statements); *In re Actimmune Mktg. Litig.*, 614 F. Supp. 2d 1037, 1052 (N.D. Cal. 2009) (dismissing claims because plaintiff consumers and insurance companies failed to allege that they, doctors, or any third party relied on the alleged misrepresentations of the efficacy of Actimmune (interferon gamma-1b)).

336. *Attorney Gen. v. Merck Sharp & Dohme Corp.*, 807 N.W.2d 343, 344 (Mich. Ct. App.

appeals court, however, held that Merck was immune from liability under a state law that exempted drug companies from products liability suits regarding FDA-approved drugs.<sup>337</sup> One judge dissented, arguing that the statutory immunity was intended to protect drug manufacturers only from suits based on defective products, and that the economic loss suffered by the state did not meet this definition.<sup>338</sup> The majority, however, countered that “product liability” suits include those that involve allegations of “damage to property,” and that damage to property included the economic losses stemming from the state’s Medicaid reimbursement policies.<sup>339</sup> Merck thus prevailed not because its claims of efficacy were accurate, nor because the state did not sustain any loss, but because of the broad interpretation given by the court to a state law that was intended to exempt drug manufacturers from product liability suits where the drug in question had been FDA-approved. Perhaps in an attempt to assuage judicial guilt for what it feared might be perceived as an unjust result, the majority offered meekly that “[i]f the plain language of the statute results in an outcome that the Legislature now deems improper, it is for the Legislature, not this Court, to narrow the application of the statute by amending or redrafting its terms.”<sup>340</sup>

Other lawsuits by state attorneys general have met with greater but hardly overwhelming success. In 2012, the attorney general of Texas brought a suit against Janssen Pharmaceutical alleging that the company overstated the effectiveness of the antipsychotic Risperdal (risperidone), among other charges.<sup>341</sup> In the middle of a four-week trial that produced testimony unflattering to Janssen, the company settled for \$158 million, though the majority of this amount can likely be attributed to issues of safety rather than efficacy (the drug company had reportedly chosen not to publish three studies suggesting a possible link between Risperdal use and diabetes, among other things).<sup>342</sup> A 2006 suit by the attorney general of West Virginia alleging deceptive overstatements of efficacy for the antipsychotic Zyprexa (olanzapine)<sup>343</sup> was settled in 2009 for \$22.5 million. As with the Risperdal (risperidone) settlement, much of the \$22.5 million may be attributable to allegations that Eli Lilly withheld side effect information and encouraged sales for unapproved uses, rather than for efficacy-related claims.

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2011).

337. *Id.* at 345.

338. *Id.* at 353 (Fitzgerald, J., dissenting).

339. *Id.* at 349 (majority opinion).

340. *Id.* at 350.

341. Tim Eaton, *State Attorney General Sues Drug Company*, STATESMAN, Jan. 8, 2012, <http://www.statesman.com/news/news/state-regional/state-attorney-general-sues-drug-company-1/nRjZR/>, archived at <http://perma.cc/3NEN-SKGF>.

342. Jef Feeley et al., *J&J to Pay \$158M to Settle Texas Drug Case*, BLOOMBERG, Jan. 19, 2012, [www.bloomberg.com/news/2012-01-19/johnson-johnson-to-pay-158-million-to-settle-texas-risperdal-drug-case.html](http://www.bloomberg.com/news/2012-01-19/johnson-johnson-to-pay-158-million-to-settle-texas-risperdal-drug-case.html).

343. Steve Korris, *AG Sues Drug Company for Fraud*, WEST VIRGINIA RECORD, Mar. 23, 2006, <http://wvrecord.com/news/176601-ag-sues-drug-company-for-fraud>, archived at <http://perma.cc/L9CE-6DSZ>.

Lilly admitted no wrongdoing.<sup>344</sup>

### *E. Lawsuits by Competitors Alleging Fraud*

Competitors may also serve as a check against false or misleading claims that overstate a drug's efficacy. One such case pitted McNeil, the maker of Extra Strength Tylenol (1000 mg acetaminophen), against Bristol-Myers Squibb (BMS), the maker of Aspirin Free Excedrin (1000 mg acetaminophen combined with 130 mg caffeine).<sup>345</sup> At the time of the litigation, BMS planned to spend \$10 million in an advertising campaign that touted Excedrin as more effective than Tylenol (acetaminophen).<sup>346</sup> Since both products contained identical amounts of acetaminophen, a pain reliever, the only difference in active ingredients was the presence in Aspirin Free Excedrin of 130 mg of caffeine. The court considered it "well settled by the FDA that caffeine acting alone is *not* effective in relieving headache pain," but noted that the FDA had not determined whether caffeine might be effective as an adjuvant, that is, a substance that is not effective itself but that increases the efficacy of the primary active pharmaceutical ingredient.<sup>347</sup> The court ultimately found the claims of Excedrin's (acetaminophen; caffeine) superiority over Tylenol (acetaminophen) to be literally false, and enjoined the advertising campaign.<sup>348</sup>

