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Pharmaceutical Federalism

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Pharmaceutical Federalism*

PATRICIA J. ZETTLER†

There is growing interest in states regulating pharmaceuticals in ways that challenge the U.S. Food and Drug Administration's (FDA) federal oversight. For example, in 2013, Maine enacted a law to permit the importation of unapproved drugs, reflecting concerns that federal requirements are too restrictive, while in 2014 Massachusetts banned an FDA-approved painkiller, reflecting concerns that federal requirements are too lax. This Article provides an account of this recent state interest in regulating drugs and considers its consequences. It argues that these state regulatory efforts, and the nascent litigation about them, demonstrate that the preemptive reach of the FDA's authority extends into medical practice regulation in some circumstances. It then begins to explore implications outside of the preemption context, arguing that state regulatory efforts may also help to inform our general understanding of both the scope of the FDA's jurisdiction and the relationship between the FDA and the states.

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INTRODUCTION

The United States is facing a severe drug abuse epidemic. The Centers for Disease Control and Prevention (CDC) reported that in 2015, drug overdoses resulted in over 52,000 deaths, and overdoses have eclipsed motor vehicle crashes as the leading cause of injury-related death in the United States.¹ Contrary to what may be popular conception, FDA-approved pharmaceuticals contribute to nearly half of all overdose deaths.² And opioids (a powerful class of pain medications) are, by far, the pharmaceuticals involved in the most overdose deaths.³

Against this backdrop, in October 2013, the FDA approved Zohydro™ ER (“Zohydro”), a new high-dose opioid that lacked abuse-deterrent properties.⁴ Shortly after the FDA approved Zohydro, politicians, physicians, and FDA advisory committee members openly questioned the agency’s decision, with one physician and medical school professor describing it as “a disaster in the making.”⁵ The Fed Up

1. BEHAVIORAL HEALTH COORDINATING COMM., U.S. DEPT. OF HEALTH & HUMAN SERVS., ADDRESSING PRESCRIPTION DRUG ABUSE IN THE UNITED STATES: CURRENT ACTIVITIES AND FUTURE OPPORTUNITIES 3 (2013), http://www.cdc.gov/drugoverdose/pdf/hhs_prescription_drug_abuse_report_09.2013.pdf [<https://perma.cc/T5XY-U2JV>]; Rose A. Rudd, Puja Seth, Felicitia David & Lawrence Scholl, *Increases in Drug and Opioid Overdose Deaths—United States, 2000–2015*, CTRS. FOR DISEASE CONTROL & PREVENTION: MORBIDITY & MORTALITY WKLY. REP. (Dec. 30, 2016), <https://www.cdc.gov/mmwr/volumes/65/wr/mm655051e1.htm> [<https://perma.cc/SD94-JH7E>].

2. *Prescription Opioid Overdose Data*, CTRS. FOR DISEASE CONTROL & PREVENTION (Dec. 16, 2016), <https://www.cdc.gov/drugoverdose/data/overdose.html> [<https://perma.cc/4WG8-AHUC>]; see also Christopher M. Jones, Karin A. Mack & Leonard J. Paulozzi, *Pharmaceutical Overdose Deaths, United States, 2010*, 309 JAMA 657, 657–59 (2013) (finding that, in 2010, 57.7% of drug overdose deaths involved FDA-approved pharmaceuticals).

3. See Rudd et al., *supra* note 1. It is worth noting that there are limitations to these findings, including that many overdose deaths involve the use of more than one drug, and there is variation in information about the causes of overdose deaths (or a lack of information). *Id.* But opioid misuse is, without question, a serious public health problem, and perhaps more importantly for this Article, politicians and the public clearly perceive opioid misuse to be of grave concern. See BEHAVIORAL HEALTH COORDINATING COMM., *supra* note 1, at 3; Roni Caryn Rabin, *New Painkiller Rekindles Addiction Concerns*, N.Y. TIMES (Apr. 21, 2014, 4:50 PM), http://well.blogs.nytimes.com/2014/04/21/new-painkiller-rekindles-addiction-concerns/?_php=true&_type=blogs&_r=0 [<https://perma.cc/6UZ3-GLWP>].

4. Rabin, *supra* note 3. Various features are thought to make drugs abuse resistant. The most commonly discussed abuse-deterrent feature is designing pills to be resistant to crushing so that the drug cannot be snorted or injected for a quick, intense high. *Id.*

5. John Fauber & Kristina Fiore, *FDA OKs High-Dose Narcotic Painkiller Zohydro, Raising Abuse Concerns*, MILWAUKEE WIS. J. SENTINEL (Oct. 28, 2013), <http://www.jsonline>

Coalition, a drug addiction advocacy group, started a Change.org petition to pressure the FDA to withdraw Zohydro's approval.⁶ And twenty-eight state attorneys general, from states across the political spectrum, wrote a letter to the FDA Commissioner asking that she reconsider the drug's approval.⁷

Once Zohydro's manufacturer began to sell the drug in March 2014, concerns about the drug not only intensified, but also motivated state action.⁸ In a highly unusual move, the governor of Massachusetts acted to prohibit the "prescribing and dispensing" of Zohydro until it was reformulated to deter abuse—effectively banning an FDA-approved drug within the state's borders.⁹ This prohibition, however, was

.com/watchdog/watchdogreports/fda-oks-high-dose-narcotic-painkiller-zohydro-raising-abuse-concerns-b99128369z1-229484621.html [https://perma.cc/5Z6Q-DZ7W].

6. Fed Up Coal., *Reconsider Approval of Dangerous New Opioid Zohydro*, CHANGE.ORG, <https://www.change.org/p/reconsider-approval-of-dangerous-new-opioid-zohydro> [https://perma.cc/2KT5-J5XP].

7. Letter from Nat'l Ass'n of Att'ys. Gen. to Margaret Hamburg, Comm'r, U.S. Food & Drug Admin. (Dec. 10, 2013), <https://web-beta.archive.org/web/20160821174802/http://www.oag.state.md.us/press/zohydro.pdf>. The FDA's 2013 decision to approve Zohydro obviously was widely criticized. But, to be clear, this Article does not examine whether those criticisms were justified. Indeed, there were also those who argued that FDA's decision to approve Zohydro in 2013 was the appropriate one. In particular, at the time of its approval, Zohydro was the only marketed drug that contained the active ingredient hydrocodone (an opioid) without also containing acetaminophen (the active ingredient in Tylenol®, among other drugs). Acetaminophen overdose is the leading cause of acute liver failure in the United States, and acetaminophen-induced liver injury is a serious problem that the FDA and public health advocates have long worked to address (albeit one that results in far fewer deaths per year than opioid overdoses do). Zohydro offered a hydrocodone option for patients without the risks of acetaminophen, which some viewed as particularly important for patients with liver problems. *See* Prescription Drug Products Containing Acetaminophen; Actions To Reduce Liver Injury From Unintentional Overdose; Notice, 76 Fed. Reg. 2691, 2692–93 (Jan. 14, 2011); Lars Noah, *State Affronts to Federal Primacy in the Licensure of Pharmaceutical Products*, 2016 MICH. ST. L. REV. 1, 3–5; Michael Ollove, *Fearing Abuse, States Challenge FDA on Painkiller Approval*, PEW CHARITABLE TR.: STATELINE (Apr. 28, 2014), <http://www.pewtrusts.org/en/research-and-analysis/blogs/stateline/2014/04/28/fearing-abuse-states-challenge-fda-on-painkiller-approval> [https://perma.cc/43AB-TSPC]; *cf.* Alison Bateman-House & Arthur Caplan, *Don't Throw Out Compassion in the War Against Opioid Abuse*, STAT (June 9, 2016), <https://www.statnews.com/2016/06/09/opioid-abuse-compassion/> [https://perma.cc/WTW3-8MPZ] (highlighting the medical value of opioids).

8. *See, e.g.,* Rita Rubin, *Critics Oppose FDA Approval of Painkiller Zohydro*, WEBMD (Feb. 27, 2014), <http://www.webmd.com/pain-management/news/20140226/new-painkiller-zohydro-criticized> [https://perma.cc/G2J5-BG6F].

9. *Zogenix, Inc. v. Patrick*, No. 14-11689-RWZ, 2014 WL 1454696, at *1 (D. Mass. Apr. 15, 2014). Numerous media reports described Massachusetts's action as the first state ban on an FDA-approved drug. *See, e.g.,* Brady Dennis, *U.S. Judge Set To Rule on Drug Firm's Suit Against Massachusetts for Painkiller Ban*, WASH. POST (Apr. 13, 2014), http://www.washingtonpost.com/national/health-science/2014/04/13/4d8c5424-c189-11e3-bcec-b71ee10e9bc3_story.html [https://perma.cc/625C-9YKL]. But that description does not fully capture the history of state regulation. Most clearly, as Lars Noah has explained, the Tennessee Board of Medical Examiners prohibited the prescribing of two FDA-approved diet drugs in the 1990s, before the FDA ultimately withdrew the drugs' approval. *See* Noah, *supra* note 7, at 21–22. In addition, several states banned the sale and distribution of FDA-approved

short-lived. A federal judge enjoined the ban in April 2014, reasoning that it was preempted by the Federal Food, Drug, and Cosmetic Act (FDCA).¹⁰

The Massachusetts Zohydro ban is just one example of a recent surge in states regulating drugs that are subject to federal oversight by the FDA.¹¹ As with the Zohydro ban, some of these state efforts have involved attempts to impose requirements stricter than the federal ones—reflecting concerns that FDA oversight is too lax. For instance, Vermont, and, after its Zohydro ban was enjoined, Massachusetts, imposed restrictions on the use of Zohydro that fell short of an outright ban but still went beyond federal requirements.¹² And California enacted a law in 2004 that was intended to secure the drug supply chain, by imposing requirements significantly more stringent than the federal ones then in place.¹³

On the other hand, states have also attempted to establish policies more permissive than federal ones—reflecting concerns that FDA oversight is too restrictive. For example, in 2013, Maine enacted a law to permit the importation of unapproved drugs from certain countries (which a judge subsequently concluded was preempted by federal law).¹⁴ At the time of writing, over thirty states have passed “right-to-try” laws that are intended to permit terminally ill patients to access unapproved drugs.¹⁵

contraceptives in 1960. *Id.* at 16–17. Those state bans, however, were enacted before Congress established the modern FDA drug approval regime, based on both safety and effectiveness, in 1962. (And were eventually struck down.) There are also several examples of state restrictions on, or ultimately unsuccessful attempts to ban, FDA-approved drugs. For instance, after the FDA approved mifepristone for terminating pregnancies in 2000, a bill was proposed in Oklahoma that would have banned that drug within the state. But it was not enacted. *See* H.B. 1038, 48th Leg., 1st Sess. (Okla. 2001); Noah, *supra* note 7, at 18–19. Additionally, since 1962, there have been a number of state laws that restrict access to human drugs (but fall short of a total ban) and a few state bans on drugs intended for use in food-producing animals that the FDA was considering, but had not yet approved. *See* Noah, *supra* note 7, at 17–27. The 2014 Massachusetts ban on Zohydro, therefore, is not the first state ban on an FDA-approved prescription drug. It is, nevertheless, unusual.

10. *See Zogenix*, 2014 WL 1454696, at *2.

11. *See infra* Part II.B.; *see also* Noah, *supra* note 7 (analyzing state efforts to ban FDA-approved drugs, focusing on the Zohydro ban). This Article uses the terms “pharmaceutical” and “drug” to include both traditional small molecule drugs and biologic therapies. But for simplicity, the Article focuses its discussion of statutory language on the language in the FDCA. *See FDA 101: Regulating Biological Products*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048341.htm> [<https://perma.cc/6BCX-6XZQ>] (last updated Nov. 18, 2015).

12. Milton J. Valencia, *Mass. Limits Use of the Potent Painkiller Zohydro*, BOS. GLOBE (Apr. 23, 2014), <https://www.bostonglobe.com/metro/2014/04/22/governor-deval-patrick-administration-enacts-new-restrictions-zohydro/GpIZM4OUOgZg7cWEI8XV5N/story.html> [<https://web-beta.archive.org/web/20170314124611/http://www.bostonglobe.com/metro/2014/04/22/governor-deval-patrick-administration-enacts-new-restrictions-zohydro/GpIZM4OUOgZg7cWEI8XV5N/story.html>].

13. *See* 2004 Cal. Stat. 6459.

14. *Ouellette v. Mills*, 91 F. Supp. 3d 1, 12 (D. Me. 2015).

15. Melissa Healy, *Dying Patients Want Easier Access to Experimental Drugs. Here's Why Experts Say That's Bad Medicine.*, L.A. TIMES (Mar. 14, 2017, 3:00 AM), <http://www.latimes.com/science/sciencenow/la-sci-right-to-try-medicines-20170314-story.html> [<https://perma.cc/247D-LMPY>].

And twenty-eight states, as well as the District of Columbia, Puerto Rico, and Guam, have enacted “comprehensive” laws to allow the use of marijuana for medical purposes, without regard to whether the FDA has approved marijuana for such purposes (or whether such laws are consistent with the federal Controlled Substances Act).¹⁶ These examples, though not exhaustive, demonstrate the range of state efforts that indirectly, and in some cases directly, challenge federal drug regulation.¹⁷

This Article provides an account of this recent state interest in regulating drugs and explores how it informs our understanding of the scope of the FDA’s authority and the relationship between state and federal drug regulation. The “crucial distinction between product and practice regulation” is the cornerstone of federalism in pharmaceutical regulation.¹⁸ That is, courts, lawmakers, and the FDA itself have long opined that state jurisdiction is reserved for medical *practice*—the activities of physicians and other health care professionals—and federal jurisdiction for medical *products*, including drugs.¹⁹ This view of the appropriate roles for state and federal regulation arises in part from both a longstanding recognition of the states’ authority to regulate medical practice pursuant to their police powers and an appreciation for the benefits of national uniformity in drug regulation.²⁰

The recent surge in drug regulation challenges this practice-products distinction, and as other commentators have recently observed, litigation over these new state regulatory efforts may provide fresh insights about the preemptive effects of the FDA’s authority.²¹ This Article argues that one such insight is that the preemptive

16. *State Medical Marijuana Laws*, NAT’L CONF. ST. LEGISLATURES (Mar. 16, 2017), <http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx> [<https://perma.cc/DMR9-ESAL>].

17. In practice, patients’ concerns often cut across many of the areas that these state laws target. For example, an article in *Wired* described a father’s attempts to obtain an unapproved marijuana product to treat his son’s recalcitrant epilepsy, raising questions about medical marijuana, seriously ill patients’ access to unapproved drugs, and drug importation, among other things. Fred Vogelstein, *Boy, Interrupted*, WIRED (July 2015), <http://www.wired.com/2015/07/medical-marijuana-epilepsy> [<https://perma.cc/4Z2A-DNJY>].

18. BJ Evans, *Distinguishing Product and Practice Regulation in Personalized Medicine*, 81 CLINICAL PHARMACOLOGY & THERAPEUTICS 288, 288 (2007).

19. See, e.g., *id.* at 288; Barbara J. Evans, *Seven Pillars of a New Evidentiary Paradigm: The Food, Drug, and Cosmetic Act Enters the Genomic Era*, 85 NOTRE DAME L. REV. 419, 500 (2010); Lars Noah, *Ambivalent Commitments to Federalism in Controlling the Practice of Medicine*, 53 KAN. L. REV. 149, 154–71 (2004); Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 SAN DIEGO L. REV. 427, 430–31 (2015). As I have done elsewhere, see Zettler, *supra*, at 430 n.7, in this Article I use a broad definition of the phrase “practice of medicine,” including within that phrase the practice of pharmacy, the practice of dentistry, and other health-related practices that states have traditionally regulated. Likewise, when I use the term “medical practitioners,” I refer to physicians, dentists, pharmacists, and other health care professionals authorized to independently practice medicine.

20. See, e.g., *Dent v. West Virginia*, 129 U.S. 114, 122–23, 128 (1889); DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA 73–75 (2010).

21. See Nathan A. Brown & Eli Tomar, *Could State Regulations Be the Next Frontier for Preemption Jurisprudence?: Drug Compounding as a Case Study*, 71 FOOD & DRUG L.J. 271 (2016); Noah, *supra* note 7, at 2–3; Catherine M. Sharkey, *States Versus FDA*, 83 GEO. WASH.

reach of the FDA's authority is broader than the practice-products distinction suggests. The Massachusetts ban on Zohydro and the Maine importation law provide instructive examples. Each was framed in terms of medical practice oversight, regulating the activities and licensing of medical practitioners, which is generally considered to be outside of the FDA's purview.²² Nevertheless, federal judges concluded that both state efforts were impliedly preempted by the FDA's regulatory regime.²³

The history of U.S. drug regulation suggests that the porousness of the practice-products distinction revealed by the recent surge in state drug regulation is not a new phenomenon. But the continued—and perhaps amplified—blurriness of the practice-products distinction is particularly important in today's regulatory environment because new technologies are also challenging the distinction. The FDA's hotly contested attempts to assert jurisdiction over innovative medical technologies, such as regenerative medicine and genetic testing, have sparked debates about whether those technologies are services that are part of medical practice, or are medical products.²⁴ The thinness of the practice-products binary, revealed by state drug regulation, thus may inform questions about the scope of the FDA's authority.

Beyond the practice-products distinction, the possibility that courts will conclude that the FDA's extensive oversight preempts state regulation raises the question of why states use their limited resources to enact and defend drug laws and regulations.²⁵ This question is further underscored by the fact that some state laws that are not preempted may, as a practical matter, have a limited impact on the pharmaceutical market. State efforts to enact policies more permissive than the FDA's do not free parties from their obligations to comply with federal requirements in many instances, and the pharmaceutical industry may have little interest in disturbing the primacy of FDA regulation.²⁶ The result is that both the legal and practical impact of at least some state regulatory efforts may be equivocal.

This Article suggests that one reason that states may, nevertheless, find value in drug regulation is because it may be a useful strategy for driving federal policy. That is, states may not be functioning as neutral innovators—"laboratories for new ideas,"

L. REV. 1609, 1613 (2015); cf. Lindsay F. Wiley, *Deregulation, Distrust, and Democracy: State and Local Action To Ensure Equitable Access to Healthy, Sustainably Produced Food*, 41 AM. J.L. & MED. 284, 286 (2015) (discussing four recent cases involving state and local food regulation "to discuss the foundational legal challenges faced by diverse food reformers"); Diana R. H. Winters, *The Benefits of Regulatory Friction in Shaping Policy*, 71 FOOD & DRUG L.J. 228 (2016) (examining the policy implications of state action in the areas of food and marijuana regulation).

22. See *Ouellette v. Mills*, 91 F. Supp. 3d 1, 9 (D. Me. 2015); *Zogenix, Inc. v. Patrick*, No. 14-11689-RWZ, 2014 WL 1454696, at *1 (D. Mass. Apr. 15, 2014).

23. *Ouellette*, 91 F. Supp. 3d at 12; *Zogenix, Inc.*, 2014 WL 1454696 at *2.

24. See, e.g., PAUL D. CLEMENT & LAURENCE H. TRIBE, LABORATORY TESTING SERVICES, AS THE PRACTICE OF MEDICINE, CANNOT BE REGULATED AS MEDICAL DEVICES 11 (2015), <http://www.acla.com/wp-content/uploads/2015/01/Tribe-Clement-White-Paper-1-6-15.pdf> [<https://perma.cc/9DAR-MTZ4>]; Usha Lee McFarling, *FDA Moves To Crack Down on Unproven Stem Cell Therapies*, STAT (Feb. 8, 2016), <http://www.statnews.com/2016/02/08/fda-crackdown-stem-cell-clinics> [<https://perma.cc/979P-2R6T>].

25. See *infra* Part III.

26. See *infra* Part III.

in the language of traditional federalism rhetoric.²⁷ Instead, states may be regulating to motivate the federal government to adopt particular policies. Put another way, even ineffectual laws and regulations may be a mechanism for states to “make[] Congress [and the FDA] . . . more honest and democratically accountable regulator[s].”²⁸ Scholars have made such arguments with respect to state regulation in other areas, including, perhaps most notably, environmental regulation.²⁹ But state drug regulation offers a new context, with a particularly powerful federal regulator, in which to examine these state pressures on federal policy.

To develop these arguments, this Article proceeds in three parts. Part I explains how federal drug regulation, and indeed the FDA itself, emerged as a response to state regulation. It also examines decades of line drawing between federal and state drug regulation, demonstrating that difficulty distinguishing between medical practice and medical products regulation is longstanding. Part II analyzes the preemptive effects of the FDA’s regulatory scheme on recent state efforts to regulate drugs, arguing that the preemptive reach of the FDA’s authority extends into state regulation of medical practice in some circumstances. Finally, Part III begins to consider the lessons to be learned from recent state drug regulation outside the preemption context. This Part first argues that the blurriness of the practice-products distinction, highlighted by state regulation, can inform debates about the proper scope of the FDA’s jurisdiction. This Part then starts to examine whether, even when state regulation is preempted or otherwise fails to significantly affect the practices of the drug industry, states may nevertheless find regulation a useful strategy for influencing federal policy.

I. THE FDA AS A RESPONSE TO STATE REGULATION

Today, the federal government rigorously regulates drugs—drugs generally cannot be sold, prescribed, or dispensed to patients until the federal government determines that they are safe and effective.³⁰ The federal government, however, did not

27. Erwin Chemerinsky, *The Values of Federalism*, 47 FLA. L. REV. 499, 525 (1995).

28. Roderick M. Hills, Jr., *Against Preemption: How Federalism Can Improve the National Legislative Process*, 82 N.Y.U. L. REV. 1, 4 (2007); see also Miriam Seifter, *States as Interest Groups in the Administrative Process*, 100 VA. L. REV. 953, 955–56 (2014) (describing other means that states use to influence agencies); Catherine M. Sharkey, *Federalism Accountability: “Agency-Forcing” Measures*, 58 DUKE L.J. 2125, 2170–72 (2009) (same); Winters, *supra* note 21 (describing the benefits of “regulatory friction” between states and the federal government in the areas of food and controlled substances).

29. See, e.g., J.R. DeShazo & Jody Freeman, *Timing and Form of Federal Regulation: The Case of Climate Change*, 155 U. PA. L. REV. 1499, 1509–10 (2007); see also Heather K. Gerken & Ari Holtzblatt, *The Political Safeguards of Horizontal Federalism*, 113 MICH. L. REV. 57, 91 (2014) (“In environmental-law scholarship, . . . ‘defensive preemption[]’ [is] used to describe how state spillovers reverse industry opposition to broadly popular legislation and thus break up congressional gridlock.”).

30. See 21 U.S.C.A. § 355(d) (Westlaw through Pub. L. No. 114-255). Federal law defines “drugs” broadly as products that are intended to diagnose, cure, mitigate, treat, or prevent disease, or to affect the structure or function of the body. 21 U.S.C.A. § 321(g)(1) (Westlaw through Pub. L. No. 114-255).

always have such extensive authority over drugs.³¹ In fact, as Part I.A explores, contrary to conventional wisdom, there is a long history of state drug regulation. Federal regulation emerged, in part, as a response to this history of disparate state laws.

A. *The Emergence of the FDA*

“[O]ur Nation has long expressed interest in drug regulation,” and that interest was evident within the states (and colonies) well before the FDA was created.³² Interestingly, many of these early state and colonial efforts to regulate drugs reflected ideas about drug contamination and misbranding that continue to permeate drug law today.³³ More importantly, early state regulation also demonstrated that the boundary between medical practice and medical products—which is thought to serve as a dividing line between federal and state jurisdiction today³⁴—has long been blurry.

Courts and historians have identified a 1736 law, enacted by the Colony of Virginia, as the first U.S. drug legislation.³⁵ The law required medical practitioners to disclose the ingredients in the drugs that they dispensed.³⁶ In other words, the *first* U.S. legislation intended to regulate drugs (and identified by the D.C. Circuit as doing so) was, in fact, a medical practice law—it restricted the activities of the medical practitioners who dispensed drugs, rather than regulating the labeling of the drugs themselves.³⁷

And many early state drug laws that followed were also framed as medical practice laws. As one example, in 1808, the Territory of Orleans enacted the first U.S.

