

PHARMACEUTICAL FEDERALISM

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ABSTRACT

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 2013 drug overdoses resulted in approximately 44,000 deaths, and, for the fifth consecutive year, overdoses eclipsed motor vehicle crashes as the leading cause of injury-related death in the United States.¹ Contrary to popular conception, pharmaceuticals contribute to more overdose deaths than illicit drugs like heroin and cocaine do.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 U.S. Food and Drug Administration (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

¹ U.S. DEPT. OF HEALTH & HUMAN SERVICES, 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 [hereinafter [HHS, DRUG ABUSE REPORT]; Rose A. Rudd et al., Ctrs. For Disease Control & Prevention, *Increases in Drug and Opioid Overdose Deaths—United States, 2000-2014*, MORBIDITY & MORTALITY WKLY. REP., Jan. 1, 2016, http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm?s_cid=mm6450a3_w#fig1

² Rudd et al., *supra* note 1; Christopher M. Jones et al., *Pharmaceutical Overdose Deaths, United States, 2010*, 309 JAMA 657-59 (2013).

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 in some cases). *Id.* But a consensus has emerged that opioid abuse is a serious public health problem, and perhaps more importantly for this paper, politicians and the public clearly perceive opioid abuse to be of grave concern. See HHS, DRUG ABUSE REPORT, *supra* note 1, at 3; Roni Caryn Rabin, *New Painkiller Rekindles Addiction Concerns*, N.Y. TIMES (Apr. 21, 2014), http://well.blogs.nytimes.com/2014/04/21/new-painkiller-rekindles-addiction-concerns/?_php=true&_type=blogs&_r=0.

⁴ See, e.g., Rabin, *supra* note 3. Various features are thought to make drugs abuse resistant. The most commonly discussed abuse deterrence 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 WISCONSIN JOURNAL SENTINEL (Oct. 28, 2013), <http://www.jsonline.com/watchdog/watchdogreports/fda-oks-high-dose-narcotic-painkiller-zohydro-raising-abuse-concerns-b99128369z1-229484621.html>.

Fed Up Coalition, a drug abuse 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 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 short-lived. A federal judge

⁶ Fed Up Coalition, Reconsider Approval of Dangerous New Opioid Zohydro, Change.org, <https://www.change.org/p/reconsider-approval-of-dangerous-new-opioid-zohydro>.

⁷ Letter from Pamela Jo Bondi, Florida Attorney General, et al. to Margaret Hamburg, Commissioner of Food and Drugs (Dec. 10, 2013), available at <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 take a position on whether those criticisms were justified. Indeed, there were also public health arguments that the FDA's decision to approve Zohydro in 2013 was the appropriate one. As one example, 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. Zohydro offered a hydrocodone option for patients without the risks of acetaminophen, which may have been 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, 2692-3 (Jan. 14, 2011); Lars Noah, *State Affronts to Federal Primacy in Licensing Pharmaceuticals*, 2016 MICH. ST. L. REV. 1, 3-5 (2016) [hereinafter Noah, *State Affronts*]; Michael Ollove, *Fearing Abuse, States Challenge FDA on Painkiller Approval*, 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>; cf. Alison Bateman-House & Arthur Caplan, *Don't Throw Out Compassion in the War Against Opioid Abuse*, STAT NEWS (June 9, 2016), <https://www.statnews.com/2016/06/09/opioid-abuse-compassion/> (highlighting the medical value of opioids).

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

⁹ *Zogenix, Inc. v. Patrick*, No. CIV.A. 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. But that description does not fully capture the

enjoined the ban in April 2014, reasoning that it was preempted by the Federal Food, Drug, and Cosmetic Act.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 now Massachusetts, have imposed restrictions on the use of Zohydro that fall short of an outright ban but still go 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

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 its approval. *See* Noah, *State Affronts*, *supra* note 7, at 21-22. In addition, several states banned the sale and distribution of FDA-approved contraceptives in 1960. *See 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, *State Affronts*, *supra* note 7. Additionally, since 1962, there have been a number 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 FDA was considering, but had not yet approved. *See* Noah, *State Affronts*, *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 *1.

¹¹ *See* Part I.C., *infra*; *see also* Noah, *State Affronts*, *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 because biologic therapies generally meet the statutory definitions of both a “biological product” (found in the Public Health Service Act) and a “drug” (found in the Federal Food, Drug, and Cosmetic Act), and are regulated much like drugs, this Article focuses its discussion of statutory language on the language in the Federal Food, Drug, and Cosmetic Act. *See* U.S. Food & Drug Admin., FDA 101: Regulating Biological Products, <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048341.htm>.

¹² *See* Milton J. Valencia, *Mass. Limits Use of the Potent Painkiller Zohydro*, BOSTON GLOBE (Apr. 23, 2014).

¹³ *See* Calif. Stat. 2004 ch. 857.

subsequently concluded was preempted by federal law).¹⁴ Twenty-eight states have passed “right-to-try” laws that are intended to permit terminally ill patients to access unapproved drugs.¹⁵ And twenty-five states, as well as the District of Columbia 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.

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.¹⁷ 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.¹⁸ This view of the appropriate roles for state and federal regulation arises in part from both 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.¹⁹

¹⁴ See *Ouellette v. Mills*, No. 1:13-CV-00347-NT, 2015 WL 751760, at *1 (D. Me. Feb. 23, 2015).

¹⁵ See Ed Silverman, *US Senator Introduces a ‘Right to Try’ Bill for Desperate Patients*, STAT NEWS (May 10, 2016), <https://www.statnews.com/pharmalot/2016/05/10/fda-experimental-drugs-right-to-try/>.

¹⁶ National Conference of State Legislatures, *State Medical Marijuana Laws*, <http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx>.

¹⁷ Barbara J. Evans, *Distinguishing Product and Practice Regulation in Personalized Medicine*, 81 CLINICAL PHARMACOLOGY & THERAPEUTICS 288, 288 (2007) [hereinafter Evans, *Product and Practice Regulation*].

¹⁸ 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) [hereinafter Evans, *Seven Pillars*]; Lars Noah, *Ambivalent Commitments to Federalism in Controlling the Practice of Medicine*, 53 U. KAN. L. REV. 149, 154-71 (2004) [hereinafter Noah, *Ambivalent Commitments*]; 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, pharmacist and other health care professionals authorized to independently practice medicine.

¹⁹ See, e.g., *Dent v. West Virginia*, 129 U.S. 114, 122-23, 128 (1889); DANIEL

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.²⁰ This Article argues that one such insight is that the preemptive 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.²¹ Nevertheless, federal judges concluded that both state efforts were impliedly preempted by the FDA's regulatory regime.²²

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.²³ The thinness of the practice-products binary, revealed by state drug regulation, thus may can inform questions about the scope of the FDA's authority.

CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA 75 (2010).

²⁰ See Nathan Brown & Eli Tomar, *Could State Regulations Be the Next Wave of Preemption Jurisprudence? Drug Compounding as a Case Study*, 71 FOOD DRUG L.J. (forthcoming 2016); Noah, *State Affronts*, *supra* note 7, at 2-3; Catherine M. Sharkey, *States vs. FDA*, 83 GEO. WASH. 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 “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. (forthcoming 2016) (examining the policy implications of state action in the areas of food and marijuana regulation).

²¹ See *Ouellette*, 2015 WL 751760, at *1; *Zogenix*, 2014 WL 1454696, at *1.