Other Lanham Act cases in the pharmaceuticals market have reached similar outcomes.<sup>349</sup> In another case involving Tylenol (acetaminophen), the Second Circuit upheld the district court's finding that claims of superiority of Anacin (aspirin; caffeine) over Tylenol (acetaminophen) were false.<sup>350</sup> Similarly, when the makers of competing heartburn medications Pepcid (famotidine) and Tagamet (cimetidine) sued each other for false claims of superiority, the court enjoined both parties' advertisements on the basis that they were false or misleading.<sup>351</sup> In another heartburn case, the Second Circuit found false or misleading claims by Procter & Gamble that Prilosec (omeprazole) provided relief for twenty-four

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344. Margaret Cronin Frisk et al., *Lilly to Pay \$22.5 Million to Settle Zyprexa Suit* (Update 3), BLOOMBERG, Aug. 20, 2009, <http://www.bloomberg.com/apps/news?pid=newsarchive&sid=a8IVc794lcs4>, archived at <http://perma.cc/6UGJ-NXX9>.

345. *McNeil-P.P.C., Inc. v. Bristol-Myers Squibb Co.*, 755 F. Supp. 1206, 1207-08 (S.D.N.Y. 1990), *aff'd*, 938 F.2d 1544 (2d Cir. 1991).

346. *Id.* at 1208.

347. *Id.* at 1211-12 (citing 42 Fed. Reg. 35,482 (1977)).

348. *Id.* at 1219.

349. See generally I. Scott Bass & Stacey Hallerman, *Prescription Drug Advertising Under the Lanham Act*, 83 TRADEMARK REP. 521 (1993).

350. *Am. Home Prods. Corp. v. Johnson & Johnson*, 577 F.2d 160, 170 (2d Cir. 1978).

351. *SmithKline Beecham Consumer Healthcare, L.P. v. Johnson & Johnson-Merck Consumer Pharms. Co.*, 906 F. Supp. 178, 183-86, 188 (S.D.N.Y. 1995); see also *SmithKline Beecham Consumer Healthcare L.P. v. Johnson & Johnson-Merck Consumer Pharms. Co.*, No. 01 Civ. 2775(DAB), 2001 WL 588846, at \*13 (S.D.N.Y. June 1, 2001) (Tums and Pepcid Complete).

hours.<sup>352</sup> And in a case by the predecessor of AstraZeneca against Eli Lilly, the court found claims that Lilly's Evista (raloxifene) reduced the risk of breast cancer to be "literally false."<sup>353</sup>

Rather than making explicit claims of superiority, companies sometimes take a more nuanced approach by seeking to convey a message of superiority by implication. In one contested television advertisement for the pain medication Aleve (naproxen), a narrator stated: "It [Aleve] lasts longer than EXTRA-STRENGTH TYLENOL. ADVIL isn't stronger, yet ALEVE is gentler to your stomach lining than aspirin."<sup>354</sup> As these words are spoken, the television viewer sees a visual of a medicine cabinet with the three competitor drugs, and each one is discarded as it is referred to.<sup>355</sup> The obvious implication is that Aleve (naproxen) is better than Advil (ibuprofen), Tylenol (acetaminophen), and aspirin, but a careful listener would notice that no claim of superiority to Advil (ibuprofen) was actually made, the only statement being that "ADVIL isn't stronger." The court held that, under Third Circuit precedent, there could be no liability for intent to mislead unless the defendant's conduct rose to "egregious proportions," which the court did not find to be present.<sup>356</sup>

Cases brought by competitors therefore appear to be among the most successful in checking exaggerated claims of efficacy. This success, however, is generally limited to checking claims of comparative, rather than absolute, efficacy. While these lawsuits may therefore represent a gain for one competitor or another, consumers can still be left with the impression that both medicines are more effective in absolute terms than they actually are. More importantly, a review of the cases just cited reveals that they address only over-the-counter products. The general absence of comparative efficacy litigation among sponsors of prescription drugs suggests that litigation is not having a substantial salutary effect on misleading claims for this class of drugs.