31. See, e.g., CARPENTER, *supra* note 20, at 1–32.

32. *Abigail All. for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 703 (D.C. Cir. 2007).

33. Cf. John P. Swann, *Food and Drug Administration*, in *A HISTORICAL GUIDE TO THE U.S. GOVERNMENT* 248, 249 (George T. Kurian & Joseph P. Harahan eds., 1998) (“Adulteration and misbranding of foods and drugs had long been a fixture in the American cultural landscape . . .”).

34. See, e.g., Zettler, *supra* note 19, at 429–31.

35. E.g., *Abigail All.*, 495 F.3d at 703–04; GLENN SONNEDECKER, KREMERS AND URDANG’S HISTORY OF PHARMACY 158 (4th ed. 1976); see also Seema Shah & Patricia Zettler, *From a Constitutional Right to a Policy of Exceptions: Abigail Alliance and the Future of Access to Experimental Therapy*, 10 YALE J. HEALTH POL’Y L. & ETHICS 135, 140–51 (2010) (describing courts’ analysis of drug regulation history in the *Abigail Alliance* litigation). Wallace F. Janssen, a historian at the FDA, also identified “An Act Respecting Chirurgions, Midwives and Physicians,” enacted in Massachusetts in 1649 and in New York in 1684, as a precursor law that evinced the public’s desire for drug legislation because it was passed with the objective of assuring safe and effective treatments for patients. The law was explicitly a medical practice law—it required practitioners to adhere to “known, approved rules of art” unless they had consulted with qualified experts and obtained consent from the patient. Wallace F. Janssen, *America’s First Food and Drug Laws*, 30 FOOD DRUG COSM. L.J. 665, 669–70 (1975).

36. See SONNEDECKER, *supra* note 35, at 158.

37. *Abigail All.*, 495 F.3d at 703–04. The law was also substantively consistent with current federal law. The Federal Food, Drug, and Cosmetic Act and FDA regulations require that a drug’s labeling reveal its ingredients. 21 U.S.C.A. § 352(e) (Westlaw through Pub. L. No. 114-255); 21 C.F.R. § 201.10 (2016).

legislation addressing drug adulteration.³⁸ It prohibited pharmacists from knowingly or intentionally selling drugs that were “injured, moulded, discomposed, or sophisticated.”³⁹ Numerous states followed suit, passing medical practice laws that prohibited pharmacists from knowingly or intentionally selling adulterated drugs, rather than regulating the drugs’ safety directly by, for example, requiring that the drugs themselves not be contaminated.⁴⁰ Yet, as with the 1736 Virginia law, both the D.C. Circuit and historians have characterized these as drug regulation laws despite their focus on the activities of medical practitioners.⁴¹

In parallel to these state efforts, interest in federally regulating drugs also began to develop. In 1813, Congress passed the Vaccine Act, the first federal consumer protection law for drugs, to ensure that physicians inoculated patients against smallpox with “genuine vaccine matter.”⁴² A mere nine years later, however, this foray into federal drug regulation ended when the newly created federal vaccine office mistakenly provided incorrect vaccine matter to a physician, several patients contracted smallpox and died as a result, and Congress repealed the law.⁴³

But recognition of the need for national drug regulation continued to grow despite this setback. In 1820, eleven delegates of state medical societies met in Washington,

38. David L. Cowen, *The Development of State Pharmaceutical Law*, 37 PHARMACY HIST. 49, 54 (1995). In addition to prohibiting the sale of adulterated drugs, the law required that pharmacists have a diploma and pass a test before dispensing any drugs, and subsequent, similar laws also generally required that pharmacists inform patients of the risks of particularly dangerous drugs. See SONNEDECKER, *supra* note 35, at 182–84; Cowen, *supra*, at 54–55.

39. Cowen, *supra* note 38, at 54. Contemporary federal law likewise prohibits drug adulteration, albeit with a significantly broader definition of what constitutes adulteration. 21 U.S.C. § 351 (2012).

40. See SONNEDECKER, *supra* note 35, at 216; Glenn Sonnedecker & George Urdang, *Legalization of Drug Standards Under State Laws in the United States of America*, 8 FOOD DRUG COSM. L.J. 741, 746 (1953).

41. See *Abigail All.*, 495 F.3d at 703–04; SONNEDECKER, *supra* note 35, at 158.

42. Vaccine Act of 1813, ch. 37, §§ 1–2, 2 Stat. 806 (repealed 1822); John P. Swann, *FDA’s Origin*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm124403.htm> [<https://perma.cc/5FVD-96XA>] (last updated June 23, 2014); see also Lars Noah, *Triage in the Nation’s Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs*, 54 S.C. L. REV. 371, 401 (2002). The official title of the law was “An Act to Encourage Vaccination.” 2 Stat. at 806. When Congress passed it, vaccination was a new phenomenon. The world’s first vaccination—against smallpox—was performed in 1796 in England, and the first U.S. smallpox vaccination was performed several years later. These early smallpox vaccinations involved exposing patients to cowpox. Because cowpox is a virus closely related to smallpox, exposure and subsequent immunity to cowpox also conferred immunity to smallpox. See Alexandra Minna Sterns & Howard Markel, *The History of Vaccines and Immunization: Familiar Patterns, New Challenges*, 24 HEALTH AFF. 611, 612–14 (2005). Shortly after physicians began to vaccinate patients in the United States, there were at least two incidents in which physicians used the wrong material to vaccinate patients—exposing patients to smallpox instead of cowpox—each leading to dozens of smallpox cases and fatalities. See Abbas M. Behbehani, *The Smallpox Story: Life and Death of an Old Disease*, 47 MICROBIOLOGICAL REVS. 455, 480 (1983). Congress enacted the 1813 law to address such problems.

43. David P. Currie, *The Vaccine Agent*, 1 GREEN BAG 245, 248–49 (1998); Noah, *supra* note 42, at 401.

D.C., for the first U.S. Pharmacopeia (USP) convention.⁴⁴ The goal of the USP was, and continues to be, to set quality standards for drugs.⁴⁵ Although the USP standards were not (and still are not) a government document, it represented an attempt to develop national standards for drug quality, and it has been recognized in federal law since Congress passed the Import Drug Act of 1848.⁴⁶ The Import Drug Act, in turn, represented the federal government's second foray into drug regulation.⁴⁷ Passed in response to concerns about contaminated foreign drugs coming into the country, the law required that all imported drugs be examined and, if found to be adulterated, stopped at the border.⁴⁸

For over fifty years, while the Import Drug Act remained the only federal law regulating drugs,⁴⁹ states continued to enact laws primarily to address intentional or knowing drug adulteration that was injurious to patients. By 1870, at least twenty-five states and territories had such laws.⁵⁰ Consistent with earlier state regulation, these were often medical practice laws, regulating the activities of drug dispensers rather than the drugs themselves.⁵¹ In the late 1800s, state regulation evolved when New Jersey enacted the first law that adopted a broader definition of adulteration—one that, like federal law today, did not require knowledge or intent on the part of the drug dispenser, nor injury to the drug recipient.⁵² And a number of other states, including New York, Massachusetts, and Michigan, followed New Jersey by enacting laws with broader definitions of adulteration.⁵³ But overall there was little consistency—James Harvey Young, a food and drug historian, described drug regulation

44. SONNEDECKER, *supra* note 35, at 261.

45. *About USP*, U.S. PHARMACOPEIAL CONVENTION, <http://www.usp.org/about-usp> [<https://perma.cc/CCA3-SS35>].

46. *See* Import Drug Act of 1848, ch. 70, § 3, 9 Stat. 237, 238 (repealed 1922); SONNEDECKER, *supra* note 35, at 261; *USP Milestones—A Timeline*, U.S. PHARMACOPEIAL CONVENTION, <http://www.usp.org/about/history-information-center/usp-milestones-timeline> [<https://perma.cc/F3W6-GXHN>].

47. *See* Wesley J. Heath, *America's First Drug Regulation Regime: The Rise and Fall of the Import Drug Act of 1848*, 59 FOOD & DRUG L.J. 169, 170 (2004).

48. § 3, 9 Stat. at 237–38. Today, the FDA similarly has authority to inspect and detain imported drugs that appear to be adulterated or otherwise in violation of the law. 21 U.S.C. § 381(a) (2012).

49. *See, e.g.*, Abigail All. for Better Access to Developmental Drugs v. von Eschenbach, 495 F.3d 695, 704–05 (D.C. Cir. 2007). In 1862, the federal Division of Chemistry, which became the Bureau of Chemistry in 1901 and is considered the predecessor to the FDA, was created. The Bureau, however, focused only on food until it established a drug division in 1903. *See, e.g.*, Terry S. Coleman, *Origins of the Prohibition Against Off-Label Promotion*, 69 FOOD & DRUG L.J. 161, 163–64 (2014).

50. SONNEDECKER, *supra* note 35, at 216; *see also* Sonnedecker & Urdang, *supra* note 40, at 746–50.

51. *See* SONNEDECKER, *supra* note 35, at 216.

52. Sonnedecker & Urdang, *supra* note 40, at 747–48; *see also* Lewis A. Grossman, *Food, Drugs, and Droods: A Historical Consideration of Definitions and Categories in American Food and Drug Law*, 93 CORNELL L. REV. 1091, 1098 n.42 (2008) (explaining that the New Jersey law mirrored National Board of Trade model legislation); *cf.* 21 U.S.C. § 351 (2012) (setting out the current federal adulteration standard).

53. Sonnedecker & Urdang, *supra* note 40, at 746; Cowen, *supra* note 38, at 54.

at the turn of the twentieth century as a “chaos of divergent and sometimes ludicrously severe state laws.”⁵⁴

This chaos—as well as two public health crises—led to significant movement toward nationwide consistency when Congress passed two federal laws regulating medicines: the Biologics Act of 1902 and the Pure Food and Drugs Act of 1906.⁵⁵ The Biologics Act of 1902 was enacted after biological diphtheria treatments contaminated with tetanus killed five children in Missouri and contaminated smallpox vaccines killed nine children in New Jersey.⁵⁶ The law required that sellers of therapeutic biological products certify that they properly prepared the products before marketing.⁵⁷ The 1902 Biologics Act, thus, was the first law creating a gatekeeping role for the federal government, albeit in a limited way and for a narrow set of drugs.⁵⁸

Although the Biologics Act was the first to create a drug approval role for the government, it is the Pure Food and Drugs Act of 1906 that is credited with establishing the FDA.⁵⁹ Reports about food contamination in Upton Sinclair’s *The Jungle*, rather than a scandal related to drugs, created the political will to pass the law.⁶⁰ But support for federal oversight of drugs had been building, and the law prohibited the sale of both food *and* drugs that were adulterated or misbranded.⁶¹

The Pure Food and Drugs Act was an important milestone in federal drug regulation, but it did not end state regulation.⁶² Instead state regulation, arguably, became more uniform, with two-thirds of states passing laws that mirrored the new federal law.⁶³ Yet a robust market of unsafe and fraudulent drugs persisted, with over 50,000 “quack” products being sold, producing over \$100 million in annual sales.⁶⁴ Indeed,

54. JAMES HARVEY YOUNG, *PURE FOOD: SECURING THE FEDERAL FOOD AND DRUGS ACT OF 1906*, at 292 (1989).

55. *See, e.g.*, CARPENTER, *supra* note 20, at 75.

56. *See, e.g.*, PHILIP J. HILTS, *PROTECTING AMERICA’S HEALTH: THE FDA, BUSINESS, AND ONE HUNDRED YEARS OF REGULATION* 69 (2003).

57. Biologics Act of 1902, ch. 1378, § 1, 32 Stat. 728, 728–29.

58. *See* CARPENTER, *supra* note 20, at 75; Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1758 n.10 (1996).

59. *See, e.g.*, Merrill, *supra* note 58, at 1758.

60. *See, e.g.*, JAMES HARVEY YOUNG, *THE TOADSTOOL MILLIONAIRES: A SOCIAL HISTORY OF PATENT MEDICINES IN AMERICA BEFORE FEDERAL REGULATION* 239 (1961).

61. Pure Food and Drugs Act of 1906, ch. 3915, §§ 1–2, 34 Stat. 768, 768. As an example of the increasing support for federal drug regulation, in 1903 Dr. Harvey W. Wiley, then-Chief Chemist of the Bureau of Chemistry and a champion of the Pure Food and Drugs Act, established a drug division within the Bureau. *See* YOUNG, *supra* note 60, at 234–39.

62. States may have continued to be interested in drug regulation in part because the Pure Food and Drugs Act had significant limitations. For example, it did not authorize premarket review of drugs, and only claims that misrepresented the ingredients in a drug would misbrand it. False or misleading claims about the safety or effectiveness of a drug, for example, were not prohibited. *See* § 7, 34 Stat. at 769–70; *United States v. Johnson*, 221 U.S. 488, 498–99 (1911).

63. *See* Sonnedecker & Urdang, *supra* note 40, at 751. A minority of states, including New York, Massachusetts, Michigan, and Illinois, retained laws inconsistent with federal law. *Id.*

64. CARPENTER, *supra* note 20, at 77–78.

in its 1910 report, the American Pharmaceutical Association's Committee on Drug Reform noted the following:

The importance of the National Food and Drugs Law of 1906 need not be impressed on pharmaceutical men, nor the benefit already realized from it and from the numerous State Laws that have been modeled largely upon it. Yet every pharmacist knows that adulteration has by no means been eliminated since these laws have been enforced. It might seem to many that these laws have operated more to expose the extent of adulteration than perceptibly to check it.⁶⁵

Given this state of affairs, it is unsurprising that adulterated drugs soon caused a public health scandal. In 1937, a Tennessee company used diethylene glycol to make a liquid form of sulfanilamide, an antibiotic.⁶⁶ Diethylene glycol was used as a solvent because of its sweet taste, but it is toxic.⁶⁷ At the time, federal and state laws did not require any premarket safety testing, and the company shipped the drug throughout the country without first conducting such testing.⁶⁸ As a result, over one hundred people, including many children, died after taking the drug.⁶⁹

And tragedy again led to legislative change. In 1938, Congress passed the FDCA.⁷⁰ The law expanded federal authority over drugs in several ways.⁷¹ Most importantly, the law created a category of “new drug[s]”—drugs that are not generally recognized as safe and effective, or that have not been marketed to a material extent and for a material time—and required that companies give the FDA time to assess a new drug's safety before it is marketed.⁷² That is, the FDCA shifted the FDA's role “from policeman to gatekeeper.”⁷³

Although the FDA's role was far more limited under the 1938 law than it is today—for example, it was not until 1962 that the companies were required to

65. *Report of Committee on Drug Reform*, 5 BULL. OF THE AM. PHARMACEUTICAL ASS'N 652, 652 (1910).

66. *See Sulfanilamide Disaster*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/aboutfda/whatwedo/history/productregulation/sulfanilamidedisaster/default.htm> [<https://perma.cc/T3CR-M9LV>] (last updated Oct. 7, 2010).

67. *Id.* Diethylene glycol is a compound used to make antifreeze. *See, e.g.*, Jeanna M. Marraffa, Michael G. Holland, Christine M. Stork, Christopher D. Hoy & Michael J. Hodgman, *Diethylene Glycol: Widely Used Solvent Presents Serious Poisoning Potential*, 35 J. EMERGENCY MED. 401 (2008).

68. *See Sulfanilamide Disaster*, *supra* note 66.

69. *Id.*

70. *See, e.g.*, Merrill, *supra* note 58, at 1761–63. For a more extensive history of the passage of the FDCA, see, for example, CHARLES O. JACKSON, *FOOD AND DRUG LEGISLATION IN THE NEW DEAL* (1970) and Vincent A. Kleinfeld, *Legislative History of the Federal Food, Drug, and Cosmetic Act*, 1 FOOD DRUG COSM. L.Q. 532 (1946).

71. *See, e.g.*, Merrill, *supra* note 58, at 1761–63.

72. Federal Food, Drug, and Cosmetic Act, ch. 675, §§ 201(p), 505(a), 52 Stat. 1040, 1041–42, 1052 (1938); Merrill, *supra* note 58, at 1761–63. The FDA's gatekeeping role is still limited to “new drug[s].” *See* 21 U.S.C.A. § 321(p) (Westlaw through Pub. L. No. 114-255); 21 U.S.C.A. 355(a) (Westlaw through Pub. L. No. 114-255).

73. Merrill, *supra* note 58, at 1776.

demonstrate both the safety *and* effectiveness of their drugs to obtain approval—the passage of the FDCA marks the beginning of federal drug regulation that resembles the gatekeeping of the modern FDA.⁷⁴ As with the federal legislation preceding it, however, it did not mark the end of state drug regulation.⁷⁵

B. Drug Regulation in the Modern Era

Since the FDCA was enacted, the FDA's authority over drugs has steadily expanded, and the Agency's gatekeeping role is now far from its only one. Indeed, the FDA now regulates drugs throughout their entire lifecycles in myriad ways, and this federal regulation continues to intersect with state regulation.

1. The FDA

Today the FDA's mission with respect to drugs is two-fold: it *protects* the public health by assuring the safety, efficacy, and quality of drugs that are marketed; and, it *promotes* the public health by helping to make drugs available and to make sure that the public has the necessary information to properly use those drugs.⁷⁶ The most well-known mechanism through which the FDA accomplishes this mission is its gatekeeping function—new drugs cannot be marketed without the FDA's approval.⁷⁷ To approve a brand-name drug, the FDA must determine that the drug is safe and effective for its proposed indication, that the proposed labeling is not false or misleading, and that the manufacturing practices used to make the drug are adequate to assure its quality.⁷⁸ The drug's safety and effectiveness must be demonstrated by “substantial evidence,” which generally consists of data from “adequate and well-controlled” clinical trials.⁷⁹ The FDA also approves generic new drugs, but through an abbreviated process based on evidence demonstrating a generic drug's similarity to the relevant brand-name drug.⁸⁰

Whether a company seeks approval of a brand-name or generic drug, it does not simply submit an application and wait for the FDA's assessment of the immense amounts of data and information in the application.⁸¹ Rather, the drug development

74. See, e.g., *id.* at 1761–63, 1764–68.

75. See, e.g., Ole Salthe, *State Food, Drug and Cosmetic Legislation and Its Administration*, 6 LAW & CONTEMP. PROBS. 165, 165 (1939).

76. See *What We Do*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/aboutfda/whatwedo> [<https://perma.cc/6TUN-7MNX>] (last updated Oct. 24, 2016).

77. 21 U.S.C.A. § 355(a).

78. *Id.* § 355(d). This Article uses the term “brand-name drug” to refer to drugs approved under a new drug application, pursuant to 21 U.S.C.A. § 355(b).

79. *Id.*; 21 C.F.R. § 314.126 (2016). In addition to reviewing new drug applications, the FDA also conducts “pre-approval inspections” of drug manufacturers to verify the authenticity, reliability, and accuracy of data in the application, and confirm that manufacturing practices comply with the FDA's requirements. See, e.g., FDA, COMPLIANCE PROGRAM GUIDANCE MANUAL § 7346.832 (2010).

80. See 21 U.S.C.A. § 355(j).

81. For a description of the content of a new drug application, see 21 C.F.R. § 314.50 (2016).

and approval process often involves significant communication between the FDA and a drug company.⁸² The FDA also frequently consults with outside experts during the approval process—through advisory committee meetings, in which drug companies and the public also participate.⁸³ When the FDA decides to approve a new drug, it publishes a lengthy document describing the data and information supporting approval, and a quick perusal of any of these “approval packages” demonstrates the depth in which the FDA examines drugs during the approval process.⁸⁴ In other words, the FDA’s approval decisions are both comprehensive and somewhat collaborative.

But it is worth emphasizing that when the FDA approves a drug, it does not make a determination that the drug is generally safe and effective. Instead, the FDA approves a drug as safe and effective only for the particular uses recommended in the approved labeling—that is, to treat a particular disease or condition, in a particular patient population, at a particular dose.⁸⁵ Once the FDA has approved a drug for a particular indication, however, medical practitioners can generally prescribe the drug for any purpose, including unapproved uses (known as “off-label” uses).⁸⁶

Although the FDA’s authority to approve drugs is critical to its public health mission, that role is just one of many ways that the agency regulates drugs. Its authorities are manifold and cover the entire lifecycle of a drug, from the beginning stages of research through its use after approval.⁸⁷ For example, before a drug’s approval, FDA regulates clinical trials and certain other research with the drug and prohibits promotion of the drug.⁸⁸ As another example, in addition to assessing the manufacturing practices for a drug at the time of its approval, the FDA requires that drugs be manufactured in compliance with “current good manufacturing practice” throughout their lifespan.⁸⁹ As a third example, after a prescription drug’s approval, the FDA oversees

82. See 21 C.F.R. § 314.102(a) (2016) (“During the course of reviewing an application[,] . . . FDA shall communicate with applicants about scientific, medical, and procedural issues that arise”); OFFICE OF INSPECTOR GEN., DEP’T OF HEALTH & HUMAN SERVS., OEI-01-01-00590, FDA’S REVIEW PROCESS FOR NEW DRUG APPLICATIONS ii (2003) (“FDA works collaboratively with sponsors.”).

83. See, e.g., OFFICE OF INSPECTOR GEN., *supra* note 82, at 10–11.

84. See 21 C.F.R. § 314.430(e) (2016).

85. See, e.g., Rebecca Dresser & Joel Frader, *Off-Label Prescribing: A Call for Heightened Professional and Government Oversight*, 37 J.L. MED. & ETHICS 476, 476 (2009).

86. See, e.g., *id.*

87. Scholars have also suggested that FDA drug regulation extends to certain areas beyond traditional public health concerns, such as patent litigation. See, e.g., Jacob S. Sherkow, *Administrating Patent Litigation*, 90 WASH. L. REV. 205, 216–17 (2015) (arguing that the FDA “acts as a litigation gatekeeper” for patent litigation).

88. 21 U.S.C.A. § 355(i) (Westlaw through Pub. L. No. 114-255); 21 C.F.R. pts. 312, 320 (2016). The FDA also regulates clinical investigations of approved drugs. 21 C.F.R. § 312.2.

89. 21 U.S.C. § 351(a)(2)(B) (2012) (“A drug . . . shall be deemed to be adulterated . . . if . . . the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform . . . with current good manufacturing practice”); see also W. Nicholson Price II, *Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing*, 55 B.C. L. REV. 491, 512–22 (2014) (discussing pre- and postapproval good manufacturing requirements).

its advertising and promotion.⁹⁰ In fact, the most-discussed area of the FDA's postapproval regulation may be its position that promoting off-label uses leads to violations of the FDCA.⁹¹

In sum, the FDA's role as a gatekeeper for drugs is vital to its public health mission. But gatekeeping is only one aspect of FDA regulation. The FDA regulates drugs across their life cycle in numerous, different ways, under numerous different authorities that have evolved over time and intersect with state efforts to regulate drugs.⁹²

2. The States

In light of the comprehensive system of FDA drug regulation, federal regulation is now generally characterized as dominant in this area.⁹³ This characterization, while fair, may obscure the continued role of states in drug regulation.⁹⁴ As this Part demonstrates, state drug regulation has evolved from its historical prominence to largely consist of tort law schemes and state Food, Drug, and Cosmetic Acts that complement or parallel FDA regulation.