²² See *id.*

²³ 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), available at <http://www.acla.com/wp-content/uploads/2015/01/Tribe-Clement-White-Paper-1-6-15.pdf>; Usha Lee McFarling *FDA Moves to Crack Down on Unproven Stem Cell Therapies*, STAT NEWS (Feb. 8, 2016), <http://www.statnews.com/2016/02/08/fda-crackdown-stem-cell-clinics/>.

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.²⁴ 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.²⁵ 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,” in the language of traditional federalism rhetoric.²⁶ 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].”²⁷ Scholars have made such arguments with respect to state regulation in other areas, including, perhaps most notably, environmental regulation.²⁸ But state drug regulation offers a new context, with a particularly powerful federal regulator, in 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,

²⁴ See Part III, *infra*.

²⁵ See *id*.

²⁶ See, e.g., Erwin Chemerinsky, *The Values of Federalism*, 47 FLA. L. REV. 499, 526 (1995).

²⁷ 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 Catherine M. Sharkey, *Federalism Accountability: "Agency-Forcing" Measures*, 58 DUKE L.J. 2125, 2172 (2009) (describing other means that states use to influence agencies); Miriam Seifter, *States As Interest Groups in the Administrative Process*, 100 VA. L. REV. 953, 956 (2014) (describing other means that states use to influence agencies); Winters, *supra* note 20 (describing the benefits of “regulatory friction” between states and the federal government in the areas of food and controlled substances).

²⁸ 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 (2007); see also Heather K. Gerken & Ari Holtzblatt, *The Political Safeguards of Horizontal Federalism*, 113 MICH. L. REV. 57, 91 (2014) (“[i]n 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”).

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 suggests that 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.²⁹ The federal government, however, did not always have such extensive authority over drugs.³⁰ In fact, as the next part 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.³¹ 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.³² More importantly, early state regulation also demonstrated that the boundary between medical

²⁹ See 21 U.S.C. § 355(d). 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. *Id.* at § 321(g).

³⁰ See, e.g., CARPENTER, *supra* note 19, at 1-33.

³¹ *Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 703 (D.C. Cir. 2007).

³² Cf. John P. Swann, *The Food and Drug Administration*, in *A HISTORICAL GUIDE TO THE U.S. GOVERNMENT* 249 (George T. Kurian, ed., 1998) (“Adulteration and misbranding of foods and drugs had long been a fixture in the American cultural landscape . . .”).

practice and medical products—which is thought to serve as a dividing line between federal and state jurisdiction today³³—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.³⁴ The law required medical practitioners to disclose the ingredients in the drugs that they dispensed.³⁵ 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.³⁶

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. legislation addressing drug adulteration.³⁷ It prohibited pharmacists from knowingly or intentionally selling drugs that were “injured, moulded, discomposed, or sophisticated.”³⁸ 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

³³ See, e.g., Zettler, *supra* note 18, at 429-31.

³⁴ See, e.g., *Abigail Alliance*, 495 F.3d at 703; EDWARD KREMERS, GLENN SONNEDECKER & GEORGE URDANG, *KREMERS AND URDANG'S HISTORY OF PHARMACY* 158 (1986); see also Seema K. Shah & Patricia J. 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, 140-52 (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*, 50 *FOOD DRUG COSM. L.J.* 665, 669-70 (1975).

³⁵ See KREMERS, SONNEDECKER & URDANG, *supra* note 34, at 158.

³⁶ 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. § 352(e); 21 C.F.R. § 201.10.

³⁷ See *id.* at 182-84; David Cowen, *The Development of State Pharmaceutical Law*, 37 *PHARMACY IN HISTORY* 49, 54 (1995); In addition to prohibiting the sale of adulterated drugs, the law required that pharmacists have a diploma, pass a test before dispensing any drugs, and inform patients of the risks of particularly dangerous drugs. See Cowen, *supra*, at 54-55.

³⁸ Cowen, *supra* note 37, at 54. Contemporary federal law likewise prohibits drug adulteration, albeit with a significantly broader definition of what constitutes adulteration. 21 U.S.C. § 351.

drugs themselves not be contaminated.³⁹ 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.⁴⁰

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.”⁴¹ 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.⁴²

But recognition of the need for national drug regulation continued to grow despite this set back. In 1820 eleven delegates of state medical societies met in Washington, D.C. to develop the first U.S. Pharmacopeia (USP).⁴³ The goal of the USP was, and continues to be, to set quality standards for drugs.⁴⁴ Although the USP was not (and still is not) a government document, it represented an attempt to develop national standards for drug quality, and has been recognized in federal law since

³⁹ See KREMERS, SONNEDECKER & URDANG, *supra* note 34, at 216; Glenn Sonnedecker & George Urdang, *Legalization of Drug Standards Under State Laws in the United States of America*, 8 FOOD DRUG COSMETIC L.J. 741, 746 (1953).

⁴⁰ See *Abigail Alliance*, 495 F.3d at 703; KREMERS, SONNEDECKER & URDANG, *supra* note 34, at 158.

⁴¹ See 2 Stat 806, §§ 1, 2; U.S. Food and Drug Administration, FDA’s Origin, <http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm124403.htm>; 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) [hereinafter “Noah, *Triage*”]. The official title of the law was “An Act to Encourage Vaccination.” 2 Stat 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 AFFAIRS, 611, 612 (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 REVIEW 455, 480 (1983). Congress enacted the 1813 law to address such problems.

⁴² David P. Currie, *The Vaccine Agent*, 1 GREEN BAG 2d 245, 248-49 (1998); Noah, *Triage*, *supra* note 41, at 401.

⁴³ See KREMERS, SONNEDECKER & URDANG, *supra* note 34, at 261.

⁴⁴ U.S. Pharmacopeial Convention, About USP, <http://www.usp.org/about-usp>.

Congress passed the Import Drug Act of 1848.⁴⁵ The Import Drug Act, in turn, represented the federal government's second foray into drug regulation.⁴⁶ 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.⁴⁷

For over fifty years, while the Import Drug Act remained the only federal law regulating drugs,⁴⁸ 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.⁴⁹ Consistent with earlier state regulation, these were often medical practice laws, regulating the activities of drug dispensers rather than the drugs themselves.⁵⁰ 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.⁵¹ And a number of other states, including New York, Massachusetts, and Michigan, followed New Jersey by enacting laws with broader definitions of adulteration.⁵² But overall there was little consistency—James Harvey Young, a food and drug regulation historian, described drug regulation at the turn of the twentieth century as a “chaos of divergent and sometimes ludicrously severe state laws.”⁵³

This chaos—as well as two public health crises—led to significant movement toward nationwide consistency when Congress passed two

⁴⁵ See ch. 70, 9 Stat. 237 § 3; KREMERS, SONNEDECKER & URDANG, *supra* note 34, at 261; U.S. Pharmacopeial Convention, USP Milestones, <http://www.usp.org/about-usp/our-history/usp-milestones-timeline>.

⁴⁶ 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).

⁴⁷ ch. 70, 9 Stat. 237 at § 3. 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).

⁴⁸ See, e.g., *Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 704 (D.C. Cir. 2007). In 1862, the federal Bureau of Chemistry, 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 (2014).

⁴⁹ See KREMERS, SONNEDECKER & URDANG, *supra* note 34, at 216; Sonnedecker & Urdang, *supra* note 39, at 746.

⁵⁰ See KREMERS, SONNEDECKER & URDANG, *supra* note 34, at 216.

⁵¹ Sonnedecker & Urdang, *supra* note 39, at 746; Lewis A. Grossman, *Food, Drugs, and Droids: A Historical Consideration of Definitions and Categories in American Food and Drug Law*, 93 CORNELL L. REV. 1091, 1098 (2008); see also 21 U.S.C. § 351.

