

**TREAT YOURSELF: IS SELF-MEDICATION THE  
PRESCRIPTION FOR WHAT AILS AMERICAN HEALTH CARE?**

*Lars Noah\**

TABLE OF CONTENTS

I. INTRODUCTION.....	359
II. FDA POLICIES AND PROCEDURES .....	364
<i>A. Experience with Internal Analgesics</i> .....	369
<i>B. Unsuccessful Switch Attempts</i> .....	372
III. LIABILITY CONSEQUENCES OF A SWITCH.....	378
IV. AGENCY “PRECEDENT” AS AN OBSTACLE .....	383
<i>A. Procedural Constraints</i> .....	384
<i>B. Constitutional Infirmities</i> .....	385
V. CONCLUSION .....	391

THE DESIRE TO TAKE MEDICINE IS PERHAPS THE GREATEST FEATURE  
WHICH DISTINGUISHES MAN FROM ANIMALS. – WILLIAM OSLER, 1925

I. INTRODUCTION

Patient “empowerment” has become something of a buzzword in debates over the future of health care delivery in this country, and the notion encompasses efforts to better equip these newly minted “consumers” of health services to exercise a role in selecting among treatment options.<sup>1</sup> Self-medication has a long tradition in this country. According to the latest official figures, annual sales of nonprescription products exceed \$31 billion, though these sales represent less than twenty percent of total spending on prescription pharmaceuticals.<sup>2</sup> In

---

\* Professor of Law, University of Florida. An earlier version of this paper was presented at a Federalist Society program on controlling pharmaceutical prices held in Washington, D.C. I would like to thank Peter Hutt for his guidance.

1. See, e.g., Marshall H. Chin, *The Patient's Role in Choice of Medications: Direct-to-Consumer Advertising and Patient Decision Aids*, 5 YALE J. HEALTH POL'Y L. & ETHICS 771, 771 (2005); see also Michael H. Cohen & Mary C. Ruggie, *Integrating Complementary and Alternative Medical Therapies in Conventional Medical Settings: Legal Quandaries and Potential Policy Models*, 72 U. CIN. L. REV. 671, 676–83 (2003) (discussing the burgeoning consumer demand for unorthodox treatments); Lars Noah, *Informed Consent and the Elusive Dichotomy Between Standard and Experimental Therapy*, 28 AM. J.L. & MED. 361, 364–69 (2002) (explaining that the expansion in physicians' duties to secure informed consent represents a perhaps futile effort to promote patient autonomy and self-determination).

2. See U.S. CENSUS BUREAU, STATISTICAL ABSTRACT OF THE UNITED STATES: 2004–2005, at 93 tbl.116 (124th ed. 2005), available at <http://www.census.gov/prod/2004pubs/>

recent years — whether a reaction to the tradition of physician paternalism, the realities of cost-containment pressures under managed care, or the need to put downward pressure on drug price inflation — demands have grown for expanded access to pharmaceuticals without first having to secure a prescription.<sup>3</sup> As the Food and Drug Administration (“FDA”) explained, nonprescription medications “have an increasingly vital role in the U.S. health care system by providing consumers easy access to certain drugs that can be used safely for conditions that consumers can self-treat without the help of a health care practitioner.”<sup>4</sup>

In 1998, WellPoint Health Networks — the parent company of Blue Cross and Blue Shield of California — petitioned the FDA to switch three popular nonsedating antihistamines from prescription (“Rx”) to over-the-counter (“OTC”) status.<sup>5</sup> The insurer thereby hoped to save nearly \$100 million annually for covered physician visits and prescription drug costs.<sup>6</sup> The manufacturers of these drugs vehemently opposed the petition because they would have had to reduce their prices substantially once consumers absorbed the entire cost out of pocket.<sup>7</sup> The two sides, however, framed their arguments in terms

---

04statab/health.pdf (listing separately expenditures for prescription drugs and for “other nondurable medical products”). The Consumer Healthcare Products Association cites retail sales of over-the-counter (“OTC”) drugs at only half of this level in 2004, but it concedes that definitions differ and that certain large retail chains were excluded. *See* Consumer Health Products Ass’n, OTC Retail Sales — 1964–2004, <http://www.chpa-info.org/ChpaPortal/PressRoom/Statistics/OTCRetailSales.htm> (last visited Apr. 29, 2006).

3. *See* Colin Bradley & Alison Blenkinsopp, *Over-the-Counter Drugs: The Future for Self-Medication*, 312 BRIT. MED. J. 835, 835 (1996); Joshua P. Cohen et al., *Switching Prescription Drugs to Over the Counter*, 330 BRIT. MED. J. 39, 40 (2005); Peter Temin, *Realized Benefits from Switching Drugs*, 35 J.L. & ECON. 351, 352 (1992) (“Concern about the rising cost of medical care has been joined by suspicion of government regulation to create a movement to revive self-medication.”).

4. Over-the-Counter Drug Products, Public Hearing, 65 Fed. Reg. 24,704, 24,705 (Apr. 27, 2000) (“In light of the continuously changing health care environment, including the growing self-care movement, the agency continues to examine its overall philosophy and approach to regulating OTC drug products.”).

5. *See* Holly M. Spencer, Comment, *The Rx-to-OTC Switch of Claritin, Allegra, and Zyrtec: An Unprecedented FDA Response to Petitioners and the Protection of Public Health*, 51 AM. U. L. REV. 999, 1000–04 (2002) (providing background and explaining that the agency never before had considered such a petition filed by an insurer and over the objections of the manufacturer).

6. *See id.* at 1001–02 & n.12, 1021, 1026–29. Health insurers could have simply removed from their drug benefit — or at least imposed a higher co-payment on — prescription antihistamines or other budget-busting drugs thought to provide too insubstantial a therapeutic benefit for patients. Because such a move surely would have triggered howls of protests from policyholders, the switch petitions put the onus on the FDA to do the dirty work.

7. *See id.* at 1010. Aside from differentials in insurance coverage, patients may claim a tax deduction for medical expenses, including uncovered expenses for prescription but not OTC drugs (except for insulin), exceeding 7.5% of their adjusted gross income. *See* Tax Equity and Fiscal Responsibility Act of 1982, Pub. L. No. 97-248, § 202(b), 96 Stat. 324, 421 (codified as amended at 26 U.S.C.A. § 213(a)–(b) (2005)); *see also* Lance W. Rook, *Listening to Zantac: The Role of Non-Prescription Drugs in Health Care Reform and the Federal Tax System*, 62 TENN. L. REV. 107, 137 n.165 (1994) (“Almost every state that

of relative safety and effectiveness, with the manufacturers suggesting that more experience with prescription marketing would provide reassuring confirmation of the evident safety of these products, while the insurers emphasized that these second-generation antihistamines enjoyed an unmistakable safety advantage over the existing (and sedating) nonprescription substitutes.<sup>8</sup> If causing drowsiness made the older antihistamines more dangerous, then perhaps WellPoint should have urged the FDA to move them to prescription status or withdraw them from the market altogether.<sup>9</sup> (Of course it would not have wanted to petition only for the withdrawal of the existing OTC antihistamines because that might have increased its tab for the prescription products.) Even so, this aspect of the petition posed a difficult policy issue for the FDA — namely, what to do with older drugs when second-generation products offer distinct therapeutic benefits.<sup>10</sup>

In 2001, a pair of advisory committees voted in favor of recommending the OTC switch,<sup>11</sup> but the FDA essentially disregarded the advice by failing to act on WellPoint's petition.<sup>12</sup> Nonetheless, because an OTC switch becomes far more appealing once a prescription drug loses patent and market exclusivity protections (and faces com-

---

imposes a sales tax exempts *prescription* drugs.”); *id.* at 133–39 (advocating that the federal tax deduction be extended to expenditures on OTC drugs); *id.* at 138–39 (“[T]he prescription/non-prescription distinction was probably a shorthand way to exclude inexpensive medication from health care insurance and tax benefits. . . . [This] might have been acceptable when there was a correlation between expense and the prescription requirement . . . [but] no longer makes sense.”).

8. See Spencer, *supra* note 5, at 1001 (explaining that the petition “argued that the three [prescription] medications are safer than the currently available OTC antihistamine medications that cause drowsiness as a side effect”); *id.* at 1019–20, 1028–29.

9. Switching the nonsedating antihistamines to OTC status without withdrawing the older products may, in fact, turn out to be entirely counterproductive if many consumers, once deprived of prescription drug coverage for the second-generation products, respond to the likely price differentials by substituting the older and still cheaper sedating antihistamines. See *id.* at 1023 & n.152; *infra* note 100 and accompanying text.

10. See Over-the-Counter Drug Products: Public Hearing, 65 Fed. Reg. 24,704, 24,705 (Apr. 27, 2000) (asking whether “older therapies that may provide less benefit or more risk [should] be removed from the OTC market”), Lars Noah, *Assisted Reproductive Technologies and the Pitfalls of Unregulated Biomedical Innovation*, 55 FLA. L. REV. 603, 654–58 (2003) (arguing that, as alternative treatments have emerged, fertility drugs previously approved by the FDA may no longer be safe and effective); Dennis Cauchon, *Better Drugs May Be Stuck Behind Counter: Makers Prefer Slow Route to OTC Market*, USA TODAY, June 27, 2000, at 9D. After all, once the agency allows OTC sale of any products to treat a particular condition, many (though by no means all) of the factors relevant to a switch decision, see *infra* notes 41–49 and accompanying text, already point in favor of nonprescription availability.

11. See Ceci Connolly, *Panel: Reclassify Allergy Pills*, WASH. POST, May 12, 2001, at A1.

12. See Melody Petersen, *Delays Possible for Over-the-Counter Allergy Drugs*, N.Y. TIMES, May 16, 2001, at C1 (explaining that, for a variety of reasons, the FDA was unlikely to act on the committee's recommendation).

petition from generics),<sup>13</sup> the manufacturer of one of the antihistamines (Claritin) soon experienced a change of heart.<sup>14</sup> Once this product reached the OTC marketplace, many health insurers limited coverage of the nonsedating antihistamines that remained in prescription status.<sup>15</sup>

Two years after the advisory committee votes, and with two of the three antihistamines still restricted to prescription dispensing, the agency briefly showed renewed interest in the question of initiating an Rx-to-OTC switch over a manufacturer's objection.<sup>16</sup> In fact, some observers wondered whether the newly created Medicare drug benefit had given the FDA's parent agency, the Department of Health and Human Services ("HHS"), the same financial incentive that had prompted WellPoint's petition.<sup>17</sup> Indeed, the agency's proposed FY2004 budget suggested that it would "become more proactive" in this area because switches could "provide an expedient way to signifi-

---

13. See Davina C. Ling et al., *Deregulating Direct-to-Consumer Marketing of Prescription Drugs: Effects on Prescription and Over-the-Counter Product Sales*, 45 J.L. & ECON. 691, 693 (2002).

14. See Spencer, *supra* note 5, at 1023–24, 1038–41. The manufacturer concurrently introduced prescription Clarinex, which contained a variation of the active ingredient in Claritin. See Rita Rubin, *Claritin Going OTC: Will Heir Be a Prescription for Success?*, USA TODAY, Apr. 23, 2002, at 11D. Similarly, when Prilosec lost patent protection and faced generic competition, AstraZeneca introduced the chemically similar drug Nexium for gastrointestinal reflux disease. See Francesca Kritz, *A Side Effect Felt in the Wallet: With Generic Prilosec Due, the \$6 Billion Drug's Maker Offers a High-Priced Successor*, WASH. POST, Mar. 13, 2001, at T6. A few years later, when persistent shortages of OTC Prilosec occurred, some observers suspected that the manufacturer had done this intentionally in order to increase the demand for Nexium. See Alex Berenson, *Where Has All the Prilosec Gone?*, N.Y. TIMES, Mar. 2, 2005, at C1.

15. See Cohen et al., *supra* note 3, at 40; see also Bruce Japsen, *New Pain Rising in Heartburn Drug Costs: Insured Prilosec Users to Pay More Over the Counter*, CHI. TRIB., July 31, 2003, at 1. Meanwhile, the manufacturer of Allegra has pressed patent infringement claims against generic competitors. See Leila Abboud, *Generic Allegra Is Launched as Patent Litigation Continues*, WALL ST. J., Sept. 7, 2005, at D5.

16. See Leila Abboud, *Firms Gird for Drug-Cost Fight: FDA May Force Over-the-Counter Sales of Some Allergy Medicines*, WALL ST. J., May 6, 2003, at A4 (explaining that, though the pharmaceutical industry strongly opposed the effort, the insurance lobby enthusiastically supported it).

17. See Rita Rubin, *FDA's Push to Switch Antihistamines to Over-the-Counter Raises Eyebrows*, USA TODAY, Apr. 24, 2003, at 9D ("Now that the Bush administration has promised to add a prescription drug benefit to Medicare, some skeptics wonder whether the FDA is looking to save the government money by taking antihistamines out of the lineup of covered medications."); see also Cohen et al., *supra* note 3, at 39 (doubting suggestions that a similar impetus accounted for the recent switch of a statin drug in the UK, but suggesting that it explains the switch of omeprazole in Sweden); Richard W. Stevenson, *Warner-Lambert in Two British Deals*, N.Y. TIMES, July 29, 1993, at D5 (noting a drug industry "belief that as governments look for ways to reduce health care costs, they will be quicker to approve nonprescription versions of drugs"). The pressure to hold down the cost of the new Medicare drug benefit continues to build. See Ceci Connolly, *Officials Defend Cost of Medicare Drug Benefit: Importation, Negotiation Ideas Rejected*, WASH. POST, Feb. 17, 2005, at A7.

cantly reduce consumer health care costs.”<sup>18</sup> Although once again it failed to act on WellPoint’s petition, the FDA confidently announced at the time that it had the power to order such a switch.<sup>19</sup> In common with any number of other bold assertions emanating from this agency, the FDA’s claim of authority may never be put to the test.

If the agency ever orders an Rx-to-OTC switch at the behest of payers rather than sellers, it could inspire similar efforts for a range of popular and pricey prescription drugs.<sup>20</sup> Even if the FDA leaves the initiative to the pharmaceutical industry, possible candidates for non-prescription marketing include various antihypertensives,<sup>21</sup> cholesterol-lowering statins,<sup>22</sup> weight-loss drugs,<sup>23</sup> proton pump inhibitors for heartburn,<sup>24</sup> and, more speculatively, treatments for urinary incontinence or erectile dysfunction. Whether such switches would serve or disserve the best interests of patients will depend on a variety of factors, but the agency should skeptically evaluate such petitions — whether initiated by insurers or manufacturers<sup>25</sup> — whenever they appear to be motivated primarily by the prospect of financial gains to the petitioner.<sup>26</sup>

---

18. Rita Rubin, *FDA Seeks to Switch to Over-Counter*, USA TODAY, Apr. 23, 2003, at 1A (quoting language from the agency’s proposed budget). Not long thereafter, Mark McClellan left his position as Commissioner of the FDA to run the Centers for Medicare and Medicaid Services (“CMS”), another unit of HHS. See Marc Kaufman, *FDA’s Reliance on Unconfirmed Chiefs Is Faulted*, WASH. POST, Dec. 19, 2004, at A1.