State tort law has been described as the primary means through which states regulate drugs.⁹⁵ Commentators, and the FDA itself, have explained that state products

90. See 21 C.F.R. pt. 202 (2016).

91. For a detailed description of the statutory provisions and regulations underlying this ban on off-label promotion, see, for example, Nathan Cortez, *The Statutory Case Against Off-Label Promotion*, 83 U. CHI. L. REV. ONLINE 124 (2016). For only a small selection of recent articles covering this topic written by both scholars and practitioners, see Ryan Abbott & Ian Ayres, *Evidence and Extrapolation: Mechanisms for Regulating Off-Label Uses of Drugs and Devices*, 64 DUKE L.J. 377, 379 (2014); Alan Bennett, Freddy Jiménez, Larry Eugene Fields & Joshua Oyster, *Back to First Principles: A New Model for the Regulation of Drug Promotion*, 2 J.L. & BIOSCIENCES 168, 179–89 (2015); Stephanie M. Greene, *After Caronia: First Amendment Concerns in Off-Label Promotion*, 51 SAN DIEGO L. REV. 645, 646 (2014); Aaron S. Kesselheim & Michelle M. Mello, *Prospects for Regulation of Off-Label Drug Promotion in an Era of Expanding Commercial Speech Protection*, 92 N.C. L. REV. 1539, 1541 (2014); Gerald Masoudi & Christopher Pruitt, *The Food and Drug Administration v. The First Amendment: A Survey of Recent FDA Enforcement*, 21 HEALTH MATRIX 111, 114–15 (2011); Lars Noah, *Truth or Consequences?: Commercial Free Speech vs. Public Health Promotion (at the FDA)*, 21 HEALTH MATRIX 31 (2011); Christopher Robertson, *When Truth Cannot Be Presumed: The Regulation of Drug Promotion Under an Expanding First Amendment*, 94 B.U. L. REV. 545, 546 (2014); Rodney A. Smolla, *Off-Label Drug Advertising and the First Amendment*, 50 WAKE FOREST L. REV. 81 (2015); James M. Spears, Jeffrey K. Francer & Natalie A. Turner, *Embracing 21st Century Information Sharing: Defining a New Paradigm for the Food and Drug Administration's Regulation of Biopharmaceutical Company Communications with Healthcare Professionals*, 70 FOOD & DRUG L.J. 143 (2015).

92. Cf. Elizabeth Y. McCuskey, *Body of Preemption: Health Law Traditions and the Presumption Against Preemption*, 89 TEMPLE L. REV. 95, 135 (2016) (describing FDA, NIH, Medicare, and Medicaid involvement in medical products regulation, concluding “[r]egulation of medical products is thus heavily and historically federal”).

93. See, e.g., *id.* at 131–35.

94. Cf. Zettler, *supra* note 19, at 474–77 (making a similar argument with respect to the federal government's longstanding regulation of medical practice).

95. See, e.g., David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts To Preempt Failure-To-Warn Claims*, 96 GEO. L.J. 461, 462–63 (2008); see also

liability schemes complement FDA regulation by providing a mechanism for privately policing postapproval drug safety and compensating injured patients.⁹⁶ Because of the FDA's extensive oversight of drug design and manufacturing, injured patients have generally sued drug manufacturers for inadequate labeling.⁹⁷ Indeed, injured patients have brought a "steady stream" of failure-to-warn cases against prescription drug manufacturers.⁹⁸ Yet, as discussed further in Part II below, recent Supreme Court opinions have significantly limited the circumstances in which such claims are available against generic drug manufacturers.

In addition to products liability regimes, states also have long had their own Food, Drug, and Cosmetic Acts that impose requirements parallel to the federal FDCA.⁹⁹ Today, the majority of states with these laws have adopted the Uniform State Food, Drug, and Cosmetic Act, which was created in 1984 by the Association of Food and Drug Officials (AFDO), the primary organization for state food and drug officials.¹⁰⁰ The AFDO was formed to foster uniformity among state food and drug laws, and its model Uniform Act includes a provision to automatically incorporate into state law changes to the federal FDCA—to produce state laws that are identical to one another and federal law.¹⁰¹ In reality, however, there is some variation between state Food, Drug, and Cosmetic Acts both because not all states have adopted this provision, and because not all states have adopted the Uniform Act.¹⁰²

Efthimios Parasidis, *Patients over Politics: Addressing Legislative Failure in the Regulation of Medical Products*, 2011 WIS. L. REV. 929, 933 ("Given the limitations of FDA review, tort law has traditionally served as a complementary means of regulating medical products and an additional layer of consumer protection.").

96. See, e.g., Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985, 67,988–89 (proposed Nov. 13, 2013) [hereinafter Generic Drug Labeling Proposed Rule]; Kessler & Vladeck, *supra* note 95, at 475–76. As Kessler and Vladeck explain, the FDA did, however, go through a period of time during President George W. Bush's administration in which it asserted that state tort law, rather than complementing FDA regulation, "threaten[ed] [the agency's] ability to protect the public health." *Id.* at 463.

97. See, e.g., Brief for the United States as Amicus Curiae Supporting Petitioner at 12, *Mutual Pharm. Co. v. Bartlett*, 133 S. Ct. 2466 (2013) (No. 12-142) ("[T]he FDCA would preempt a pure design-defect claim where . . . the claim does not require the plaintiff to prove that the manufacturer knew or should have known of new and scientifically significant evidence that rendered the drug 'misbranded' under federal law.").

98. Kessler & Vladeck, *supra* note 95, at 462.

99. See, e.g., FDA, INVESTIGATIONS OPERATIONS MANUAL § 3.3.3 (2016), <https://www.fda.gov/downloads/ICECI/Inspections/IOM/UCM497756.pdf> [<https://perma.cc/77Y7-JVS5>]; see also *supra* Part I.A; cf. Matt Lamkin, *Regulating Identity: Medical Regulation as Social Control*, 2016 BYU L. REV. 501, 539 (2016) ("[S]tates regulate controlled substances in ways that mirror the federal [Controlled Substances Act].").

100. See FDA, *supra* note 99; *About*, ASS'N OF FOOD & DRUG OFFICIALS, <http://www.afdo.org/about> [<https://perma.cc/G8UU-KDP5>]. As of 2012, forty-two states had adopted all or some of the Uniform State Food, Drug, and Cosmetic Act. PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, *FOOD AND DRUG LAW: CASES AND MATERIALS* 290 (4th ed. 2014).

101. See HUTT ET AL., *supra* note 100, at 290; *About*, *supra* note 100.

102. See, e.g., FDA, *supra* note 99, at § 3.3.3; HUTT ET AL., *supra* note 100, at 290.

State laws identical (or almost identical) to federal law, of course, do not substantively add to or challenge the FDA's regulatory scheme. Instead, such laws may show that states (and the AFDO) recognize that the FDA's resources are limited.¹⁰³ The agency simply cannot monitor and penalize every violation of the FDCA, and state laws identical to the FDCA could allow states to fill these gaps by enforcing requirements related to drug safety and efficacy, just as the FDA does.¹⁰⁴ Consistent with this idea, states do not regulate drugs under their laws in isolation from the FDA.¹⁰⁵ Many states have an agreement with the FDA that permits information sharing and coordination.¹⁰⁶ In some areas where the FDA's statutory authority has been challenged or otherwise is less clear, such as drug compounding, states have played a significant regulatory role in the modern era.¹⁰⁷ But state enforcement of their own Food, Drug, and Cosmetic Acts appears to be rare.¹⁰⁸ Nevertheless, regardless of how strictly states enforce state Food, Drug, and Cosmetic Acts or how vigorously private parties pursue products liability claims, these state schemes ultimately represent efforts to complement or amplify the reach of the FDA's requirements.

II. PRACTICE, PRODUCTS, AND PREEMPTION

Unlike products liability regimes and state Food, Drug, and Cosmetic Acts intended to complement FDA requirements, recent state drug regulation efforts seem intended to challenge the FDA's regulatory scheme. This recent surge in state drug regulation, thus, may provide new insights about the preemptive reach of the FDA's authority.¹⁰⁹ To consider these insights, this Part starts by discussing preemption in

103. Cf. Catherine M. Sharkey, *Tort-Agency Partnerships in an Age of Preemption*, 15 THEORETICAL INQUIRIES L. 359, 360 (2014) (describing parallel requirements in the food and drug context).

104. See, e.g., William F. Reindollar, *The Association of Food and Drug Officials*, 6 FOOD DRUG COSM. L.J. 52, 53–54 (1951).

105. See FDA, *supra* note 99, at § 3.3.3; see also Salthe, *supra* note 75, at 165 (“The consumer will receive the greatest amount of this protection when federal, state and municipal food and drug officials cooperate in the enforcement of a uniform law.”); cf. Anna Wexler, *A Pragmatic Analysis of the Regulation of Consumer Transcranial Direct Current Stimulation (TDCS) Devices in the United States*, 2 J.L. & BIOSCIENCES 669, 687–91 (2015) (describing an example of federal cooperation with a state enforcement action related to devices).

106. See FDA, *supra* note 99, at § 3.3.2.

107. See, e.g., Kevin Outtersson, *Regulating Compounding Pharmacies After NECC*, 367 NEW ENG. J. MED. 1969 (2012). Drug compounding refers to a manufacturing practice that involves a medical practitioner combining, mixing, or altering drug ingredients to create an individualized medication for a patient. See *Pharmacy Compounding: Implications of the 2012 Meningitis Outbreak: Hearing Before the S. Comm. on Health, Educ., Labor, and Pensions*, 112th Cong. 21 (2012) (testimony of Margaret A. Hamburg, Comm’r, Food & Drug Admin.).

108. See, e.g., John Shaeffer, *Prescription Drug Advertising—Should States Regulate What Is False and Misleading?*, 58 FOOD & DRUG L.J. 629, 629 (2003) (“States have delegated much of their enforcement of drug safety to private citizens, who are empowered to bring tort actions.”); cf. Marc T. Law, *The Origins of State Pure Food Regulation*, 63 J. ECON. HIST. 1103, 1107–09 (2003) (discussing the history of weak state enforcement in the context of food).

109. See Brown & Tomar, *supra* note 21; Noah, *supra* note 7; Sharkey, *supra* note 21.

the products liability context, where state drug regulation is more widely understood to coexist and where the Supreme Court has spoken. This Part then describes and considers five examples of the recent surge of state drug regulation, arguing that one insight from this surge is that the preemptive effects of the FDA's authority extend into state regulation of medical practice in some instances.

A. Products Liability

Although “the States possess sovereignty concurrent with that of the Federal Government,” the basic premise of preemption is that Congress may choose to displace state law.¹¹⁰ That is, when federal and state law conflict, the state law is “without effect.”¹¹¹ A preemption analysis “start[s] with the assumption that the historic police powers of the States [are] not to be superseded . . . unless that [was] the clear and manifest purpose of Congress.”¹¹² Accordingly, courts’ preemption analyses ultimately center on congressional intent.¹¹³

Preemption is express when a federal law explicitly provides that it displaces state oversight.¹¹⁴ Federal law may also impliedly preempt state law in several ways. Field preemption occurs when Congress intended federal law to occupy the entire regulatory field.¹¹⁵ Conflict preemption, however, is the more commonly relied-upon theory of implied preemption in food and drug law.¹¹⁶ State law can conflict with federal law, and thus be impliedly preempted, either when compliance with both state and federal requirements is impossible (impossibility preemption), or when state law thwarts the purpose of the federal law (obstacle preemption).¹¹⁷ Implied preemption theories are generally most relevant in drug products liability cases because there is no provision in the FDCA that expressly preempts products liability claims against drug manufacturers.¹¹⁸

110. *Gregory v. Ashcroft*, 501 U.S. 452, 456 (1991) (quoting *Tafflin v. Levitt*, 493 U.S. 455, 458 (1990)).

111. *Cipollone v. Liggett Grp., Inc.*, 505 U.S. 504, 516 (1992) (quoting *Maryland v. Louisiana*, 451 U.S. 725, 746 (1981)).

112. *Id.* (first and second alterations in original) (quoting *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947)); *cf. McCuskey*, *supra* note 92 (discussing and critiquing a broad presumption against preemption, based on a history of state regulation, in health law).

113. *See, e.g., Cipollone*, 505 U.S. at 516.

114. *E.g., id.*

115. *E.g., id.*

116. *See, e.g., Richard C. Ausness, The Impact of Wyeth v. Levine on FDA Regulation of Prescription Drugs*, 65 FOOD & DRUG L.J. 247, 247–49 (2010).

117. *See, e.g., Cipollone*, 505 U.S. at 516; *see also Wyeth v. Levine*, 555 U.S. 555, 563–64 (2009) (discussing impossibility and obstacle preemption).

118. *See, e.g., Wyeth*, 555 U.S. at 574–75. The FDCA does contain a provision that expressly preempts state and local requirements for over-the-counter drug labeling that differ from federal requirements, but that provision also indicates that it is not intended “to modify or otherwise affect . . . the liability of any person under the product liability law of any State.” 21 U.S.C. § 379r(e) (2012). Thus, preemption disputes about over-the-counter drugs frequently focus on whether the case in fact involves products liability law. *See, e.g., Kanter v. Warner-Lambert Co.*, 122 Cal. Rptr. 2d 72, 80 (Cal. Ct. App. 2002). The FDCA also contains an express preemption provision regarding state and local requirements for certain devices,

Case law and scholarship in the products liability context—the area in which most FDA preemption litigation has occurred, and in which the Supreme Court has recently spoken—are helpful for considering the preemptive effects of FDA regulation on divergent state regulation.¹¹⁹ In *Wyeth v. Levine*, a patient sued the manufacturer of a brand-name, injectable medication for failing to adequately warn of the risks of gangrene associated with certain methods of injection.¹²⁰ Although the drug manufacturer argued that the plaintiff’s case was impliedly preempted under both impossibility and obstacle theories, the Court disagreed.¹²¹ The Court explained that the “powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress.”¹²² In other words, the Court underscored the presumption against concluding that Congress intended federal law to preempt state law.¹²³ And the Court concluded that, in this instance, Congress intended to preserve state tort law noting, among other things, that FDA regulations permit manufacturers of brand-name drugs to update their drug’s labeling with new warnings before the FDA approves the change, and the 1962 amendments to the FDCA included a provision “indicating that a . . . state law would only be invalidated upon a ‘direct and positive conflict’ with the FDCA.”¹²⁴

But several Supreme Court decisions after *Wyeth* clarified that the preemptive effect of the FDA’s regulation of *generic* drugs is more extensive and chipped away at the notion that Congress intended to preserve state drug law in all circumstances.¹²⁵

which the Supreme Court has interpreted as preempting some state common law causes of action; however, that provision is outside the scope of this Article. 21 U.S.C. § 360k (2012); *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 322–24 (2008); *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 492–502 (1996).

119. See, e.g., Brown & Tomar, *supra* note 21; Catherine M. Sharkey, *Products Liability Preemption: An Institutional Approach*, 76 GEO. WASH. L. REV. 449, 450 (2008); see also Lars Noah, *Reconceptualizing Federal Preemption of Tort Claims as the Government Standards Defense*, 37 WM. & MARY L. REV. 903, 907–908 (1996) (describing the Supreme Court’s increasing willingness to find tort law, as well as positive law, preempted).

120. *Wyeth*, 555 U.S. at 558–60; see also Ausness, *supra* note 116, at 280 (explaining the *Wyeth* decision).

121. *Wyeth*, 555 U.S. at 563–64, 581; see also Erika Fisher Lietzan & Sarah E. Pitlyk, *Thoughts on Preemption in the Wake of the Levine Decision*, 13 J. HEALTH CARE L. & POL’Y 225, 229–252 (2010) (discussing the *Wyeth* majority’s analysis of impossibility and obstacle preemption claims).

122. *Wyeth*, 555 U.S. at 565 (quoting *Lohr*, 518 U.S. at 485).

123. See Ausness, *supra* note 116, at 280–81.

124. *Wyeth*, 555 U.S. at 567 (quoting Drug Amendments of 1962, Pub. L. No. 87-781, sec. 202, 76 Stat. 780, 793); see also Noah, *supra* note 7, at 8 (noting this language as one piece of evidence that Congress intended to preserve state authority).

125. *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466 (2013); *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011). The Supreme Court’s findings of implied preemption in *PLIVA* and *Bartlett* are not inconsistent with the 1962 provision cited in *Wyeth*. The language stating that state laws are invalidated only upon a “direct and positive conflict” with the FDCA can be viewed as a restatement of the impossibility theory of implied preemption. And, indeed, some courts have interpreted similar savings clauses in this way. See *S. Blasting Servs., Inc. v. Wilkes County*, 288 F.3d 584, 591 (4th Cir. 2002); Christine H. Kim, *The Case for Preemption of Prescription Drug Failure-To-Warn Claims*, 62 FOOD & DRUG L.J. 399, 410 (2007); Noah, *supra* note 7, at 8–9.

In *PLIVA, Inc. v. Mensing*, patients who developed tardive dyskinesia—a neurological disorder—from long-term use of a generic drug sued the drug manufacturer.¹²⁶ At the time that the patients were prescribed the drug, its labeling did not include a warning about the link between long-term use and tardive dyskinesia.¹²⁷ The plaintiffs argued that the drug manufacturers breached a state tort law duty by failing to add such a warning, and, by the time the case reached the Supreme Court, the FDA had required that manufacturers add the warning.¹²⁸ Nevertheless, the majority concluded that the drug manufacturers were not liable to the plaintiffs on impossibility preemption grounds.¹²⁹ The majority noted that the FDCA and the FDA’s implementing regulations require that a generic drug’s labeling be the “same” as the brand-name drug’s labeling, and the brand-name drug’s labeling lacked a warning about long-term use and tardive dyskinesia at the time of the plaintiffs’ injuries.¹³⁰ In the majority’s view, it, therefore, was impossible for the drug manufacturers to comply both with federal labeling requirements, and with the state-law duty to update their drug’s labeling with a new warning.¹³¹

Two years later, in *Mutual Pharmaceutical Company v. Bartlett*, the Supreme Court faced a very similar case.¹³² The plaintiff, again, was a patient who had been injured by a generic drug—in this case, a nonsteroidal anti-inflammatory pain reliever.¹³³ The plaintiff argued that the drug manufacturer was liable for her injuries on the theory that the design of the drugs was unreasonably unsafe, because the drugs’ labeling failed to warn of the rare and serious skin reaction that the plaintiff suffered.¹³⁴ Relying on its decision in *PLIVA, Inc. v. Mensing* and applying the same impossibility rationale, the majority held that design-defect claims against generic drug manufacturers that turn on the adequacy of the drug’s labeling are preempted.¹³⁵ The majority found unpersuasive the plaintiff’s argument that, because the generic drug manufacturer could have simply chosen not to sell the drug in states with requirements that conflict with federal law, it was not impossible for the manufacturer to comply with both state and federal requirements.¹³⁶

Regardless of one’s view of the merits of this outcome,¹³⁷ *Bartlett* may signal trouble for some of the recent state drug regulatory efforts. The majority opinion

126. 564 U.S. at 610.

127. *Id.*

128. *Id.* at 609–10.

129. *Id.* at 618.

130. *Id.*

131. *Id.* As the majority did in *Wyeth*, in dissent in *PLIVA* Justice Sotomayor cited the provision in the 1962 amendments to the FDCA preserving state authority as evidence that Congress did not intend to preempt state tort law claims against drug manufacturers. *Id.* at 633 (Sotomayor, J., joined by Ginsburg, J., dissenting).

132. 133 S. Ct. 2466, 2470 (2013).

133. *Id.*

134. *Id.* at 2471–72.

135. *Id.* at 2476–77.

136. *Id.* at 2477.

137. Numerous scholars have criticized *PLIVA* and *Bartlett* on both legal and policy grounds. See, e.g., LARS NOAH, LAW, MEDICINE, AND MEDICAL TECHNOLOGY 556–57 (3d ed. 2012); Aaron S. Kesselheim & Jonathan J. Darrow, *Hatch-Waxman Turns 30: Do We Need a Re-Designed Approach for the Modern Era?*, 15 YALE J. HEALTH POL’Y L. & ETHICS 293,

suggested that imposing tort liability in the factual circumstances in *Bartlett* would be similar to a state “directly prohibiting the product’s sale”¹³⁸—indicating that the Court may find a prohibition on an FDA-approved drug, or other types of state positive law, to be preempted on impossibility grounds in some circumstances.¹³⁹ Justice Breyer’s dissent (which was joined by Justice Kagan) also suggested a path forward for challenging recent state regulation on implied preemption grounds. Although Justice Breyer agreed with the plaintiff’s argument that it was not impossible for the manufacturer to comply with both state and federal requirements, his dissent acknowledged that state requirements may pose an obstacle to federal ones in some circumstances.¹⁴⁰ An obstacle preemption argument, in his view, becomes stronger the more “medically valuable” a particular drug is.¹⁴¹ Justice Sotomayor’s dissenting opinion (joined by Justice Ginsburg) was more skeptical of an obstacle preemption argument but, nevertheless, similarly acknowledged obstacle preemption “presents a closer question than the impossibility argument.”¹⁴² Taken together, the dissents and the majority opinion, thus, suggest for the potential to persuade a majority of the Court that recent state regulatory efforts are preempted by the FDCA, depending on the circumstances.

Although *PLIVA* and *Bartlett* significantly limit the role of state tort law regimes in drug regulation,¹⁴³ viable avenues for bringing products liability claims against drug manufacturers may remain or reemerge.¹⁴⁴ So-called “parallel claims” are perhaps the most widely applicable avenue left for products liability claims against generic drug manufacturers.¹⁴⁵ Parallel claims are based on state tort-law duties that are

343–45 (2015); Stacey B. Lee, *PLIVA v. Mensing: Generic Consumers’ Unfortunate Hand*, 12 *YALE J. HEALTH POL’Y L. & ETHICS* 209, 235–45 (2012).

138. *Bartlett*, 133 S. Ct. at 2478 n.5; see also Noah, *supra* note 7, at 34 n.137.

139. See *Bartlett*, 133 S. Ct. at 2478 n.5; Noah, *supra* note 7, at 34 n.137.

140. *Bartlett*, 133 S. Ct. at 2480–81 (Breyer, J., joined by Kagan, J., dissenting); Noah, *supra* note 7, at 31.

141. *Bartlett*, 133 S. Ct. at 2480–81 (Breyer, J., joined by Kagan, J., dissenting).

142. *Id.* at 2493 (Sotomayor, J., joined by Ginsburg, J., dissenting).

143. This is because generic drugs comprise approximately eighty-eight percent of prescription drugs used in the United States. GENERIC PHARM. ASS’N, *GENERIC DRUG SAVINGS IN THE U.S.* 1 (2015), http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf [<https://perma.cc/736L-75UR>].

144. Perhaps most obviously, Supreme Court jurisprudence has not foreclosed failure-to-warn, and other labeling-based claims, against the manufacturers of *brand-name* drugs. *Wyeth v. Levine*, 555 U.S. 555 (2009). But as explained, see *supra* note 143, brand-name drugs are only a small part of the market. Additionally, because of changes to the FDCA that were enacted after the events that gave rise to *Wyeth*, the case may not foreclose all findings of implied preemption against brand-name manufacturers. See Evans, *supra* note 19, at 517. Contract, rather than tort, claims may be another avenue for injured patients. See Max N. Helveston, *Preemption Without Borders: The Modern Conflation of Tort and Contract Liabilities*, 48 *GA. L. REV.* 1085, 1105 (2014).