⁵² See *id.*; Cowen, *supra* note 37, at 54.

⁵³ JAMES HARVEY YOUNG, *PURE FOODS: SECURING THE FEDERAL FOOD AND DRUGS ACT OF 1906* 292 (1989) [hereinafter “YOUNG, PURE FOODS”].

federal laws regulating medicines: The Biologics Act of 1902 and the Pure Food and Drugs Act of 1906.⁵⁴ The Biologics Act of 1902 was enacted after biological diphtheria treatments contaminated with tetanus killed twenty-one children in Missouri and New Jersey.⁵⁵ The law required that sellers of therapeutic biological products certify that they properly prepared the products, before marketing.⁵⁶ 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.⁵⁷

Although the Biologics Act was the first to create a drug approval role for the government, it was the Pure Food and Drugs Act of 1906 that established the FDA.⁵⁸ 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.⁵⁹ 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.⁶⁰

Although the Pure Foods and Drugs Act was an important milestone in federal drug regulation, it did not end state regulation.⁶¹ Instead state regulation, arguably, became more uniform, with two-thirds of states passing laws that mirrored the new federal law.⁶² Yet a robust market of unsafe and fraudulent drugs persisted with over 50,000 “quack” products being sold, producing over one hundred million dollars in annual sales.⁶³ Indeed, its 1910 report, the American Pharmaceutical Association's

⁵⁴ See, e.g., CARPENTER, *supra* note 19, at 75.

⁵⁵ See, e.g., PHILLIP J. HILTS, PROTECTING AMERICA'S HEALTH 69 (2003).

⁵⁶ ch. 1378, 32 stat. 728-29 § 1.

⁵⁷ See CARPENTER, *supra* note 19, at 75; Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1758 n.10 (1996).

⁵⁸ See, e.g., Merrill, *supra* note 57, at 1758.

⁵⁹ See, e.g., JAMES HARVEY YOUNG, TOADSTOOL MILLIONAIRES: A SOCIAL HISTORY OF PATENT MEDICINES IN AMERICA BEFORE FEDERAL REGULATION 239 (1961) [hereinafter “YOUNG, TOADSTOOL MILLIONAIRES”].

⁶⁰ Ch. 3915, 34 Stat. 768 §§ 1, 2 (1907). 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, TOADSTOOL MILLIONAIRES, *supra* note 59, at 234-39.

⁶¹ 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 pre-market 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 Ch. 3915, 34 Stat. 768 (1907); *United States v. Johnson*, 221 U.S. 488, 498-99 (1911).

⁶² See Sonnedecker & Urdang, *supra* note 39, at 751. A minority of states, including New York, Massachusetts, Michigan, and Illinois, retained laws inconsistent with federal law. *Id.*

⁶³ CARPENTER, *supra* note 19, at 77-78.

Committee on Drug Reform noted:

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.⁶⁴

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.⁶⁵ Diethylene glycol was used as a solvent because of its sweet taste, but it is toxic.⁶⁶ 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.⁶⁷ As a result, over one hundred people, including many children, died after taking the drug.⁶⁸

And tragedy again led to legislative change. In 1938, Congress passed the Federal Food, Drug, and Cosmetic Act (FDCA).⁶⁹ The law expanded federal authority over drugs in several ways.⁷⁰ Most importantly, the law created a category of “new drugs”—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.⁷¹ That is,

⁶⁴ *Report of Committee on Drug Reform*, 5 BULLETIN OF THE AMERICAN PHARMACEUTICAL ASS’N 652, 652 (1910).

⁶⁵ See U.S. Food & Drug Admin, About FDA, Sulfanilimide Disaster [hereinafter “FDA, Sulfanilimide Disaster”], <http://www.fda.gov/aboutfda/whatwedo/history/productregulation/sulfanilamidedisaster/default.htm>

⁶⁶ *Id.* Diethylene glycol is related to the compound used to make antifreeze. See, e.g., Jeanna M. Marraffa et. al, *Diethylene Glycol: Widely Used Solvent Presents Serious Poisoning Potential*, 35 J. EMERGENCY MED. 401 (2008).

⁶⁷ See FDA, Sulfanilimide Disaster, *supra* note 65.

⁶⁸ *Id.*

⁶⁹ See, e.g., Merrill, *supra* note 57, at 1761-63. For a more extensive history of the passage of the Federal Food, Drug, and Cosmetic Act, 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.J. 532 (1946).

⁷⁰ See, e.g., Merrill, *supra* note 57, at 1761-63.

⁷¹ See Ch. 675, 52 Stat. 1040 §§ 201(p), 505(a) (1938); Merrill, *supra* note 57, at 1761-

the FDCA shifted the FDA’s role from “policeman to gatekeeper.”⁷²

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 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.⁷³ As with the federal legislation preceding it, however, it did not mark the end of state drug regulation.⁷⁴

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.⁷⁵ 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.⁷⁶ 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.⁷⁷ The drug’s safety and effectiveness must be demonstrated by “substantial evidence,” which generally consists of data from “adequate and well-controlled” clinical

63. The FDA’s gatekeeping role is still limited to “new drugs.” See 21 U.S.C. § 321(p), 355(a).

⁷² Merrill, *supra* note 57, at 1776.

⁷³ See, e.g., *id.* at 1761-63, 1764-68.

⁷⁴ See, e.g., Ole Salthe, *State Food, Drug and Cosmetic Legislation and Its Administration*, 6 LAW & CONTEMP. PROBS. 165, 165 (1939).

⁷⁵ See U.S. Food & Drug Admin., What We Do, <http://www.fda.gov/aboutfda/whatwedo/>.

⁷⁶ 21 U.S.C § 355(a).

⁷⁷ *Id.* at § 355(d).

trials.⁷⁸ 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.⁷⁹

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.⁸⁰ Rather, the drug development and approval process often involves significant communication between the FDA and a drug company.⁸¹ 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.⁸² 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 FDA examines drugs during the approval process.⁸³ 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—*e.g.*, to treat a particular disease or condition, in a particular patient population, at a particular dose.⁸⁴ 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).⁸⁵

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

⁷⁸ *Id.* § 355(d); 21 C.F.R. § 314.126. 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.*, U.S. FOOD & DRUG ADMIN, COMPLIANCE PROGRAM GUIDANCE MANUAL § 7346.832.

⁷⁹ *See* 21 U.S.C. § 355(j).

⁸⁰ For a description of the content of a new drug application, *see* 21 C.F.R. § 314.50.

⁸¹ *See* 21 C.F.R. § 314.102(a) (“[d]uring the course of reviewing an application . . . FDA shall communicate with applicants about scientific, medical, and procedural issues that arise . . .”); DEPT. OF HEALTH AND HUMAN SERVS., OFFICE OF INSPECTOR GENERAL, FDA’S REVIEW PROCESS FOR NEW DRUG APPLICATIONS ii (Mar. 2003) (“FDA works collaboratively with sponsors”) [hereinafter “OIG, FDA’S REVIEW PROCESS”].

⁸² *See, e.g.*, OIG, FDA’S REVIEW PROCESS, *supra* note 81, at 10-11.

⁸³ *See* 21 C.F.R. § 314.430(e).

⁸⁴ *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).

⁸⁵ *See, e.g., id.*

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. For example, before a drug's approval, FDA regulates clinical trials and certain other research with the drug, and prohibits promotion of the drug.⁸⁶ 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.⁸⁷ As a third example, after a prescription drug's approval, the FDA oversees its advertising and promotion.⁸⁸ In fact, the most-discussed area of the FDA's post-approval regulation may be its ban on the promotion of off-label uses.⁸⁹

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 lifecycle in numerous different ways, under numerous different authorities that have evolved over time and

⁸⁶ 21 U.S.C. § 355(i); 21 C.F.R. pts. 312, 320. The FDA also regulates clinical investigations of approved drugs. *See* 21 C.F.R. § 312.2.