19. See Marc Kaufman, *FDA Says It Can Take Away Drugs’ Prescription Status*, WASH. POST, Apr. 26, 2003, at A1.

20. See Dennis Cauchon, “Complex Issues” Require Much Study Before Action, *FDA Says: Administration’s Decision on Allergy Drugs Could Have Wide Repercussions*, USA TODAY, Apr. 12, 2000, at 5A.

21. See *Over-the-Counter Drug Products*, Public Hearing, 65 Fed. Reg. 24,704, 24,705 (Apr. 27, 2000).

22. See Brian L. Strom, *Statins and Over-the-Counter Availability*, 352 NEW ENG. J. MED. 1403, 1404–05 (2005) (canvassing the competing arguments, and noting that an FDA advisory committee recently recommended against granting a switch petition).

23. See Diedra Henderson, *Glaxo Plans Sales Curbs for Diet Pill*, BOSTON GLOBE, Jan. 13, 2006, at F1 (reporting that the manufacturer of Xenical has petitioned to switch a low-dose version and is prepared to adopt mechanisms to enforce an age restriction if the agency has concerns about abuse by adolescents); Shari Roan, *Diet Drug May Go Over the Counter: Xenical Would Be the First of Its Kind to Go from Prescription Use to Pharmacy Shelves*, L.A. TIMES, Oct. 24, 2005, at F3.

24. See Hope Cristol, *Heartburn of Another Kind: For Some Patients, Self-Treating with New OTC Drugs May Invite Trouble*, WASH. POST, Sept. 30, 2003, at F1; Gardiner Harris, *F.D.A. Approves Over-Counter Sales of Top Ulcer Drug*, N.Y. TIMES, June 21, 2003, at A1 (reporting that earlier efforts to switch Prilosec had faltered).

25. One might even imagine a switch petition initiated (perhaps covertly) by a competitor anxious to have the prescription market for a particular class of drugs entirely to itself, which again should counsel against uncritical FDA acceptance. See Lars Noah, *Sham Petitioning as a Threat to the Integrity of the Regulatory Process*, 74 N.C. L. REV. 1, 5–11, 66 & n.272 (1995).

26. These various economic interests can play themselves out in an entirely different manner should the FDA reject a manufacturer-initiated switch request — generic versions of the prescription drug enter the marketplace, substantially reducing prices, which will remove many of the financial incentives for seeking a switch from both the brand-name

This Article analyzes the drive to switch more pharmaceutical products to nonprescription status. Part II offers more detailed background about the mechanisms and criteria used by the FDA to distinguish between prescription and OTC drugs. Part III views the distinction through the lens of tort law, suggesting a number of reasons why an Rx-to-OTC switch might increase a seller's exposure to liability. Part IV unpacks the oft-repeated point that an involuntary switch would be "unprecedented," which connotes both procedural and substantive objections (arising under both statute and the Constitution), focusing in particular on the possibility of pressing a regulatory takings claim.

## II. FDA POLICIES AND PROCEDURES

When it passed the Federal Food, Drug, and Cosmetic Act ("FDCA") in 1938,<sup>27</sup> Congress drew no distinction between prescription and OTC pharmaceuticals, and it apparently had "not intended to restrict in any way the availability of drugs for self-medication."<sup>28</sup> Nonetheless, when the FDA issued regulations to implement the new legislation later that year, it for the first time provided that certain drugs could not be sold directly to consumers.<sup>29</sup> Six years later, the agency promulgated a rule designating a class of drugs that would be safe only when used "by or under the supervision of a physician."<sup>30</sup> In

---

manufacturer and health insurers. Generic manufacturers also will have no real reason to make the investment to ask the FDA to revisit its original decision to reject a switch, which creates a "prescription orphan." See Letter from Peter Barton Hutt, Senior Counsel, Covington & Burling, to author (Jan. 24, 2006) (on file with author). Precisely this seems to have happened in the case of Zovirax (acyclovir), an antiviral indicated for the treatment of genital herpes, shingles, and other conditions, which the FDA refused to switch one decade ago. See *FDA Urged to Bar Sales of Burrough's Acyclovir Drug Without a Prescription*, WALL ST. J., Jan. 13, 1995, at B6. Although good reasons exist to doubt that the agency later might have reconsidered its decision, see *infra* note 90, the arrival of much cheaper generic competitors in the wake of the FDA's rejection meant that no one subsequently pressed the matter. If, in fact, Zovirax satisfied the criteria for OTC marketing and readier access would have proven beneficial to patients, then the alignment of the various parties' interests after the entry of generic prescription substitutes results in a suboptimal outcome.

27. Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-396 (2000)).

28. H.R. REP. NO. 75-2139, at 8 (1938), *quoted in* *United States v. Articles of Drug*, 625 F.2d 665, 672 (5th Cir. 1980). "On the contrary, it [wa]s intended to make self-medication safer and more effective." *Id.*

29. See Promulgation of Regulations Under the Federal Food, Drug, and Cosmetic Act, 3 Fed. Reg. 3161, 3168 (Dec. 28, 1938); see also Peter Temin, *The Origin of Compulsory Drug Prescriptions*, 22 J.L. & ECON. 91, 98-100, 103-05 (1979) (criticizing this development for reducing consumer freedom of choice).

30. See Regulations for the Enforcement of the Federal Food, Drug, and Cosmetic Act, 9 Fed. Reg. 12,255, 12,255-56 (Oct. 10, 1944) (codified at 21 C.F.R. pt. 2 (1950)); see also Alan H. Kaplan, *Over-the-Counter and Prescription Drugs: The Legal Distinction Under Federal Law*, 37 FOOD DRUG COSM. L.J. 441, 442 (1982) (explaining that this rule sought to discourage prescription marketing of drugs that did not genuinely require physician supervision).

practice, under early federal law, decisions concerning the appropriate status of a drug were largely left to manufacturers.<sup>31</sup>

Not until 1951, when it passed the Durham-Humphrey Amendments,<sup>32</sup> did Congress expressly recognize prescription drugs as a separate category. New section 503(b)(1) of the FDCA provided in relevant part that a drug, which “because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug, . . . shall be dispensed only” upon a prescription.<sup>33</sup> The statute also allowed — but did not require — the FDA to exempt drugs from this requirement if it was “not necessary for the protection of the public health,”<sup>34</sup> though one can read the legislative history to suggest a preference for unrestricted marketing whenever possible.<sup>35</sup>

When it considers an application for approval of a new drug, the FDA can demand modifications in the drug’s proposed labeling.<sup>36</sup> One fundamental question that the agency must ask is whether to make a product available only upon a prescription from — or through direct administration by — a licensed health care professional. At least initially, virtually all new ingredients are available only by prescription while the FDA collects additional adverse event data.<sup>37</sup> Thus, a product later switched OTC will have survived not only the

---

31. See Peter Barton Hutt, *A Legal Framework for Future Decisions on Transferring Drugs from Prescription to Nonprescription Status*, 37 FOOD DRUG COSM. L.J. 427, 429 (1982).

32. See Pub. L. No. 215, ch. 578, § 1, 65 Stat. 648 (1951). Industry representatives opposed an earlier version of this legislation for granting the FDA greater authority to decide which drugs would require a prescription. See Temin, *supra* note 29, at 102–03.

33. 21 U.S.C. § 353(b)(1)(A) (2000). Separately, however, a new drug may have to abide by prescription-only availability if so provided in the labeling at the time of approval. See *id.* § 353(b)(1)(B).

34. *Id.* § 353(b)(3).

35. See Advance Notice of Proposed Rulemaking, Drug Approvals: Circumstances Under Which an Active Ingredient May Be Simultaneously Marketed in Both a Prescription Drug Product and an Over-the-Counter Drug Product, 70 Fed. Reg. 52,050, 52,051 (Sept. 1, 2005) (explaining that one of Congress’ “primary objectives” was “to relieve retail pharmacists and the public from burdensome and unnecessary restrictions on the dispensing of drugs that are safe for use without the supervision of a physician” (citing S. REP. No. 946, at 1 (1951), *reprinted in* 1951 U.S.C.C.A.N. 2454)).

36. See 21 C.F.R. § 314.110 (2005). For instance, the FDA may refuse to approve a new drug application if “proposed labeling is false or misleading in any particular,” *id.* § 314.125(b)(6), which would be the case if an exempt product proposed to use prescription labeling, see *infra* note 53 and accompanying text.

37. See Stephen Paul Mahinka & M. Elizabeth Bierman, *Direct-to-OTC Marketing of Drugs: Possible Approaches*, 50 FOOD & DRUG L.J. 49, 56–57 (1995) (listing the handful of new drugs approved from the outset without prescription restrictions). OTC marketing further complicates the already difficult process of collecting adverse event reports — instead of relying on information about side effects observed in patients under the supervision of physicians, the agency would receive sporadic and indiscriminate consumer complaints. See, e.g., Jane E. Allen, *Over-the-Counter Zinc Nasal Sprays Reviewed for Destroying Sense of Smell*, L.A. TIMES, Mar. 15, 2004, at F3; see also Strom, *supra* note 22, at 1403.

agency's rigorous premarket review process for new chemical entities but also the test of time and a second round of FDA scrutiny.<sup>38</sup> Even so, risks may not come to light until long after a switch occurs.<sup>39</sup>

Although the statute and regulations provide some general criteria for differentiating between prescription and OTC products, ultimately that determination must be made on an ad hoc basis and without clear guidance.<sup>40</sup> The 1951 amendments and the FDA's regulations mention toxicity, other harmful effects, methods of use, and the need for collateral measures,<sup>41</sup> but they fail to indicate the point at which one or more of these factors will necessitate prescription-only availability. Toxicity concerns may relate to either acute or chronic effects,<sup>42</sup> and this factor is often operationalized by reference to a product's "margin of safety" and the extent to which it needs to be carefully titrated for each patient.<sup>43</sup> Other harmful effects may include the risk of interactions with food or other drug products and the potential for abuse.<sup>44</sup>

---

38. See Over-the-Counter Human Drugs, Proposed Labeling Requirements, 62 Fed. Reg. 9024, 9027 (proposed Feb. 27, 1997) (to be codified at 21 C.F.R. pts. 201, 330, 358). In the early 1990s, for example, the FDA considered requests to switch the nonsedating antihistamines Seldane and Hismanal to nonprescription status after several years of prescription marketing, only to see the products withdrawn because of the belated discovery of potentially fatal cardiac side effects. See Bruce Ingersoll, *FDA Proposes to Force Seldane Off the Market*, WALL ST. J., Jan. 14, 1997, at B1. Before switching Claritin, the FDA looked into reports of unexpected side effects that arose one decade after original approval. See *F.D.A. Reviews Nonprescription Claritin*, N.Y. TIMES, Apr. 30, 2002, at C12 (discussing a cluster of birth defects in Sweden). More recently, in seeking to switch a reduced dosage version of Xenical six years after the FDA's approval of the prescription version, the manufacturer pointed out that 22 million people around the world had taken the drug and that it had been studied in more than one hundred clinical trials enrolling approximately 30,000 subjects. See Sally Squires, *Weighing a Pill for Weight Loss*, WASH. POST, Jan. 24, 2006, at F1.

39. See, e.g., Sandra Dial et al., *Use of Gastric Acid-Suppressive Agents and the Risk of Community-Acquired Clostridium difficile-Associated Disease*, 294 JAMA 2989 (2005); Jeff Gerth & Sheryl Gay Stolberg, *Another Part of the Battle: Keeping a Drug on the Shelves of Stores*, N.Y. TIMES, Dec. 13, 2000, at A31 (offering a detailed history of phenylpropanolamine, a decongestant ingredient used in OTC weight-loss and cough-cold products, that the FDA belatedly withdrew after scientists confirmed a long suspected association with hemorrhagic stroke); see also Scott Hensley, *Rethinking Over-the-Counter Drugs: Finding on Aleve Underscores Dearth of Overall Research*, WALL ST. J., Dec. 22, 2004, at D1.

40. See Hutt, *supra* note 31, at 428–31; Linda M. Katz, *Prescription to Over-the-Counter Drug Switches*, 48 FOOD & DRUG L.J. 567 (1993).

41. See 21 U.S.C. § 353(b)(1) (2000); 21 C.F.R. § 330.10(a)(4)(vi) (2005).

42. See *United States v. El-O-Pathic Pharmacy*, 192 F.2d 62, 74–75 (9th Cir. 1951) (discussing the considerations going into the labeling of hormones); Gerald M. Rachanow, *The Switch of Drugs from Prescription to Over-the-Counter Status*, 39 FOOD DRUG COSM. L.J. 201, 204–05 (1984).

43. See Hutt, *supra* note 31, at 433.

44. The Drug Enforcement Administration ("DEA") can recommend to the FDA prescription status for an OTC drug with an abuse potential. See 21 U.S.C. § 829(d). Under Schedule V, those narcotics with only a limited abuse potential can remain OTC, but a number of states have mandated dispensing of these drugs only by pharmacists and sometimes only with a physician's prescription. See Gregory M. Fisher, *Third Class of Drugs — A Current View*, 46 FOOD DRUG COSM. L.J. 583, 606–07 (1991) (adding that, before passage of the Controlled Substances Act in 1970, the FDA would handle such concerns by



Methods of use and “collateral measures” may pose questions about the ability of laypersons to self-diagnose and self-administer as well as the need for periodic clinical monitoring.<sup>45</sup> No single factor is determinative, however, as there are a number of approved OTC products that raise toxicity, drug interaction, self-diagnosis, and method of administration concerns.<sup>46</sup>

Ultimately, the decision may turn on whether appropriate labeling can help to minimize these problems.<sup>47</sup> FDA regulations provide that OTC drug product labeling must include directions and warnings “in such terms as to render them likely to be read and understood by the ordinary individual, including individuals of low comprehension, under customary conditions of purchase and use.”<sup>48</sup> In theory, therefore, the agency would not permit OTC marketing if overly complex labeling were necessary to ensure safe use. In practice, however, the FDA

---

mandating prescription status); *cf.* *Carey v. Population Servs. Int'l*, 431 U.S. 678, 686–91 & n.9 (1977) (invalidating a state law allowing only licensed pharmacists to sell OTC contraceptives).

45. In particular, the agency sometimes worries that symptomatic relief may mask a serious underlying condition and cause the consumer to delay seeking medical attention. *See, e.g.,* *United States v. Article of Drug Labeled “Decholin,”* 264 F. Supp. 473 (E.D. Mich. 1967).