145. See, e.g., Sharkey, *supra* note 103, at 362–63. The other pathways for suing generic drug manufacturers that exist or may reemerge may not be as widely applicable, or may be challenged, for a variety of reasons. First, failure-to-warn claims against generic drug manufacturers may once again be viable if the FDA finalizes a proposed rule that would permit generic drug manufacturers to unilaterally add or strengthen warnings in the labeling, just as

identical to or incorporate, rather than conflict with, federal requirements and generally have survived preemption challenges.¹⁴⁶ For example, after *PLIVA* and *Bartlett*, failure-to-warn claims against generic drug manufacturers who have failed to update their labeling to match the brand-name drug's labeling—as required by both state and federal law—have continued to withstand preemption challenges.¹⁴⁷ Likewise, where state Food, Drug, and Cosmetic Acts incorporate the federal FDCA's prohibitions, plaintiffs' state-law tort claims that are premised on violations of sections of the state law that mirror federal law may survive preemption.¹⁴⁸

Nevertheless, courts have concluded that parallel claims are preempted in some circumstances. For example, in *Buckman Co. v. Plaintiffs' Legal Committee*, and subsequent interpretations of the case, the Supreme Court articulated the idea that even parallel state requirements can be preempted when they “encroach[] upon an agency's territory.”¹⁴⁹ That is, state enforcement of parallel requirements might

brand-name drug manufacturers can do. *See* Generic Drug Labeling Proposed Rule, *supra* note 96, at 67,988–89. But whether the FDA has the statutory authority to make the proposed changes to generic drug labeling requirements is hotly disputed. *See, e.g.*, Generic Pharmaceutical Association, Comments on the Proposed Rule “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products” at 2–4 (Mar. 13, 2014), <https://www.regulations.gov/contentStreamer?documentId=FDA-2013-N-0500-0067&attachmentNumber=1&contentType=pdf> [<https://perma.cc/3AQ2-WVPX>]. Second, a few courts have held that, in certain circumstances, brand-name drug manufacturers may be held liable for the injuries caused by generic copies of their drugs, if the brand-name manufacturers provided false or misleading information that led to the injury. *See Kellogg v. Wyeth, Inc.*, 762 F. Supp. 2d 694 (D. Vt. 2010); *Wyeth, Inc. v. Weeks*, 159 So. 3d 649 (Ala. 2014); *Conte v. Wyeth, Inc.*, 85 Cal. Rptr. 3d 299 (Ct. App. 2008). But such decisions are in the clear minority—indeed, in Alabama, the legislature overrode the court's decision in *Wyeth v. Weeks*, eliminating, by statute, brand-name drug companies' liability for injuries caused by generic copies of their drugs. *See* 2015 Ala. Acts 106 (2015); *Wyeth*, 159 So. 3d at 696 (Murdock, J. dissenting) (describing the majority rule); *see also* Katie Thomas, *Man Taking Generic Drug Can Sue Branded Maker*, N.Y. TIMES (Jan. 11, 2013), <http://www.nytimes.com/2013/01/12/business/court-says-pfizer-can-be-sued-by-man-who-took-generic.html> [<https://perma.cc/CTL7-FMQR>] (quoting a drug industry lawyer as stating that the Alabama decision “is contrary to the overwhelming weight of authority on this issue nationwide”).

146. *See* *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 330 (2008); Sharkey, *supra* note 103, at 362–63.

147. *See* *Fulgenzi v. PLIVA, Inc.*, 711 F.3d 578 (6th Cir. 2013); *Teva Pharm. USA, Inc. v. Superior Court*, 158 Cal. Rptr. 3d 150, 152 (Cal. Ct. App. 2013); Sharkey, *supra* note 103, at 362–63.

148. Brief for United States as Amicus Curiae Supporting Petitioner, *supra* note 97, at 23. Additionally, in at least one circumstance outside the products liability context, such a parallel claim has survived a preemption argument. In *Allergan, Inc. v. Athena Cosmetics*, Allergan successfully obtained a permanent injunction prohibiting its competitor, Athena Cosmetics, from selling a product within California because Athena Cosmetics was violating California's Unfair Competition Law (UCL) by selling a new drug without FDA approval. *Allergan, Inc. v. Athena Cosmetics, Inc.*, 738 F.3d 1350 (Fed. Cir. 2013). The Federal Circuit held that the relevant provisions of California's UCL were not preempted by the FDCA because the “provisions . . . parallel the FDCA, such that the statutes have consistent goals.” *Id.* at 1356.

149. Sharkey, *supra* note 103, at 374; *see also* *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 350 (2001) (“State-law fraud-on-the-FDA claims inevitably conflict with the

conflict with federal requirements, for example by undermining federal agencies' prerogative to exercise discretion in how they enforce federal law. The parallel claims context, as with the failure-to-warn and design-defect contexts, therefore suggests that courts are willing to conclude in at least some circumstances that Congress intended FDA oversight to displace the states' role in drug regulation—and may foretell courts finding that certain recent state drug regulation efforts may be preempted.

B. Divergent State Regulation

Because recent state efforts to regulate drugs, unlike state tort law regimes and state Food, Drug, and Cosmetic Acts, are generally intended to diverge from the FDA's regulatory scheme, these efforts present an opportunity to consider the preemptive reach of the FDA's drug authority in a fresh context.¹⁵⁰ Indeed, scholars and commentators have begun to weigh in, with varying views of the viability of claims that FDA regulation preempts particular areas of state positive law.¹⁵¹

Examining the potential clash between existing state regulation of drug compounding and the FDA's recently expanded authority in this area, two attorneys, Nathan Brown and Eli Tomar, have predicted that courts may conclude that certain state regulation of drug compounding presents an obstacle to the mission of the FDA.¹⁵² Drawing on cases about food and cosmetic regulation, they argued that

FDA's responsibility to police fraud consistently with the Administration's judgment and objectives." *Buckman* involved a device rather than a drug, but is nevertheless instructive. In *Buckman*, the plaintiffs claimed to be injured by orthopedic bone screws, which, the plaintiffs argued, the FDA authorized for marketing on the basis of fraudulent information submitted by the company. The plaintiffs sought damages under state tort law on the basic theory that the company's fraudulent representations were "a 'but for' cause of injuries that plaintiffs sustained from the implantation of these devices: Had the representations not been made, the FDA would not have approved the devices, and plaintiffs would not have been injured." 531 U.S. at 343; *see also* *Arizona v. United States*, 132 S. Ct. 2492, 2502 (2012) ("Permitting the State to impose its own penalties for the federal offenses here would conflict with the careful framework Congress adopted.").

150. Recent state regulatory efforts also present an opportunity to assess some of the possible preemptive effects of the Food and Drug Administration Amendments Act (FDAAA) of 2007, which amended the FDCA to significantly expand the FDA's postmarket drug safety authorities. *Cf.* Evans, *supra* note 19, at 515–17 (discussing the effect of FDAAA on brand-name manufacturers' products liability); Parasidis, *supra* note 95, at 937–49 (discussing the evolution of the FDA's postmarket authorities, including FDAAA). Among other things, FDAAA authorized the FDA to require Risk Evaluation and Mitigation Strategies (REMS) for certain prescription drugs. For further discussion of REMS and preemption, see *infra* Part II.B.2.

151. *See* Brown & Tomar, *supra* note 21; Noah, *supra* note 7; *cf.* Sharkey, *supra* note 21 (arguing that courts should consider the FDA's view of state regulation in obstacle preemption cases).

152. *See generally* Brown & Tomar, *supra* note 21. Congress passed the Drug Quality and Security Act of 2013 in part to expand the FDA's authority over drug compounding after a fatal fungal meningitis outbreak in 2012 that was linked to compounded drugs. *E.g.*, Kevin Outterson, *The Drug Quality and Security Act—Mind the Gaps*, 370 NEW ENG. J. MED. 97, 97 (2014).

courts are “more willing to strike state regulations that are not impossible to abide, but which complicate industry’s compliance with an overarching federal program.”¹⁵³ For example, courts have struck down, on implied preemption grounds, a California law establishing a standard for weight variance in bagged flour that differed from the federal law and a Minnesota law that required cosmetics to bear a warning about chlorofluorocarbons additional to the federally required one.¹⁵⁴ Neither state law made compliance with federal law impossible; the courts’ reasoning in both cases focused on the states’ disruption of the federal governments’ balancing of numerous considerations, such as the public health benefits of stricter regulation and the costs to industry and consumers.¹⁵⁵ In other words, according to Brown and Tomar, this line of cases—and, arguably, Justice Breyer’s dissent in *Bartlett* and some of the parallel claims decisions—suggests that courts may have an increasingly favorable view towards obstacle preemption arguments. These cases, therefore, may suggest an obstacle preemption rationale for courts to strike down certain recent state efforts to regulate drugs.

Lars Noah has argued that state bans on FDA-approved drugs—for which there will often be strong arguments that state action disrupts the careful balancing of the FDA’s approval decisions—may not always be preempted.¹⁵⁶ Although *Bartlett* suggests that at least some Supreme Court Justices are inclined to conclude that such state bans are preempted, the outcome of any preemption litigation will ultimately depend on the precise context within which a state imposes such a ban.¹⁵⁷ For example, a state ban might be more likely to survive a preemption challenge if it reflects unique local concerns or is implemented many years after a drug’s initial approval as a result of new information that the FDA did not consider.¹⁵⁸ Additionally, the language from the 1962 amendments to the FDCA preserving state authority except where it “direct[ly] and positive[ly] conflict[s]” with those amendments, cited by the majority in *Wyeth*, provides evidence that Congress did not intend FDA approval decisions to preempt state bans on any theory other than impossibility.¹⁵⁹

153. Brown & Tomar, *supra* note 21, at 285; cf. Lars Noah, *A Miscarriage in the Drug Approval Process?: Mifepristone Embroils the FDA in Abortion Politics*, 36 WAKE FOREST L. REV. 571, 601 (2001) (“To the extent that recent Supreme Court cases have reinvigorated implied preemption in cases where state law stands as an ‘obstacle’ to the achievement of federal purposes, one could argue that any state efforts to prohibit or restrict distribution of mifepristone would create an impermissible conflict with federal law.” (footnote omitted)).

154. See *Jones v. Rath Packing Co.*, 430 U.S. 519, 540–43 (1977); *Cosmetic, Toiletry & Fragrance Ass’n, Inc. v. Minnesota*, 440 F. Supp. 1216, 1222 (D. Minn. 1977), *aff’d*, 575 F.2d 1256 (8th Cir. 1978).

155. See *Jones*, 430 U.S. at 540–43; *Cosmetic, Toiletry & Fragrance Ass’n*, 440 F. Supp. at 1222.

156. E.g., Noah, *supra* note 7. Noah also examines dormant commerce clause and substantive due process objections to state bans on FDA-approved drugs, likewise concluding the outcome of such challenges would depend on the precise factual context in which a ban is established. See *id.* at 35–54.

157. See *id.* at 3–16, 27–35.

158. See *id.* at 53–54.

159. Drug Amendments of 1962, Pub. L. No. 87-781, sec. 202, 76 Stat. 780, 793; see Noah, *supra* note 7, at 8–9. Although this language clearly presents a hurdle to the success of implied preemption theories other than impossibility, it may not be an insurmountable hurdle. The

This Part considers these preemption arguments within the context of specific examples of state regulation that diverge from federal requirements, starting with examples for which there is a stronger case that state regulation is preempted. The examples provided are not meant to be exhaustive; rather, they illustrate the varied ways that state regulatory efforts intersect with the FDA's authority.¹⁶⁰ Ultimately, these examples do not provide a categorical answer to when state drug regulation is preempted.¹⁶¹ But they do demonstrate that in many cases there are plausible arguments that, because of the FDA's wide-ranging oversight, its regulation preempts divergent state regulatory efforts.

language was not codified and expressly applied only to the 1962 amendments to the FDCA. Sec. 202, 76 Stat. at 793. Congress has changed and expanded the FDA's authority numerous times since 1962, and many recent state regulatory efforts intersect with these newer aspects of FDA regulation. *E.g.*, *Significant Dates in U.S. Food and Drug Law History*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/WhatWeDo/History/Milestones/ucm128305.htm> [<https://perma.cc/XS4J-BD5A>] (last updated Dec. 19, 2014). And in the recent Supreme Court preemption decisions in the products liability context, there is evidence to suggest that various Justices believed that, although this language is some evidence of Congress's intent not to displace state law absent an impossibility argument, it is not dispositive. *See* *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2480–81 (2013) (Breyer, J., joined by Kagan, J., dissenting) (acknowledging obstacle preemption as a possibility); *Wyeth v. Levine*, 555 U.S. 555, 612 n.4 (2009) (Alito, J. dissenting) (arguing this language “simply recognizes the background principles of conflict pre-emption”); *cf. Bartlett*, 133 S. Ct. at 2493 (Sotomayor, J., joined by Ginsburg, J., dissenting) (noting obstacle preemption “presents a closer question than the impossibility argument” despite this language); *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 870–72 (2000) (arguing that a similar savings clause does not preclude obstacle theories).

160. As one example, this Article does not discuss in depth state laws restricting the use of drugs intended for pregnancy termination. Nineteen states require that a physician be physically present when a patient takes such drugs. And several states also require that pregnancy termination drugs be used according to their FDA-approved labels, whereas off-label use is generally permitted in other contexts. (These on-label use laws, however, no longer meaningfully restrict access to pregnancy termination drugs because in March 2016, the FDA approved updated labeling for the drugs that reflects the current standard of care.) As with the Maine and Massachusetts regulatory efforts, state laws governing pregnancy termination drugs are generally medical practice laws, limiting how practitioners may prescribe the drug. Whether FDA authority preempts these laws may raise similar issues to those discussed with respect to Vermont and Massachusetts's restrictions on the use of Zohydro, albeit complicated by the constitutional questions around access to abortion. *See, e.g.*, Zettler, *supra* note 19, at 449, 449 n. 123; Sandhya Somashekhar & Laurie McGinley, *The FDA Just Made the Abortion Pill Easier To Get*, WASH. POST (Mar. 30, 2016), https://www.washingtonpost.com/national/fda-updates-recommendations-for-abortion-pill/2016/03/30/426407de-f681-11e5-8b23-538270a1ca31_story.html [<https://perma.cc/8VP5-QBLU>]; *State Laws and Policies: Medication Abortion*, GUTTMACHER INST., <https://www.guttmacher.org/state-policy/explore/medication-abortion> [<https://perma.cc/8R9R-C25U>] (last updated Apr. 1, 2017). As another example, several states and localities require a prescription for pseudoephedrine, a decongestant that, under federal law, may be sold over-the-counter. *See, e.g.*, OFFICE FOR STATE, TRIBAL, LOCAL & TERRITORIAL SUPPORT, CTRS. FOR DISEASE CONTROL & PREVENTION, PSEUDOEPHEDRINE: LEGAL EFFORTS TO MAKE IT A PRESCRIPTION-ONLY DRUG (2013), <https://www.cdc.gov/phlp/docs/pseudo-brief112013.pdf> [<https://perma.cc/24VK-MWQP>].

161. *See* Noah, *supra* note 7, at 53–54.

1. Maine's Drug Importation Law

Because prescription drugs are notoriously expensive in the United States, patients sometimes want to purchase them from countries where they are cheaper.¹⁶² Although it is illegal for individuals to import drugs not approved by the FDA (or that otherwise violate the FDCA), the FDA does not stop individuals from importing such drugs for personal use in certain circumstances.¹⁶³ Nevertheless, the FDA has been criticized for too strictly enforcing drug import requirements and chilling even the personal importation to which the agency does not object.¹⁶⁴

In response, states have explored allowing their citizens access to inexpensive imported drugs.¹⁶⁵ The FDA has consistently opined that importing unapproved drugs from other countries is prohibited under federal law and that such drugs raise significant safety concerns because they may be counterfeit or low quality.¹⁶⁶ The FDA has also said that state drug importation laws are impliedly preempted by the FDCA under theories of field, impossibility, and obstacle preemption.¹⁶⁷

162. See Patricia M. Danzon & Michael F. Furukawa, *Prices and Availability of Pharmaceuticals: Evidence from Nine Countries*, 3 HEALTH AFF. WEB EXCLUSIVES 521 (2003); see also Aaron S. Kesselheim, Jerry Avorn & Ameet Sarpatwari, *The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform*, 316 JAMA 858, 859 (2016) (discussing “growing concern” about increasing prescription drug prices).

163. The conditions that must be met for the FDA to use its discretion to permit personal importation include that the individual has a serious condition for which no effective treatment is available in the United States. See *Is It Legal for Me To Personally Import Drugs?*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm194904.htm> [<https://perma.cc/C2AZ-7PHX>] (last updated Mar. 4, 2016).

164. See, e.g., Peter S. Reichertz & Melinda S. Friend, *Hiding Behind Agency Discretion: The Food and Drug Administration's Personal Use Drug Importation Policy*, 9 CORNELL J.L. & PUB. POL'Y 493 (2000).

165. See *Importing Prescription Drugs: Letters to State and Local Officials*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DrugSafety/ucm170594.htm> [<https://perma.cc/A2CV-UGCV>] (last updated Sept. 29, 2014).

166. See, e.g., Letter from William K. Hubbard, Assoc. Comm'r for Policy & Planning, U.S. Food & Drug Admin., to Gregory Gonot, Deputy Att'y Gen., Cal. Dep't of Justice (Aug. 25, 2003), <https://www.fda.gov/Drugs/DrugSafety/ucm179893.htm> [<https://perma.cc/84FK-CP5K>]; Letter from Randall W. Lutter, Deputy Comm'r for Policy, U.S. Food & Drug Admin., to Linda Lingle, Governor, State of Haw. (Aug. 14, 2008), <https://www.fda.gov/Drugs/DrugSafety/ucm179204.htm> [<https://perma.cc/WT3M-Y5L4>]; see also Letter from Robert M. Califf, Margaret B. Hamburg, Mark B. McClellan & Andrew Von Eschenbach to Members of Congress (Mar. 16, 2017), https://healthpolicy.duke.edu/sites/default/files/atoms/files/2017_03_16_commissioners_letter_final.pdf [https://webcache.googleusercontent.com/search?q=cache:UmGcEUmUPIUJ:https://healthpolicy.duke.edu/sites/default/files/atoms/files/2017_03_16_commissioners_letter_final.pdf+&cd=1&hl=en&ct=clnk&gl=us] (explaining four former FDA commissioners' concerns about importing unapproved drugs).

167. See, e.g., Letter from William K. Hubbard to Gregory Gonot, *supra* note 166. In its letters, the FDA does not address the language in the 1962 amendments preserving state authority except in cases of a “direct and positive” conflict. This may be because the FDA's letters primarily focus on statutory provisions that were not enacted as part of the 1962 amendments, because the FDA does not view that language as dispositive of preemption questions, or because of the unique intersection between the FDA's importation authority and federal

Nevertheless, in 2013, Maine enacted a law to allow its citizens to purchase prescription drugs from certain foreign pharmacies.¹⁶⁸ The law was cleverly crafted to be within states' traditional powers to regulate medical practice, and outside the FDA's sphere of medical products regulation. Like all states, Maine requires pharmacies to be licensed.¹⁶⁹ The 2013 drug importation law, however, exempted from this state licensing requirement retail pharmacies located in Canada, the U.K., Ireland, Australia, or New Zealand.¹⁷⁰ According to Maine, the law "reduce[d] the reach of [Maine's unauthorized practice of pharmacy law] . . . 'leaving to the federal government the enforcement of any federal laws that regulate the sale of prescription drugs to Mainers by pharmacies located in certain foreign countries.'"¹⁷¹

Framing the drug importation law as medical practice regulation was not, however, sufficient to save it from a preemption challenge.¹⁷² In her opinion striking down the law, Judge Nancy Torresen of the District of Maine explained that, despite its framing, the law "extend[ed] beyond the regulation and licensure of pharmacies and pharmacists in Maine" to the field of "the importation of foreign pharmaceuticals."¹⁷³ And, in light of the Maine law's scope, she struck it down on the basis of field preemption, finding that Congress intended "to occupy the field of pharmaceutical importation."¹⁷⁴ Judge Torresen, thus, considered the underlying intent of the law—to allow drug importation—as well as the practical effect of the law in determining how the law may intersect with the FDA's jurisdiction.

This case, however, may not be particularly informative for other state drug regulation efforts because Maine's law not only intersects with the FDA's authority, but also with federal oversight of foreign commerce.¹⁷⁵ As Judge Torresen explained, there is a "presumption in favor of preemption where a state legislates in the traditional federal area of foreign affairs . . . based in part on a need for federal uniformity regarding foreign commerce."¹⁷⁶ Moreover, the opinion notes that Congress expressly considered drug importation from Canada when enacting the Medicare Prescription Drug, Improvement, and Modernization Act (MMA).¹⁷⁷ Under the MMA, Canadian drug imports are permissible only when the Secretary of the Department of Health and Human Services determines that such imports would be safe and cost-effective—and no Secretary has made such a determination.¹⁷⁸ Field

oversight of foreign commerce generally.

168. ME. REV. STAT. ANN. tit. 32, § 13731 (Supp. 2016).

169. *See id.*; *see also* Zettler, *supra* note 19, at 450 ("[A]ll fifty states have boards that are responsible for licensing medical practitioners.").

170. Tit. 32, § 13731(1)(B).

171. *See Ouellette v. Mills*, 91 F. Supp. 3d 1, 5–6 (D. Me. 2015).

172. *Id.* at 5–6, 9, 12.

173. *Id.* at 9.

174. *Id.* at 12.

175. *Cf.* Daniel A. Farber, *Climate Change, Federalism, and the Constitution*, 50 ARIZ. L. REV. 879, 882 (2008) (making a similar argument with respect to state climate change regulation).

176. *Ouellette*, 91 F. Supp. 3d at 8.

177. *Id.* at 10. Another reason is, of course, that this decision only reflects the opinion of one federal judge.

178. *See id.* at 5.

preemption arguments may face challenges in other FDA contexts in which it is less clear that Congress intended the federal government to dominate drug regulation.¹⁷⁹

2. The Zohydro Ban and Restrictions

Unlike the Maine importation law, state efforts to regulate Zohydro reflect concerns that the FDA's requirements are not strict enough. Concerned that the FDA's 2013 approval of Zohydro, an opioid that lacked abuse-deterrent properties, would contribute to the opioid misuse epidemic, Massachusetts banned Zohydro in 2014.¹⁸⁰ Massachusetts's Zohydro ban was framed as part of its regulation of the practice of medicine. Following the governor's direction, the Department of Public Health prohibited the prescribing, dispensing, or administering of Zohydro until it was reformulated to be abuse deterrent.¹⁸¹ Because the ban covered healthcare providers' prescribing and dispensing decisions—rather than the drug manufacturer's sale activities—the state argued that this ban was part of its traditional regulation of medical practice.¹⁸²

But, as with Maine's importation law, framing the Zohydro ban as medical practice regulation was not sufficient to save it.¹⁸³ After Massachusetts implemented its ban, Zogenix, Inc., Zohydro's then-manufacturer,¹⁸⁴ sought a preliminary injunction, arguing that, among other things, the ban was preempted by the FDCA.¹⁸⁵ Judge Rya Zobel of the District of Massachusetts concluded that the ban obstructed "the FDA's Congressionally-given charge" because if Massachusetts "were able to countermand the FDA's [approval] determinations and substitute its own requirements, it would undermine the FDA's ability to make drugs available to promote and protect the public health."¹⁸⁶ In other words, the judge relied on an obstacle preemption rationale

179. *Cf.* *Camps Newfound/Owatonna, Inc. v. Town of Harrison*, 520 U.S. 564, 616–17 (1997) (Thomas, J., dissenting) ("[F]ield pre-emption is itself suspect, at least as applied in the absence of a congressional command that a particular field be pre-empted."); *Hillsborough County v. Automated Med. Labs., Inc.*, 471 U.S. 707, 716–19 (1985) (holding that county ordinances governing blood plasma centers were not preempted under a field preemption theory).

180. *Zogenix, Inc. v. Patrick*, No. 14-11689-RWZ, 2014 WL 1454696, at *1 (D. Mass. Apr. 15, 2014).

181. *Id.* The language of the ban prohibited the use of any extended-release drugs that lacked abuse-deterrent properties and contained hydrocodone as their only active ingredient. At the time of the ban, Zohydro was the only such drug on the market. Accordingly, this Article refers to the ban as a ban on Zohydro.

182. *See* Defendant's Memorandum in Opposition to Application for Preliminary Injunctive Relief at 15–16, *Zogenix*, 2014 WL 1454696.

183. *See Zogenix*, 2014 WL 1454696, at *1.

184. In March 2015, Zogenix sold Zohydro to another drug company, Pernix Therapeutics. But for simplicity, this Article refers to Zogenix as the drug's manufacturer and relevant plaintiff. News Release, Zogenix Announces Agreement of Sale of Zohydro(R) ER Business to Pernix for \$100 Million at Closing Plus Potential Milestones of \$283.5 Million, (Mar. 10, 2015), <http://ir.zogenix.com/phoenix.zhtml?c=220862&p=irol-newsArticle&id=2024400> [<https://perma.cc/2EMS-4HWN>].

185. *See Zogenix*, 2014 WL 1454696, at *2.

186. *Id.*

to enjoin the ban.¹⁸⁷ Thus, as Judge Torresen did with Maine's drug importation law, Judge Zobel looked to the underlying intent of the ban, and its practical effect, to assess the preemption question before her.