⁸⁷ *See generally* 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, 512-522 (2014) (discussing pre- and post-approval good manufacturing requirements).

⁸⁸ *See* 21 C.F.R. pt. 202.

⁸⁹ For a detailed description of the statutory provisions and regulations underlying this ban on off-label promotion, *see, for example*, Alan Bennett et al, *Back to First Principles: A New Model for the Regulation of Drug Promotion*, 2 J.L. & BIOSCIENCES 1, 12-22 (2015). 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); 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, 133-34 (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).

intersect with state efforts to regulate drugs.⁹⁰

2. The States

In light of the comprehensive system of FDA drug regulation, state regulation is now generally characterized as limited.⁹¹ This characterization, however, may obscure the continued role of states in drugs regulation.⁹² 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.⁹³ Commentators, and the FDA itself, have explained that state products liability schemes complement FDA regulation by providing a mechanism for privately policing post-approval drug safety and compensating injured patients.⁹⁴ Because of the FDA's extensive oversight of drug design and manufacturing, injured patients have generally sued drug manufacturers for inadequate labeling.⁹⁵ Indeed, injured patients have brought a “steady stream” of failure-to-warn cases against prescription drug manufacturers.⁹⁶ Yet, as discussed further in Part II below, recent

⁹⁰ Cf. Elizabeth Y. McCuskey, *Body of Preemption: Health Law Traditions and the Presumption Against Preemption*, 89 *TEMPLE L. REV.* (forthcoming 2017) (describing FDA, NIH, Medicare, and Medicaid involvement in medical products regulation, concluding “[r]egulation of medical products is thus heavily and historically federal”).

⁹¹ See, e.g., Evans, *Product and Practice Regulation*, *supra* note 18, at 288.

⁹² Cf. Zettler, *supra* note 18 (making a similar argument with respect the federal government's longstanding regulation of medical practice).

⁹³ 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, 463 (2008); see also Efthimios Parasidis, *Patients over Politics: Addressing Legislative Failure in the Regulation of Medical Products*, 2011 *WIS. L. REV.* 929, 933 (2011) (“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.”)

⁹⁴ See, e.g., Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 *Fed. Reg.* 67985, 67988-89 (proposed Nov. 13, 2013) [hereinafter “Generic Drug Labeling Proposed Rule”]; Kessler & Vladeck, *supra* note 93, 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.

⁹⁵ See, e.g., Brief for the United States as Amicus Curiae Supporting Petitioner, *Mutual Pharmaceutical Company, Inc. v. Bartlett*, 2013 WL 314460 (U.S.) (“[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.”).

⁹⁶ Kessler & Vladeck, *supra* note 93, at 462.

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.⁹⁷ 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.⁹⁸ 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.⁹⁹ 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.¹⁰⁰

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.¹⁰¹ 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.¹⁰² Consistent with this idea, states do not regulate drugs under their laws in isolation from the FDA.¹⁰³ Each state has an agreement with the FDA that permits information-sharing

⁹⁷ See, e.g., U.S. FOOD & DRUG ADMIN., INVESTIGATIONS OPERATIONS MANUAL § 3.3.3 (2014); Part I.A., *supra*.

⁹⁸ See U.S. FOOD & DRUG ADMIN., INVESTIGATIONS OPERATIONS MANUAL § 3.3.3 (2014); Assoc'n of Food & Drug Officials, About, <http://www.afdo.org/about>. As of 2012, 42 states had adopted all or some of the Uniform State Food, Drug, and Cosmetic Act. PETER BARTON HUTT ET AL., FOOD AND DRUG LAW 290 (4th ed. 2014).

⁹⁹ See Assoc'n of Food & Drug Officials, About, <http://www.afdo.org/about>.

¹⁰⁰ See, e.g., HUTT, *supra* note 98, at 290; U.S. FOOD & DRUG ADMIN., INVESTIGATIONS OPERATIONS MANUAL § 3.3.3 (2014).

¹⁰¹ 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).

¹⁰² See, e.g., William F. Reindollar, *The Association of Food and Drug Officials*, 6 FOOD DRUG COSM. L.J. 52, 53-54 (1951).

¹⁰³ See U.S. FOOD & DRUG ADMIN., INVESTIGATIONS OPERATIONS MANUAL § 3.3.3 (2014); see also Salthe, *supra* note 74, 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. BIOSCI. 669, 687-691 (2015) (describing an example of federal cooperation with a state enforcement action related to devices).

and coordination.¹⁰⁴ 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.¹⁰⁵ But state enforcement of their own Food, Drug, and Cosmetic Acts appears to be rare.¹⁰⁶ 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.¹⁰⁷ To consider these insights, this Part starts by discussing preemption in 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

¹⁰⁴ See FDA, INVESTIGATIONS OPERATIONS MANUAL, *supra* note 100, at § 3.3.3.

¹⁰⁵ See, e.g., Kevin Outterson, *Regulating Compounding Pharmacies after NECC*, 367 NEJM 1969 (2012). Drug compounding refers to 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, Education, Labor, and Pensions*, (2012) (testimony of Margaret A. Hamburg, Commissioner, Food & Drug Admin.), <http://www.help.senate.gov/hearings/hearing/?id=5f5def0d-5056-a032-5297-eab57634d209>.

¹⁰⁶ See, e.g., John Shaeffer, *Prescription Drug Advertising—Should States Regulate What Is False and Misleading?*, 58 FOOD & DRUG L.J. 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. HISTORY 1103, 1107-1109 (2003) (discussing the history of weak state enforcement in the context of food).

¹⁰⁷ See Brown & Tomar, *supra* note 20; Noah, *State Affronts*, *supra* note 7; Sharkey, *States vs. FDA*, *supra* note 20.

Federal Government,” the basic premise of preemption is that Congress may choose to displace state law.¹⁰⁸ That is, when federal and state law conflict, the state law is “without effect.”¹⁰⁹ A “preemption analysis starts 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.”¹¹⁰ Accordingly, courts’ preemption analyses ultimately center on Congressional intent.¹¹¹

Preemption is express when a federal law explicitly provides that it displaces state oversight.¹¹² 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.¹¹³ Conflict preemption, however, is the more commonly relied upon theory of implied preemption in food and drug law.¹¹⁴ 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).¹¹⁵ 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.¹¹⁶

Caselaw and scholarship in the products liability context—the area in which most FDA preemption litigation has occurred, and the Supreme

¹⁰⁸ *Gregory v. Ashcroft*, 111 S. Ct. 2395, 2399 (1991).

¹⁰⁹ *See, e.g., Cipollone v. Liggett Grp., Inc.*, 112 S. Ct. 2608, 2617 (1992).

¹¹⁰ *Id.* (internal quotations and citations omitted); *cf. McCuskey, supra* note 90 (discussing and critiquing a broad presumption against preemption, based on a history of state regulation, in health law).

¹¹¹ *See, e.g., Cipollone*, 112 S. Ct. at 2617.

¹¹² *See, e.g., id.*

¹¹³ *See, e.g., id.*

¹¹⁴ *See, e.g., Richard C. Ausness, The Impact of Wyeth v. Levine on FDA Regulation of Prescription Drugs*, 65 *FOOD & DRUG L.J.* 247, 247-48 (2010).