46. *See* Hutt, *supra* note 31, at 433–40. For example, some OTC drug labels instruct patients to use the product only after having gotten a physician’s diagnosis of a particular condition. *See, e.g.,* Martin S. Lipsky & Theresa Waters, *The “Prescription-to-OTC Switch” Movement: Its Effects on Antifungal Vaginitis Preparations*, 8 ARCHIVES FAM. MED. 297, 298 (1999). At one time, diabetic patients needing insulin injections could purchase this product without a prescription notwithstanding possible difficulties with self-administration and diagnosis. *See* Kaplan, *supra* note 30, at 443–44 (speculating that OTC status reflected the need to ensure ready access by these patients); *see also* Gardiner Harris & Robert Pear, *Drug Maker’s Efforts to Compete in Lucrative Insulin Market Are Under Scrutiny*, N.Y. TIMES, Jan. 28, 2006, at A14 (discussing efforts to promote the use of newer forms of insulin, which require a prescription). Blood-glucose monitors have raised separate concerns about reliability and the ability of laypersons to calibrate these home-use diagnostic devices. *See* Jennifer Corbett Dooren, *J&J Unit Gets an FDA Warning on Glucose Tests*, WALL ST. J., Dec. 21, 2005, at D4; *see also* Joyce Gemperlein, *Ask the Pharmacists: Why Are Nonprescription Items Behind the Counter?*, WASH. POST, Dec. 25, 2005, at F6 (reporting that pharmacies often hold such items behind the counter). Nonetheless, recent research suggests that patients may enjoy better outcomes using risky prescription drugs when they monitor themselves rather than rely on continuing medical supervision. *See* C. Heneghan et al., *Self-Monitoring of Oral Anticoagulation: A Systematic Review and Meta-Analysis*, 367 LANCET 404 (2006).

47. *See* Hutt, *supra* note 31, at 438 (“[P]roblems of toxicity, self-diagnosis, and self-treatment, can either be accentuated by inadequate labeling, or alleviated by adequate labeling. Thus, labeling must be regarded as central to all future determinations of prescription/nonprescription status.”).

48. 21 C.F.R. § 330.10(a)(4)(v) (2005); *see also* Warner-Lambert/Parke-Davis & Co., *Benlylin*, 44 Fed. Reg. 51,512, 51,525 (FDA Aug. 31, 1979) (final decision) (“Suitable labeling of an OTC drug may provide sufficient safeguards for a drug that presents such indirect risks [from drowsiness]. When a drug presents serious direct risks (e.g., of cancer or other serious disease), adequate labeling for lay use without medical supervision generally cannot be written.”). In 1999, the agency issued uniform formatting rules designed to improve the readability of OTC drug labels. *See* *Over-the-Counter Human Drugs, Labeling Requirements*, 64 Fed. Reg. 13,254, 13,286 (Mar. 17, 1999) (codified at 21 C.F.R. § 201.66).

has required fairly detailed labeling for OTC products as a means of addressing toxicity concerns, serious drug interactions, fears about delaying medical intervention, and so forth.<sup>49</sup>

For drugs that do not require the supervision of a physician, have a history of safe use, and present no abuse potential, the FDA has a pair of ways to authorize OTC marketing.<sup>50</sup> First, a company may sell an OTC drug if it abides by the terms of the applicable “monograph,” which specifies for a particular category of products the active ingredients and dosages that the agency has determined to be safe and effective, along with the precise labeling necessary to facilitate appropriate consumer use.<sup>51</sup> As an illustration of this stringency, the FDA recently barred any references to “sinusitis” in the labeling of certain OTC cough-cold products.<sup>52</sup> Any continued prescription marketing of active ingredients for indications recognized in an OTC monograph would constitute a misbranding violation under the FDCA.<sup>53</sup> Nonmonograph ingredients, dosages, and indications could continue to be marketed as prescription products under an approved new drug application (“NDA”). The FDA has used the monograph process as a mechanism to switch dozens of prescription drugs.<sup>54</sup>

The second route to OTC marketing requires that a company secure a supplemental NDA for a reformulation (including revised labeling and perhaps reduced dosage) of a product previously approved for prescription use.<sup>55</sup> Manufacturers generally initiate switches of

---

49. See Lars Noah, *The Imperative to Warn: Disentangling the “Right to Know” from the “Need to Know” About Consumer Product Hazards*, 11 YALE J. ON REG. 293, 320–26 (1994); *id.* at 320 (“Because few drugs are entirely risk free, OTC drug products can be marketed only if consumers are given information adequate to minimize the danger of any side effects.”); *id.* at 326 (“Because OTC products are intended for self-treatment, the [FDA’s] emphasis on instructional warnings rather than [chronic] risk disclosures seems entirely appropriate.”).

50. Anyone may initiate an effort to exempt a product from prescription status. See 21 C.F.R. § 310.200(b) (“A proposal to exempt a drug . . . may be initiated by the Commissioner or any interested person.”).

51. See 21 C.F.R. pt. 330; *see also* Cutler v. Hayes, 818 F.2d 879, 883–85 (D.C. Cir. 1987) (describing the OTC drug review process). After the agency issues a final monograph, marketing of an OTC product outside of its scope would require favorable FDA action on either a petition to amend the monograph or an application for new drug approval. *See Farquhar v. FDA*, 616 F. Supp. 190 (D.D.C. 1985).

52. See Jennifer Corbett Dooren, *FDA to Bar Use of Term “Sinusitis” on Decongestants*, WALL ST. J., Oct. 12, 2005, at D4.

53. See 21 C.F.R. § 310.200(d); *see also* 21 U.S.C. § 353(b)(4)(B) (2000) (providing that a drug exempted from prescription requirements would be misbranded if it used the prescription warning statement or otherwise suggested that it was for prescription use).

54. See Fisher, *supra* note 44, at 612; *id.* at 627 (“[T]he OTC Drug Review greatly accelerated the prescription-to-nonprescription switch movement, reflecting the conclusions of experts that at least forty theretofore prescription ingredients are safe and effective for use by consumers on a nonprescription basis.”).

55. See 21 C.F.R. § 330.11; *id.* § 310.201(a) (listing these previously approved active ingredients); Over-the-Counter Drug Products, Public Hearing, 65 Fed. Reg. 24,704, 24,704–05 (Apr. 27, 2000). If the seller of an OTC drug fails to follow one of these routes to market, then it may face sanctions. *See United States v. Articles of Drug . . . Promise Toothpaste for*

drugs that remain subject to NDAs, though they sometimes fail to persuade the FDA to take this action.<sup>56</sup> The agency may require that the applicant conduct so-called actual use and label comprehension studies. Dual marketing of an ingredient for both prescription and OTC use is possible under limited circumstances. For instance, the agency has approved the active ingredient ibuprofen at different dosages as a prescription and as an OTC analgesic.<sup>57</sup> Of course, in the event of reduced dosage formulations, it did not take long for consumers to realize that they could self-medicate with prescription strength simply by exceeding the dose recommended in the OTC labeling.<sup>58</sup>

#### A. Experience with Internal Analgesics

Because analgesics relieve symptoms and do not purport to treat any underlying disease process, they would seem to represent natural

---

Sensitive Teeth, 624 F. Supp. 776 (N.D. Ill. 1985), *aff'd*, 826 F.2d 564 (7th Cir. 1987). Similar issues may arise with medical devices. *See, e.g.*, United States v. Snoring Relief Labs Inc., 210 F.3d 1081, 1087 (9th Cir. 2000); Gen. Med. Co. v. FDA, 770 F.2d 214, 217 & n.1 (D.C. Cir. 1985). Occasionally, the FDA accomplishes what amounts to an OTC switch from a different baseline — namely, prohibiting sale as a dietary supplement or food but allowing sale as a nonprescription drug product. *See* Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk, 69 Fed. Reg. 6788, 6793 (Feb. 11, 2004) (codified at 21 C.F.R. pt. 119); Saccharin and Its Salts, 42 Fed. Reg. 19,996, 20,004 (proposed Apr. 15, 1977) (to be codified at scattered parts of 21 C.F.R.); *see also* Patrick R. Jones, Note, *Protecting the Consumer from Getting Burned: The FDA, the Administrative Process, and the Tentative Final Monograph on Over-the-Counter Sunscreens*, 20 AM. J.L. & MED. 317, 328–29 (1994) (explaining that the FDA classified cosmetics that incorporated sunscreens as OTC drugs).

56. *See* United States v. An Undetermined Quantity of Drug Labeled as Benylin Cough Syrup, 583 F.2d 942, 944–46 (7th Cir. 1978). In connection with new animal drugs, for example, the agency has rejected Rx-to-OTC switch applications. *See, e.g.*, Am. Cyanamid Co. v. Young, 770 F.2d 1213, 1220 (D.C. Cir. 1985) (affirming the FDA's decision to reject a supplemental application for OTC marketing of the flea-killer Proban); *see also* United States v. Colahan, 635 F.2d 564, 567–68 (6th Cir. 1980) (rejecting a challenge to FDA regulations governing prescription status for animal drugs).

57. *See* Chattem, Inc. v. Heckler, Food Drug Cosm. L. Rep. (CCH) ¶ 38,339 (D.D.C. 1985), *aff'd mem.*, 787 F.2d 675 (D.C. Cir. 1986). Even more rarely, the FDA has permitted prescription marketing of an active ingredient for prescription indications while the same strength product was on the OTC market for certain other indications. *See* Advance Notice of Proposed Rulemaking, Drug Approvals: Circumstances Under Which an Active Ingredient May Be Simultaneously Marketed in Both a Prescription Drug Product and an Over-the-Counter Drug Product, 70 Fed. Reg. 52,050, 52,051 (Sept. 1, 2005).

58. *See* Emilie Le Beau, *A Dose of Caution: Whether You're Big or Small, Don't Self-Correct Drug Amounts*, CHI. TRIB., Dec. 18, 2005, at Q9 (“Forty-eight percent of people admitted to taking more than the recommended dose of an OTC drug, believing it would make the drug more effective, according to a recent survey by the National Council on Patient Information and Education.”). As health insurers have begun to demand through their coverage decisions the dispensing of higher dosage versions of prescribed drugs that patients must then split in half, *see* Tara Parker-Pope, *Health Insurers Push Pill Splitting As a Way to Save Money on Drugs*, WALL ST. J., Nov. 22, 2005, at D1, one wonders whether insurers also would encourage patients to pay out of pocket for lower dosage OTC versions (when available) and take the higher dose prescribed by their doctor.

candidates for OTC marketing.<sup>59</sup> Nonetheless, even if most consumers would not need a physician's diagnostic skills in order to decide whether to select a particular pain reliever, the safety profile of such products may justify restrictions on access. Thus, the FDA requires prescription labeling when it first approves a new analgesic product, and many of these drugs never get switched OTC.<sup>60</sup>

The agency's OTC drug review for internal analgesics began with a call for data in 1972.<sup>61</sup> Five years later, the advisory panel, which had considered forty-nine active ingredients, issued its recommendations.<sup>62</sup> More than one decade later, the FDA published a tentative final monograph ("TFM") for this OTC drug category.<sup>63</sup> In brief, this proposed rule includes aspirin and acetaminophen as permitted active ingredients and allows labeling "[f]or the temporary relief of minor aches and pains" with directions against taking the product for more than ten days, accompanied by an assortment of warning statements.<sup>64</sup> After more than thirty years, however, the OTC monograph for internal analgesics remains unfinished.<sup>65</sup>

---

59. Lars Noah, *Challenges in the Federal Regulation of Pain Management Technologies*, 31 J.L. MED. & ETHICS 55, 57 (2003); see also *United States v. Article of Drug Labeled "Decholin"*, 264 F. Supp. 473, 482 n.9 (E.D. Mich. 1967) (noting that the FDA would not limit aspirin to prescription use even though "at the root of a headache may lie anything from nervous tension to a malignant brain tumor"). On the flimsiness of the distinction between symptoms and disease, see Lars Noah, *Pigeonholing Illness: Medical Diagnosis as a Legal Construct*, 50 HASTINGS L.J. 241, 262-63 (1999).

60. See Noah, *Challenges in the Federal Regulation of Pain Management Technologies*, *supra* note 59, at 56-58. After all, Cox-2 inhibitors (e.g., Vioxx) looked like potential switch candidates because they avoided a side-effect associated with OTC analgesics (and were costing insurers a mint), see Cauchon, *supra* note 20, at 5A, but the belated discovery of cardiac risks put an end to any such possibility, see Alex Berenson et al., *Despite Warnings, Drug Giant Took Long Path to Vioxx Recall*, N.Y. TIMES, Nov. 14, 2004, § 1, at 1.

61. See Over-the-Counter Internal Analgesic and Antirheumatic Drug Products, Safety and Efficacy Review, Request for Data and Information, 37 Fed. Reg. 14,633 (July 21, 1972).

62. See Establishment of a Monograph for OTC Internal Analgesic, Antipyretic, and Antirheumatic Products, 42 Fed. Reg. 35,346 (proposed July 8, 1977) (to be codified at 21 C.F.R. pt. 343) (concluding, for instance, that a few ingredients used in then-marketed analgesics (e.g., phenacetin) were not generally recognized as safe and/or effective).

63. See Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use, Tentative Final Monograph, 53 Fed. Reg. 46,204 (proposed Nov. 16, 1988) (to be codified at 21 C.F.R. pts. 310, 343, 369).

64. See *id.* at 46,255-56. The TFM includes a number of warnings applicable to aspirin. See *id.* at 46,256 (to be codified at 21 C.F.R. § 343.50(c)). In addition, with the OTC drug review for internal analgesics still pending, the FDA promulgated a requirement that any nonprescription products containing aspirin include a special warning against use during pregnancy. See Labeling for Oral and Rectal Over-the-Counter Aspirin and Aspirin-Containing Products, Final Rule, 55 Fed. Reg. 27,776, 27,784 (July 5, 1990) (codified at 21 C.F.R. § 201.63(e)); see also Martha M. Werler et al., *Use of Over-the-Counter Medications During Pregnancy*, 193 AM. J. OBSTET. & GYNEC. 771, 776 (2005) (finding that use of aspirin by pregnant women has decreased while their use of other OTC drugs has increased); *id.* at 777 ("The common use of OTC medicines in pregnancy necessitates further studies to establish safety or to identify risks.").