The Zohydro story, however, did not end there. Massachusetts declined to appeal Judge Zobel's decision to enjoin the ban, and instead, as Vermont had done, imposed restrictions on the use of Zohydro that fall short of a complete ban.¹⁸⁸ Specifically, the Massachusetts medical board required healthcare providers to take certain steps before prescribing Zohydro, including thoroughly assessing the patient's risk factors of drug abuse, entering into a "Pain Management Treatment Agreement" with the patient, and documenting that other pain treatments were inadequate.¹⁸⁹ Massachusetts also established requirements for pharmacies that handle Zohydro.¹⁹⁰ These requirements include that the drug be stored in a securely locked cabinet and dispensed in a child-proof container, that the pharmacist verify that the prescriber has documented that other pain treatments are inadequate, that the pharmacist provide a written warning to patients about the risks of abuse, and that the pharmacist check the patient's medical history in the state-wide database for drugs of abuse.¹⁹¹ Zogenix challenged these new regulations, arguing that they amount to a de facto ban on Zohydro.¹⁹² Although Judge Zobel explained that the preemption claim could succeed if the new regulations did, in fact, affect the availability of Zohydro, she declined to enjoin the new regulations.¹⁹³

Although Zogenix did not advance this argument, the state Zohydro restrictions may also be vulnerable to a different obstacle preemption challenge because the state regulations went beyond the federal restrictions on Zohydro's use imposed by the FDA.¹⁹⁴ The FDA has required a "Risk Evaluation and Mitigation Strategy (REMS)"

187. *Id.*

188. *See, e.g.,* Valencia, *supra* note 12.

189. 243 MASS. CODE REGS. 2.07(25) (2015). Vermont has imposed similar requirements on prescribers, including that they assess the patient's risks for drug abuse, enter into a Treatment Agreement with the patient, and document that Zohydro is required for the management of the patient's pain. *See* Letter from Ronald J. Klein, Exec. Officer, Vt. Bd. of Pharmacy, & Linda Davidson, Exec. Dir., Vt. Bd. of Nursing, to Health Care Prescribers and Dispensers (Apr. 15, 2014), <https://www.sec.state.vt.us/media/474524/Zohydro-Memo-and-Rules.pdf> [<https://perma.cc/VK7K-JNCK>].

190. 247 MASS. CODE REGS. 9.04(8) (2014).

191. *Id.*

192. *Zogenix, Inc. v. Baker*, No. 14-11689-RWZ, 2015 WL 1206354, at *2 (D. Mass. Mar. 17, 2015).

193. *See id.* at *4; Sharkey, *supra* note 21, at 1619–20.

194. Because Zohydro is a controlled substance, its use is also subject to restrictions under the federal Controlled Substances Act (CSA). Under the CSA, Zohydro—like all painkillers with hydrocodone as an active ingredient—is subject to Schedule II controls, which include a prohibition on prescription refills and a requirement that prescriptions be written, rather than oral. *See, e.g.,* 21 U.S.C.A. § 829(a) (Westlaw through Pub. L. 114-198); Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II, 79 Fed. Reg. 49,661, 49,662, 49,675 (Aug. 22, 2014) (codified at 21 C.F.R. pt. 1308). The focus of this Article, however, is the intersection of state law with the FDA's authority. Moreover, the CSA contains language indicating that Congress intended it to displace state law only when "there is a positive conflict between [a] provision of [the CSA] and

for Zohydro (and other similar opioids).¹⁹⁵ The FDA is authorized to require a REMS for a prescription drug when the agency determines that a risk-mitigation program is necessary to ensure that the drug's benefits outweigh its risks.¹⁹⁶ In short, through a REMS, the FDA can impose requirements on the drug's manufacturer that go beyond providing warnings and other information in a drug's labeling.¹⁹⁷ These requirements may include, among other things, that a manufacturer ensure that practitioners who prescribe or dispense the drug have special training, that a drug is dispensed only in certain settings such as hospitals, or that certain test results are documented before a drug is dispensed.¹⁹⁸

Although medical practitioners ultimately carry out many of these REMS requirements, the requirements apply only to drug manufacturers.¹⁹⁹ Thus, regardless of their content, the Massachusetts and Vermont restrictions on the use of Zohydro—which apply to medical practitioners—do not make it “impossible” for any party to comply with both state and federal requirements. Likewise, a field preemption argument is unlikely to be successful because of courts' reluctance to conclude that Congress implicitly reserved the entire field of drug regulation for the federal government (absent an intersection with foreign commerce).²⁰⁰

That the FDA has required a REMS for Zohydro, however, may provide a plausible basis for challenging state Zohydro restrictions on obstacle preemption grounds. Through its REMS, the FDA requires that Zogenix make training available

... State law so that the two cannot consistently stand together.” 21 U.S.C. § 903 (2012); Noah, *supra* note 7, at 8–9.

195. See *Approved Risk Evaluation and Mitigation Strategies (REMS): Extended-Release and Long-Acting (ER/LA) Opioid Analgesics*, U.S. FOOD & DRUG ADMIN., <http://www.accessdata.fda.gov/scripts/cder/remis/index.cfm?event=RemsDetails.page&REMS=17> [<https://perma.cc/U4UU-DC6A>] (last updated Sept. 30, 2016).

196. See 21 U.S.C.A. § 355-1(a), (b) (Westlaw through Pub. L. No. 114-255).

197. See, e.g., Jennifer L. Bragg & Maya P. Florence, *Life with a REMS: Challenges and Opportunities*, 13 J. HEALTH CARE L. & POL'Y 269 (2010); Evans, *supra* note 19, at 511–16; Kristen Underhill, *Risk-Taking and Rulemaking: Addressing Risk Compensation Behavior Through FDA Regulation of Prescription Drugs*, 30 YALE J. ON REG. 377, 426–28 (2013).

198. See 21 U.S.C.A. § 355-1(f)(3). Under the FDCA, REMS requirements apply to the person(s) who submit certain new drug or biological license applications for approval, or who hold certain approved applications. *Id.* § 355-1(a). Because these persons are generally the drug's manufacturer, this Article describes the REMS requirements as applying to a drug's manufacturer.

199. See Zettler, *supra* note 19, at 463.

200. See *supra* Part II.A.2. Additionally, mitigating the risks of drugs may be a field that, however it is defined, is one where courts conclude that state and federal regulation coexist. For example, before Congress authorized the FDA to require REMS in 2007, numerous states had established prescription drug monitoring programs for controlled substances, to collect data and deter abuse (and these programs continue in the present). Such programs could be characterized as risk mitigation programs—and indeed, the FDA can require a registry to collect information about a drug as part of a REMS. 21 U.S.C.A. § 355-1(f). As the Supreme Court has explained, “[t]he case for federal pre-emption is particularly weak where Congress has indicated its awareness of the operation of state law in a field of federal interest, and has nonetheless decided to ‘stand by both concepts and to tolerate whatever tension there [is] between them.’” *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 166–67 (1989) (second alteration in original) (quoting *Silkwood v. Kerr-McGee Corp.*, 464 U.S. 238, 256 (1984)).

to Zohydro prescribers, but declined to impose additional requirements, such as that pharmacies be certified to dispense the drug or only dispense the drug with certain documentation.²⁰¹ That is, the FDA chose not to impose some of the requirements imposed by Vermont and Massachusetts—for example, that the inadequacy of other pain treatments be documented before Zohydro is dispensed.

Generally, the federal government's failure to act or impose a requirement does not create a strong case for preemption.²⁰² But in this context, Congress has arguably required the FDA to do a complex balancing of numerous considerations, both in determining whether a REMS is necessary at all, and in determining what to include in a REMS when one is needed.²⁰³ To require a REMS, the agency must consider the risks and benefits of a drug, and determine that a REMS is "necessary to ensure that the benefits of the drug outweigh [its] risks."²⁰⁴ If the FDA determines that a REMS is necessary, Congress expressly required that certain REMS elements be "commensurate with [a] specific serious risk" listed in the drug's labeling, not be "unduly burdensome on patient access to the drug," and "to the extent practicable . . . minimize the burden on the healthcare delivery system."²⁰⁵ Thus, a court might reasonably conclude that state requirements additional to those in an FDA-required REMS pose an obstacle to the FDA's responsibility to satisfy these Congressional objectives, particularly if courts increasingly view federal regulatory choices as an effort to find the optimal balance between competing policy goals.²⁰⁶

3. California's Track and Trace Law

Unlike the Massachusetts Zohydro ban and Maine's drug importation law, California's "track and trace" law provides an example of *express* preemption—and an example of a state that apparently *wanted* its law, which was more stringent than federal law, to be preempted by the FDCA. California enacted this law in 2004 to prevent counterfeit drugs and substandard drugs from reaching patients.²⁰⁷ To that end, the law required a "pedigree" for prescription drugs.²⁰⁸ A pedigree documents every "stop" a drug makes as it travels through the supply chain, from the point of manufacturing through its arrival at a pharmacy for dispensing to a patient.²⁰⁹ A pedigree is intended to prevent counterfeit and other potentially substandard drugs from

201. See *Approved Risk Evaluation and Mitigation Strategies (REMS)*, *supra* note 195; see also 21 U.S.C.A. § 355-1(f) (describing all of the measures that FDA may require as part of REMS).

202. See, e.g., David C. Vladeck, *FDA Preemption, Wyeth, Congress, and A Crystal Ball*, 32 *HAMLIN L. REV.* 707, 719 (2009).

203. 21 U.S.C.A. § 355-1(f)(2).

204. *Id.* at § 355-1(a).

205. *Id.* at § 355-1(f)(2).

206. See Brown & Tomar, *supra* note 21, at 284–85.

207. See 2004 Cal. Stat. 6459; Lisa A. Daigle, *ASHP Policy Analysis: Following Pharmaceutical Products Through the Supply Chain*, AM. SOC'Y OF HEALTH-SYSTEM PHARMACISTS 2–3 (2012), <https://www.ashp.org/DocLibrary/Advocacy/AnalysisPaper/Following-Pharmaceutical-Products.aspx> [<https://perma.cc/TW8H-T8YG>].

208. Daigle, *supra* note 207, at 3.

209. See *id.*; see also CAL. BUS. & PROF. CODE § 4034 (West 2011 & Supp. 2016) (repealed).

entering the supply chain, and, if that fails, to enable regulators and industry to track such drugs and remove them from the supply chain—hence the name “track and trace.”²¹⁰ The California requirements, similar to the Maine drug importation law and the Massachusetts Zohydro ban, were codified in the state laws regulating pharmacy practice and overseen by the state board of pharmacy.²¹¹

When California enacted its law, the FDA had not established a federal track and trace system—and likely lacked the statutory authority to do so.²¹² Interestingly, however, California’s law contained a provision inviting federal preemption.²¹³ The law stated that it would “become inoperative” “[u]pon the effective date of federal legislation or adoption of a federal regulation.”²¹⁴ Additionally, any FDA “rule, standard, or . . . other action that [was] inconsistent with any provision of California law governing . . . a pedigree” would render that provision of California law “inoperative.”²¹⁵ This invitation for preemption was remarkably broad. For example, because any federal “action” would render conflicting California law inoperative, even voluntary federal standards may have replaced California’s standards, even though a court otherwise would almost certainly hold that nonbinding federal recommendations do not preempt binding state law.

Although California’s requirements never fully went into effect, they ultimately motivated federal action.²¹⁶ In 2013, the federal Drug Quality and Security Act was enacted, which created a federal track and trace system similar to what would have been required by California law.²¹⁷ The Drug Quality and Security Act also provides that “no State . . . may establish or continue in effect any requirements for tracing products through the distribution system . . . which are inconsistent with, more stringent than, or in addition to, any [federal] requirements.”²¹⁸ Consistent with the

2015). A few other states also enacted a similar laws. *See, e.g.*, 2003 Fla. Laws 940. This Article uses the California law as its case study because of the unique preemption provisions in the law and because it has been credited with driving industry support for a federal pedigree requirement. *See* FDA, DETERMINATION OF SYSTEM ATTRIBUTES FOR THE TRACKING AND TRACKING OF PRESCRIPTION DRUGS; FDA PUBLIC WORKSHOP SUMMARY (2011), <https://web.archive.org/web/20170113074119/http://www.fda.gov/downloads/Drugs/NewsEvents/UCM249331.pdf>.

210. *See, e.g.*, Stephanie Feldman Aleong, *Green Medicine: Using Lessons from Tort Law and Environmental Law To Hold Pharmaceutical Manufacturers and Authorized Distributors Liable for Injuries Caused by Counterfeit Drugs*, 69 U. PITT. L. REV. 245, 270–71 (2007).

211. 2004 Cal. Stat. 6459.

212. At the time the laws were enacted, the FDCA required the FDA to establish “standards” for a track and trace system but did not authorize the FDA to take enforcement actions if those standards were not met. Accordingly, any federal standards in 2004 would likely have been voluntary. Additionally, the FDA’s 2006 attempt to require a pedigree for drugs, which would have been less extensive than California’s requirements, was successfully challenged in court. For further discussion of federal law at the time that California enacted its law, see Aleong, *supra* note 210, at 252–57.

213. CAL. BUS. & PROF. CODE § 4034.1 (West 2011 & Supp. 2016) (repealed 2015).

214. *Id.* at § 4034.1(a)(1).

215. *Id.* at § 4034(b)(1).

216. *See* Daigle, *supra* note 207, at 3.

217. Drug Quality and Security Act, Pub. L. No. 113-54, 127 Stat. 587, 599–640 (2013).

218. *Id.* at sec. 205, § 585, 127 Stat. at 638.

express preemption provision in the Drug Quality and Security Act, and the invitation for preemption in California's own law, California repealed its track and trace law after the federal law was enacted.²¹⁹

4. Medical Marijuana

State medical marijuana laws offer one example of state laws for which there is a weaker case for FDA preemption. In 1996, California enacted the first "comprehensive" medical marijuana law, and since then, twenty-eight states, the District of Columbia, Puerto Rico, and Guam, have followed suit.²²⁰ These state laws generally remove state criminal penalties for medical marijuana use, permit access to marijuana through home cultivation or dispensaries, and permit various forms of marijuana use, including smoking or vaporizing.²²¹ The mechanisms through which state laws permit and regulate access to medical marijuana often resemble medical practice laws, including licensing requirements for marijuana cultivators, dispensers, and prescribers, and limits on the conditions for which patients may obtain medical marijuana. For example, a recently enacted state law, signed by the governor of Ohio in June 2016, authorizes licensing requirements for marijuana cultivators, processors, dispensers, and prescribers, requires registration of patients and caregivers, and specifies the twenty-one conditions for which marijuana may be prescribed, including cancer, intractable pain, and multiple sclerosis.²²²

Although medical marijuana laws are obviously focused on patients and medical care, one purpose of them also may be to eliminate the prohibition on recreational marijuana.²²³ And the intersection between state medical marijuana laws and the

219. 2014 Cal. Stat. 3601 sec. 3 (effective Jan. 1, 2015).

220. See *State Medical Marijuana Laws*, *supra* note 16. Four states and the District of Columbia have enacted laws permitting the recreational use of marijuana. *Id.* This Article focuses on medical, rather than recreational, marijuana laws as an example of state drug regulation because they are more widespread. But marketing marijuana for recreational uses may also result in it falling within the FDA's jurisdiction because the FDCA includes in its definition of "drugs" products that are "intended to affect the structure or any function of the body." 21 U.S.C.A. § 321(g) (Westlaw through Pub. L. No. 114-255). A drug intended to provide a "high" is intended to affect the function of the body. See 21 U.S.C.A. § 321(g); see also FDA, U.S. DEP'T OF HEALTH & HUMAN SERVS., BOTANICAL DRUG DEVELOPMENT: GUIDANCE FOR INDUSTRY 2-3 (2016), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm458484.pdf> [<https://perma.cc/2X25-4QJX>] (explaining the statutory definition of a drug).

221. See, e.g., *State Medical Marijuana Laws*, *supra* note 16. Another seventeen states have enacted limited medical marijuana laws, which permit access only to marijuana with low tetrahydrocannabinol (THC) content or only to cannabidiol, the ingredient thought to be the source of marijuana's purported medical benefit. *Id.*

222. H.B. 523, 131st Gen. Assemb. (Ohio 2016), <https://www.legislature.ohio.gov/legislation/legislation-summary?id=GA131-HB-523> [<https://perma.cc/EL7K-RXCQ>] (click "View Current Version"). The law also permits the state medical board to add more conditions.

223. See, e.g., *About Us*, MARIJUANA POL'Y PROJECT, <https://www.mpp.org/about> [<https://perma.cc/5WV4-7RH2>].

federal Controlled Substances Act (CSA) has been widely discussed.²²⁴ The CSA currently classifies marijuana as a “Schedule I” drug, the category for drugs with a high likelihood of addiction, no safe dose, and no “currently accepted” medical use.²²⁵ Accordingly, the CSA prohibits the manufacturing, distribution, dispensing, and possession of marijuana.²²⁶ Although the federal government cannot force states to enact laws that prohibit these activities,²²⁷ and has had a policy of not enforcing federal law against certain individuals distributing or using marijuana in compliance with state law,²²⁸ state laws that expressly permit marijuana manufacture, distribution, dispensing, or possession are clearly inconsistent with the CSA.²²⁹

But medical marijuana laws also intersect with the FDA’s jurisdiction.²³⁰ Any substance that is “intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease”—as medical marijuana is—meets the FDCA’s definition of a drug.²³¹ Given the paucity of high-quality data supporting many medical uses of marijuana, marijuana is also likely a “new drug” that cannot be marketed for many of its intended uses without the FDA’s approval.²³² In fact, the FDA has approved

224. See, e.g., Brannon P. Denning, *Vertical Federalism, Horizontal Federalism, and Legal Obstacles to State Marijuana Legalization Efforts*, 65 CASE W. RES. L. REV. 567, 568 (2015); Todd Grabarsky, *Conflicting Federal and State Medical Marijuana Policies: A Threat to Cooperative Federalism*, 116 W. VA. L. REV. 1, 2 (2013); Robert A. Mikos, *On the Limits of Supremacy: Medical Marijuana and the States’ Overlooked Power To Legalize Federal Crime*, 62 VAND. L. REV. 1421, 1422 (2009) [hereinafter Mikos, *Limits of Supremacy*]; Robert A. Mikos, *Preemption Under the Controlled Substances Act*, 16 J. HEALTH CARE L. & POL’Y 5, 12 (2013) [hereinafter Mikos, *Preemption*].

225. 21 U.S.C. § 812(b)(1), (c)(c)(10); *All. for Cannabis Therapeutics v. Drug Enf’t Admin.*, 15 F.3d 1131, 1133 (D.C. Cir. 1994).

226. 21 U.S.C. § 841 (2012).

227. See, e.g., *Printz v. United States*, 521 U.S. 898, 933 (1997); Erwin Chemerinsky, Jolene Forman, Allen Hopper & Sam Kamin, *Cooperative Federalism and Marijuana Regulation*, 62 UCLA L. REV. 74, 102 (2015).

228. Consolidated Appropriations Act, 2016, Pub. L. No. 114-113, § 542, 129 Stat. 2242, 2332–33 (2015); Memorandum from James M. Cole, Deputy Att’y Gen., U.S. Dep’t of Justice, to all U.S. Att’ys 1–2 (Aug. 29, 2013) [hereinafter DOJ Memo], <https://www.justice.gov/iso/opa/resources/3052013829132756857467.pdf> [<https://perma.cc/47W2-YFSK>].

229. But as explained in note 194, *supra*, the CSA expressly disclaims congressional intent to occupy the field of criminal drug enforcement, possibly because most drug arrests and prosecutions are carried out by local and state officials, under local and state law.

230. See Alex Kreit, *What Will Federal Marijuana Reform Look Like?*, 65 CASE W. RES. L. REV. 689, 698 (2015); Kevin A. Sabet, *Much Ado About Nothing: Why Rescheduling Won’t Solve Advocates’ Medical Marijuana Problem*, 58 WAYNE L. REV. 81, 101 (2012).

231. 21 U.S.C.A. § 321(g) (Westlaw through Pub. L. No. 114-255).

232. See 21 U.S.C.A. §§ 321(p), 355(a) (Westlaw through Pub. L. No. 114-255); Deepak Cyril D’Souza & Mohini Ranganathan, *Medical Marijuana: Is the Cart Before the Horse?*, 313 JAMA 2431 (2015); Kevin P. Hill, *Medical Marijuana for Treatment of Chronic Pain and Other Medical and Psychiatric Problems: A Clinical Review*, 313 JAMA 2474 (2015); Penny F. Whiting, Robert F. Wolff, Sohan Deshpande, Marcello Di Nisio, Steven Duffy, Adrian V. Hernandez, Christiaan Keurentjes, Shona Lang, Kate Misso, Steve Ryder, Simone Schmidkofer, Marie Westwood & Jos Kleijnen, *Cannabinoids for Medical Use: A Systematic Review and Meta-Analysis*, 313 JAMA 2456 (2015). But see Richard J. Schrot & John R. Hubbard, *Cannabinoids: Medical Implications*, 48 ANNALS OF MED. 128, 128 (2016) (arguing

synthetic THC and THC analogue drugs, which suggests that the FDA understands marijuana to be a “new drug.”²³³ Accordingly, state medical marijuana laws represent an attempt to permit access to medicine outside of the FDA approval process.

Because the FDA’s jurisdiction is limited to drugs that move in interstate commerce (including drugs with components that move in interstate commerce),²³⁴ medical marijuana laws could be written to avoid the FDA altogether by permitting only wholly *intrastate* production and sale of marijuana. There is historical precedent for such state laws. In the 1970s and 1980s, many states enacted laws that permitted the *intrastate* production and sale of laetrile.²³⁵ Laetrile is a compound derived from apricot pits that was marketed as a cancer cure.²³⁶ Despite a lack of evidence supporting this use, healthcare providers and patients challenged the FDA’s restrictions on the sale of the unapproved drug.²³⁷ This challenge led to an unsuccessful lawsuit against the FDA, congressional hearings, and ultimately the state laws that permitted the intrastate sale of laetrile.²³⁸ However, although some marijuana products similarly might be produced, sold, and used wholly within a state such that they are outside the FDA’s jurisdiction, medical marijuana laws generally are not limited to such intrastate products.²³⁹ Thus medical marijuana laws pose the question of whether the FDCA preempts them.

An FDA preemption challenge to medical marijuana laws is less likely to be successful than the challenges to the Maine importation law and the Massachusetts Zohydro ban and restrictions. First, a court is unlikely to conclude that state medical marijuana laws are preempted by the FDCA on an impossibility theory.²⁴⁰ Marketing medical marijuana pursuant to a state law but without the approval of the FDA would violate federal law (assuming that the drug travels in interstate commerce),²⁴¹ but nothing in the state medical marijuana laws *compels* a person to violate federal law by selling marijuana without FDA approval.²⁴² A person could comply with both state and federal law by obtaining FDA approval to market marijuana before doing

that “substantial evidence” supports the use of marijuana for “chronic cancer and neuropathic pain and certain symptoms of multiple sclerosis”).

233. See *Cesamet*, U.S. FOOD & DRUG ADMIN., http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677s011lbl.pdf [<https://perma.cc/KZ2C-GTZC>]; *Marinol*, U.S. FOOD & DRUG ADMIN., http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018651s025s026lbl.pdf [<https://perma.cc/6SUK-LUA6>].

234. 21 U.S.C.A. §§ 321(g), 331 (Westlaw through Pub. L. No. 114-255).

235. Noah, *supra* note 7, at 22–23; Comment, *Laetrile: Statutory and Constitutional Limitations on the Regulation of Ineffective Drugs*, 127 U. PA. L. REV. 233, 234 (1978).

236. See, e.g., *United States v. Rutherford*, 442 U.S. 544, 548–49 (1979).

237. See *id.* at 548; Irving J. Lerner, *Laetrile: A Lesson in Cancer Quackery*, 31 CA 91, 93 (1981).

238. See, e.g., Lerner, *supra* note 237, at 94.

239. Some popular marijuana products, such as edibles, may be likely to contain components that cross state lines. Cf. Robert J. MacCoun & Michelle M. Mello, *Half-Baked—The Retail Promotion of Marijuana Edibles*, 372 NEW ENG. J. MED. 989 (2015) (explaining edible marijuana products).