¹¹⁵ *See, e.g., Cipollone* 112 S. Ct. at 2617; *see also Wyeth v. Levine*, 129 S. Ct. 1187, 1193 (2009) (explaining conflict and obstacle preemption).

¹¹⁶ *See, e.g., Wyeth*, 129 S. Ct. at 1200. 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. 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.*, 99 Cal. App. 4th 780, 784, 122 Cal. Rptr. 2d 72, 76 (2002). The FDCA does contain an express preemption provision regarding state and local requirements for devices, which the Supreme Court has interpreted as preempting state common law causes of action; however, that provision is outside the scope of this Article. 21 U.S.C. § 360k; *Riegel v. Medtronic, Inc.*, 128 S. Ct. 999, 1007 (2008); *Medtronic, Inc. v. Lohr*, 116 S. Ct. 2240, 2263 (1996).

Court has recently spoken—are helpful for considering the preemptive effects of FDA regulation on divergent state regulation.¹¹⁷ 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.¹¹⁸ Although the drug manufacturer argued that the plaintiff’s case was impliedly preempted under both impossibility and obstacle theories, the Court disagreed.¹¹⁹ 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.”¹²⁰ In other words, the Court underscored the presumption against concluding that Congress intended federal law to preempt state law.¹²¹ 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.”¹²²

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.¹²³ In *Pliva v. Mensing*, patients who developed tardive dyskinesia—a neurological disorder—from long-

¹¹⁷ See, e.g., Brown & Tomar, *supra* note 20; 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 (1996) (explaining that the Supreme Court has described tort law as equivalent to positive law for preemption purposes).

¹¹⁸ *Wyeth*, 129 S. Ct. at 1191-92; see also Ausness, *supra* note 114, at 280 (explaining the *Wyeth* decision).

¹¹⁹ *Id.*

¹²⁰ *Id.* at 1195.

¹²¹ See Ausness, *supra* note 114, at 280.

¹²² *Wyeth*, 129 S. Ct. at 1195, 1196 (citing Drug Amendments of 1962, Pub. L. No. 87-781, § 202, 76 Stat. 780, 793); see also Noah, *State Affronts*, *supra* note 7, at 8 (noting this language as one piece of evidence that Congress intended to preserve state authority).

¹²³ *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466 (2013); *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011). The Supreme Court’s findings of implied preemption in *Pliva* and *Bartlett* are not inconsistent with 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 Christine H. Kim, *The Case for Preemption of Prescription Drug Failure-to-Warn Claims*, 62 FOOD & DRUG L.J. 399, 410 (2007); Noah, *State Affronts*, *supra* note 7, at 8-9; *Blasting Servs. v. Wilkes County*, 288 F.3d 584, 591 (4th Cir. 2002).

term use of a generic drug sued the drug manufacturer.¹²⁴ 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.¹²⁵ 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.¹²⁶ Nevertheless, the majority concluded that the drug manufacturers were not liable to the plaintiffs on impossibility preemption grounds.¹²⁷ 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.¹²⁸ 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.¹²⁹

Two years later, in *Mutual Pharmaceutical Company v. Bartlett*, the Supreme Court faced a very similar case.¹³⁰ The plaintiff, again, was a patient who had been injured by a generic drug—in this case, a non-steroidal anti-inflammatory pain reliever.¹³¹ 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.¹³² Relying on its decision in *Pliva 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.¹³³ The majority found unpersuasive the plaintiff’s argument that it was not impossible for the generic drug manufacturer to comply with both state and federal requirements because it could have simply chosen not to sell the drug in states with requirements that conflict with federal law.¹³⁴

¹²⁴ *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011).

¹²⁵ *See id.*

¹²⁶ *See id.*

¹²⁷ *See id.*

¹²⁸ *See id.*

¹²⁹ *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 2586 (Sotomayor, J., joined by Ginsburg, J., dissenting).

¹³⁰ *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2470 (2013).

¹³¹ *Id.*

¹³² *Id.*

¹³³ *Id.*

¹³⁴ *Id.*

Regardless of one's view of the merits of this outcome,¹³⁵ *Bartlett* may signal trouble for some of the recent state drug regulatory efforts. The majority opinion suggested that imposing tort liability in the factual circumstances in *Bartlett* would be similar to a state “directly prohibiting the product's sale”¹³⁶—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.¹³⁷ 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.¹³⁸ An obstacle preemption argument, in his view, becomes stronger the more “medically valuable” a particular drug is.¹³⁹ 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.”¹⁴⁰ Taken together, the dissents and the majority opinion, thus, suggest that there may be a path for persuading 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,¹⁴¹ viable avenues for bringing products liability claims against drug manufacturers may remain or reemerge.¹⁴² So-

¹³⁵ Numerous scholars have criticized *Pliva* and *Bartlett* on both legal and policy grounds. See, e.g., LARS NOAH, LAW, MEDICINE, AND MEDICAL TECHNOLOGY 557 (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, 343 (2015); Stacey B. Lee, *Pliva v. Mensing: Generic Consumers' Unfortunate Hand*, 12 YALE J. HEALTH POL'Y, L. & ETHICS 209, 235-45 (2012).

(Foundation Press, 3d ed. 2012).

¹³⁶ *Bartlett*, 133 S. Ct. at 2478 n.5 (2013); Noah, *State Affronts*, *supra* note 7, at 34 n.137.

¹³⁷ See *id.*

¹³⁸ *Bartlett*, 133 S. Ct. at 2480-81 (Breyer, J., joined by Kagan, J., dissenting); Noah, *State Affronts*, *supra* note 7, at 31.

¹³⁹ *Bartlett*, 133 S. Ct. at 2480-81 (Breyer, J., joined by Kagan, J., dissenting).

¹⁴⁰ *Id.* at 2493 (Sotomayor, J., joined by Ginsburg, J., dissenting).

¹⁴¹ This is because generic drugs comprise approximately 88% of prescription drugs used in the United States. Generic Pharmaceutical Association, *Generic Drug Savings in the US—Seventh Annual Edition* (Nov. 2015), http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf.

¹⁴² 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*, 129 S. Ct. 1187 (2009). But as explained in note 141, *supra*, brand-name

called “parallel claims” are perhaps the most widely applicable avenue left for products liability claims against generic drug manufacturers.¹⁴³ Parallel claims are based on state tort-law duties that are identical to or incorporate, rather than conflict with, federal requirements and generally have survived preemption challenges.¹⁴⁴ 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.¹⁴⁵ Likewise, where state Food, Drug, and Cosmetic Acts incorporate the federal FDCA’s prohibitions, plaintiffs state tort-law claims

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, *Seven Pillars*, *supra* note 18, 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).

¹⁴³ See, e.g., Catherine M. Sharkey, *Tort-Agency Partnerships in an Age of Preemption*, 15 THEORETICAL INQUIRIES L. 359, 362 (2014). 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 brand-name drug manufacturers can do. See Generic Drug Labeling Proposed Rule, *supra* note 94, at 67988-89. 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 Ass’n, Comments on the Proposed Rule “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” Docket No. FDA-2013-N-0500 (Mar. 13, 2014). Second, a few state 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 *Wyeth, Inc. v. Weeks*, No. 1:10-cv-602, 2014 WL 4055813 (Ala. Aug. 15, 2014); *Conte v. Wyeth, Inc.*, 85 Cal. Rptr. 3d 299 (Ct. App. 2008); *Kellogg v. Wyeth, Inc.*, 762 F. Supp. 2d 694 (D. Vt. 2010). 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 Ala. Act 2015-106; *Wyeth, Inc. v. Weeks*, 159 So. 3d at 696 (Murdock, J. dissenting); see also Katie Thomas, *Man Taking Generic Drug Can Sue Branded Maker*, N.Y. TIMES (Jan. 11, 2013) (quoting a drug industry lawyer as stating that the Alabama decision “is contrary to the overwhelming weight of authority on this issue nationwide”).