#### *F. Antitrust Actions*

Fraud may be the most likely legal doctrine to assail false claims of pharmaceutical efficacy, but it is not the only one. Antitrust law also provides a possible means for redress, at least where a defendant has attempted to obtain or maintain a monopoly position through unfair means. In *Walgreen Company v. AstraZeneca Pharmaceuticals*, Walgreen, Eckerd, Rite Aid, and other retailers alleged that AstraZeneca had attempted to monopolize the market, in violation of Section 2 of the Sherman Act, by "us[ing] distortion in its efforts to persuade

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352. *Johnson & Johnson-Merck Consumer Pharms. Co. v. Procter & Gamble Co.*, 90 Fed. App'x 8, at \*9 (2d Cir. 2003).

353. *Zeneca Inc. v. Eli Lilly & Co.*, No. 99 Civ. 1452(JGK), No. 99 CIV. 1452(JGK), 1999 WL 509471, at \*43 (S.D.N.Y. July 19, 1999).

354. *Am. Home Prods. Corp. v. Procter & Gamble Co.*, 871 F. Supp. 739, 745-46 (D.N.J. 1994).

355. *Id.*

356. *Id.* at 751-52.

doctors . . . that Nexium offered advantages to Prilosec and in its advertising directed to lay persons.”<sup>357</sup> As with the alleged efficacy-related fraud cases above, however, the court dismissed the claim, noting that the antitrust laws do not prohibit “market switching through sales persuasion” absent allegations of false representation or fraud.<sup>358</sup> In dismissing the antitrust claim, the *Walgreen* court noted that “[c]ourts and juries are not tasked with determining which product among several is superior.”<sup>359</sup> The issue thus devolved to one of fraud, as in the cases above, and in this regard the court noted that “Plaintiffs cannot hope to make such a showing [of reliance] because Nexium sales necessarily depended on prescriptions written by medical professionals.”<sup>360</sup> In other words, the learned intermediary doctrine once again barred recovery. Another district court dismissed a similar Sherman Act counterclaim brought by a generic drug manufacturer that sought to compete with AstraZeneca.<sup>361</sup>

### G. Synthesis of Litigation and Implications

An examination of cases alleging fraudulent overstatement of efficacy reveals that the large majority of these cases have been dismissed, not because the drugs were found to in fact be very effective or even because plaintiffs did not experience a loss, but because plaintiffs did not adequately allege that the overstatements of efficacy *caused* the economic harm that resulted.<sup>362</sup> The clear message from the judiciary is that the various plaintiffs could not prove that they would not have purchased or reimbursed the drug, but for the statements of the manufacturer.

Legally, this outcome is understandable, even if not inevitable. If an action did not cause an adverse outcome, then the actor cannot be held responsible. What the cases fail to adequately answer, however, is the puzzling question of why the plaintiffs did not adequately allege causation, a traditional and well-known element of any fraud claim.<sup>363</sup> The failure of plaintiffs is all the more

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357. *Walgreen Co. v. AstraZeneca Pharms. L.P.*, 534 F. Supp. 2d 146, 152 (D.D.C. 2008).

358. *Id.*

359. *Id.* at 151.

360. *Id.* at 152.

361. *AstraZeneca AB v. Mylan Labs., Inc.*, Nos. 00 Civ. 6749, 03 Civ. 6057, 2010 WL 2079722, at \*7 (S.D.N.Y. May 19, 2010).

362. See Joseph J. Leghorn, *Defending an Emerging Threat: Consumer Fraud Class Action Suits in Pharmaceutical and Medical Device Products-Based Litigation*, 61 *FOOD & DRUG L.J.* 519, 520 (2006) (noting four principal bases of dismissal of consumer fraud class action suits against pharmaceutical companies: “1) challenging standing to sue; 2) summoning the protections of [state consumer protection act] ‘safe harbor’ provisions; 3) asserting preemption under the Food, Drug, and Cosmetic Act (FDCA) . . . and 4) invoking the learned intermediary doctrine.”).

363. See, e.g., *Kevin M. Ehringer Enters., Inc. v. McData Servs. Corp.*, 646 F.3d 321, 325 (5th Cir. 2011) (“To state a claim for fraudulent inducement under Texas law, a plaintiff must prove the basic elements of fraud: (1) a material misrepresentation; (2) that is false; (3) when the defendant made the representation, the defendant knew it was false or made the statement without any

puzzling in later cases, when attorneys were presumably aware of the earlier opinions where judges had emphasized the need for alleging causation in this particular context.