240. Cf. Mikos, *Preemption*, *supra* note 224, at 8 (making the same point with respect to the CSA).

241. 21 U.S.C.A. §§ 331, 355(a) (Westlaw through Pub. L. No. 114-255).

242. See, e.g., Sabet, *supra* note 230, at 101.

so.²⁴³ Moreover, to the extent state marijuana laws involve prescriber and dispenser licensing, or prescribing decisions, the laws would apply to parties—that is, medical practitioners—to whom FDA requirements generally do not directly apply.²⁴⁴

A challenge to medical marijuana laws under an obstacle preemption theory would be a stronger case, but still may be unlikely to succeed.²⁴⁵ Some courts have been convinced by obstacle preemption arguments with respect to the CSA by, for example, concluding that state laws prohibiting employment discrimination against medical marijuana users are an obstacle to the execution of the objectives of the CSA.²⁴⁶ By permitting the sale of drugs for which there is little evidence of safety and effectiveness at least for some uses,²⁴⁷ state medical marijuana laws arguably “stand[] as an obstacle to the accomplishment and execution of the full purposes and objectives” of the FDA’s congressionally mandated mission of ensuring the safety and effectiveness of drugs.²⁴⁸ And courts have echoed the idea that Congress intended the FDA to be the gatekeeper for drugs both inside the preemption context—such as in the litigation challenging Maine’s drug importation law²⁴⁹—and outside the preemption context. For example, in *United States v. Evers*, a case involving allegedly illegal drug promotion, the Fifth Circuit noted that the FDA “was obviously intended to control the *availability of drugs* for prescribing by physicians.”²⁵⁰ Moreover, medical marijuana laws do not present a theoretical obstacle to the FDA’s mission. Evidence suggests that state medical marijuana laws are in fact utilized by a large group of patients—one group that researches controversial policy issues estimates that over one million patients obtain medical marijuana under state laws.²⁵¹

This theory, however, has significant weaknesses, even if courts are increasingly

243. Obtaining FDA approval for marijuana admittedly may be somewhat complicated because it is a “botanical,” that is, plant-based, drug. As the FDA has explained in guidance, if a botanical product is marketed for use in diagnosing, curing, mitigating, or treating disease, as medical marijuana is, it is subject to all regulatory requirements for drugs, including approval. But because of the “heterogeneous nature” of botanical drugs, sponsors may face difficulty ensuring and demonstrating that the effectiveness of the drug is the same across batches. *See* FDA, *supra* note 220, at 4.

244. *See supra* Part II.2.B. for the discussion of REMS.

245. Under similar reasoning, there may be a plausible claim that medical marijuana laws are preempted because the FDA wholly occupies the field of determining whether drugs are safe and effective—although such an argument would be weaker, facing the earlier mentioned challenges of a field preemption argument outside the context of foreign commerce. *See supra* Part II.B.2.

246. *See, e.g.,* Washburn v. Columbia Forest Prods., Inc., 134 P.3d 161, 166–67 (Or. 2006) (Kistler, J., concurring).

247. *See supra* note 232.

248. *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941).

249. *See Ouellette v. Mills*, 91 F. Supp. 3d 1, 8–11 (D. Me. 2015).

250. 643 F.2d 1043, 1048 (5th Cir. 1981) (emphasis in original).

251. *Number of Legal Medical Marijuana Patients*, PROCON.ORG, <http://medicalmarijuana.procon.org/view.resource.php?resourceID=005889> [<https://perma.cc/S48R-YUYD>] (last updated Mar. 3, 2016). Moreover, if the FDA were to approve a marijuana product for a condition for which state law prohibited it, a court could conclude that state laws were preempted under an obstacle preemption theory, just as Judge Zobel did in the Zohydro litigation.

inclined to rely on obstacle preemption to strike down state laws that disrupt the careful balancing that the federal government has struck with a particular policy.²⁵² In general, where state regulation has existed for decades, and Congress is well aware of that regulation, as is the case with medical marijuana, courts may be reluctant to rely on an obstacle preemption.²⁵³ Additionally, recent congressional attempts to federally legalize marijuana that have largely ignored the FDA's jurisdiction provide some evidence that Congress does not intend the FDA to occupy the field of marijuana regulation.²⁵⁴ Moreover, the evidence that the FDA has done a careful balancing of competing federal goals with respect to marijuana is weaker than it is for Zohydro. Unlike with Zohydro, where there is evidence that the FDA carefully considered the safety and effectiveness (and potential for abuse) of Zohydro in both its approval decision and its decision to require a REMS,²⁵⁵ there is no publicly available documentation that the FDA has considered the use of marijuana for the full range to indications for which states have authorized its use, and rejected those uses.²⁵⁶ In sum, while there are colorable arguments that the FDCA preempts medical marijuana laws, the chances of success of such a challenge may be remote.

5. "Right To Try" Laws

State "right to try" laws provide another example of state drug laws intended to provide access to drugs outside of the FDA process, for which there is a weaker case for FDA preemption. "Right to try" laws are intended to provide terminally and seriously ill patients easy access to unapproved drugs (and devices) for treatment purposes, outside of clinical trials.²⁵⁷ The term for such treatment use in the FDA's regulations is "expanded access."²⁵⁸ FDA regulations specify a process for requesting expanded access, and the agency authorizes approximately ninety-nine percent of

252. Brown & Tomar, *supra* note 21, at 289–84.

253. See, e.g., *Gade v. Nat'l Solid Wastes Mgmt. Ass'n*, 505 U.S. 88, 116 (1992) (Souter, J., dissenting); *Lefavre v. KV Pharm. Co.*, 630 F.3d 733, 739 (8th Cir. 2011); *Chemerinsky et al.*, *supra* note 227, at 101, 101 n.97.

254. See, e.g., H.R. 1227, 115th Cong. (2017); S. 683, 114th Cong. (2015).

255. See, e.g., FDA, SUMMARY MINUTES OF MEETING OF THE ANESTHETIC AND ANALGESIC DRUG PRODUCTS ADVISORY COMMITTEE (2012), <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/UCM336475.pdf> [<https://perma.cc/8HSA-V8WC>].

256. The two FDA-approved THC products are approved for various nausea- and vomiting-related indications. See *Cesamet*, *supra* note 233; *Marinol*, *supra* note 233.

257. See, e.g., Rebecca Dresser, *The "Right To Try" Investigational Drugs: Science and Stories in the Access Debate*, 93 TEX. L. REV. 1631, 1640 (2015); Noah, *supra* note 7, at 23–24; Brady Dennis & Ariana Eunjung Cha, *'Right To Try' Laws Spur Debate Over Dying Patients' Access to Experimental Drugs*, WASH. POST (May 16, 2014), http://www.washingtonpost.com/national/health-science/right-to-try-laws-spur-debate-over-dying-patients-access-to-experimental-drugs/2014/05/16/820e08c8-dcfa-11e3-b745-87d39690c5c0_story.html [<https://perma.cc/M642-R8W6>]. The debate about the appropriate balance between early access to drugs and demonstrated safety and effectiveness of those drugs has been ongoing for decades. See, e.g., Patricia J. Zettler & Henry T. Greely, *The Strange Allure of State "Right-To-Try" Laws*, 174 JAMA INTERNAL MED. 1885 (2014).

258. 21 C.F.R. pt. 312, subpt. I (2016).

patients' requests.²⁵⁹ But advocacy groups and patients have criticized the FDA process for being slow and burdensome.²⁶⁰ Although there is good reason to think such criticisms of the FDA are not deserved,²⁶¹ since 2014, over thirty states have enacted "right to try" laws, and additional states are considering proposed legislation.²⁶²

"Right to try" laws are based on model legislation drafted by the Goldwater Institute, an organization that advocates for a "constitutionally limited government."²⁶³ The laws permit access to experimental drugs that have successfully completed phase 1 trials—small, first-in-human studies intended to show only that a drug is safe enough for further study.²⁶⁴ A few additional requirements generally must be met, including that the patient's physician documents the patient's illness and that the patient has considered all approved treatment options, and that the patient has provided informed consent.²⁶⁵ The laws also typically provide that a state medical board cannot discipline a physician solely for recommending an unapproved drug under these laws and stipulate both that companies may charge for the unapproved drugs and insurers are not required to cover them.²⁶⁶

These "right to try" laws provide significantly fewer safeguards for patients than the FDA's expanded access regulations do.²⁶⁷ For example, under the FDA's regulations, the patient must go beyond merely considering approved treatment options and demonstrate that he or she lacks "comparable or satisfactory" approved treatment options.²⁶⁸ As another example, in addition to requiring that patients provide informed consent, the FDA requires that an independent ethics review committee—known as an institutional review board (IRB)—reviews and approves the

259. *See id.*; *IND Activity Reports, Expanded Access INDs and Protocols*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/ucm373560.htm> [<https://perma.cc/8WR7-W88P>] (last updated Mar. 13, 2017).

260. *See e.g.*, CHRISTINA CORIERI, GOLDWATER INST., *EVERYONE DESERVES THE RIGHT TO TRY: EMPOWERING THE TERMINALLY ILL TO TAKE CONTROL OF THEIR TREATMENT* (2014), https://goldwater-media.s3.amazonaws.com/cms_page_media/2015/1/29/Right%20To%20Try.pdf [<https://perma.cc/4LA4-M895>]; Dennis & Cha, *supra* note 257.

261. *See infra* Part III.; *cf.* Dresser, *supra* note 257, at 1648–53 (describing positive and negative patient experiences with access).

262. *See* Healy, *supra* note 15.

263. *About*, GOLDWATER INST., <http://goldwaterinstitute.org/en/about> [<https://perma.cc/LJ9X-9VUH>].

264. *See* 21 C.F.R. § 312.21(a) (2016).

265. *See, e.g.*, Right To Try Act, 2015 N.C. Sess. Laws 335; *see also* Lisa Kearns & Alison Bateman-House, *Who Stands To Benefit? Right To Try Law Provisions and Implications*, 51 THERAPEUTIC INNOVATION & REGULATORY SCI. 170 (2017); GOLDWATER INST., *RIGHT TO TRY MODEL LEGISLATION*, https://goldwater-media.s3.amazonaws.com/cms_page_media/2015/1/28/RIGHT%20TO%20TRY%20MODEL%20LEGISLATION%20%282%29_1.pdf [<https://perma.cc/52KY-2SSK>].

266. *See* GOLDWATER INST., *supra* note 265, §§ 2, 3, 5.

267. *See, e.g.*, Alison Bateman-House, Laura Kimberly, Barbara Redman, Nancy Dubler & Arthur Caplan, *Right-To-Try Laws: Hope, Hype, and Unintended Consequences*, 163 ANNALS INTERNAL MED. 796, 796 (2015).

268. 21 C.F.R. § 312.305(a)(1) (2016).

expanded access program before the patient receives the experimental drug.²⁶⁹ The FDA also requires some evidence to support the treatment use of the unapproved drug, albeit far short of the level of evidence required for drug approval.²⁷⁰

“Right to try” laws, therefore, offer the opportunity to consider the preemptive effects of the FDA’s authority in another context in which states have established requirements less stringent than the FDA’s. “Right to try” advocates assert that any preemption challenge to the laws would fail because, under the Tenth Amendment, “federal regulations that violate constitutional liberties can never trump state laws.”²⁷¹ They argue that “right to try” laws “preserve constitutionally protected rights, such as a person’s right to life and medical self-preservation.”²⁷² Although patients often have very sympathetic claims for access to unapproved therapies (and understandable reasons for wanting access),²⁷³ courts have declined to recognize such access as a constitutionally protected right.²⁷⁴ Accordingly, “right to try” laws are not likely to survive preemption challenges on the ground that they protect a constitutional right.²⁷⁵

Yet “right to try” advocates may not be wrong that preemption challenges to the laws are likely to fail. Nothing in the state laws makes it impossible for a drug manufacturer to comply with the FDA’s expanded access regulations because the FDA’s requirements are more stringent.²⁷⁶ As long as the FDA has authorized the treatment use of the unapproved drug under its regulations (and the manufacturer complies with the other requirements in FDA regulations), a drug manufacturer would comply

269. *Id.* at § 312.305(c)(4).

270. *See* 21 C.F.R. §§ 312.305(a)(2), .310(a), .315(b), .320(a) (2016).

271. Kurt Altman & Christina Sandefur, *Right-To-Try Laws Fulfill The Constitution’s Promise of Individual Liberty*, HEALTH AFF.: BLOG (July 14, 2015), <http://healthaffairs.org/blog/2015/07/14/right-to-try-laws-fulfill-the-constitutions-promise-of-individual-liberty> [https://perma.cc/6H7Q-JRWH]; Clint Bolick, *The End of FDA Paternalism?*, HOOVER INST.: DEFINING IDEAS (Aug. 14, 2014), <http://www.hoover.org/research/end-fda-paternalism> [https://perma.cc/652Z-6H9C]; *see also* Sam Adriance, *Fighting for the “Right To Try” Unapproved Drugs: Law As Persuasion*, 124 YALE L.J. FORUM 148, 151 (2014) (“Right to Try’s supporters have successfully framed the laws as both a boon to personal liberty and a remedy for bureaucratic failure.”).

272. Altman & Sandefur, *supra* note 271.

273. *Cf.* Arthur Caplan & Alison Bateman-House, *Compassion for Each Individual’s Own Sake*, 14 AM. J. BIOETHICS 16, 16 (2014) (“When people face dire outcomes, we are compelled, morally and psychologically, to try to help them.”).

274. *Abigail All. for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 697 (D.C. Cir. 2007); Shah & Zettler, *supra* note 35, at 140–51.

275. Likewise, anticommandeering concerns grounded in the Tenth Amendment are irrelevant to considering the legal effect of state drug regulation—because in no instance is the FDA forcing states to enact laws or enforce federal law. Rather, the issue is whether states may, of their own volition, enact laws that intersect with the FDA’s drug regulatory scheme. *See, e.g.*, *Printz v. United States*, 521 U.S. 898 (1997); Chemerinsky et al., *supra* note 227, at 102.

276. *Compare* 21 C.F.R. pt. 312, subpt. I (2016), with GOLDWATER INSTIT., *supra* note 265. *But see* Caitlyn Martin, Note, *Questioning the “Right” in State Right To Try Laws: Assessing the Legality and Effectiveness of These Laws*, 77 OHIO ST. L.J. 159, 178 (2016) (arguing that “right to try” laws are preempted on impossibility grounds).

with both federal and state law if it chose to supply its unapproved drug to a patient in one of the “right to try” states.²⁷⁷

As in the medical marijuana context, an obstacle preemption challenge to “right to try” laws is a closer call but may face some difficulties.²⁷⁸ In support of such a challenge, there is considerable evidence that Congress intended the FDA to determine when access to drugs is appropriate. In section 561 of the FDCA, Congress explicitly authorized the FDA to establish an expanded access program and required the FDA to balance various considerations when reviewing patients’ access requests, including the data supporting the use of the unapproved drug and whether expanded access to the unapproved drug will interfere with its approval process.²⁷⁹ And there is evidence—in the form of detailed regulations—that the FDA has in fact carefully considered the complex ethical and scientific issues associated with expanded access to establish a process that the agency believes strikes the right balance.²⁸⁰ To the extent “right to try” laws deviate from the FDA process, they, therefore, could be viewed as undermining the objectives of the federal program.

But unlike medical marijuana, there is no convincing evidence that any patients have received unapproved drugs pursuant to state laws outside the FDA’s process.²⁸¹ Without such evidence, it may be difficult to argue that these state laws thwart the FDA’s expanded access policy—to the extent courts conclude that a party must demonstrate *actual* frustration of federal objectives to succeed on an obstacle

277. See 21 U.S.C. § 360bbb (2012).

278. *But see* David Farber, Preeya Noronha Pinto, Arthur Caplan & Alison Bateman-House, *How State Right-To-Try Laws Create False Expectations*, HEALTH AFF. BLOG (May 22, 2015), <http://healthaffairs.org/blog/2015/05/22/how-state-right-to-try-laws-create-false-expectations> [<https://perma.cc/M7T7-K2GV>] (arguing generally that “right to try” laws are impliedly preempted by the FDCA, without focusing on which specific theory of implied preemption supports that assertion). Also similar to medical marijuana, there may be a plausible case that “right to try” laws are preempted because Congress intended FDA to wholly occupy the field of determining when early access to unproven drugs is appropriate. Again, however, such a case would face the previously mentioned impediments to bringing a successful field preemption challenge outside the context of foreign commerce. See *supra* Part II.B.2.

279. 21 U.S.C. § 360bbb.

280. See 21 C.F.R. pt. 312, subpt. I.

281. See Michele Munz, *Missouri’s ‘Right To Try’ Law No Guarantee Patient Will Get Experimental Drugs*, ST. LOUIS POST-DISPATCH (May 20, 2015), http://www.stltoday.com/news/local/metro/missouri-s-right-to-try-law-no-guarantee-patient-will/article_05c07958-5217-5c3f-9f15-1a43c8a3e740.html [<https://perma.cc/Z3JK-MSMG>]. In 2016 congressional hearings, a representative of the Goldwater Institute asserted that over twenty patients have received drugs pursuant to “right to try” laws. However, it is unclear whether the FDA had also authorized that access, and other sources report that no drug company has provided its drugs without FDA authorization. See Zachary Brennan, *Congressional Hearings Focus on Compassionate Use, FDA Issues*, REG. AFF. PROFS. SOC’Y (Feb. 25, 2016), <http://raps.org/Regulatory-Focus/News/2016/02/25/24410/Congressional-Hearings-Focus-on-Compassionate-Use-FDA-Issues/> [<https://perma.cc/Q8DR-P8SK>]; see also Julie Turkewitz, *Patients Seek ‘Right To Try’ New Drugs*, N.Y. TIMES (Jan. 10, 2015), <http://www.nytimes.com/2015/01/11/us/patients-seek-right-to-try-new-drugs.html> [<https://web-beta.archive.org/web/20161018215120/http://www.nytimes.com/2015/01/11/us/patients-seek-right-to-try-new-drugs.html>] (“The laws do not seem to have helped anyone obtain experimental medicine . . .”).

preemption theory. Moreover, certain aspects of state “right to try” laws either may be consistent with FDA oversight, such as provisions noting that drug manufacturers are not required to provide unapproved drugs to patients and may charge patients for the cost of the drug, or may not directly intersect with FDA oversight, such as provisions eliminating drug manufacturers’ liability for providing access or stating that insurers are not required to cover unapproved drugs.²⁸² As with marijuana, therefore, it is unclear that an obstacle preemption challenge to “right to try” laws would succeed.

C. Preempting Medical Practice Regulation

The above Part demonstrates that there are plausible arguments that FDA oversight preempts much divergent state regulation—but determining whether FDA oversight preempts state drug regulation is a fact-intensive inquiry that does not yield a categorical answer. This, however, is not to say that examining recent drug regulation provides no new insights into the scope of the FDA’s authority. Rather, the analysis suggests that in one area—medical practice regulation—the preemptive reach of the FDA’s authority may be more extensive than previously thought.

Conventional wisdom in health law and policy holds that states regulate the practice of medicine, while the federal government—specifically the FDA—regulates drugs.²⁸³ This adage has been cited by lawmakers, courts, and the FDA itself when discussing the limits on the agency’s jurisdiction.²⁸⁴ For example, in a 1972 proposed rule, the FDA explained “it is clear that Congress did not intend the [FDA] to regulate . . . the practice of medicine.”²⁸⁵ As a more recent example, in the litigation about its drug importation law, Maine argued that the regulation of medical practice—in that case, requirements for pharmacy licensing—is “an area traditionally reserved for the states,” and Judge Torresen did not dispute that proposition.²⁸⁶

The history of drug and medical practice regulation explained in Part I raises questions about whether this conventional wisdom ever accurately described the intersection (or lack thereof) of state and federal regulation. State drug regulation—often

282. See FDA, U.S. DEP’T OF HEALTH & HUMAN SERVS., CHARGING FOR INVESTIGATIONAL DRUGS UNDER AN IND—QUESTIONS AND ANSWERS: GUIDANCE FOR INDUSTRY (2016) [hereinafter FDA CHARGING GUIDANCE], <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351264.pdf> [<https://perma.cc/L98R-4X95>]; FDA, U.S. DEP’T OF HEALTH & HUMAN SERVS., EXPANDED ACCESS TO INVESTIGATIONAL DRUGS FOR TREATMENT USE—QUESTIONS AND ANSWERS: GUIDANCE FOR INDUSTRY (2016) [hereinafter FDA EXPANDED ACCESS GUIDANCE], <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf> [<https://perma.cc/VFX4-MTXG>]; GOLDWATER INST., *supra* note 265.

283. See, e.g., Evans *supra* note 18, at 288; Noah, *supra* note 19, at 154–71; Zettler, *supra* note 19, at 430–31.

284. See Evans, *supra* note 18, at 288; Noah, *supra* note 19, at 154–71; Zettler, *supra* note 19, at 430–31.

285. Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the FDA, 37 Fed. Reg. 16,503, 16,504 (proposed Aug. 15, 1972).

286. Ouellette v. Mills, 91 F. Supp. 3d 1, 9 (D. Me. 2015). *But cf.* McCuskey, *supra* note 92, at 146 (questioning whether a tradition of state regulation is “compelling evidence” with respect to congressional intent to preempt).

framed as medical practice regulation—dates back to the colonies and continues today in various forms, including state Food, Drug, and Cosmetic Acts that mimic federal law. Likewise, the federal government has long regulated medical practice. For example, during the prohibition era in the early twentieth century, federal law limited the amount of liquor that physicians could prescribe.²⁸⁷ Nevertheless, the idea that the practice-products distinction serves as the dividing line between state and federal regulation persists.²⁸⁸

However, a preemption analysis of recent state drug laws and regulations underscores that the distinction between regulating medical practice and medical products is nebulous. If the FDA has no role in directly or indirectly regulating medical practice, state medical practice laws and regulations should not be preempted by the FDA's authority. But as litigation over the Maine drug importation law and the Massachusetts Zohydro ban show most clearly, the FDA's preemptive reach can extend into medical practice regulation in certain circumstances.²⁸⁹

The Maine drug importation law exempted foreign pharmacies from Maine's licensing requirements but did not purport to "approve" foreign drugs.²⁹⁰ The Massachusetts ban prohibited medical practitioners from prescribing and dispensing Zohydro, but did not prohibit the drug manufacturer from selling Zohydro in Massachusetts.²⁹¹ Yet Judges Torresen and Zobel concluded that FDA oversight preempted both state efforts, implicitly collapsing the distinction between regulating medical practice and regulating medical products to reach those conclusions.²⁹² Both judges acknowledged the long history of state medical practice regulation pursuant to states' police powers, and that the state laws and regulations at issue purported to continue in this tradition.²⁹³ Nevertheless they looked beyond that framing to the underlying intent of the regulatory efforts, concluding that they were intended to challenge particular aspects of the FDA's scheme.²⁹⁴ They did so because, as Judge Torresen

287. See *Lambert v. Yellowley*, 272 U.S. 581, 596–97 (1926); Zettler, *supra* note 19, at 440–41; cf. Nicole Huberfeld, *Federalizing Medicaid*, 14 U. PA. J. CONST. L. 431, 476 (2011) ("The practice of medicine is increasingly nationalized . . .").

288. See, e.g., Zettler, *supra* note 19, at 442–46. This persistence may exist in part because characterizing proposed federal laws as medical products regulation, rather than medical practice regulation, arguably has helped to garner political support from organized medicine for those laws. See *id.*

289. See Sharkey, *supra* note 21, at 1618. California's track and trace law also provides an example of the blurriness of the practice-products distinction, albeit a less compelling one. California lawmakers established the drug pedigree requirements within the state's pharmacy practice laws. Because that law expressly invited federal preemption, lawmakers apparently did not think that placing the requirements within its pharmacy practice regulations would prevent FDA preemption. See CAL. BUS. & PROF. CODE § 4034.1 (West 2011 & Supp. 2016) (repealed 2015).