65. See Regulatory Agenda, 70 Fed. Reg. 26,818, 26,839 (May 16, 2005).

Apart from this still-pending monograph process, some sponsors of analgesics approved for prescription-only sale filed supplemental NDAs requesting OTC status. Among its most prominent switches, the FDA authorized nonprescription sale of a lower dose product containing the non-steroidal anti-inflammatory drug ("NSAID") ibuprofen (e.g., Motrin).<sup>66</sup> It later switched a number of other NSAIDs, including ketoprofen and naproxen, to nonprescription status.<sup>67</sup>

OTC analgesics may pose significant risks,<sup>68</sup> which the agency generally has tried to handle through revisions in labeling. For instance, researchers have linked prolonged use of NSAIDs to sometimes fatal gastrointestinal bleeding.<sup>69</sup> In the early 1980s, the FDA became aware of a link between Reye syndrome and the use of aspirin by children suffering from viral infections,<sup>70</sup> and labels of OTC drug products containing aspirin now must include a warning of this risk.<sup>71</sup> Notably, the agency rejected suggestions urging "more drastic measures [such as] banning use of aspirin in products for individuals under 21 years of age or limiting such products to prescription use."<sup>72</sup> More recently, after it received reports of an association between acetaminophen and liver toxicity, the FDA imposed special warning requirements.<sup>73</sup>

---

66. See Irvin Molotsky, *Agency Approves Painkiller for Over-the-Counter Sales*, N.Y. TIMES, May 19, 1984, § 1, at 1. Many years later, the FDA proposed amending the TFM to add ibuprofen as a monograph ingredient. See Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use, Proposed Amendment of the Tentative Final Monograph, and Related Labeling, 67 Fed. Reg. 54,139 (proposed Aug. 21, 2002) (to be codified at 21 C.F.R. pt. 201); see also Sunscreen Drug Products for Over-the-Counter Human Use, Amendment to the Tentative Final Monograph, 61 Fed. Reg. 48,645, 48,645–46 (Sept. 16, 1996) (to be codified at 21 C.F.R. pt. 352) (issuing a similar proposal to include an ingredient in the TFM for sunscreen products after several years of OTC marketing under an NDA).

67. See Gary Mays, *Pain-Killer Wars Can Be a Pain for Ailing Consumers*, CHI. TRIB., Nov. 24, 1995, at B1.

68. See Sandra G. Boodman, *Painful Choices: Consumers Face a Baffling Wall of Choices — and a Surprising Number of Serious Risks — When They Seek Relief from Minor Pains and Illnesses in the Drug Aisle*, WASH. POST, Feb. 11, 2003, at F1; Mary Duenwald, *Choosing a Pain Remedy Carefully*, N.Y. TIMES, July 6, 2004, at F5.

69. See Noah, *Challenges in the Federal Regulation of Pain Management Technologies*, *supra* note 59, at 65 nn.19–20, 67 n.52; *id.* at 62 ("NSAIDs may . . . contribut[e] to thousands of patient deaths each year.").

70. See Proposed Labeling for Oral Aspirin-Containing Drug Products, 50 Fed. Reg. 51,400, 51,401 (proposed Dec. 17, 1985) (to be codified at 21 C.F.R. pt. 201); see also Pub. Citizen Health Research Group v. Comm'r, FDA, 740 F.2d 21, 34–35 (D.C. Cir. 1984) (remanding for lower court to consider a claim of unreasonable delay by the FDA in acting on a citizen petition urging it to require a warning of this risk); Am. Home Prods. Corp. v. Johnson & Johnson, 672 F. Supp. 135, 137–41 (S.D.N.Y. 1987) (offering a detailed account of the history behind the early Reye syndrome warning efforts).

71. See 21 C.F.R. § 201.314(h)(1) (2005).

72. Labeling for Oral and Rectal Over-the-Counter Aspirin and Aspirin-Containing Drug Products, Reye Syndrome Warning, 53 Fed. Reg. 21,633, 21,635 (June 9, 1988) (codified at 21 C.F.R. pt. 201).

73. See Over-the-Counter Drug Products Containing Analgesic/Antipyretic Active Ingredients for Internal Use, Required Alcohol Warning, 63 Fed. Reg. 56,789, 56,801–02 (Oct.

*B. Unsuccessful Switch Attempts*

The agency's mechanisms and criteria for OTC marketing also came to the fore in struggles over the need for prescription status of two other types of products: bronchodilators and exocrine pancreatic insufficiency products. In both cases, the FDA took the initiative in proposing that these drugs should be made available without a prescription. After receiving extensive feedback, the FDA decided that most bronchodilators (other than those containing metaproterenol sulfate) should be made available OTC, but that exocrine pancreatic insufficiency products should remain limited to prescription sale. These examples suggest two competing conclusions: first, that the FDA is not easily convinced that a product needs to remain in prescription status, but, second, that it may be more conservative about agency-initiated switches in the future, especially given the risk of receiving criticism from the medical community.<sup>74</sup> This Subpart then introduces some newer contested cases for comparison.

In 1982, the FDA proposed switching metaproterenol sulfate to nonprescription status.<sup>75</sup> The decision was based on nine years of safe marketing as a prescription drug (sold under the brand-name Alupent), and the fact that metaproterenol was as safe and somewhat more effective than other OTC bronchodilators (e.g., epinephrine). In response to widespread criticism received from physicians and others, the agency scheduled an advisory committee meeting to address the issue. The committee recommended against OTC availability, and the

---

23, 1998) (codified at 21 C.F.R. pt. 201) (warning against the use of internal analgesics in combination with heavy alcohol consumption); see also *Benedi v. McNeil-P.P.C., Inc.*, 66 F.3d 1378, 1387, 1389 (4th Cir. 1995) (sustaining a negligence claim and punitive damage award against the seller of Tylenol where it had delayed submitting adverse reaction reports — concerning liver toxicity resulting from interactions between acetaminophen and alcohol — to the FDA during the OTC monograph review process for internal analgesics). Even in the absence of alcohol consumption, reports of liver toxicity from accidental overdoses have increased with the expanding use of acetaminophen in combination OTC products. See Deborah Franklin, *Poisonings from a Popular Pain Reliever Are on the Rise*, N.Y. TIMES, Nov. 29, 2005, at F5; *Tylenol Misuse Seems to Climb*, WALL ST. J., Dec. 27, 2005, at D5.

74. In some instances, criticism from the medical community emerges long after the agency has authorized OTC marketing. See, e.g., Rita Rubin, *Cough Syrup Left out in the Cold: Over-the-Counter Drugs Don't Help, Report Says*, USA TODAY, Jan. 10, 2006, at 1A; see also Lars Noah, *Medicine's Epistemology: Mapping the Haphazard Diffusion of Knowledge in the Biomedical Community*, 44 ARIZ. L. REV. 373, 385, 387–89, 413–14 (2002) (explaining that rigorous new research often discredits prevailing medical wisdom).

75. See Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use, Tentative Final Monograph for OTC Bronchodilator Drug Products, 47 Fed. Reg. 47,520, 47,524 (proposed Oct. 26, 1982) (to be codified at 21 C.F.R. pt. 341); see also Spencer, *supra* note 5, at 1017 n.116 (“The FDA set precedent for initiating an Rx-to-OTC switch with the asthma drug, Alupent.”).

FDA accepted this advice.<sup>76</sup> The agency continued, however, to defend its original conclusions.

First, the FDA reiterated that adequate patient labeling could be drafted for metaproterenol sulfate products: "Whether the drug is 'safe' for OTC use is a matter of judgment, and that judgment relates to one's expectations about patient behavior. . . . FDA believes that persons who suffer from severe asthma are capable of understanding and heeding instructions for the safe use of metaproterenol sulfate."<sup>77</sup> The agency also repeated its conclusion with regard to the risk of overuse and masking of serious conditions such as a life-threatening asthmatic attack: "[T]hese patients are most likely to be under close medical supervision, and thus have the readiest access to professional advice on the appropriate use of any drugs they may be taking."<sup>78</sup> Finally, the agency dismissed the concern that children may misuse the drug if made available OTC, emphasizing that labeling set forth a clear age limitation and that parents were no less likely to abide by this restriction for OTC than for prescription products.<sup>79</sup> Notwithstanding these conclusions, the FDA explained that it "cannot fail to respect the judgment of specialists in the field who believe that OTC availability of metaproterenol sulfate metered-dose inhaler poses a health risk."<sup>80</sup>

The final monograph for bronchodilators excluded metaproterenol sulfate because of the lack of consensus about its nonprescription use.<sup>81</sup> The agency left open the possibility, however, that it might approve a supplemental NDA to switch the drug,<sup>82</sup> and it rejected comments opposed to the OTC marketing of any other metered-dose inhalers for asthma patients.<sup>83</sup> With regard to other bronchodilators,

---

76. See Metaproterenol Sulfate Metered-Dose Inhaler Drugs for Use as a Bronchodilator, Marketing Status, Proposed Rule-Related Notice, 48 Fed. Reg. 24,925, 24,926 (proposed June 3, 1983) (to be codified at 21 C.F.R. pt. 341).

77. *Id.* ("There seems to be little or no controversy about whether adequate directions for the safe use of metaproterenol sulfate can be written for lay persons. There is controversy, however, about whether patients can be depended on to follow carefully those directions.").

78. *Id.* ("Under these circumstances, the OTC availability of metaproterenol sulfate metered-dose inhaler does not appear to pose a serious threat that the patient will overuse the drug or rely inappropriately on the drug's relief-giving properties.").

79. See *id.*

80. *Id.* at 24,927; see also Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Combination Drug Products Containing Promethazine Hydrochloride, Marketing Status, Policy Statement, 54 Fed. Reg. 36,762, 36,764 (Sept. 5, 1989) (deferring to an advisory committee recommendation against the agency's proposal to allow OTC marketing of the antihistamine promethazine hydrochloride until it could resolve safety questions such as the risk of sudden infant death syndrome).

81. See Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use, Final Monograph for OTC Bronchodilator Drug Products, 51 Fed. Reg. 35,326, 35,328 (Oct. 2, 1986) (codified at 21 C.F.R. pts. 341, 369).

82. *Id.* at 35,330.

83. *Id.* at 35,327. The agency did restrict single-ingredient uses of theophylline to prescription status because it "requires careful dosage titration" in each patient. *Id.* at 35,331.

the FDA concluded that safety concerns could be adequately addressed through appropriate labeling.<sup>84</sup> These products must provide the following directions and warnings: (1) that the product be used only after a physician has diagnosed asthma, (2) that patients with active and serious asthma not rely on the product, (3) that persons with certain chronic conditions or on other medications not take the product without first consulting their physician, (4) that medical assistance should be sought immediately if symptoms are not relieved in the indicated time interval, and (5) that certain side effects may occur.<sup>85</sup>

In the OTC drug review concerning exocrine pancreatic insufficiency products (which may, for instance, be used with cystic fibrosis patients), the FDA first proposed but then rejected the idea of nonprescription marketing. A number of health professionals commented that “continuous physician monitoring of patients appears to be one of several important factors in the increased survival rates of exocrine pancreatic insufficiency patients, [so] the agency conclude[d] that such collateral measures necessary to the use of these drug products require that the[y] . . . be available by prescription only.”<sup>86</sup> These collateral measures were not required for the proper use of the drugs but instead were deemed beneficial in the treatment of the underlying disease.

Recent switch efforts have raised questions that arguably range beyond the traditional factors considered by the FDA. For instance, notwithstanding favorable internal and advisory committee recommendations, the agency repeatedly has declined to act on petitions requesting OTC status for emergency contraceptives (the so-called “morning after pill”),<sup>87</sup> though it considered the idea of an age restric-

---

84. *Id.* at 35,327.

85. See 21 C.F.R. § 341.76(c) (2005).

86. Exocrine Pancreatic Insufficiency Drug Products for Over-the-Counter Human Use, Proposed Rulemaking, 56 Fed. Reg. 32,282, 32,285 (proposed July 15, 1991) (to be codified at 21 C.F.R. pts. 310, 357). The agency had rejected a number of other seemingly compelling arguments against OTC use:

The agency reiterates its position that the requirement for a physician's diagnosis of a condition does not, by itself, necessitate prescription status of a drug as long as the patient can self-monitor the drug's effectiveness and adequate OTC labeling can be developed for the product's safe and effective use. . . . Also, the agency disagrees with the comments which stated that OTC availability of exocrine pancreatic insufficiency drug products would lead to abuse or cause harm to individuals not suffering from exocrine pancreatic insufficiency who might use the products by mistake or for some other (nonlabeled) use.

*Id.* Nonetheless, the FDA applied a broad notion of “collateral measures” to justify its decision against a switch.

87. See Marc Kaufman, *FDA: Plan B Sales Rejected Against Advice: Official Denies That Politics Blocked Contraceptive's Over-the-Counter Status*, WASH. POST, May 8, 2004, at A2. Proponents of this OTC switch even filed a judicial challenge to the agency's inac-



tion in response to fears expressed by social conservatives that readier access by teenagers would promote sexual promiscuity.<sup>88</sup> In rejecting a switch application for lovastatin, a lower-dose version of the prescription cholesterol-lowering drug Mevacor, the agency responded in part to fears that patients might fail to make critical dietary and other lifestyle changes.<sup>89</sup> Proponents of both of these switch candidates had argued that readier access would serve public health purposes — in preventing, respectively, unwanted pregnancies after contraceptive failures and in reducing the risk of cardiovascular disease. Nonetheless, the agency appeared to give these benefits short shrift relative to its more traditional focus on the potential detriments associated with OTC availability.<sup>90</sup>

---

tion. See Marc Kaufman, *Contraception Debate Delays Nomination of FDA Chief*, WASH. POST, Apr. 7, 2005, at A7.

88. See Marc Kaufman, *Compromise May Restrict "Morning-After" Pill*, WASH. POST, Apr. 8, 2004, at A2; Marc Kaufman, *FDA Delays Decision on Plan B Contraceptive*, WASH. POST, Aug. 27, 2005, at A1 ("Crawford said a formal rulemaking process would begin immediately on the question of whether a drug can be prescription-only and over the counter for different age groups . . . , though he acknowledged that several drugs with such dual status are already on the market."). The agency's request for comments asserted that no dual-marketed products differed solely according to age. See Advance Notice of Proposed Rulemaking, Drug Approvals: Circumstances Under Which an Active Ingredient May Be Simultaneously Marketed in Both a Prescription Drug Product and an Over-the-Counter Drug Product, 70 Fed. Reg. 52,050, 52,051 (Sept. 1, 2005); see also Marc Kaufman, *FDA Comment Period on "Morning-After Pill" Ends*, WASH. POST, Nov. 2, 2005, at A14 (reporting that the FDA had received as many as 10,000 comments). Nonetheless, critics pointed to nicotine gum as an example of such a product. See Gardiner Harris, *U.S. Again Delays Decision on Sale of Next-Day Pill*, N.Y. TIMES, Aug. 27, 2005, at A1. The Commissioner also suggested that teenagers might find it difficult to interpret the instructions, see *id.*, but this question would arise with any OTC drug product.

89. See Rob Stein, *Nonprescription Sales of Cholesterol Drug Rejected: FDA Panel Says Risk of Side Effects Outweighs Benefits*, WASH. POST, Jan. 15, 2005, at A3 (reporting that some members of the advisory committee expressed concerns "that many people might take the drug instead of doing other beneficial things — such as eating better and exercising more"); *id.* (noting that past switches had always involved drugs intended to treat an acute illness, while favorable action on the statin petition "would have marked the first time approval had been granted for nonprescription sale of a medication that would be taken for years to prevent a disease").