The seeming mystery, however, has an obvious explanation. Plaintiffs cannot allege that the defendant's misrepresentations caused the *plaintiff* (as opposed to his doctor) to rely to his detriment, because such reliance is barred by the learned intermediary doctrine.<sup>364</sup> In the words of one court:

Even if [the plaintiffs] had offered evidence indicating that they had relied in some way on Defendants' misrepresentations, it would ultimately be of no consequence. The learned intermediary breaks the chain in terms of reliance, since the patient cannot obtain prescription drugs without the physician no matter what they believe about them.<sup>365</sup>

Therefore, in order to adequately allege causation, a plaintiff has to establish that the doctor who prescribed the medication would not have done so if that doctor had not viewed the television advertisements of (or other communications from) the manufacturer. The court must then be willing to allow a fraud claim to proceed based upon reliance by one party (the doctor) that caused harm to another party (the patient or insurance company). Fraud claims traditionally require reliance by the same party that experiences the loss,<sup>366</sup> but in the learned intermediary context, courts seem willing to flexibly apply the elements of fraud to allow recovery.<sup>367</sup>

The stumbling block, however, is that it is not easy for a physician to admit reliance, because to do so would be to admit that the principal reason she prescribed a drug was that she had recently viewed a television advertisement or other promotional material. Professional pride and the need to project an aura of competence in order to maintain an effective doctor-patient relationship make such a statement awkward at best. In addition, if causation derives not from a single discrete event, but rather from the accumulation of a number of communications that come to the doctor both directly and indirectly over a period of time, it may be difficult for the doctor to precisely determine which particular communication or communications caused her to prescribe, issues of professional image aside.

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knowledge of its truth; (4) the defendant intended the plaintiff to rely on the representation, and the plaintiff actually relied on the representation; and (5) the defendant's actions caused an injury.”)

364. *Heindel v. Pfizer Inc.*, 381 F. Supp. 2d 364, 384 (D.N.J. 2004).

365. *Id.*

366. *See, e.g., Mason v. Threshman*, No. 3:12cv259, 2012 WL 3696177, at \*4 (M.D. Pa. Aug. 27, 2012); *Guigey v. Bombardier*, 615 A.2d 1169, 1173 (Me. 1992).

367. *See, e.g., In re Avandia Mktg., Sales Practices & Prods. Liab. Litig.*, No. 10-2401, 2011 WL 4006639, at \*2 (E.D. Pa. Sept. 7, 2011); *Lee v. Mylan, Inc.*, 806 F. Supp. 2d 1320, 1323-24 (M.D. Ga. 2011); *Kline v. Pfizer, Inc.*, No. 08-3238, 2008 WL 4787577, at \*3 (E.D. Pa. Oct. 31, 2008).

## CONCLUSION

Patients, doctors, insurance companies, government regulators, and courts make poor gatekeepers for a variety of reasons, including lack of information, soft corruption, lack of financial incentives, and lack of statutory mandate. Part of the problem, however, ironically lies in the simple fact that there are so many regulators that responsibility becomes complex or even unclear; each potential gatekeeper assumes that the others are either individually or collectively performing the gatekeeper role. The FDA, for example, screens out drugs whose risks are not offset by sufficient efficacy or who have absolutely no efficacy at all, but otherwise assumes that patients and their doctors will determine whether a drug is worth using.<sup>368</sup> Similarly, the PTO issues patents on drugs (or any invention) that can meet the extremely minimal utility hurdle, leaving it to “the market” to weed out low value inventions.<sup>369</sup> Patients and doctors are willing to try anything that might work, so long as the risks are not too high, and assume that the FDA has done its job in only allowing sufficiently effective drugs onto the market.<sup>370</sup> Insurance companies may have a financial interest in preventing the consumption of ineffective drugs when cheaper alternatives would do as well, but cannot intrude too far into the physician (or patient) arena without risking a significant publicity backlash.<sup>371</sup> It is a complex web in which the buck is passed once and passed again but never settles with any one party. Regardless of responsibility or blame, however, it is ultimately the public that suffers.

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368. *See supra* Part III.B.

369. *See supra* Part III.A.

370. *See supra* Part I.C.

371. *See supra* Part I.B.