¹⁴⁴ See *Riegel v. Medtronic, Inc.*, 128 S. Ct. 999, 1011 (2008); Sharkey, *Tort-Agency Partnerships in an Age of Preemption*, *supra* note 143, at 362.

¹⁴⁵ See *Fulgenzi v. PLIVA, Inc.*, 711 F.3d 578 (6th Cir. 2013); *Teva Pharm. USA, Inc. v. Superior Court*, 217 Cal. App. 4th 96, 100, 158 Cal. Rptr. 3d 150, 152 (2013), review denied (Sept. 25, 2013), cert. denied sub nom. *Teva Pharm. USA, Inc. v. Superior Court of Cal., Orange Cnty.*, 135 S. Ct. 1152, 190 L. Ed. 2d 911 (2015); Catherine M. Sharkey, *Tort-Agency Partnerships*, *supra* note 143, at 362.

that are premised on violations of sections of the state law that mirror federal law may survive preemption.¹⁴⁶

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.”¹⁴⁷ That is, state enforcement of parallel requirements might 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

¹⁴⁶ Brief for United States as Amicus Curiae Supporting Petitioner at 23, *Bartlett*, 133 S. Ct. 2466 (No. 12-142). 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. 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.” *Allergan, Inc. v. Athena Cosmetics, Inc.*, 738 F.3d 1350, 1359 (Fed. Cir. 2013) *cert. denied*, 135 S. Ct. 2886 (2015).

¹⁴⁷ Catherine M. Sharkey, *Tort-Agency Partnerships*, *supra* note 143, at 374; *see also* *Buckman Co. v. Plaintiffs' Legal Comm.*, 121 S. Ct. 1012, 1018 (2001) (“State-law fraud-on-the-FDA claims inevitably conflict with the FDA’s responsibility to police fraud consistently with the Administration’s judgment and objectives.”); *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.”). *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, 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.” 121 S. Ct. at 1015.

opportunity to consider the preemptive reach of the FDA’s drug authority in a fresh context.¹⁴⁹ Indeed, scholars and commentators have begun to weigh in, with varying views of the viability of claims that FDA regulation preempts various areas of state positive law.¹⁵⁰

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.¹⁵¹ Drawing on cases about food and cosmetic regulation, they argued that courts are “increasingly willing to strike state regulations that are not impossible to abide, but which complicate compliance with an overarching federal program.”¹⁵² 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.¹⁵³ 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

¹⁴⁹ 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 post-market drug safety authorities. *Cf.* Evans, *Seven Pillars*, *supra* note 18, at 515-17 (discussing the effect of FDAAA on brand-name manufacturers’ products liability); Parasidis, *supra* note 93, at 937-43 (discussing the evolution of the FDA’s post-market 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 Part II.B.2, *infra*.

¹⁵⁰ *See generally* Brown & Tomar, *supra* note 20; Noah, *State Affronts*, *supra* note 7; *cf.* Sharkey, *States vs. FDA*, *supra* note 20 (arguing that courts should consider the FDA’s view of state regulation in obstacle preemption cases).

¹⁵¹ *See generally* Brown & Tomar, *supra* note 20. 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. *See, e.g.*, Kevin Outterson, *The Drug Quality and Security Act—Mind the Gaps*, 370 NEJM 97, 97 (2014).

¹⁵² Brown & Tomar, *supra* note 20 at * 14; *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.”).

¹⁵³ *See* Jones v. Rath Packing Co., 97 S. Ct. 1305, 1316 (1977); *Cosmetic, Toiletry & Fragrance Ass’n., Inc. v. State of Minn.*, 440 F. Supp. 1216, 1222 (D. Minn. 1977).

the costs to industry and consumers.¹⁵⁴ 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—suggest 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.¹⁵⁵ 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.¹⁵⁶ 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 its initial approval as a result of new information that the FDA did not consider.¹⁵⁷ 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.¹⁵⁸

¹⁵⁴ See *id.*

¹⁵⁵ See generally Noah, *State Affronts*, *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.

¹⁵⁶ See *id.* at 3-16, 27-35.

¹⁵⁷ See *id.* at 53-54.

¹⁵⁸ Pub. L. No. 87-781, § 202, 76 Stat. 780, 783; Noah, *State Affronts*, *supra* note 7, at 8-9. Although this language clearly presents a hurdle to the success of preemption theories other than impossibility, it may not be an insurmountable hurdle. The language was not codified and expressly applied only to the 1962 amendments to the FDCA. Pub. L. No. 87-781, § 202, 76 Stat. 780, 783. 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.*, U.S. Food & Drug Admin., Significant Dates in U.S. Food and Drug Law History, <http://www.fda.gov/AboutFDA/WhatWeDo/History/Milestones/ucm128305.htm>. 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 *Wyeth v. Levine*, 129 S. Ct. 1187, 1222 (2009) (Scalia, J. dissenting) (arguing this language “simply recognizes the background principles of conflict pre-emption”); *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); *cf.*

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.¹⁵⁹ Ultimately, these examples do not provide a categorical answer to when state drug regulation is preempted.¹⁶⁰ 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.

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.¹⁶¹ Although it is illegal for individuals to import drugs not

Id. 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.*, 120 S. Ct. 1913, 1920 (2000) (arguing that a similar savings clause does not preclude obstacle theories).

¹⁵⁹ As one example, this Article does not discuss in depth state laws restricting the use of drugs intended for pregnancy termination. Sixteen 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, where-as 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 raises similar issues to those discussed with respect to Vermont and Massachusetts’s restrictions on the use of Zohydro. *See, e.g.,* Zettler, *supra* note 18, at 449; Sandhya Somashekhar & Laurie McGinley, *The FDA Just Made the Abortion Pill Easier to Get*, Wash. Post. (March 30, 2016), https://www.washingtonpost.com/national/fda-updates-recommendations-for-abortion-pill/2016/03/30/426407de-f681-11e5-8b23-538270a1ca31_story.html; Guttmacher Institute, *State Policies in Brief, Medication Abortion*, http://www.guttmacher.org/statecenter/spibs/spib_MA.pdf. Additionally, patients’ concerns often cut across many of the areas that these state laws target. For example, a recent 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, expanded access, and drug importation, among other things. Fred Vogelstein, *Boy Interrupted*, WIRED.COM, <http://www.wired.com/2015/07/medical-marijuana-epilepsy/>.

¹⁶⁰ *See* Noah, *State Affronts*, *supra* note 7, at 53-54.

¹⁶¹ *See* Patricia M. Danzon & Michael F. Furukawa, *Prices and Availability of Pharmaceuticals: Evidence from Nine Counties*, HEALTH AFFAIRS (Oct. 29, 2003); *see also* Aaron S. Kesselheim et al., *The High Cost of Prescription Drugs in the United States:*

approved by the FDA (or that otherwise violated the FDCA), the FDA does not stop individuals from importing such drugs for personal use in certain circumstances.¹⁶² 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.¹⁶³

In response, states have explored allowing their citizens access to inexpensive imported drugs.¹⁶⁴ 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.¹⁶⁵ The FDA has also said that state drug importation laws are impliedly preempted by the FDCA under theories of field, impossibility, and obstacle preemption.¹⁶⁶

Nevertheless, in 2013 Maine enacted a law to allow its citizens to purchase prescription drugs from certain foreign pharmacies.¹⁶⁷ 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.¹⁶⁸

Origins and Prospects for Reform, 316 JAMA 858 (2016) (discussing “growing concern” about increasing prescription drug prices).