90. For the same reason, the agency presumably would not switch antimicrobials to non-prescription status. Most of these pharmaceuticals enjoy a wide margin of safety, but the agency would take into account the societal consequences of further worsening already serious problems of antibiotic resistance. See Hutt, *supra* note 31, at 435; see also Eric Kades, *Preserving a Precious Resource: Rationalizing the Use of Antibiotics*, 99 NW. U. L. REV. 611 (2005); David Brown, *Two Common Flu Drugs Called Ineffective Against Virus*, WASH. POST, Jan. 15, 2006, at A9 (reporting a similar development with antiviral drugs). In addition, though fears of an avian flu pandemic have led to calls for readier consumer access to antiviral drugs such as Tamiflu, the agency may worry about hoarding and resulting shortages. See *Shipments of Flu Drug Suspended: Tamiflu Maker Moves to Foil Hoarding, Meet Winter Demand*, WASH. POST, Oct. 28, 2005, at A2. Nonetheless, the FDA did approve the OTC drug Abreva for cold sores, and, last year, British regulators switched chloramphenicol eye drops. See Richard Wise, Letter, *Antibiotics for Acute Infective Conjunctivitis in Children*, 366 LANCET 1431 (2005).

In the face of the FDA's intransigence over switching emergency contraceptives,<sup>91</sup> state efforts to facilitate easier access to these products have included systems (referred to as collaborative practice arrangements) that allow pharmacists to dispense such drugs without first getting a physician's prescription for a particular patient.<sup>92</sup> Conversely, recent concerns about methamphetamine have prompted legislators and retailers to place OTC cough-cold products containing the methamphetamine precursor pseudoephedrine behind the counter.<sup>93</sup> Retailers also have begun to limit access to other OTC cough-cold products in response to problems with teenagers purchasing them for recreational purposes.<sup>94</sup> Perhaps it would make sense to codify the notion of a pharmacist-controlled class of drugs to serve as a transitional step between prescription and OTC status when switching a new category of prescription pharmaceuticals.<sup>95</sup> Other industrialized countries use just such an intermediate category of products,<sup>96</sup> though the FDA emphatically has rejected proposals to create a "third class" of drugs.<sup>97</sup>

---

91. Despite agency officials' protests to the contrary, politics arguably influenced the FDA's decision-making process. See Alastair J.J. Wood et al., *A Sad Day for Science at the FDA*, 353 NEW ENG. J. MED. 1197 (2005); see also Lars Noah, *A Postmodernist Take on the Human Embryo Research Debate*, 36 CONN. L. REV. 1133, 1145-46 (2004); Marc Kaufman, *Memo May Have Swayed Plan B Ruling: FDA Received "Minority Report" from Conservative Doctor on Panel*, WASH. POST, May 12, 2005, at A2.

92. See Scott S. Greenberger, *Lawmakers Override Governor's Contraception Veto*, BOSTON GLOBE, Sept. 16, 2005, at B4 (reporting that Massachusetts became the eighth state to take this route). See generally Lars Noah, *Ambivalent Commitments to Federalism in Controlling the Practice of Medicine*, 53 U. KAN. L. REV. 149, 175-76, 179-80 (2004); *id.* at 171 ("[F]ederal agencies normally designate which products require a prescription but then defer to state rules about who may issue such prescriptions."). A trend toward "conscientious objection" by pharmacists, however, may undermine such efforts to expand access. See Monica Davey & Pam Belluck, *Pharmacies Balk on After-Sex Pill and Widen Fight*, N.Y. TIMES, Apr. 19, 2005, at A1. This movement suggests yet another reason for switching emergency contraceptives to OTC status, assuming that retailers do not then take it upon themselves to limit consumer access.

93. See Margaret Webb Pressler, *Retailers Restrict Some Cold Medicines: Ingredient Can Be Used to Make Meth*, WASH. POST, May 14, 2005, at A1. Federal law now requires "behind-the-counter" status for this ingredient. See Combat Methamphetamine Epidemic Act, Pub. L. No. 109-177, tit. VII, § 711(b)(1), 120 Stat. 256, 257-61 (2006) (to be codified at 21 U.S.C. § 830(e)).

94. See Rebecca Dana, *Household Medicine Abused by the Young: Trend Alarms Activists, Officials*, WASH. POST, Oct. 8, 2004, at A1.

95. Cf. Fisher, *supra* note 44, at 594 ("Recent 'third class of drugs' efforts have arisen primarily because of the FDA's switch in recent years of many ingredients to 'nonprescription' from 'prescription' status . . ."); *id.* at 628 (concluding, however, that this would be unjustified).

96. See *id.* at 625 (noting that the U.S. "is one of the few developed countries with only two classes of drugs," but explaining that the European systems reflect peculiar customs and other factors unrelated to safety).

97. See OTC Drugs: Proposed General Conditions, 39 Fed. Reg. 19,880, 19,881 (proposed June 4, 1974) (to be codified at 21 C.F.R. pt. 330); U.S. GEN. ACCOUNTING OFFICE, No. PEMD-95-12, NONPRESCRIPTION DRUGS: VALUE OF A PHARMACIST-CONTROLLED CLASS HAS YET TO BE DEMONSTRATED 75-80 (1995) (concluding that little support exists in this country for an intermediate class of drug products available only on the recommenda-

Finally, when it considered the WellPoint petition to switch the nonsedating antihistamines, the agency repeatedly emphasized that it would disregard cost-savings (to insurers and patients).<sup>98</sup> Nonetheless, responsiveness to anticipated changes in price will have a central impact on likely changes in patterns of use (for better or for worse),<sup>99</sup> and the elasticity in demand should get factored into the equation. For instance, if consumers respond to their increased out-of-pocket costs by substituting the older (and cheaper) OTC antihistamines that cause sedation,<sup>100</sup> then more traffic accidents might result;<sup>101</sup> if, however, consumers respond by instead demanding newer (and more expensive but covered by insurance) prescription products for allergy relief, then they may encounter greater risks of side effects.<sup>102</sup>

---

tion of licensed pharmacists); Fisher, *supra* note 44, at 596 (“The federal government has often considered and has consistently rejected the establishment of a third class of drugs.”); *id.* at 596–604 (elaborating). Along similar lines, some commentators have recommended creating gradations among certain prescription drugs. See, e.g., Noah, *supra* note 10, at 654 (suggesting that only reproductive endocrinologists enjoy access to fertility drugs); Scott B. Makow, Note, *Penetrating the Walls of Drug-Resistant Bacteria: A Statutory Prescription to Combat Antibiotic Misuse*, 87 GEO. L.J. 531, 546–47 (1998) (suggesting that only infectious disease specialists in hospitals be permitted to use the latest antibiotics).

98. See Spencer, *supra* note 5, at 1002 n.16, 1018–19 n.123.

99. See Hutt, *supra* note 31, at 438–39 (“The cost of adequate professional care for the poor and the elderly will undoubtedly be a major factor in future decisions about the possibility of transferring drugs used in chronic disease from prescription to OTC status. These are valid considerations, to be encouraged rather than discouraged . . .”). The former chair of FDA’s Nonprescription Drugs Advisory Committee published an article discussing a broad range of issues relevant when considering an Rx-to-OTC switch. See Eric P. Brass, *Changing the Status of Drugs from Prescription to Over-the-Counter Availability*, 345 NEW ENG. J. MED. 810, 815 (2001) (concluding that “the overall effect on health care costs is complex”); see also Mahinka & Bierman, *supra* note 37, at 59 (“As a practical matter, the Nonprescription Drugs Advisory Committee increasingly has considered elements not closely related to safety and efficacy determinations, such as drug reimbursement, without opposition from the FDA.”); *id.* at 62 (“Some FDA Advisory Committee members have suggested that the FDA examine practical issues that are raised by a prescription-to-OTC switch, although these are not related to the legal standards of safety and efficacy . . .”).

100. See Ceci Connolly, *Allergy Pills Spark Dispute: Insurer Urges FDA to Reclassify Drugs as Over-the-Counter*, WASH. POST, May 10, 2001, at A1; Christopher Rowland, *Over-the-Counter Versions Seen Raising Costs for Insured*, BOSTON GLOBE, Jan. 31, 2004, at A1; see also Strom, *supra* note 22, at 1403 (explaining that after a switch OTC prices may exceed co-payments, so that “patients with insurance that covers medications face the paradox of increased, rather than reduced, costs for their medications”). But cf. Dennis Cauchon, *Why Allergy Drugs Cost So Much*, USA TODAY, Apr. 12, 2000, at 1A (assuming that a switch would reduce demand for sedating antihistamines).

101. Cf. Jeff Zeleny, *NTSB Says Drugs Need More Label Warnings: Drowsiness Cited as Contributing to Many Crashes*, CHI. TRIB., Nov. 15, 2001, at N24.

102. See Francesca Lunzer Kritz, *Blowing Money: Your Allergy Medications May Cost More This Year — or Be Changed Entirely*, WASH. POST, Mar. 25, 2003, at F1 (predicting that, after the Claritin switch and the resulting insurer reimbursement limits on the remaining nonsedating antihistamines, prescription nasal steroids such as Flonase may become more popular for allergy sufferers). As one commentator explained:

At first glance, a drug’s switch from prescription to OTC status seems very positive for the consumer. The change may allow her to avoid a doctor’s appointment which would save time and money, and the OTC incarnation of the drug may cost less than its prescription ver-

In short, the FDA should stop pretending that Rx-to-OTC switches turn solely on questions of a drug's intrinsic safety and efficacy. When the agency announced that it had ample authority to force an Rx-to-OTC switch over a manufacturer's objection, FDA officials pointed to their power to ensure drug safety.<sup>103</sup> Although this authority would no doubt justify switching an erstwhile OTC drug to prescription status in light of newly discovered safety concerns, it is difficult to understand how switching from prescription to OTC status would ever promote the safe use of a drug. A switch may serve any number of other valuable ends, and such a move may not present any untoward risk to the public health, but, all other things being equal, is it not inherently (even if only marginally) safer to use a pharmaceutical under the supervision of a health care professional?<sup>104</sup> Thus, in deciding whether to switch a drug, the FDA must openly confront a wide range of factors while not losing sight of its primary obligation to promote the public health.

### III. LIABILITY CONSEQUENCES OF A SWITCH

Pharmaceutical manufacturers may resist OTC switches for reasons other than loss of revenue. In particular, they would face increased exposure to tort liability,<sup>105</sup> both because patterns of usage

---

sion. However, our insurance and tax systems make the switch to OTC status disadvantageous for many consumers.

Rook, *supra* note 7, at 110. As a consequence, patients may seek out more expensive (but covered and/or tax deductible) — and perhaps less safe or effective — prescription substitutes. *See id.* at 109, 112–13 & n.25; Gina Kolata, *There's a Blurry Line Between Rx and O.T.C.*, N.Y. TIMES, Dec. 21, 2003, § 4, at 3; *see also* Niteesh K. Choudry & Jerry Avorn, *Over-the-Counter Statins*, 142 ANNALS INTERNAL MED. 910, 912 (2005) (worrying that less affluent patients may lose access to valuable preventive therapies in the wake of an Rx-to-OTC switch).

103. *See* Kaufman, *supra* note 19 (“FDA officials . . . rested their conclusion, in part, on the FDA’s legal authority to regulate the safety of all drugs, including whether or not they require a doctor’s prescription to ensure the protection of patients.”).

104. *See* Brass, *supra* note 99, at 814–15 (“[I]t is assumed that the role of the health care professional as an intermediary in the process of making drugs available to patients increases the likelihood that the drugs will be used appropriately and decreases the risk of inappropriate use . . . .”); *cf. supra* note 86 and accompanying text (using an expansive notion of “collateral measures” in rejecting an Rx-to-OTC switch of exocrine pancreatic insufficiency products). The agency must, however, resist the temptation to use prescription status simply as a mechanism for inducing physician visits to promote patient welfare more generally. *See* Hutt, *supra* note 31, at 438 (“It is doubtful, indeed, that the prescription status of many drugs can be justified in the future solely on the basis of the physician’s need to monitor the progress of the patient.”).

105. *See* Temin, *supra* note 3, at 353 (speculating that pharmaceutical manufacturers are not “anxious to increase their [liability] exposure by selling powerful drugs on the over-the-counter market”); *id.* at 356 (“[D]rug companies are exceedingly sensitive to the costs of being sued for the apparently negligent marketing of their products.”); Daniel W. Whitney, *Product Liability Issues for the Expanding OTC Drug Category*, 48 FOOD & DRUG L.J. 321, 349 (1993) (predicting that a switch to OTC status “may be accompanied by a greater frequency of personal injury claims”).

would change in ways that present heightened risks of inappropriate use and because of differences in the applicable tort doctrine. For instance, courts typically apply a forgiving design defect standard to prescription drug products.<sup>106</sup> Sellers of nonprescription drugs, however, receive no such protection.

In addition, the learned intermediary doctrine substantially limits the availability of inadequate warning claims against sellers of prescription drugs by imposing a duty to warn only health care professionals. When drug products can be purchased without a prescription, the manufacturer's duty to warn runs directly to consumers and requires that the information make sense to a layperson.<sup>107</sup> In switching a product, the FDA invariably abridges the package insert, which means that some of the risk information previously communicated to physicians will not appear on the label of the OTC drug. When a consumer then experiences such a known but undisclosed side effect, the manufacturer may find itself hard-pressed to defend against a failure-to-warn claim.<sup>108</sup>

The increasing movement of prescription pharmaceuticals to the OTC marketplace, whether at the manufacturer's behest or otherwise, may justify rethinking the stark doctrinal distinctions that have emerged.<sup>109</sup> With inadequate warning claims, the differential treatment seems inevitable — after all, FDA approval of OTC sale usually removes the learned intermediary from the selection process and turns

---

106. See *infra* notes 112–14 and accompanying text.

107. See, e.g., *O'Gilvie v. Int'l Playtex, Inc.*, 821 F.2d 1438, 1441–42 (10th Cir. 1987); *Hahn v. Sterling Drug, Inc.*, 805 F.2d 1480, 1482–83 (11th Cir. 1986). Normal rules of causation would, however, still apply and should protect manufacturers against liability claims for unsubstantiated side effects. See, e.g., *Porter v. Whitehall Labs., Inc.*, 9 F.3d 607, 614–16 (7th Cir. 1993) (ibuprofen and kidney failure); *Wade-Greaux v. Whitehall Labs., Inc.*, 874 F. Supp. 1441, 1477–85 (D.V.I. 1994) (Primatene and birth defects); cf. *Glaser v. Thompson Med. Co.*, 32 F.3d 969 (6th Cir. 1994) (finding sufficient evidence that the phenylpropanolamine in Dexatrim could have caused the plaintiff's stroke). Similarly, no liability should attach for failures to warn of previously unknowable allergic reactions. See, e.g., *Burlison v. Warner-Lambert Co.*, 842 F.2d 991 (8th Cir. 1988) (anaphylactic reaction to menthol in cough drops); *Griggs v. Combe, Inc.*, 456 So. 2d 790, 792 (Ala. 1984) (reaction to benzocaine in Vagisil).