290. See ME. REV. STAT. ANN. tit. 32, § 13731 (Supp. 2016).

291. *Zogenix, Inc. v. Patrick*, No. 14-11689-RWZ, 2014 WL 1454696, at *1 (D. Mass. Apr. 15, 2014).

292. *Ouellette v. Mills*, 91 F. Supp. 3d 1, 9 (D. Me. 2015); *Zogenix*, 2014 WL 1454696, at *2.

293. See *Ouellette*, 91 F. Supp. 3d at 9; *Zogenix*, 2014 WL 1454696, at *2; cf. McCuskey, *supra* note 92, at 146 (questioning whether a tradition of state regulation is "compelling evidence" with respect to congressional intent to preempt).

294. *Ouellette*, 91 F. Supp. 3d at 9; *Zogenix*, 2014 WL 1454696, at *2.

explained, “[w]hen undertaking preemption analysis, courts . . . evaluate whether the aim of the state law is to affect an area of federal regulation or interest.”²⁹⁵

Indeed, examining the underlying intent of the state regulation seems to be the appropriate legal approach. Importantly, there is no constitutional bar on FDA regulation of medical practice.²⁹⁶ Because there is no constitutional significance to a state applying its oversight to medical practitioners rather than to drug manufacturers or the drugs themselves, in these preemption cases, courts are simply faced with the question of whether Congress intended FDA oversight to displace state regulation.²⁹⁷ And as the Supreme Court has explained, “the words of a statute must be read in their context and with a view to their place in the overall statutory scheme.”²⁹⁸ Consistent with this idea, in considering preemption questions, courts are right to consider states’ intent to regulate drugs, even when the requirements of a state statute or regulation technically apply only to medical practitioners.

Even with courts considering the underlying purpose of state regulation, however, states may be able to avoid impossibility challenges by applying their requirements to medical practitioners—whom the FDA generally does not directly regulate. As an example, because the terms of the Massachusetts ban on Zohydro prohibited practitioners from prescribing and dispensing—and FDA requirements do not directly apply to practitioners—arguably, it was not impossible for any particular party to comply with both state and federal law.²⁹⁹ That is, under the ban it would have been legal for Zohydro’s manufacturer to sell its drug within Massachusetts; there, however, would have been no buyers, because it would not have been legal for medical practitioners to prescribe or dispense the drug. Thus, obstacle (and perhaps even field)

295. *Ouellette*, 91 F. Supp. 3d at 8.

296. See Noah *supra* note 19, at 154–71; Zettler, *supra* note 19, at 467–74; cf. LEIGHANNE OLSEN, W. ALEXANDER GOOLSBY & J. MICHAEL MCGINNIS, INST. OF MED., LEADERSHIP COMMITMENTS TO IMPROVE VALUE IN HEALTHCARE: FINDING COMMON GROUND 242–43 (2009), https://www.ncbi.nlm.nih.gov/books/NBK52851/pdf/Bookshelf_NBK52851.pdf [<https://perma.cc/Z67C-BFKU>] (“The states directly regulate the practice of medicine and the healthcare workforce. This regulatory authority has its foundation in the 10th Amendment to the U.S. Constitution. Because these duties are not assigned to the federal government by the Constitution, this amendment provides the states the right to enact laws and regulations to protect the health and general welfare of their residents.”); David Orentlicher, *Off-Label Drug Marketing, the First Amendment, and Federalism*, 50 WASH. U. J.L. & POL’Y 89, 99 (2016) (arguing FDA regulation of practitioners’ off-label prescribing raises “serious federalism concerns,” but conceding that such regulation would not exceed the federal government’s constitutional authority).

297. See *supra* Part II.A.

298. *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000) (quoting *Davis v. Mich. Dep’t of Treasury*, 489 U.S. 803, 809 (1989)).

299. *Zogenix*, 2014 WL 1454696, at *1. To be clear, one might also argue that Judge Zobel should have concluded that the Massachusetts Zohydro ban was preempted on the basis of impossibility, rather than obstacle, preemption. It would have been impossible for Zogenix to reformulate its drug to be abuse deterrent, to satisfy Massachusetts’s requirements for prescribing and dispensing, without violating the FDA’s requirement that such a change not be made without the FDA’s preapproval. See Noah, *supra* note 7, at 8–12; cf. *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2478 n.5 (2013) (“[T]he mere fact that a manufacturer may avoid liability by leaving the market does not defeat a claim of impossibility.”).

preemption may have an important role to play if such preemption challenges to state medical practice regulation are to be successful. But, at the very least, challenges asserting that state oversight is preempted by FDA regulation should not fail solely because a state action is framed as medical practice regulation.

III. BEYOND PREEMPTION

Beyond providing insights into the preemptive reach of the FDA's authority, examining recent state interest in drug regulation may also inform our general understanding of both the scope of the FDA's jurisdiction and the relationship between the FDA and the states. This Part explores two such lessons. First, this Part argues that the nebulosity of the practice-products binary revealed by recent state drug regulation may have ramifications for debates about the confines of the FDA's authority to regulate innovative technologies such as regenerative medicine and genetic testing. Second, this Part considers the relationship between the FDA and the states, by beginning to explore why states might choose to spend their limited resources enacting and defending drug regulation despite the specter of preemption litigation and the existing (and extensive) federal regulatory scheme. One possibility that emerges is that state drug regulation is an effective means to influence federal policy.

A. Blurring the Practice-Products Distinction

The blurriness of the practice-products distinction revealed by recent state drug regulation may have significance for debates about the proper scope of the FDA's jurisdiction outside the preemption context—because these debates often involve questions about where to draw the line between medical practice and medical products oversight.³⁰⁰ And this line drawing may be particularly difficult when the FDA is faced with questions about whether, and how, to regulate new medical technologies that may not fit comfortably within the agency's existing framework.³⁰¹ Two examples—regenerative medicine and genetic testing—highlight the challenges of relying on the practice-products binary to determine the boundaries of the FDA's jurisdiction.

1. Regenerative Medicine

Regenerative medicine offers one example of a medical technology in which the practice-products distinction has come into play. Therapies involving stem cell

300. See, e.g., CLEMENT & TRIBE, *supra* note 24, at 11; Evans, *supra* note 18, at 288.

301. The FDA's attempts to assert authority over new technologies are not the only context in which the argument that the FDA cannot regulate medical practice is put forth. Stakeholders have also raised this argument when the FDA has tried to change the way it regulates products that are clearly within its jurisdiction, including traditional pharmaceuticals. For example, when the FDA proposed regulations in the 1990s to create risk-mitigation programs for drugs that were similar to REMS, it received comments asserting that the FDA lacked authority to implement these programs because they “interfere with the practice of medicine.” New Drug, Antibiotic, and Biological Drug Product Regulations; Accelerated Approval, 57 Fed. Reg. 58,942, 58,951–52 (Dec. 11, 1992) (codified at 21 C.F.R. pts. 314 & 601).

transplantation are one area of regenerative medicine widely believed to hold great promise for treating myriad serious or life-threatening illnesses—albeit a promise that has yet to be realized for most conditions.³⁰² Nevertheless, clinics offering autologous stem cell therapies for a range of conditions, including joint problems, asthma, autism, muscular dystrophy, and Alzheimer’s disease, have proliferated in the United States.³⁰³ In part because autologous stem cell therapies involve the transplantation of stem cells that are derived from the patient’s own tissue, some clinics, medical practitioners, and commentators have argued that these therapies are surgical procedures that are part of the practice of medicine and outside the FDA’s purview.³⁰⁴

In at least one case, however, courts were unconvinced by this logic. In 2010, the FDA sought to enjoin three Colorado physicians and their company Regenerative Sciences, LLC from giving patients an autologous stem cell therapy, on the ground that it was a drug that violated the FDA’s requirements.³⁰⁵ The specific treatment involved removing the patient’s own bone marrow, isolating stem cells from that bone marrow, processing those stem cells, and then reimplanting the mixture back into the same patient.³⁰⁶ In the subsequent litigation, *United States v. Regenerative Sciences*, the physicians asserted that the FDA lacked authority over their stem cell treatment because it was a procedure that fell within Colorado’s definition of medical

302. See, e.g., PAUL KNOEPFLER, *STEM CELLS: AN INSIDER’S PERSPECTIVE* 10 (2013); Kalina Kamenova & Timothy Caulfield, *Stem Cell Hype: Media Portrayal of Therapy Transplantation*, *SCI. TRANSLATIONAL MED.*, Mar. 11, 2015, at ps4 (2015). Thus far, the safety and effectiveness of stem cell transplantation has been established only for hematopoietic stem cell transplantation for certain blood cancers and genetic disorders. See, e.g., Kamenova & Caulfield, *supra*, at ps4; Aaron D. Levine & Leslie E. Wolf, *The Roles and Responsibilities of Physicians in Patients’ Decisions About Unproven Stem Cell Therapies*, 40 *J.L. MED. & ETHICS* 122, 122 (2012).

303. See, e.g., R. Alta Charo, *On the Road (to a Cure?)—Stem-Cell Tourism and Lessons for Gene Editing*, 374 *NEW ENG. J. MED.* 901, 902 (2016); Leigh Turner & Paul Knoepfler, *Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry*, 19 *CELL STEM CELL F.* 154, 156 (2016); cf. Levine & Wolf, *supra* note 302 (describing stem cell clinics in other countries).

304. See, e.g., RICHARD EPSTEIN, *CTR. FOR LEGAL POLICY, THE FDA’S MISGUIDED REGULATION OF STEM-CELL PROCEDURES: HOW ADMINISTRATIVE OVERREACH BLOCKS MEDICAL INNOVATION* 2 (2013), http://www.manhattan-institute.org/pdf/lpr_17.pdf [<https://perma.cc/E9F5-8MNH>]; Margaret Foster Riley, *Twenty-First-Century Technology with Twentieth-Century Baggage: FDA Regulation of Regenerative Medicine*, in *FDA IN THE TWENTY-FIRST CENTURY* 455, 460 (Holly Fernandez Lynch & I. Glenn Cohen, eds., 2015); Charo, *supra* note 303, at 902; *FDA, CELL SURGICAL NETWORK*, <http://stemcellrevolution.com/fda> [<https://perma.cc/EA88-9266>]; see also 21 C.F.R. § 1271.3 (2016) (defining “autologous use”). Other issues are also prominent in the debate about FDA jurisdiction over autologous stem cell therapies, including whether a product has traveled in interstate commerce, and whether it satisfies the criteria in FDA regulations necessary for human cells or cellular products to fall outside of the regulatory scheme for drugs, devices, or biologics that requires premarket review. See generally *United States v. Regenerative Scis., LLC*, 741 F.3d 1314 (D.C. Cir. 2014); 21 C.F.R. § 1271.10(a) (2016); *supra* notes 234–39 and accompanying text.

305. *United States v. Regenerative Scis., LLC*, 878 F. Supp. 2d 248, 251–52 (D.D.C. 2012), *aff’d*, 741 F.3d 1314 (D.C. 2014).

306. *Id.*

practice and “the [FDA] was not intended to infringe on states’ traditional role in regulating the practice of medicine.”³⁰⁷ This argument did not persuade the D.C. Circuit in part because the court concluded that the stem cell therapy was a product, rather than a procedure.³⁰⁸ The court also expressed skepticism about the practice-products distinction.³⁰⁹ It dismissed the physicians’ practice of medicine argument as a “syllogism,” concluding that the scope of the FDA’s authority cannot depend “on state-by-state definitions of the ‘practice of medicine’” and its “breadth . . . and applicability to doctors” is evident.³¹⁰

Nevertheless, some providers of autologous stem cell therapies continue to rely on the practice-products distinction to assert that they are not subject to FDA oversight.³¹¹ Indeed, this argument resurfaced at a public meeting that the FDA held to obtain input on its policies related to the regulation of cells and cellular products.³¹² But, consistent with *Regenerative Sciences* and a preemption analysis of recent state drug regulation, relying on the practice-products distinction may not be particularly useful for identifying the borders of the FDA’s jurisdiction.³¹³

2. Genetic Testing

Genetic testing offers a second example of an innovative technology for which FDA oversight implicates the practice-products distinction.³¹⁴ Many (though not all)

307. 741 F.3d at 1319.

308. *See id.*

309. *See id.*

310. *Id.* But see Lars Noah, *Growing Organs in the Lab: Tissue Engineers Confront Institutional “Immune” Responses*, 55 JURIMETRICS 297, 315–17 (2015) (questioning the court’s reasoning).

311. *See, e.g.*, Charo, *supra* note 303, at 902 (“U.S. clinics have sprung up offering various ‘treatments’ that they argue merely represent the practice of medicine using a patient’s own tissues and therefore aren’t subject to the jurisdiction of the [FDA].”); McFarling, *supra* note 24 (explaining that one provider “plans to attend [an FDA hearing scheduled for September 2016] to argue, as other clinics have, that the injections are not drugs, but simple outpatient surgeries that should not be regulated”); FDA, *supra* note 304 (“[T]he treatment centers provide surgical procedures only and are not involved in the use or manufacture of any investigational drugs.”).

312. *See* Draft Guidances Relating to the Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products; Rescheduling of Public Hearing; Request for Comments, 81 Fed. Reg. 23,661 (Apr. 22, 2016); Laurie McGinley, *Stem-Cell Clinics Face New Scrutiny from Federal Regulators*, WASH. POST (Sept. 12, 2016), https://www.washingtonpost.com/national/health-science/for-stem-cell-clinics-new-scrutiny-from-federal-regulators/2016/09/12/7b101896-7540-11e6-b786-19d0cb1ed06c_story.html?postshare=7201473775905391&tid=ss_tw [<https://perma.cc/6XAM-CQBM>].

313. Indeed, some have few qualms about the FDA’s authority over autologous stem cell therapies and assert that the FDA should more vigorously enforce applicable requirements. *See, e.g.*, Turner & Knoepfler, *supra* note 303; Andrew Joseph, *Drive To Get More Patients Experimental Stem Cell Treatments Stirs Concern*, STAT (June 30, 2016), <https://www.statnews.com/2016/06/30/stem-cell-political-fight> [<https://perma.cc/2T3V-KTUU>].

314. *See, e.g.*, James P. Evans & Michael S. Watson, *Genetic Testing and FDA Regulation: Overregulation Threatens the Emergence of Genomic Medicine*, 313 JAMA 669, 669 (2015);

genetic tests fall within a category known as “laboratory developed tests” (LDTs).³¹⁵ LDTs are in vitro diagnostic tests that are designed, manufactured, and used within a single laboratory.³¹⁶ This category includes tests of varying complexity, from simple tests like those measuring sodium levels to more complicated tests like many genetic tests.³¹⁷

Although, according to the FDA, various requirements of the FDCA (including premarket review) apply to LDTs, for decades the FDA has declined to enforce these requirements for policy reasons.³¹⁸ Because of changes to the LDT industry and testing technology, in 2014 the FDA proposed phasing in enforcement of applicable regulatory requirements for “high and moderate risk” LDTs, including many genetic tests.³¹⁹ This proposal was controversial, and various stakeholders and commentators criticized it on numerous legal and policy grounds.³²⁰

see also Lars Noah, *The Coming Pharmacogenomics Revolution: Tailoring Drugs To Fit Patients’ Genetic Profiles*, 43 JURIMETRICS J. 1, 24–25 (2002) (arguing that pharmacogenomics may collapse the practice-products distinction in tort law). Although genetic tests within the scope of FDA’s jurisdiction are devices rather than drugs, *see* 21 U.S.C.A. § 321 (g), (h) (Westlaw through Pub. L. No. 114-255), the practice-products distinction presents similar issues in the device and drug context. It is also worth noting that not all genetic tests are devices as defined in the FDCA. For example, genetic tests that provide only raw data or ancestry information—without any health information or interpretation—are generally thought not to meet the definition of a device. *See, e.g.*, Kayte Spector-Bagdady & Elizabeth Pike, *Consuming Genomics: Regulating Direct-to-Consumer Genetic and Genomic Information*, 92 NEB. L. REV. 677, 728–31 (2014).

315. Barbara J. Evans, Wylie Burke, & Gail P. Jarvik, *The FDA and Genomic Tests—Getting Regulation Right* 372 NEW ENG. J. MED. 2258, 2258 (2015). Direct-to-consumer genetic tests, such as those famously offered by 23andMe, do not fall within the FDA’s LDT policies. FDA, U.S. DEP’T OF HEALTH & HUMAN SERVS., DRAFT GUIDANCE FOR INDUSTRY, FOOD AND DRUG ADMINISTRATION STAFF, AND CLINICAL LABORATORIES: FRAMEWORK FOR REGULATORY OVERSIGHT OF LABORATORY DEVELOPED TESTS (LDTs) 5 n.4 (2014), <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm416685.pdf> [https://perma.cc/NQ6A-4562].

316. FDA, *supra* note 315, at 5.

317. *Laboratory Developed Tests*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/LaboratoryDevelopedTests/default.htm> [https://perma.cc/247S-EMBB] (last updated Jan. 13, 2017).

318. *See id.*

319. FDA, *supra* note 315, at 12–13.

320. *See, e.g.*, CLEMENT & TRIBE, *supra* note 24; Evans & Watson, *supra* note 314, at 669; Gail Javitt, *FDA’s Legally-Suspect Shift of Clinical Lab Test Regulation Through Guidance Documents*, WASH. LEGAL FOUND. LEGAL PULSE (Aug. 20, 2014), <https://wfllegalpulse.com/2014/08/20/fdas-legally-suspect-shift-of-clinical-lab-test-regulation-through-guidance-documents> [https://perma.cc/7VPC-X2EE]; *see also* Evans et al., *supra* note 315, at 2258 (arguing for “a relatively modest set of statutory reforms” to improve FDA oversight); Bradley Merrill Thompson, *The LDT Debate: Understanding FDA’s Jurisdiction Over IVDs Made at a Clinical Lab*, HEALTH L. ADVISOR (Jan. 16, 2015), <http://www.healthlawadvisor.com/2015/01/16/the-ldt-debate-understanding-fdas-jurisdiction-over-ivds-made-at-a-clinical-lab/#.VLmaImmAVbY.twitter> [https://perma.cc/N8PQ-4Z7K] (analyzing several legal questions raised by the FDA’s proposal).

Although the agency does not currently plan to move forward with finalizing the proposed policy on LDTs until there is an opportunity for further public discussion and, possibly, congressional action,³²¹ it is worth noting that one argument against the proposed policy that some laboratory stakeholders advanced was that LDTs are outside the scope of the FDA's jurisdiction because LDTs are services provided as part of the practice of medicine, rather than medical products.³²² A challenge to the FDA's authority over LDTs based solely on this argument, however, seems unlikely to succeed.³²³ As in the regenerative medicine and preemption contexts, in which courts have seemed willing to explicitly or implicitly dismiss the practice-products distinction, the line between practice and products oversight for LDTs may simply be too unclear to be useful.

This is not to say that the FDA has the authority to regulate all aspects of medical practice (or to regulate all aspects of regenerative medicine and genetic testing). And to be clear, this Article does not attempt to determine in what circumstances the FDA possesses or lacks the authority to regulate LDTs and regenerative medicine. Rather, this Article posits that relying on the practice-products distinction may not be particularly helpful for answering these jurisdictional questions because the line between practice and products oversight can be quite unclear. Whether a particular technology is within the FDA's jurisdiction simply depends on the relevant language of the FDA's enabling statutes³²⁴—and if the statute authorizes the FDA to take a particular regulatory action, it can do so, even if that action affects or regulates medical practice.

B. Beginning To Explore the Reasons for State Regulation

In addition to informing debates about the proper scope of the FDA's jurisdiction over new technologies, recent state interest in drug regulation that challenges FDA oversight raises a question about why this state interest has emerged, particularly given the possibility of preemption litigation. This Part first argues that this question about the reasons for state interest is heightened by the mixed practical impact of state regulation. It then begins to explore one reason that states may be interested in drug regulation that challenges FDA oversight—it may be an effective strategy to influence federal policy, even when a particular state action has limited legal or practical impact.

321. FDA, DISCUSSION PAPER ON LABORATORY DEVELOPED TESTS (2017), <https://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/LaboratoryDevelopedTests/UCM536965.pdf> [<https://perma.cc/6FFU-2SVV>].

322. See, e.g., CLEMENT & TRIBE, *supra* note 24, at 4–6; Evans & Watson, *supra* note 314, at 670; Thompson, *supra* note 320; cf. Evans, *supra* note 18, at 288–92 (discussing the practice-products distinction in the context of personalized medicine); W. Nicholson Price, *Regulating Black-Box Medicine*, 116 MICH. L. REV. (forthcoming 2017) (noting complications applying the practice-products distinction to medical algorithms).

323. See Thompson, *supra* note 320; cf. Evans et al., *supra* note 315, at 2258 (“[T]here is little doubt that the FDA has ample power to impose at least some new regulatory requirements on genomic testing . . .”).

324. See, e.g., *United States v. Regenerative Scis., LLC*, 741 F.3d 1314 (D.C. Cir. 2014).

1. The Mixed Practical Effect of State Regulation

Preemption is not the only reason that state drug regulation may be without significant effect. State regulation that establishes a scheme more permissive than the FDA's does not exempt drug manufacturers from federal requirements.³²⁵ For example, marketing marijuana for conditions for which state governments have given their approval does not confer approval of such drugs under federal law.³²⁶ Likewise, drug companies would violate the FDA's expanded access requirements if they choose to provide patients their unapproved drugs pursuant to a "right to try" law but without the FDA's authorization.³²⁷ That is, the very argument that would render an impossibility preemption challenge unsuccessful—that compliance with both state and federal requirements is possible—limits the legal impact of these laws.

That federal requirements remain intact means that the practical effect of some state regulation may turn on whether there are incentives for the drug industry to take advantage of the state policies that diverge from federal law. Mainstream pharmaceutical and biotechnology companies are immensely profitable businesses that are designed around the FDA's role as the gatekeeper and regulator of drugs. The perception within the drug industry is that failing to cooperate with the FDA, or violating its requirements and policies, is costly.³²⁸ Therefore, without significant financial incentives or a publicly announced federal enforcement discretion policy, much of the drug industry may not be likely to risk violating the FDA's requirements pursuant to an untested state law.

The dramatically different practical impacts of the equivalently widespread state medical marijuana and "right to try" laws demonstrate the importance of industry incentives. Despite the continued prohibition on marijuana under the federal CSA and FDCA,³²⁹ state medical marijuana laws have created a robust, openly conducted marijuana market. One organization estimates that over one million patients have obtained medical marijuana consistent with state laws.³³⁰ And in 2014, retailers sold \$386 million of medical marijuana (and another \$313 million of recreational marijuana) in Colorado alone.³³¹

One reason for this vigorous, but federally illegal, marijuana market is almost certainly that the federal government announced that it would not pursue prosecution

325. Other reasons might also include dormant commerce clause and substantive due process challenges. See Noah, *supra* note 7, at 35–54.

326. See 21 U.S.C.A. §§ 321(g), 355(a) (Westlaw through Pub. L. No. 114-255); FDA, *supra* note 220.

327. See 21 C.F.R. pt. 312, subpt. I (2016).

328. See, e.g., Lars Noah, *Governance by the Backdoor: Administrative Law(lessness?) at the FDA*, 93 NEB. L. REV. 89, 123 (2014); Elizabeth C. Price, *Teaching the Elephant To Dance: Privatizing the FDA Review Process*, 51 FOOD & DRUG L.J. 651, 654 (1996).