¹⁶² The conditions that must be met for the FDA to use its discretion of permit personal importation include that the individual has a serious condition for which no effective treatment is available in the United States. *See* U.S. Food & Drug Admin., Is it legal for me to personally import drugs?, <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm194904.htm>

¹⁶³ *See, e.g.*, Peter S. Reichertz & Melinda S. Friend, *Hiding Behind Agency Discretion: The Food and Drug Administrations' Personal Use Drug Importation Policy*, 9 CORNELL J.L. & POLICY 494 (1999).

¹⁶⁴ *See* U.S. Food & Drug Admin., Importing Prescription Drugs, Letters to State and Local Officials, <http://www.fda.gov/Drugs/DrugSafety/ucm170594.htm>.

¹⁶⁵ *See, e.g.*, Letter from William K. Hubbard, Associate Commissioner for Policy and Planning, FDA, to Mr. Gregory Gonot, Deputy Attorney General, State of California Department of Justice (Aug. 25, 2003); Letter from Randall W. Lutter, Deputy Commissioner for Policy, FDA, to The Honorable Linda Lingle, Governor, State of Hawaii (Aug. 14, 2008).

¹⁶⁶ *See, e.g.*, Letter from William K. Hubbard, Associate Commissioner for Policy and Planning, FDA, to Mr. Gregory Gonot, Deputy Attorney General, State of California Department of Justice (Aug. 25, 2003), <http://www.fda.gov/Drugs/DrugSafety/ucm179893.htm>. 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, or 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 oversight of foreign commerce generally.

¹⁶⁷ *See* Me. Rev. Stat. tit. 32, § 13731.

¹⁶⁸ *See id.*; *see also* Zettler, *supra* 18 (describing state licensing requirements for

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.¹⁶⁹ 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 federal laws that regulate the sale of prescription drugs to Mainers by pharmacies located in certain foreign countries.”¹⁷⁰

Framing the drug importation law as medical practice regulation was not, however, sufficient to save it from a preemption challenge.¹⁷¹ 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.”¹⁷² 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.”¹⁷³ 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.¹⁷⁴ 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.”¹⁷⁵ Moreover, the opinion notes that Congress expressly considered drug importation from Canada when enacting the Medicare Prescription Drug, Improvement, and Modernization Act (MMA).¹⁷⁶ Under the MMA, Canadian drug imports are permissible only when the Secretary of the Department of Health and Human Services determines that such

physicians and pharmacies).

¹⁶⁹ Me. Rev. Stat. tit. 32, § 13731.

¹⁷⁰ See *Ouellette v. Mills*, No. 1:13-CV-00347-NT, 2015 WL 751760, at *5 (D. Me. Feb. 23, 2015).

¹⁷¹ *Id.* At *1, 5.

¹⁷² *Id.* at *5-6.

¹⁷³ *Id.* at *8.

¹⁷⁴ 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).

¹⁷⁵ *Ouellette v. Mills*, No. 1:13-CV-00347-NT, 2015 WL 751760, at *5 (D. Me. Feb. 23, 2015).

¹⁷⁶ *Id.* at *5. Another reason is, of course, that this decision only reflects the opinion of one federal judge.

imports would be safe and cost-effective—and no Secretary has made such a determination.¹⁷⁷ Field 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.¹⁷⁸

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 abuse epidemic, Massachusetts banned Zohydro in 2014.¹⁷⁹ 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 administration of Zohydro until it was reformulated to be abuse deterrent.¹⁸⁰ 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.¹⁸¹

But, as with Maine's importation law, framing the Zohydro ban as medical practice regulation was not sufficient to save it.¹⁸² After Massachusetts implemented its ban, Zogenix, Inc., Zohydro's then-manufacturer,¹⁸³ sought a preliminary injunction, arguing that, among other

¹⁷⁷ *See id.*

¹⁷⁸ *Cf. Hillsborough Cnty., Fla. v. Automated Med. Labs., Inc.*, 105 S. Ct. 2371 (1985) (holding that county ordinances governing blood plasma centers were not preempted under a field preemption theory); *Camps Newfound/Owatonna, Inc. v. Town of Harrison, Me.*, 117 S. Ct. 1590, 1618 (1997) (J. Thomas, dissenting) (“field pre-emption is itself suspect, at least as applied in the absence of a congressional command that a particular field be pre-empted”).

¹⁷⁹ *Zogenix, Inc. v. Patrick*, No. CIV.A. 14-11689-RWZ, 2014 WL 1454696, at *1 (D. Mass. Apr. 15, 2014).

¹⁸⁰ *Id.* at *1. 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, for simplicity, this Article refers to the ban as a ban on Zohydro.

¹⁸¹ *See* Defendant's Memorandum in Opposition to Application for Preliminary Injunctive Relief, 2014 WL 1454696.

¹⁸² *See Zogenix*, at *1.

¹⁸³ 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. *Zogenix Inc., Zogenix Announces Agreement of Sale of Zohydro* (Mar. 10, 2015), <http://ir.zogenix.com/phoenix.zhtml?c=220862&p=irol-newsArticle&iid=2024400>.

things, the ban was preempted by the FDCA.¹⁸⁴ 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.”¹⁸⁵ In other words, the judge relied on an obstacle preemption rationale to enjoin the ban.¹⁸⁶ Thus, as Judge Torreson 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.¹⁸⁷ 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.¹⁸⁸ Massachusetts also established requirements for pharmacies that handle Zohydro.¹⁸⁹ 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.¹⁹⁰ Zogenix challenged these new regulations, arguing that they amount to a *de facto* ban on Zohydro.¹⁹¹ Although Judge Zobel explained that the preemption

¹⁸⁴ *See id.*

¹⁸⁵ *Id.*

¹⁸⁶ *Id.*

¹⁸⁷ *See, e.g.,* Milton J. Valencia, *Mass. Limits use of the potent painkiller Zohydro*, BOSTON GLOBE (Apr. 23, 2014), <http://www.bostonglobe.com/metro/2014/04/22/governor-deval-patrick-administration-enacts-new-restrictions-zohydro/GpIZM4OUOgZg7cWEI8XV5N/story.html>.

¹⁸⁸ 243 Mass. Code Regs. 2.07. 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 Vermont Board of Pharmacy to Health Care Providers (Apr. 15, 2014), <https://www.sec.state.vt.us/media/474524/Zohydro-Memo-and-Rules.pdf>.

¹⁸⁹ 247 Mass. Code Regs. 9.04.

¹⁹⁰ *Id.*

¹⁹¹ *Zogenix, Inc. v. Baker*, No. CIV.A. 14-11689-RWZ, 2015 WL 1206354, at *2 (D. Mass. Mar. 17, 2015).

claim could succeed if the new regulations did, in fact, affect the availability of Zohdro, she declined to enjoin the new regulations.¹⁹²

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 go beyond the federal restrictions on Zohydro's use imposed by the FDA.¹⁹³ The FDA has required a “Risk Mitigation and Evaluation Strategy (REMS)” for Zohydro (and other similar opioids).¹⁹⁴ 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.¹⁹⁵ 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.¹⁹⁶ 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.¹⁹⁷

¹⁹² See *Zogenix*, 2015 WL 1206354, at *2; Catherine M. Sharkey, *States vs. FDA*, 83 GEO. WASH. L. REV. 1609, 1610 (2015).