108. See J. Warren Rissier, Note, *The FDA's Proposed Labeling Rules for Over-the-Counter Drugs and Preemption of State Tort Law*, 71 S. CAL. L. REV. 1387, 1399 (1998) (“OTC drug manufacturers are especially vulnerable to state tort lawsuits for failure to warn since ‘switch’ products will inevitably have fewer warnings on the OTC drug label than previously included on the prescription label.”); *id.* at 1399–400 (using Pepcid to illustrate); Terrence E. McCartney & Paul D. Rheingold, *From Prescription to Over-the-Counter: Watered-Down Warnings*, TRIAL, Mar. 1996, at 24; see also Noah, *supra* note 49, at 338 (describing differences in consumer and professional labeling for otherwise identical drugs).

109. See Thomas M. Moore & Scott L. Hengesbach, *Comment k: A Prescription for the Over-the-Counter Drug Industry*, 22 PAC. L.J. 43, 55 n.57, 61–86 (1990) (arguing that sellers of OTC drugs should receive the same exemption from strict liability claims granted to sellers of prescription drugs); Whitney, *supra* note 105, at 324 (“[I]t is difficult to fathom how a Rx drug would lose its social utility merely because it is being made available OTC.”).

on the agency's judgment that average consumers will manage to comprehend instructions and warnings. Even so, the relatively recent phenomenon of advertising prescription drugs directly to consumers, as well as the advent of Internet prescribing and dispensing, may have made these products more similar to OTC drugs.<sup>110</sup> It is not clear whether these changes throw into doubt the traditional protections afforded to prescription drugs, as some have argued,<sup>111</sup> or instead suggest that these protections also might extend to increasingly potent and useful nonprescription drugs.

Similar arguments might apply to design defect claims. In an earlier era, when OTC drugs offered marginal symptomatic relief and generally posed only trivial risks, it made sense to apply the same standard used for cosmetics, appliances, and other consumer goods. Now that OTC drugs may offer some genuine clinical utility accompanied by non-trivial risks, courts may conclude that these products qualify as "unavoidably unsafe" and deserve some protection from strict liability claims.<sup>112</sup> After all, the movement of a product from prescription to nonprescription status does not alter its intrinsic character so much as the means of access and the method of marketing. Nonetheless, in common with prevailing interpretations of this aspect of the *Restatement (Second) of Torts*,<sup>113</sup> the latest *Restatement* views OTC drugs as appropriately subject to the general provisions applicable to all other consumer products rather than the specialized rules governing prescription drugs.<sup>114</sup>

---

110. Indeed, now that manufacturers enjoy the freedom to advertise prescription pharmaceuticals directly to consumers (coupled with the spread of insurance coverage for prescription drugs), many of the older incentives to secure OTC status appear to have vanished.

111. See Timothy S. Hall, *Reimagining the Learned Intermediary Rule for the New Pharmaceutical Marketplace*, 35 SETON HALL L. REV. 193, 226–35, 240–44 (2004); Lars Noah, *Advertising Prescription Drugs to Consumers: Assessing the Regulatory and Liability Issues*, 32 GA. L. REV. 141, 160–61, 169–79 (1997) (canvassing and rebutting these arguments). Health care professionals may, of course, become involved in consumer decisions to use OTC drugs. See Temin, *supra* note 3, at 358–59; see also Whitney, *supra* note 105, at 329–30 (arguing that the learned intermediary rule should remain applicable in such cases).

112. See RESTATEMENT (SECOND) OF TORTS § 402A cmt. k (1965).

113. See Ruiz-Guzman v. Amvac Chem. Corp., 7 P.3d 795, 803 (Wash. 2000); Joanne Rhoton Galbreath, Annotation, *Products Liability: What Is an "Unavoidably Unsafe" Product*, 70 A.L.R.4th 16 (1989 & 2005 Supp.).

114. See RESTATEMENT (THIRD) OF TORTS: PROD. LIAB. § 2 cmt. k (1998). With regard to design defect claims, this makes sense because its specialized standard asks whether a fully informed health care professional would select a prescription drug for any class of patients. See *id.* § 6(c); see also James A. Henderson, Jr. & Aaron D. Twerski, *Drug Designs Are Different*, 111 YALE L.J. 151, 156, 170–73, 178–79 (2001) (emphasizing physician involvement to justify the distinctive doctrinal treatment of prescription drugs); *id.* at 169 ("[S]uch differentiation [in design defect standards based on users] is not possible for nonprescription products, which are available to everyone on the open market."); *id.* at 173 n.91 (conceding that, if physicians routinely acquiesced in patient demands for heavily advertised prescription drugs, "[t]his breakdown of the learned intermediary as a screening device would make marketing of prescription drugs not substantially different from that of nonprescription products"). In contrast, jurisdictions that retain the warranty-inspired con-

In addition to making drugs more vulnerable to both inadequate warning and design defect claims, switching a prescription pharmaceutical product to OTC status may prompt injured parties to pursue a peculiar theory of recovery akin to negligent marketing.<sup>115</sup> If an OTC drug with otherwise unassailable labeling and design causes an injury, then the victim might argue that the product should have been made available only under professional medical supervision and never sold directly to consumers.<sup>116</sup> Such a claim would represent something of a hybrid between more traditional defects in labeling and design, challenging a manufacturer's choice about appropriate channels for distributing potentially hazardous products in a way that resembles novel (and so far largely unsuccessful) theories asserted against gun sellers.<sup>117</sup> In particular, such claims find their closest parallel in lawsuits alleging that manufacturers of certain types of weapons or ammunition should not have sold these products to civilians, instead limiting their distribution to law-enforcement professionals and the military.<sup>118</sup>

Even if the FDA had authorized OTC marketing, a plaintiff might argue that a reasonable drug manufacturer would never have undertaken marketing directly to consumers. The manufacturer could respond by noting that it would violate federal law to sell an OTC drug

---

sumer expectations test may apply it to judge design defect claims against OTC products. See, e.g., *Haddix v. Playtex Fam. Prods. Corp.*, 138 F.3d 681, 684–86 (7th Cir. 1998) (affirming summary judgment for a tampon manufacturer because the plaintiff could not opt to use the risk-utility test for such a simple product and her design defect claim failed under the consumer expectations test where the labeling included a clear warning of the risk of toxic shock syndrome).

115. Cf. *Hunnings v. Texaco, Inc.*, 29 F.3d 1480, 1485–87 (11th Cir. 1994) (holding that a negligence claim could proceed against the supplier of mineral spirits where it knew that a retailer packaged the chemical in used milk jugs and sold the product without warnings); Richard C. Ausness, *Will More Aggressive Marketing Practices Lead to Greater Tort Liability for Prescription Drug Manufacturers?*, 37 WAKE FOREST L. REV. 97, 133–36 (2002); *id.* at 123 (“The concept of negligent marketing is based on the notion that manufacturers should be required to market their products in a way that minimizes the risk that consumers will injure themselves or others.”); *id.* at 136 (forecasting that such claims will be brought against manufacturers of prescription drugs when patients suffer injuries as a result of dispensing by unscrupulous Internet pharmacies).

116. See *Whitney*, *supra* note 105, at 328–29 (predicting that consumers injured by a drug switched from prescription status may argue that it “was so dangerous no warning would be sufficient” and that “the drug should not be available OTC because of the need for supervision and control by a qualified physician”); cf. *Ramirez v. Plough, Inc.*, 863 P.2d 167, 177–78 (Cal. 1993) (rejecting plaintiff’s claim that defendant should not have marketed OTC children’s aspirin because of the risk of Reye syndrome).

117. See, e.g., *Merrill v. Navegar, Inc.*, 28 P.3d 116 (Cal. 2001); *Chicago v. Beretta U.S.A. Corp.*, 821 N.E.2d 1099 (Ill. 2004); *Hamilton v. Beretta U.S.A. Corp.*, 750 N.E.2d 1055 (N.Y. 2001).

118. See, e.g., *McCarthy v. Olin Corp.*, 119 F.3d 148, 152, 156–57 (2d Cir. 1997) (noting, in the course of rejecting such a claim, that the manufacturer of Black Talon bullets subsequently limited sales to professionals); *id.* at 163 (Calabresi, J., dissenting) (“Selling tanks to the armed forces is fine; selling them to the general public is, I would think, clearly negligent.”).

product with prescription labeling,<sup>119</sup> but a court nonetheless might allow such a claim to proceed on the notion that a reasonable manufacturer then would not have brought the product to market at all.<sup>120</sup> In instances where the impetus for a switch came from the FDA, perhaps a federal preemption argument might relieve the manufacturer of tort liability under these circumstances, but even in that respect sellers of nonprescription products may find themselves more exposed than sellers of prescription drugs, whether the victim asserts claims of inadequate warning, design defect, or negligent marketing. Courts have become somewhat more receptive to implied preemption arguments as a defense to tort claims involving FDA-regulated products.<sup>121</sup> With respect to OTC drugs, however, Congress made such an argument more difficult in 1997 when it amended the statute to displace state regulation but expressly saved tort claims.<sup>122</sup>

Along similar lines, retailers may face enhanced exposure to tort liability after an Rx-to-OTC switch. Pharmacists encounter only limited liability in selling prescription products, but pharmacies and other businesses that sell nonprescription drugs face the same strict liability imposed on retailers of regular consumer goods.<sup>123</sup> Indeed, retailers may have greater flexibility than manufacturers after an Rx-to-OTC

---

119. See 21 U.S.C. § 353(b)(4)(B) (2000); 21 C.F.R. § 310.200(d) (2005).

120. Cf. *Tobin v. Astra Pharm. Prods., Inc.*, 993 F.2d 528, 537–40 (6th Cir. 1993); RESTATEMENT (THIRD) OF TORTS: PROD. LIAB., § 6 cmt. f & illus. 1 (1998).

121. See *Buckman v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 347–53 (2001) (holding fraud-on-the-FDA claim involving medical device approval impliedly preempted); *R.F. v. Abbott Labs.*, 745 A.2d 1174, 1192–94 (N.J. 2000); see also Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3934–36 (Jan. 24, 2006) (codified at 21 C.F.R. pts. 201, 214, 601) (arguing that courts should impliedly preempt certain failure-to-warn claims involving prescription drugs); Lars Noah, *Rewarding Regulatory Compliance: The Pursuit of Symmetry in Products Liability*, 88 GEO. L.J. 2147, 2158–59 (2000). Courts continue to find express preemption of tort claims against sellers of medical devices, including those sold directly to consumers. See, e.g., *Papike v. Tambrands, Inc.*, 107 F.3d 737, 740–42 (9th Cir. 1997) (finding preemption for tort claims against tampon sellers).

122. See Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 412(a), 111 Stat. 2296, 2373 (codified at 21 U.S.C. § 379r (2000)); Over-the-Counter Human Drugs, Labeling Requirements, 64 Fed. Reg. 13,254, 13,272 (Mar. 17, 1999) (codified at scattered parts of 21 C.F.R.). Nonetheless, courts may still entertain implied preemption arguments. Cf. *Geier v. Am. Honda Motor Co.*, 529 U.S. 861 (2000) (rejecting express preemption because of statutory savings clause, but finding implied preemption of tort claim premised on the failure to install airbags in automobiles). Thus, an effort to use California's Proposition 65, which Congress also had saved from the operation of the express preemption clause, to require reproductive toxicity warnings on smoking cessation products foundered on the basis of implied preemption because it would frustrate the purposes underlying the FDA's decision not to mention this risk. See *Dowhal v. SmithKline Beecham Consumer Healthcare*, 88 P.3d 1, 9–11, 15 (Cal. 2004); cf. *Green v. BDI Pharms.*, 803 So. 2d 68, 74–75 (La. Ct. App. 2001) (finding express preemption of failure-to-warn claim involving OTC ephedrine product, ignoring entirely the impact of the savings clause).

123. See, e.g., *Morales v. Am. Home Prods. Corp.*, 214 F. Supp. 2d 723, 726 (S.D. Tex. 2002); see also RESTATEMENT (THIRD) OF TORTS: PROD. LIAB. § 6(e) & cmt. h (1998); David J. Marchitelli, Annotation, *Liability of Pharmacist Who Accurately Fills Prescription for Harm Resulting to User*, 44 A.L.R.5th 393 (1996 & 2005 Supp.).



switch when it comes to regulating consumer access to such products, as demonstrated by chains that opted for behind-the-counter sales of drugs containing pseudoephedrine,<sup>124</sup> which may make them more vulnerable to negligent marketing claims if they fail to adopt such safeguards.

#### IV. AGENCY “PRECEDENT” AS AN OBSTACLE

The previous discussion of tort liability applies with equal force to switches that manufacturers initiate and those that they resist, though it offers another explanation for hesitation about premature OTC marketing.<sup>125</sup> This Part focuses on the potential legal objections to involuntary switches. In connection with the FDA’s consideration of the WellPoint petition, observers repeatedly alluded to the “unprecedented” nature of the case.<sup>126</sup> If understood to connote an objection to (rather than praise for) the agency’s initiative, then this point can mean one of two things. First, a departure from settled FDA precedent may raise concerns about administrative procedure. Second, and more interestingly, a constitutional concern may underlie the objection to “unprecedented” agency action insofar as it raises a potential takings problem. Even if valid, one or both of these concerns would not forever disable FDA initiatives to force Rx-to-OTC switches, but they could present serious obstacles for the inaugural attempt, and a regime countenancing agency-initiated (and manufacturer resisted) switches may have adverse consequences for pharmaceutical innovation in the future. This Part takes up each of these variants of the precedent-based objection in turn.

---

124. See *supra* note 93 and accompanying text. Only once before has the manufacturer of an OTC drug created a “behind-the-counter” system of distribution. See Francesca Lunzer Kritz, *Over the Counter but Not Easy to Reach*, WASH. POST, Oct. 8, 2002, at F3 (Mucinex).

125. In addition, an Rx-to-OTC switch also affects regulatory jurisdiction over advertising of these products: the FDA has the authority to supervise advertising for prescription drugs, see 21 U.S.C. § 352(n) (2000), while the Federal Trade Commission (“FTC”) supervises nonprescription drug marketing, see Memorandum of Understanding Between Federal Trade Commission and the Food and Drug Administration, 36 Fed. Reg. 18,539 (Sept. 16, 1971); *Thompson Med. Co. v. FTC*, 791 F.2d 189, 192–93 (D.C. Cir. 1986) (holding that the FDA’s review of labeling claims for OTC drugs did not prevent an FTC enforcement action against OTC drug product advertising). Although the Commission’s standards offer somewhat greater flexibility than those of the FDA, it also may impose more sweeping sanctions for regulatory infractions. See *Novartis Corp. v. FTC*, 223 F.3d 783, 786–89 (D.C. Cir. 2000) (rejecting a challenge to a corrective advertising order for a nonprescription analgesic product); *FTC v. Pantron I Corp.*, 33 F.3d 1088, 1097–103 (9th Cir. 1994) (suspending an enforcement action for false advertising against the seller of a baldness remedy).