329. See *supra* Part II.B.4.

330. See *Number of Legal Medical Marijuana Patients*, *supra* note 251.

331. Christopher Ingraham, *Colorado's Legal Weed Market: \$700 Million in Sales Last Year, \$1 Billion by 2016*, WASH. POST (Feb. 12, 2015), <http://www.washingtonpost.com/news/wonkblog/wp/2015/02/12/colorados-legal-weed-market-700-million-in-sales-last-year-1-billion-by-2016/> [<https://perma.cc/6BNR-DS7M>].

in many circumstances in which marijuana is sold in compliance with state law.³³² Congress subsequently gave teeth to this enforcement discretion policy through a rider in the omnibus appropriations bill that prohibited the U.S. Department of Justice from using funds on actions that would prevent states from implementing their medical marijuana laws.³³³ But medical marijuana laws were also utilized before this enforcement discretion policy was in place.³³⁴ Another reason that state laws have created a prospering marijuana market despite federal prohibitions may be that marijuana sellers are outside of the mainstream pharmaceutical industry.³³⁵ Without other products subject to FDA oversight or a business model designed around FDA approval and regulation, marijuana sellers may not have the same aversion to bypassing the FDA as the traditional drug industry does. For example, although current federal policy suggests that the FDA is unlikely to enforce violations of its requirements that comply with state laws,³³⁶ mainstream drug companies might nevertheless wish to seek approval for any marijuana products because insurers often consider FDA approval when making coverage decisions.³³⁷

Yet unlike the substantial market created by state medical marijuana laws, there is no convincing evidence that any patients have received an unapproved drug pursuant to a “right to try” law (and outside of the FDA’s expanded access program).³³⁸ “Right to try” laws may have limited impact because the laws are new compared with medical marijuana laws, because they do not require drug companies to provide unapproved drugs to terminally ill patients, and because the laws do not address many valid industry concerns regarding the complicated practical and ethical questions that expanded access raises.³³⁹ But another reason might be that the mainstream drug industry has little incentive to risk a federal enforcement action by circumventing the FDA expanded access process. Indeed, the industry does not appear interested in providing unapproved drugs pursuant to “right to try” laws.³⁴⁰ For example, the primary trade organizations for brand-name drug manufacturers, the

332. DOJ Memo, *supra* note 228.

333. See Consolidated Appropriations Act, 2016, Pub. L. No. 114-113, § 542, 129 Stat. 2242, 2332–33 (2015); *United States v. McIntosh*, 833 F.3d 1163, 1169 (9th Cir. 2016).

334. See, e.g., *United States v. Oakland Cannabis Buyers’ Coop.*, 532 U.S. 483 (2001).

335. Cf. Alex Halperin, *How To Brand, Market, and Sell Marijuana Without Breaking the Law*, FASTCOMPANY (Apr. 23, 2015, 4:20 AM), <http://www.fastcompany.com/3045240/rebranding-pot/how-to-brand-market-and-sell-weed-without-breaking-the-law> [<https://perma.cc/2TU7-NZAV>] (describing the “best-known” cannabis brands in Colorado).

336. See § 542, 129 Stat. at 2332–33; DOJ Memo, *supra* note 228.

337. See, e.g., *Frequently Asked Questions About Drugs: Why Won’t My Insurance Company Pay for Certain Drugs?*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm082690.htm#6> [<https://perma.cc/9B4K-GV67>] (last updated Nov. 27, 2015).

338. See, e.g., Munz, *supra* note 281.

339. See, e.g., Right To Try Act, 2015 N.C. Sess. Laws 335; GOLDWATER INST., *supra* note 265; see also Shah & Zettler, *supra* note 35, at 140–52 (explaining some of the concerns for industry that expanded access raises). Although “right to try” laws seem to leave many industry concerns unaddressed, they do offer industry some incentives to provide expanded access to unapproved drugs. For example, many offer some protection from liability. See, e.g., 2015 N.C. Sess. Laws 335.

340. See, e.g., Dennis & Cha, *supra* note 257; Zettler & Greely, *supra* note 257.

Pharmaceutical Research and Manufacturers Association (PhRMA) and the Biotechnology Industry Organization (BIO), have publicly expressed reservations about “right to try” laws.³⁴¹ Neuralstem, Inc., is one of the few, if not the only company, to have publicly indicated interest in providing unapproved drugs under these state laws.³⁴²

In sum, the “right to try” and medical marijuana laws demonstrate that preemption is not the only reason that state drug laws and regulations may have a limited impact. Together, these examples suggest that the practical effect of certain state regulation that is more permissive than federal law will be limited when the pharmaceutical industry is the major industry involved, and the industry generally lacks incentives to risk violating FDA requirements by testing the legality of the more permissive state programs.

2. Influencing Federal Policy

The uncertain practical impact of some state drug regulation, combined with the possibility that courts will conclude that the FDA’s extensive oversight preempts state regulation, raises the question of why states use their limited resources to enact and defend drug laws. One possibility is that states find regulation to be a useful tool for influencing federal policy.³⁴³

The federal government itself, as well as commentators, have recognized that states ought to have a voice in federal policy.³⁴⁴ Indeed, administrative agencies have been directed to provide states the opportunity to participate in agency decision making.³⁴⁵ The FDA’s own policy is that “[f]ederal, state, and local cooperation shall be fostered whenever possible,”³⁴⁶ and it established an “Office of Partnerships” to facilitate that goal.³⁴⁷

341. See, e.g., Zettler & Greely, *supra* note 257.

342. Neuralstem is developing a stem cell therapy for the treatment of amyotrophic lateral sclerosis (ALS), or Lou Gehrig’s disease. The company’s therapy has completed phase 1 trials, and thus could be provided to terminally ill patients under the terms of the “right to try” laws. See, e.g., Damian Garde, *Neuralstem Wades into Murky Water with Plan To Offer Unapproved Therapy*, FIERCE BIOTECH (June 6, 2014, 11:25 AM), <http://www.fiercebiotech.com/story/neuralstem-wades-murky-water-plan-offer-unapproved-therapy/2014-06-06> [<https://perma.cc/4YET-AWAB>]. It makes sense that a stem cell therapy company would be more interested than other drug companies in taking advantage of “right to try” laws because some stem cell therapy providers have argued that they are outside the FDA’s jurisdiction altogether, and because there is a great deal of hype (and hope) regarding stem cell therapies for a variety of serious and terminal conditions. See Kamenova & Caulfield, *supra* note 302; *supra* Part III.A.1.

343. Cf. Gerken and Holzblatt, *supra* note 29, at 91 (“[D]efensive preemption’ [is] used to describe how state spillovers reverse industry opposition to broadly popular legislation and thus break up congressional gridlock.”).

344. See, e.g., Exec. Order No. 13,132, 3 C.F.R. § 206 (2000); Miriam Seifter, *supra* note 28, at 959.

345. See Exec. Order No. 13,132, 3 C.F.R. § 206.

346. FDA, *supra* note 99, § 3.1.1.

347. *FDA Contacts for Regulatory Partners*, U.S. FOOD & DRUG ADMIN. (Apr. 11, 2016), <https://www.fda.gov/ForFederalStateandLocalOfficials/Office%20of%20Partnerships%20Contacts/default.htm#CT1> [<https://perma.cc/94KM-92GK>].

In addition to formal pathways for federal-state cooperation, state officials can participate in or comment on any public FDA proceeding, including proposed regulations, guidance documents, and public meetings (just as any member of the public can). For example, before approving Zohydro, the FDA sought input on the drug's safety and efficacy at a public advisory committee meeting.³⁴⁸ Although no state officials spoke at the meeting, they could have chosen to voice their concerns then.³⁴⁹

Despite these avenues for states to communicate their concerns to the FDA, states may have logical reasons for enacting divergent drug regulation instead of, or in addition to, communicating with the FDA through existing channels. States are undoubtedly confronted with public health problems associated with FDA-regulated drugs. With Zohydro, for example, states bear many of the costs of prescription drug abuse, and state policies have had some success in decreasing abuse.³⁵⁰ Accordingly, state officials may rightfully have strong views about how best to prevent and address drug abuse. More cynically, because public opinion of the federal government is low,³⁵¹ the political climate may be ripe for state lawmakers to reclaim territory within the health-and-safety sphere traditionally subject to the states' police powers.³⁵² State politicians may have much to gain politically—and little to lose—by inserting themselves into areas typically considered the domain of the federal government, like drug regulation, particularly when those areas touch on politically charged issues such as prescription drug abuse and marijuana. This political climate may also lead advocacy organizations to lobby for legal change at the state, rather than federal, level.³⁵³

Moreover, federal agencies have a “dismal track record” in considering states' input.³⁵⁴ Commentators have expressed concern that federal agencies—which, today, are the federal entities that often make “[c]ritical decisions about the actual scope of state powers and autonomy”³⁵⁵—are not adequately protecting state regulatory

348. See FDA, *supra* note 255.

349. See *id.*; Sharkey, *supra* note 21, at 1616–17.

350. See, e.g., Yuhua Bao, Yijun Pan, Aryn Taylor, Sharmini Radakrishnan, Feijun Luo, Harold Alan Pincus & Bruce R. Schackman, *Prescription Drug Monitoring Programs Are Associated With Sustained Reductions in Opioid Prescribing by Physicians*, 35 HEALTH AFF. 1045 (2016); Dennis Thompson, *The States with the Worst Prescription Painkiller Problem*, CBS NEWS (July 1, 2014, 6:36 PM), <http://www.cbsnews.com/news/the-states-with-the-worst-prescription-painkiller-problem> [<https://perma.cc/XKC6-8YQF>].

351. See *State Governments Viewed Favorably as Federal Rating Hits New Low*, PEW RES. CTR. (Apr. 15, 2013), <http://www.people-press.org/2013/04/15/state-governments-viewed-favorably-as-federal-rating-hits-new-low> [<https://perma.cc/JP6R-KUG3>].

352. Cf. Nathan G. Cortez, *The Local Dilemma: Preemption and the Role of Federal Standards in State and Local Immigration Laws*, 61 SMU L. REV. 47, 47 (2008) (describing “a persistent stream of immigration-related laws” recently enacted by states); DeShazo & Freeman, *supra* note 29, at 1509 (describing a similar wave of state and local efforts in environmental regulation); Huberfeld, *supra* note 287, at 435 (“[S]ome would oppose centralization [of Medicaid] on the ideological grounds that more federal government power is bad, and more state or local power is good.”); Justin Weinstein-Tull, *Election Law Federalism*, 114 MICH. L. REV. 747, 789–90 (2016) (describing state resistance to federal election statutes).

353. See, e.g., Gerken and Holzblatt, *supra* note 29, at 91.

354. Sharkey, *supra* note 28, at 2125 (italics omitted).

355. Gillian E. Metzger, *Federalism Under Obama*, 53 WM. & MARY L. REV. 567, 570

interests.³⁵⁶ To remedy this problem, scholars have proposed mechanisms through which states could negotiate with agencies during decision-making processes, or through which Congress, the executive, or the courts might force agencies to take state interests into account.³⁵⁷

Recent state drug laws and regulations—regardless of their practical impact on the drug market, or their legal effect—might be another way for the states, themselves, to force the FDA (or Congress) to account for their interests. One reason that state laws and regulations might influence federal policy, or industry support for federal policy change, is that they garner significant media attention. For example, the ban and restrictions on Zohydro in just two states elicited far more media coverage than did a letter from twenty-eight state attorneys general to the FDA requesting that it reconsider Zohydro’s approval.³⁵⁸

And the Zohydro ban may have achieved Massachusetts’s desired policy outcome—even though the ban was enjoined.³⁵⁹ In January 2015, the FDA approved a version of Zohydro that includes abuse-deterrent properties, which was a primary goal of Massachusetts’s initial ban.³⁶⁰ As additional examples, in the wake of the Zohydro ban and restrictions, Congress has considered several bills that, if enacted, would make it more difficult for the FDA to approve new opioids that lack abuse-deterrent properties going forward;³⁶¹ the Centers for Disease Control and Prevention

(2011); cf. Abbe R. Gluck, *Federalism from Federal Statutes: Health Reform, Medicaid, and the Old-Fashioned Federalists’ Gamble*, 81 *FORDHAM L. REV.* 1749, 1750 (2013) (“[F]ederal statutes may now be the primary way in which state power is created and protected.” (emphasis omitted)).

356. See, e.g., Miriam Seifter, *States, Agencies, and Legitimacy*, 67 *VAND. L. REV.* 443, 445 (2014); Seifter, *supra* note 28, at 956; Sharkey, *supra* note 28, at 2172.

357. See Seifter, *supra* note 356, at 445; Seifter, *supra* note 28, at 956; Sharkey, *supra* note 28, at 2172.

358. A search for “Zohydro” in ProQuest’s News and Newspapers Database, which includes over 2000 publications, indicates that in the two months after the state attorneys general letter, there were eleven articles about Zohydro. In the two months after Massachusetts banned Zohydro and Vermont restricted its use (which occurred within the span of one week), there were 171 articles about Zohydro.

359. See *supra* Part II.B.2.

360. See Letter from Shannon Hertz, Acting Dir., Div. of Anesthesia, Analgesia, & Addiction Prods., FDA, to Zogenix, Inc. (Jan. 30, 2015), http://www.accessdata.fda.gov/drugsatfda_docs/applletter/2015/202880Orig1s003ltr.pdf [<https://perma.cc/D2B9-VTNK>]; cf. *Zogenix, Inc. v. Patrick*, No. 14-11689-RWZ, 2014 WL 1454696, at *1 (D. Mass. Apr. 15, 2014) (noting the ban applied to hydrocodone-only products that lacked abuse-deterrent properties). From the time of Zohydro’s initial approval, Zogenix publicly said that it intended to develop an abuse-deterrent version—but state interest in Zohydro may have encouraged the company to fulfill this intention as quickly as possible. See News Release, Zogenix, Inc., Zogenix Receives FDA Approval for Zohydro(TM) ER (hydrocodone bitartrate) Extended-Release Capsules (Oct. 28, 2013), <http://ir.zogenix.com/phoenix.zhtml?c=220862&p=irol-newsArticle&ID=1868848> [<https://perma.cc/GRZ4-H47E>].

361. See, e.g., FDA Accountability for Public Safety Act, S. 954, 114th Cong. (2015); Alexander Gaffney, *Tougher FDA Approval Process for Opioids Sought by Congress*, REG. AFF. PROFS. SOC’Y (Apr. 16, 2015), <http://www.raps.org/Regulatory-Focus/News/2015/04/16/21987/Tougher-FDA-Approval-Process-for-Opioids-Sought-by-Congress> [<https://perma.cc/VTK7-UCE6>].

released new guidelines on opioid prescribing intended to combat opioid misuses and overdoses;³⁶² and the FDA requested a report from a National Academies of Sciences, Engineering, and Medicine committee to identify actions that the agency could take to better address the opioid misuse epidemic.³⁶³

Similarly, although Maine's drug importation law was struck down, it too has received congressional and media attention. For example, after Maine enacted its drug importation law, congressional bills were introduced in 2013, 2015, and 2017 that would allow U.S. patients to purchase cheaper, foreign drugs from certain countries.³⁶⁴ And following Judge Torresen's decision invalidating Maine's law, a spokesperson for one bill's sponsor, Senator John McCain, said "[t]his decision highlights the importance that Congress act to change federal law."³⁶⁵

Likewise, although "right to try" laws have had no practical effect on the drug market,³⁶⁶ they have received significant media attention, and Congress has taken note. In July 2015, May 2016, and January 2017, lawmakers introduced a federal "right to try" bill, which would prevent the FDA from enforcing its expanded access requirements on companies that provide unapproved drugs pursuant to a state "right to try" law.³⁶⁷ Additionally, the FDA recently has taken steps to clarify and

362. Press Release, Ctrs. for Disease Control & Prevention, CDC Releases Guideline for Prescribing Opioids for Chronic Pain (Mar. 15, 2016), <http://www.cdc.gov/media/releases/2016/p0315-prescribing-opioids-guidelines.html> [<https://perma.cc/S6LD-LJKZ>]. Massachusetts also continues to consider how best to address prescription drug abuse at the state level. *See, e.g.*, H. 3817, 189th Gen. Court (Mass. 2015) (as filed), <https://malegislature.gov/Bills/189/House/H3817> [<https://perma.cc/78FY-8RA2>].

363. *Committee on Pain Management and Regulatory Strategies To Address Prescription Opioid Abuse: Activity Description*, NAT'L ACADS. SCI. ENGINEERING & MED. <http://nationalacademies.org/hmd/activities/publichealth/addressprescriptionopioidabuse.aspx> [<https://perma.cc/ET9M-CP8J>].

364. Affordable and Safe Prescription Drug Importation Act, S. 469, 115th Cong. (2017); Safe and Affordable Drugs from Canada Act of 2015, S. 122, 114th Cong. (2015); Personal Drug Importation Fairness Act of 2013, H.R. 3715, 113th Cong. (2013); Ed Silverman, *Senators Re-Introduce Bill To Allow Imported Medicines from Canada*, WALL ST. J. (Jan. 9, 2015, 9:13 AM), <http://blogs.wsj.com/pharmalot/2015/01/09/senators-re-introduce-bill-to-allow-imported-medicines-from-canada> [<https://web-beta.archive.org/web/20150922231743/http://blogs.wsj.com/pharmalot/2015/01/09/senators-re-introduce-bill-to-allow-imported-medicines-from-canada>].

365. Ed Silverman, *Judge Strikes Down Maine Law for Importing Prescription Medicines*, WALL ST. J. (Feb. 25, 2015, 11:38 AM), <http://blogs.wsj.com/pharmalot/2015/02/25/judge-strikes-down-maine-law-for-importing-prescription-medicines> [<https://web-beta.archive.org/web/20150906212837/http://blogs.wsj.com/pharmalot/2015/02/25/judge-strikes-down-maine-law-for-importing-prescription-medicines/>].

366. *See, e.g.*, Farber et al., *supra* note 278.

367. Trickett Wendler Right To Try Act of 2017, S. 204, 115th Cong. (2017); Trickett Wendler Right To Try Act of 2016, S. 2912, 114th Cong. (2016); Right To Try Act of 2015, H.R. 3012, 114th Cong. (2015). In addition, in 2017, the Compassionate Freedom of Choice Act was introduced in the House, which, if enacted, would provide broader access to unapproved drugs without regard to whether a state has passed a "right to try" law. H.R. 1020, 115th Cong. (2017). However, the 21st Century Cures Act, enacted in December 2016, did not include any federal "right to try" provisions, although it did include a provision addressing expanded access. H.R. 34, 114th Cong. (2016).

streamline its expanded access process.³⁶⁸ After states began to enact these laws, the FDA simplified its application for the most-frequently-used expanded access program, and the agency issued a final version of its guidance document on expanded access.³⁶⁹ The agency is also now developing an “expanded access navigator,” to serve as a resource for interested patients and medical practitioners.³⁷⁰

State marijuana laws also appear to have instigated change to federal policy. In 2013, the Department of Justice issued a memorandum explaining that it does not intend to prosecute certain marijuana activities that violate federal CSA but are permissible under state law.³⁷¹ Although the memorandum is not binding on the federal government, such enforcement discretion policies are a well-known means through which the federal government can accomplish its policy goals more quickly than statutory change occurs.³⁷² In addition to this change to federal policy, as with Zohydro, drug importation, and “right to try” laws, Congress has recently considered proposals to change federal law to legalize medical marijuana use—and, as previously noted, included a rider in the omnibus appropriations bill that prohibits the Department of Justice from using funds to prevent states from implementing their medical marijuana laws.³⁷³

While the previous examples involve *proposed* legislative change (or limits on how the federal government may use its funding), California’s track and trace law arguably realized change to federal law. Although California’s track and trace requirements were never fully implemented, in 2013 Congress authorized the FDA to establish a federal track and trace system similar to the one required under California

368. The agency has not suggested that its efforts are a response to the “right to try” movement. But the increased public attention to expanded access may have encouraged the FDA to take some of these steps.

369. FDA EXPANDED ACCESS GUIDANCE, *supra* note 282; Press Announcement, U.S. Food & Drug Admin., Statement from FDA Commissioner Robert Califf, MD, on the Release of the Final Individual Patient Expanded Access Form (June 2, 2016), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm504579.htm> [<https://perma.cc/34K2-BW2E>]. The FDA implemented the new application for “individual patient” expanded access, the program that accounts for approximately ninety-six percent of all expanded access requests. See *Expanded Access Submission Receipts Reports Oct. 1, 2013–Sept. 30, 2014*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/UCM430188.pdf> [<https://perma.cc/9LGV-YC56>].

370. *Public Workshop: Expanded Access Navigator—May 16, 2016*, REAGAN-UDALL FOUND. FOR THE FOOD & DRUG ADMIN., <http://www.reaganudall.org/news-and-events/events-2/public-workshop-expanded-access-navigator> [<https://perma.cc/XE2U-ERMP>].

371. DOJ Memo, *supra* note 228.

372. See, e.g., Zachary S. Price, *Enforcement Discretion and Executive Duty*, 67 VAND. L. REV. 671, 681 (2014).

373. See, e.g., Consolidated Appropriations Act, 2016, Pub. L. No. 114-113, § 542, 129 Stat. 2242, 2332–33 (2015); *United States v. McIntosh*, 833 F.3d 1163, 1169 (9th Cir. 2016); Compassionate Access Act, H.R. 715, 115th Cong. (2017); CARERS Act of 2015, S. 683, 114th Cong. (2015); Press Release, Drug Policy All., Senators Cory Booker (D-NJ), Rand Paul (R-KY), and Kirsten Gillibrand (D-NY) Introduce Historic Medical Marijuana Legislation (Mar. 10, 2015), <http://www.drugpolicy.org/news/2015/03/senators-cory-booker-d-nj-rand-paul-r-ky-and-kirsten-gillibrand-d-ny-introduce-historic> [<https://perma.cc/LG2P-ZTE2>].

law.³⁷⁴ For many years preceding the 2013 federal law (and the 2015 effective date of California's requirements), there was scant industry support for a federally required system, likely because implementing a track and trace system is very expensive, and proposals for a federal track and trace system were unsuccessful.³⁷⁵ But California, which is a large market for drugs, has been credited with motivating industry to support for a federal system.³⁷⁶ When California enacted its own track and trace requirements, it created the prospect of varied, and possibly stricter, state requirements, and also provided a clear way for industry to avoid that outcome—through the law's express invitation for federal preemption. The California law, thus, suggests a way for states to use invitations for federal preemption to create industry support for federal policy change.

In sum, taken together, these examples of recent state efforts to regulate drugs suggest that state regulation may be an effective strategy for affecting federal law and policy, at least in certain instances. And even those state laws and regulations that are preempted, or have little practical impact on the pharmaceutical market, may be influential.

CONCLUSION

There is growing state interest in regulating drugs that are subject to federal oversight by the FDA. Although states have a long history of drug regulation, states traditionally complemented or copied FDA regulation. Recent state efforts, however, diverge from the FDA's regulatory schemes. These efforts, thus, offer the opportunity to consider the intersection of state and federal pharmaceutical regulation in a new light. Analyzing five examples of state regulation demonstrates that the preemptive effects of the FDA's authority may extend into state regulation of medical practice in some circumstances—and this blurriness of the practice-products distinction has ramifications for debates about the scope of the FDA's jurisdiction outside the preemption context as well. But even when state regulation is preempted or otherwise fails to change the practices of the drug industry, such regulation may be a useful strategy for states to influence policy change at the federal level, at least in some instances.

374. Drug Quality and Security Act, Pub. L. No. 113-54, 127 Stat. 587 (2013).

375. See, e.g., *Drug Quality and Security Act Becomes Law*, PHARMACEUTICAL COMM. (Jan. 20, 2014), http://pharmaceuticalcommerce.com/index.php?pg=legal_regulatory&articleid=27095&keyword=Drug%20Quality%20and%20Security%20Act-supply%20chain-monitoring [<https://perma.cc/HW4S-QCT5>]; FDA, FDA PUBLIC WORKSHOP SUMMARY: DETERMINATION OF SYSTEM ATTRIBUTES FOR THE TRACKING AND TRACING OF PRESCRIPTION DRUGS, <http://www.fda.gov/downloads/Drugs/NewsEvents/ucm249331.pdf> [<https://web-beta.archive.org/web/20170211121431/http://www.fda.gov/downloads/Drugs/NewsEvents/ucm249331.pdf>].

376. See, e.g., David Pittman, *House Passes 'Track and Trace' Drug Bill*, MEDPAGETODAY (June 4, 2013), <http://www.medpagetoday.com/Washington-Watch/Washington-Watch/39616> [<https://perma.cc/F3R7-XB2A>].