126. See, e.g., Spencer, *supra* note 5, at 999, 1003–04, 1022, 1027, 1033; see also Marc Kaufman, *Staff Scientists Reject FDA’s Plan B Reasoning*, WASH. POST, June 18, 2004, at A2 (reporting that internal reviewers called the agency’s rejection of this switch petition unprecedented).

### A. Procedural Constraints

Although administrative agencies enjoy tremendous leeway in construing their enabling statutes and implementing regulations, they face some outer limits on the freedom to shift gears.<sup>127</sup> Principles of *stare decisis* operate much more weakly than they do in the judicial context,<sup>128</sup> but agencies cannot change position entirely at whim.<sup>129</sup> At the very least, courts demand that regulators explain the rationale for departures from precedent.<sup>130</sup> Although the FDA enjoys largely unreviewable discretion in exercising its enforcement powers,<sup>131</sup> courts have chastised the agency when it acts inconsistently in regulating similarly-situated products.<sup>132</sup> If, however, the FDA can offer a cogent explanation for taking a novel approach to a regulatory issue, then courts will defer to its expertise.<sup>133</sup>

Whatever its obligations to explain a departure from settled practice, an Rx-to-OTC switch initiated by the agency at the very least might trigger a statutory right to a hearing. Although the FDA may prevail on a sponsor to revise the labeling of a previously approved

127. See Lars Noah, *Divining Regulatory Intent: The Place for a "Legislative History" of Agency Rules*, 51 HASTINGS L.J. 255, 290–99 (2000).

128. See *NLRB v. Wyman-Gordon Co.*, 394 U.S. 759, 766 (1969) (plurality) (alluding to “the qualified role of *stare decisis* in the administrative process”); Richard J. Pierce, Jr., *Reconciling Chevron and Stare Decisis*, 85 GEO. L.J. 2225, 2237 (1997) (“Both courts and agencies rely on some version of *stare decisis*, but agencies generally are more willing to depart from precedent than are courts.”).

129. See Lars Noah, *The FDA's New Policy on Guidelines: Having Your Cake and Eating It Too*, 47 CATH. U. L. REV. 113, 130–35 (1997).

130. See *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 41–43 (1983); *Orion v. FCC*, 131 F.3d 176, 181 (D.C. Cir. 1997) (“Although the Commission is not necessarily bound by its prior decisions, particularly in cases where it must weigh the public interest and the equities in an individualized fashion, the Commission is bound to provide an explanation when it departs from a clear precedent.”); *Ins. Premium Fin. Ass'n v. N.Y. State Dep't of Ins.*, 668 N.E.2d 399, 403 (N.Y. 1996) (explaining that courts “impose[] a *stare decisis* constraint on administrative agencies requiring them to explain inconsistent [adjudicatory] decisions”).

131. See *Heckler v. Chaney*, 470 U.S. 821, 831–32 (1985).

132. See *United States v. Diapulse Corp. of Am.*, 748 F.2d 56, 61–62 (2d Cir. 1984); *Rhodia, Inc. v. FDA*, 608 F.2d 1376, 1379 (D.C. Cir. 1979); *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 28 (D.D.C. 1997); *United States v. Undetermined Quantities of an Article of Drug Labeled as "Exachol,"* 716 F. Supp. 787, 795 (S.D.N.Y. 1989). *But cf.* *United States v. Sage Pharm., Inc.*, 210 F.3d 475, 480 (5th Cir. 2000) (holding that the FDA could target one firm for selling unapproved new drugs even though it had not yet acted against others who distributed substantially similar products).

133. In the course of deferring to the agency, one court noted:

FDA conceded that it had never before approved a new biological drug on the basis of a clinical study of a “comparable” drug, but FDA demonstrated by reference to public documents that the principle of comparability was not unknown and that, in fact, it had been previously applied in other situations.

*Berlex Labs., Inc. v. FDA*, 942 F. Supp. 19, 25 (D.D.C. 1996).

drug, especially to reflect newly discovered risk information,<sup>134</sup> a demand to remove the prescription restriction looks more like the partial withdrawal of the license.<sup>135</sup> In the case of new drugs, the FDA's enabling statute grants a sponsor the right to demand an evidentiary hearing before the agency withdraws an NDA.<sup>136</sup> The statute also spells out the grounds that would justify such an action, typically the discovery of some new information casting doubt on the agency's original findings of safety and effectiveness.<sup>137</sup> Although the agency clearly enjoys the authority to remove prescription restrictions unilaterally when that would serve the public health,<sup>138</sup> a desire to improve consumer access and reduce prices (or at least reduce the expenses borne by health insurers) probably would not suffice. In short, a drug manufacturer facing an involuntary Rx-to-OTC switch may have valid objections — both procedural and substantive — if the FDA summarily alters this central aspect of the labeling that it had approved at the time of original licensure.

### B. Constitutional Infirmities

Apart from these arguable deviations from the statute, an involuntary Rx-to-OTC switch may well trigger constitutional objections. It might promote clarity to understand such switches as a two-step process: the FDA revokes the NDA for the original drug, which carried prescription labeling, but offers to issue a new (though financially less desirable) license for an OTC version of the same drug as a substitute.<sup>139</sup> It also could be understood as tantamount to revoking a license

---

134. See, e.g., Thomas M. Burton & Gardiner Harris, *Bristol-Myers Squibb Must Label Serzone with Liver Warning*, WALL ST. J., Dec. 7, 2001, at B4; Jennifer Corbett Dooren, *FDA Will Label Two Eczema Salves for Cancer Risk*, WALL ST. J., Mar. 11, 2005, at B6.

135. See *infra* notes 139–41 and accompanying text.

136. See 21 U.S.C. § 355(e) (2000); see also *Warner-Lambert Co. v. Heckler*, 787 F.2d 147, 151 (3d Cir. 1986). Only in cases of an “imminent hazard to the public health” did Congress empower the FDA to suspend a product's approval without first providing any hearing. See 21 U.S.C. § 355(e) (entitling the manufacturer to an expedited hearing after withdrawal); *Forsham v. Califano*, 442 F. Supp. 203, 207–10 (D.D.C. 1977) (sustaining the FDA's first and only attempted exercise of this authority).

137. Lars Noah, *A Miscarriage in the Drug Approval Process?: Mifepristone Embroils the FDA in Abortion Politics*, 36 WAKE FOREST L. REV. 571, 593 (2001). The sponsor of a withdrawn NDA would, of course, retain a right to seek judicial review of the basis for the FDA's decision, though courts show tremendous deference to the agency's scientific judgments. See, e.g., *Henley v. FDA*, 77 F.3d 616, 620–21 (2d Cir. 1996); *Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d Cir. 1995).

138. See 21 U.S.C. § 353(b)(3). This provision also authorizes the agency to do so “by regulation,” which seriously weakens the possibility of a procedural objection based on the failure to grant the sponsor an evidentiary hearing.

139. This way of thinking about the issue parallels inquiries about “conceptual severance” when evaluating partial takings of property. See John E. Fee, Comment, *Unearthing the Denominator in Regulatory Taking Claims*, 61 U. CHI. L. REV. 1535, 1550 (1994) (explaining that severance is inescapable); *id.* at 1537–45 (distinguishing among horizontal, vertical, temporal, and functional definitions of the targeted parcel of land); Courtney C.

several months after approval because patients and health insurers (and their representatives in Congress) complained about exorbitant pricing, but offering to reissue the NDA if the sponsor promises to lower prices by 75%.<sup>140</sup> Alternatively, imagine that the agency responds to such pressure by prematurely approving lower-priced generic copies of a newly licensed drug, ignoring any applicable patents and the market exclusivity period granted to the NDA sponsor by statute.<sup>141</sup> In either case, the innovator pharmaceutical companies that devoted tremendous resources in bringing the brand-name drugs to market would have reason to complain about unfair surprise and substantial interference in their reasonable investment-backed expectations.<sup>142</sup> Any of these scenarios should raise constitutional hackles about a deprivation of property without due process of law or confiscatory government action without just compensation.

The Supreme Court has long recognized that licenses represent a form of property protected under the Due Process Clause, at least for purposes of triggering procedural rights.<sup>143</sup> Although objections to

---

Tedrowe, Note, *Conceptual Severance and Takings in the Federal Circuit*, 85 CORNELL L. REV. 586, 592–93, 598–601 (2000). If the first hypothesized step qualifies as a “taking” by the FDA, then the second step’s quid pro quo probably would not satisfy the just compensation requirement. Cf. *Nollan v. Cal. Coastal Comm’n*, 483 U.S. 825, 833 n.2 (1987).

140. See Lars Noah, *Administrative Arm-Twisting in the Shadow of Congressional Delegations of Authority*, 1997 WIS. L. REV. 873, 883–84, 887–89, 892–93; *id.* at 933 (“[T]he FDA presumably understands that it cannot condition product approvals on voluntary price controls or charitable contributions . . . .”); see also *Forsham v. Califano*, 442 F. Supp. at 210 (upholding the FDA’s withdrawal of its approval for phenformin while allowing continued distribution to a limited class of patients); Noah, *supra* note 1, at 396–97 & n.184 (explaining that the FDA withdrew the NDA for Lotronex because of safety concerns but then negotiated with the sponsor for its return to the market under more limited circumstances); Marc Kaufman, *FDA Reapproves Bowel Drug After Pulling It for Safety*, WASH. POST, June 8, 2002, at A4 (same).

141. In connection with a program to make cheaper AIDS drugs available in developing countries, the FDA had to resort to the artifice of “tentatively” approving generic versions because the products still enjoyed patent protection. See Joyce Howard Price, *FDA to Allow Generic Version of Life-Prolonging AIDS Drug*, WASH. TIMES, July 14, 2005, at A11. Finally, one might imagine that the agency approved a new drug for two separate indications but later decided to require a revision in labeling that removed the more lucrative use, not because of any newly discovered safety or efficacy information but out of a concern that, thanks to aggressive marketing for that indication, physicians were selecting this drug instead of cheaper alternatives, thereby contributing to the overall escalation in health care costs. Cf. *Kuhn v. Sandoz Pharm. Corp.*, 14 P.3d 1170, 1174–75 (Kan. 2000) (summarizing negotiations between the FDA and the manufacturer of Parlodel that led, after the agency initiated procedures to withdraw a part of the NDA, to the removal from the originally approved labeling of the indication for the suppression of lactation).

142. See Ceci Connolly, *Price Tag for a New Drug*, WASH. POST, Dec. 1, 2001, at A10 (reporting estimates that place the average investment for an approved new drug at more than \$800 million); Peter Landers, *Cost of Developing a New Drug Increases to About \$1.7 Billion*, WALL ST. J., Dec. 8, 2003, at B4.

143. See, e.g., *Barry v. Barchi*, 443 U.S. 55, 64 (1979) (holding that an occupational license constituted property); *Dixon v. Love*, 431 U.S. 105, 112 (1977) (holding that a commercial driver’s license constituted property); *Indus. Safety Equip. v. EPA*, 837 F.2d 1115, 1122 (D.C. Cir. 1988) (“There is no question that [manufacturers] possess cognizable property interests in their respirator certifications [from the EPA].”).

FDA license withdrawals usually focus on the hearing rights defined by the statute, constitutional requirements for procedural due process remain fully applicable.<sup>144</sup> Thus, even if the agency could modify the NDA without having to comply with the procedures for withdrawal provided by statute, it might have to satisfy the right to a hearing guaranteed by the Fifth Amendment if an involuntary Rx-to-OTC switch qualified as a partial deprivation of property.

Even absent a procedural due process problem, the Takings Clause would constrain any effort to override a license to sell a pharmaceutical product. Here again the Fifth Amendment restriction applies equally to this form of intangible property.<sup>145</sup> At its most basic level, a taking occurs when the government seizes private property for public use, and courts regard such confiscatory actions as “per se” takings that entitle the owner to just compensation.<sup>146</sup> More controversially, a “regulatory taking” may occur when governmental restrictions on the use of private property drastically interfere with an owner’s reasonable investment-backed expectations.<sup>147</sup>

Licenses never represent unconditional forms of property,<sup>148</sup> however, and a license holder cannot complain if the government revokes or modifies a license on previously-specified grounds. The government remains free to regulate property without paying just compensation if it does so consistently with the existing law, which would have limited the scope of the property holder’s original expectations.<sup>149</sup> In order to present the takings issue in more concrete terms,

---

144. See *Weinberger v. Hynson Westcott & Dunning*, 412 U.S. 609, 621–22 (1973).

145. Not all interests that trigger rights to procedural due process qualify as property protected by the takings clause, but intellectual property does count. See, e.g., *Pittman v. Ch. Bd. of Educ.*, 64 F.3d 1098, 1104 (7th Cir. 1995) (“‘[P]roperty’ as used in [the takings] clause is defined much more narrowly than in the due process clauses. It encompasses real property and personal property, including intellectual property.”); Thomas W. Merrill, *The Landscape of Constitutional Property*, 86 VA. L. REV. 885, 955–60, 969–81 (2000).

146. See, e.g., *United States v. Pewee Coal Co.*, 341 U.S. 114 (1951) (involving government seizure of a coal mine to prevent a strike); *Kimball Laundry Co. v. United States*, 338 U.S. 1 (1949) (calculating just compensation for laundry temporarily seized and operated by the government during WWII); *Liggett & Myers Tobacco Co. v. United States*, 274 U.S. 215, 218–20 (1927) (taking of tobacco products for use by the armed forces during WWI).

147. See *Penn Cent. Transp. Co. v. City of New York*, 438 U.S. 104, 124 (1978) (applying a balancing approach); *Pa. Coal Co. v. Mahon*, 260 U.S. 393, 415 (1922) (“[W]hile property may be regulated to a certain extent, if regulation goes too far it will be recognized as a taking.”); see also *Lingle v. Chevron U.S.A. Inc.*, 125 S. Ct. 2074, 2082 (2005) (explaining that “our regulatory takings jurisprudence . . . aims to identify regulatory actions that are functionally equivalent to the classic taking in which government directly appropriates private property or ousts the owner from his domain”). The Court has treated the nearly complete destruction of the value of real property as a categorical regulatory taking. See *Lucas v. S.C. Coastal Council*, 505 U.S. 1003, 1015, 1019 (1992).

148. See *Barsky v. Bd. of Regents*, 347 U.S. 442, 451–52 (1954) (medical license); *FCC v. Sanders Bros. Radio Station*, 309 U.S. 470, 475 (1940) (radio broadcasting permit); see also *Prometheus Radio Project v. FCC*, 373 F.3d 372, 428 (3d Cir. 2004) (explaining that broadcast licenses do not qualify as protected property); *id.* at 430 (adding that contracting parties operating in highly regulated fields could not reasonably expect regulatory stasis).

149. As the *Lucas* Court noted in dicta:

imagine that someone has purchased a plot of land in an undeveloped area hoping to resell it as a site for a high-rise luxury apartment building but is unsure initially whether local land-use authorities will authorize this use. If the zoning board rejects the proposal, then no one can complain about a regulatory taking. Suppose, however, that the board approves the proposal but, after the owner of the land resells the plot to a developer for a premium, the board has a change of heart, prompted by an adjacent land owner with plans to build a competing apartment complex, and allows only the construction of a low-income housing complex, reducing the value of the land by 90%. In such a case, a regulatory taking may have occurred.<sup>150</sup> In connection with intangible property, the Supreme Court has held that, to the extent that a federal statute created some reasonable investment-backed expectation of confidential treatment of trade secret information filed with the EPA in connection with a pesticide registration application, the agency's unauthorized disclosure of that data amounted to a taking without just compensation.<sup>151</sup>

An NDA does more than simply entitle a company to commercialize a new drug — it grants the recipient a period of market exclusivity against generic competition. Like patents, which clearly qualify

---

[I]n the case of personal property, by reason of the State's traditionally high degree of control over personal dealings, [an owner] ought to be aware of the possibility that new regulation might even render his property economically worthless (at least if the property's only economically productive use is sale or manufacture for sale).

505 U.S. at 1027–28. When Congress amended patent laws to promote the introduction of generic pharmaceuticals, it defended the changes against retroactivity and takings objections on a variety of grounds. See H.R. REP. NO. 98-857(II), at 27–30 (1984), *reprinted in* 1984 U.S.C.A.N. 2686, 2711–14; see also Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, 65 Fed. Reg. 1000, 1041–43 (Jan. 6, 2000) (codified at 21 C.F.R. pt. 101) (explaining why restricting the types of health and nutrient content claims that sellers could make, including implied claims appearing in trademarked brand-names, did not constitute a regulatory taking).

150. See John C. O'Quinn, *Protecting Private Intellectual Property from Government Intrusion: Revisiting SmithKline and the Case for Just Compensation*, 29 PEPP. L. REV. 435, 521–22 (2002) (suggesting such an analogy in the course of evaluating whether the FDA's authorization of copyright infringement of an approved drug's labeling by a generic competitor seeking agency approval constituted a regulatory taking); *id.* at 460, 517–23 (characterizing the agency's action as an appropriation of intellectual property, but concluding that it probably would not amount to a taking). The hypothetical is not entirely fanciful. See, e.g., *A.A. Profiles, Inc. v. City of Ft. Lauderdale*, 253 F.3d 576, 579–80, 582 (11th Cir. 2001); *Town of Orangetown v. Magee*, 665 N.E.2d 1061, 1064–65 (N.Y. 1996).

151. See *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1001–04, 1010–14 (1984); see also *Nixon v. United States*, 978 F.2d 1269, 1284–87 (D.C. Cir. 1992) (finding that the government had taken without just compensation Richard Nixon's presidential papers); *Phillip Morris Inc. v. Reilly*, 113 F. Supp. 2d 129, 142–45 (D. Mass. 2000) (striking down a state law mandating the disclosure of tobacco industry trade secrets), *aff'd*, 312 F.3d 24 (1st Cir. 2002) (plurality); Robert K. Hur, Note, *Takings, Trade Secrets, and Tobacco: Mountain or Molehill?*, 53 STAN. L. REV. 447 (2000) (discussing the *Phillip Morris* litigation).

as property,<sup>152</sup> an NDA provides the sponsor with the right to exclude others and recoup its substantial investment in research and development.<sup>153</sup> When proponents of Rx-to-OTC switches forecast substantial net savings to the health care system,<sup>154</sup> those sums represent potential revenues lost to the license-holder, at least where the manufacturer did not initiate the requested switch.<sup>155</sup> In short, aside from costs shifted

---

152. See *Hartford-Empire Co. v. United States*, 323 U.S. 386, 415 (1945) (“That a patent is property, protected against appropriation both by individuals and government, has long been settled.”); *Genentech, Inc. v. Regents of the Univ. of Cal.*, 939 F. Supp. 639, 643 (S.D. Ind. 1996) (“[A] patent is a protectable property right and to permit the State to infringe that property right without redress for the patent owner would deprive that owner of property without due process of law.”).

153. See *supra* note 142; cf. *Kaiser Aetna v. United States*, 444 U.S. 164, 179–80 (1979) (explaining that, though it did not have to grant a dredging permit and create reasonable expectations of exclusive rights to use a private marina, once it did so the government could not defeat those expectations without paying just compensation to the property holder). As one commentator pointed out with regard to a *pending* license application, “when the FDA refuses to approve a drug for human medical use, it can eliminate the value of both tangible stocks of the drug and the intellectual property behind it. Few would argue that such routine regulatory conduct gives rise to a valid claim for compensation by affected property-holders.” Eduardo Moisés Peñalver, *Is Land Special? The Unjustified Preference for Land-ownership in Regulatory Takings Law*, 31 *ECOLOGICAL L.Q.* 227, 284 (2004) (footnote omitted). This entirely unremarkable proposition — namely, that pharmaceutical manufacturers that have amassed some inventory and secured patent protection nowadays fully realize that they also must secure a license from the FDA — does not, however, mean that, once it has granted such a license, the agency enjoys unlimited freedom to revoke or restrict it on grounds not previously disclosed to the holder.

154. See, e.g., Temin, *supra* note 3, at 366–68 (calculating the “consumer surplus,” a measure of the extent to which demand exceeded actual prices, generated by making remedies for the common cold available without a prescription, and concluding that “the net annual benefit of switching cough-and-cold medicines from prescription to OTC is approximately three-quarters of a billion dollars”); Peter Temin, *Costs and Benefits in Switching Drugs from Rx to OTC*, 2 *J. HEALTH ECON.* 187 (1983) (conducting a similar analysis of topical hydrocortisone).

155. Temin’s studies, however, focused on categories of drugs switched at the behest of manufacturers. Another economist calculated the out-of-pocket savings from switching two prescription non-sedating antihistamines, concluding that insurers would save approximately \$700 million annually while increasing costs to consumers by only approximately \$50 million. See Frank R. Lichtenberg, *The Expected Financial Impact of Rx-to-OTC Switches of Allegra and Zyrtec* (June 2003), [http://www.centerforindividualfreedom.org/education/lichtenberg\\_etc\\_study.pdf](http://www.centerforindividualfreedom.org/education/lichtenberg_etc_study.pdf) (assuming that the OTC prices would be 39% of the prescription prices and that volume would not change); see also Spencer, *supra* note 5, at 1009 n.60 (citing predictions of an 80% drop in prices). Those net savings, of course, represent lost revenues to the sellers of these drugs. See Susan Warner, *Should Three Drugs for Allergies Be Nonprescription?: Drugmakers Are Fighting a Proposal to Change Claritin, Allegra and Zyrtec into Over-the-Counter Medicines*, *PHILA. INQUIRER*, May 6, 2001, at C1. Separately, savings to consumers (and health insurers) resulting from reduced physician visits, see Temin, *supra* note 3, at 358 (finding that, by 1989, the FDA’s switching of cough-cold products had resulted in 1.65 million fewer visits to physicians, and concluding that this resulted in savings of almost \$70 million), represent lost revenues to health care professionals. Thus, allergists may have had selfish reasons for objecting to WellPoint’s petition to switch the non-sedating antihistamines. See Liz Kowalczyk, *Nothing to Sneeze At: Allergy Drug Debate Raises Self-Diagnosis, Cost Issues*, *BOSTON GLOBE*, May 11, 2001, at E1; see also Brass, *supra* note 99, at 815 (“[Physicians] are often concerned when drugs used in their own specialty are proposed for over-the-counter status. Depending on one’s perspec-

from insurers to patients, aggregate savings realized in switching prescription drugs to nonprescription status represent financial losses suffered by the pharmaceutical industry.

In a related vein, sponsors of NDAs for prescription drugs generally enjoy an additional right that an involuntary switch would undermine. Under the statute, a sponsor may file a supplemental approval application for any number of reasons, such as additional indications or altered dosage forms. If the FDA required the sponsor to conduct additional studies in order to support approval, then the successful applicant would receive an extra three-year period of market exclusivity.<sup>156</sup> When sponsors file supplements with supporting research in pursuit of an Rx-to-OTC switch, this right has additional value insofar as it normally would prevent altogether the marketing of generic versions of the original prescription product and entirely delay generic versions of the new OTC product for three years.<sup>157</sup> When a switch occurs at another party's behest, however, the sponsor does not receive this extension and permanently loses the opportunity to take advantage of this incentive at a later date.<sup>158</sup>

When the government grants a valuable privilege such as a license and then revokes it or renders it essentially valueless, and does so for reasons not previously announced as a basis for such action, courts may entertain a regulatory takings claim. In fact, even more clearly than claims about stranded investments in the utilities context,<sup>159</sup> one might argue that a "deregulatory taking" occurs if the

---

tive, this may be viewed as parochial self-interest on the part of a group being threatened . . . ." (footnote omitted)).

156. See *Apotex, Inc. v. Shalala*, 53 F. Supp. 2d 454, 458 & n.4 (D.D.C. 1999); Kevin J. Kraushaar, *Market Exclusivity After a Prescription to Nonprescription Drug Switch: Striking the Right Balance Between Innovation and Competition*, 54 FOOD & DRUG L.J. 243 (1999); Berenson, *supra* note 14 (reporting that Prilosec had received this additional period of marketing exclusivity); see also *Upjohn Co. v. Kessler*, 938 F. Supp. 439 (W.D. Mich. 1996) (declining to issue a preliminary injunction where the manufacturer of Rogaine failed to establish a likelihood of success on the merits of its claim that the FDA should have granted its request for market exclusivity after an Rx-to-OTC switch); *id.* at 441 n.1 (noting that Upjohn's takings claim was not before the court).

157. See *Rook*, *supra* note 7, at 122 ("[T]he period of OTC market exclusivity has allowed the drug's manufacturer to position the branded drug as the premium product in the field which helps immunize it from generic competition."); see also *SmithKline Beecham Consumer Healthcare, L.P. v. Watson Pharms., Inc.*, 211 F.3d 21, 23–24, 29 (2d Cir. 2000) (rejecting an effort by the sponsor of a switched smoking cessation product to assert a copyright claim in an effort to extend protection from generic competition beyond this additional three-year period of market exclusivity). In contrast, if the sponsor of an approved prescription drug receives market exclusivity for a supplemental indication, this would not prevent generic versions using the original labeling from entering the market and free-riding by virtue of off-label uses for the new indication. See *Sigma-Tau Pharms., Inc. v. Schwetz*, 288 F.3d 141, 145–48 (4th Cir. 2002).

158. See *Spencer*, *supra* note 5, at 1049 n.295.

159. See J. Gregory Sidak & Daniel F. Spulber, *Deregulatory Takings and Breach of the Regulatory Contract*, 71 N.Y.U. L. REV. 851, 857–62, 995–98 (1996); see also William P. Barr et al., *The Gild That Is Killing the Lily: How Confusion over Regulatory Takings Doctrine Is Undermining the Core Protections of the Takings Clause*, 73 GEO. WASH. L. REV.



FDA grants a company the exclusive right to commercialize a therapeutic invention for a specified period of time but then unilaterally alters the terms of this monopoly in a fashion that substantially erodes the value of the investment.<sup>160</sup> No taking would occur if Congress decided to deregulate the drug industry across the board by, for example, no longer requiring product licensure or physician intervention before dispensing prescription pharmaceuticals; when done on a case-by-case basis and against the backdrop of such longstanding regulatory barriers to entry, however, a manufacturer may well cry foul.<sup>161</sup>

## V. CONCLUSION

The choice between prescription and OTC distribution for a pharmaceutical product is nothing to sneeze at. Apart from the potentially enormous financial stakes for all involved — manufacturers, health insurers, and patients/consumers — the classification could

---

429, 430–36 (2005) (arguing that the failure to allow utilities to recover their investments constitutes a per se taking of private capital for public use). The drug industry lacks the features of a public utility (i.e., a command to produce and a prohibition on exit from the marketplace, *see id.* at 438–44, 491–92), but that would not grant the government license to take advantage of a manufacturer's sunken investments by, for instance, requiring charitable donations:

[A]n attempt effectively to compel the business to transfer the use of property by threatening to prevent the recovery of sunk costs . . . would occur if, for example, the government conditioned a firm's ability to sell a pharmaceutical product, in which the firm had invested a large amount, on the firm's agreement to supply some of it for free to indigents.

*Id.* at 494.

<sup>160</sup> In the context of infrastructure industries, controversy surrounds such claims for a number of reasons, particularly the point that a legislature's initial decision to create barriers to entry does not come with an assurance of permanence, so an incumbent firm cannot claim to have reasonably relied on perpetual freedom from competition when making its investment decisions. *See* Susan Rose-Ackerman & Jim Rossi, *Disentangling Deregulatory Takings*, 86 VA. L. REV. 1435, 1457–68 (2000).

<sup>161</sup> *Cf. id.* at 1483–85 (offering illustrations of cases where utilities should receive just compensation). *See generally* John E. Fee, *The Takings Clause As a Comparative Right*, 76 S. CAL. L. REV. 1003, 1007, 1060–66 (2003) (arguing that the clause protects against differential treatment of similarly situated property owners); Ronald J. Krotoszynski, Jr., *Expropriatory Intent: Defining the Proper Boundaries of Substantive Due Process and the Takings Clause*, 80 N.C. L. REV. 713, 739–40, 755–56, 768–72 (2002) (urging courts to recognize takings claims only when government regulations represent veiled exercises of the eminent domain power). It would differ little from a governmental effort at compulsory licensing of a patented product. *See* Lars Noah, *Triage in the Nation's Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs*, 54 S.C. L. REV. 741, 767–68 (2003) (discussing patent buyouts and compulsory licensing). As another set of commentators noted:

However accomplished, when the government mandates that the economic opportunities inhering in any of these forms of property are to be made available to others, such actions are appropriations [as opposed to regulations limiting an owner's use of property so as to provide a diffuse benefit to the public] and are "takings" . . .

Barr et al., *supra* note 159, at 437; *see also id.* at 469–99 (elaborating on this argument).

have profound public health consequences, either positive or negative. Given changes in both technology and the marketplace, the FDA must grapple with an increasingly difficult balancing act when manufacturers or health insurers petition the agency for an Rx-to-OTC switch. Although scientific judgments about safety and effectiveness must remain the focal point, the FDA should not entirely blind itself to the larger economic forces at play, but it also must understand statutory and constitutional limitations on the extent to which it might begin to take cost into account. For their part, manufacturers must factor the possible liability consequences into decisions about pursuing a switch to nonprescription status.