¹⁹³ 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 2 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. § 829(a); Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II, 79 Fed. Reg. 49661, 49662, 49675 (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 . . . State law so that the two cannot consistently stand together.” 21 U.S.C. § 903; Noah, *State Affronts*, *supra* note 7, at 8-9.

¹⁹⁴ U.S. Food & Drug Admin., Extended-Release and Long-Acting (ER/LA) Opioid Analgesics Shared System REMS, <http://www.accessdata.fda.gov/scripts/cder/remis/index.cfm?event=RemsDetails.page&REMS=17>.

¹⁹⁵ See 21 U.S.C. § 355-1(a), (b).

¹⁹⁶ 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, *Seven Pillars*, *supra* note 18, at 419; Kristen Underhill, *Risk-Taking and Rulemaking: Addressing Risk Compensation Behavior Through FDA Regulation of Prescription Drugs*, 30 YALE J. ON REG. 377, 426 (2013).

¹⁹⁷ See 21 U.S.C. § 355-1. 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.

Although medical practitioners ultimately carry out many of these REMS requirements, REMS requirements apply only to drug manufacturers.¹⁹⁸ 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).¹⁹⁹

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 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.²⁰⁰ That is, 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.²⁰¹ 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.²⁰² To require a REMS, the agency must consider the risks and benefits of a drug, and determine that a REMS is “necessary to

¹⁹⁸ See Zettler *supra* note 18, at 430.

¹⁹⁹ See, e.g., Part II.2.A, *supra*. 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 co-exist. For example, both 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. Such programs could be characterized as risk mitigation programs—and indeed, FDA can require a registry to collect information about a drug as part of a REMS. 21 U.S.C. § 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.*, 109 S. Ct. 971, 986 (1989) (internal quotations and citations omitted).

²⁰⁰ See ER/LA Opioid REMS, *supra* note 194; see also 21 U.S.C. § 355-1 (describing all of the measures that FDA may require as part of REMS).

²⁰¹ See, e.g., David C. Vladeck, *FDA Preemption, Wyeth, Congress, and A Crystal Ball*, 32 *HAMLIN L. REV.* 707, 719 (2009)

²⁰² 21 U.S.C. § 355-1(f)(2).

ensure that the benefits of the drug outweigh [its] risks.”²⁰³ 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.”²⁰⁴ 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.²⁰⁵

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 *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.²⁰⁶ To that end, the law required a “pedigree” for prescription drugs.²⁰⁷ 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.²⁰⁸ A pedigree is intended to prevent counterfeit and other potentially substandard drugs from entering the supply chain, and, if that fails, to enable to track such drugs and remove them from the supply chain—hence the name “track and trace.”²⁰⁹ The California requirements, similar to the Maine drug importation law and the Massachusetts Zohydro

²⁰³ *Id.* at § 355-1(a).

²⁰⁴ *Id.* at § 355-1(f)(2).

²⁰⁵ See Brown & Tomar, *supra* note 20, at *14.

²⁰⁶ See Calif. Stat. 2004 Chapter 857; Lisa A. Daigle, *Following Pharmaceutical Products Through the Supply Chain*, ASHP POLICY ANALYSIS 2-3 (Aug. 2012), <https://www.ashp.org/DocLibrary/Advocacy/AnalysisPaper/Following-Pharmaceutical-Products.aspx>.

²⁰⁷ See Daigle, *supra* note 206.

²⁰⁸ See *id.*; West’s Ann.Cal.Bus. & Prof.Code § 4034. A few other states also enacted a similar laws. See, e.g., Fla. Stat. 2003 Chapter 155. This Article uses the California law as its case study because of the unique preemption provisions in the law, and because it is often credited with driving industry support for a federal pedigree requirement. See 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, 252 (2007).

²⁰⁹ See, e.g., Aleong, *supra* note 208, at 270-71

ban, were codified in the state laws regulating pharmacy practice and overseen by the state board of pharmacy.²¹⁰

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.²¹¹ Interestingly, however, California’s law contained a provision inviting federal preemption.²¹² The law stated that it would “become inoperative” “upon the effective date of federal legislation or adoption of federal regulation.”²¹³ 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.”²¹⁴ 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 non-binding federal recommendations do not preempt binding state law.

Although California’s requirements never fully went into effect, it ultimately motivated federal action.²¹⁵ 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.²¹⁶ 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] requirement.”²¹⁷ Consistent with the 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.²¹⁸

²¹⁰ Calif. Stat. 2004 Chapter 857.

²¹¹ 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 208, at 252.

²¹² Cal. Bus. & Prof. Code § 4034.1 (West) (repealed 2015).

²¹³ *Id.*

²¹⁴ *Id.*

²¹⁵ See Daigle, *supra* note 206.

²¹⁶ See Drug Quality and Security Act of 2013, Pub. L. No. 113-54, 127 Stat. 587, 599-640 (2013).

²¹⁷ *Id.* at 638.

²¹⁸ See Stats. 2014, c. 492 (S.B.600), § 3, eff. Jan. 1, 2015.

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-four states, the District of Columbia, and Guam, have followed suit.²¹⁹ 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.²²⁰ 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, the most 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 21 conditions for which marijuana may be prescribed, including cancer, intractable pain, and multiple sclerosis.²²¹

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.²²² And the intersection between state medical marijuana laws and the federal Controlled Substances Act (CSA) has been widely discussed.²²³ The CSA currently classifies marijuana as a

²¹⁹ See State Medical Marijuana Laws, *supra* note 16. Four states and the District of Columbia have enacted laws permitting the recreational use of marijuana. 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.” A drug intended to provide a “high” is intended to affect the function of the body. See 21 U.S.C. § 321(g); FDA Draft Guidance on Botanical Drug Development (Aug. 2015), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm458484.pdf>.

²²⁰ 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.*

²²¹ H.B. 523, <https://www.legislature.ohio.gov/legislation/legislation-summary?id=GA131-HB-523>. The law also permits the state medical board to add more conditions.

²²² See, e.g., Marijuana Policy Project, About Us, <https://www.mpp.org/about/>

²²³ See, e.g., Brannon P. Denning, *Vertical Federalism, Horizontal Federalism, and*

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

But medical marijuana laws also intersect with the FDA’s jurisdiction.²²⁹ 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.²³⁰ 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.²³¹ In fact, the FDA has approved

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, *Preemption Under the Controlled Substances Act*, 16 J. HEALTH CARE L. & POL’Y 5, 12 (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).

²²⁴ 21 U.S.C. §§ 812(b)(1), 812(c)(c)(10); *Alliance for Cannabis Therapeutics v. Drug Enforcement Admin.*, 15 F.3d 1131, 1133 (D.C. Cir. 1994).

²²⁵ 21 U.S.C. § 841.

²²⁶ *See, e.g.,* *Printz v. United States*, 117 S. Ct. 2365 (1997); Erwin Chemerinsky et al., *Cooperative Federalism and Marijuana Regulation*, 62 UCLA L. REV. 74 (2015).

²²⁷ DEP’T OF JUSTICE, MEMORANDUM FOR ALL UNITED STATES ATTORNEYS: GUIDANCE REGARDING MARIJUANA ENFORCEMENT 1-2 (2013), available at <http://www.justice.gov/iso/opa/resources/3052013829132756857467.pdf> [hereinafter “DOJ Memo”].

²²⁸ But as explained in note 193, *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.

²²⁹ *See* Kevin A. Sabet, Ph.D., *Much Ado About Nothing: Why Rescheduling Won’t Solve Advocates’ Medical Marijuana Problem*, 58 WAYNE L. REV. 81, 101 (2012); Alex Kreit, *What Will Federal Marijuana Reform Look Like?*, 65 CASE W. RES. L. REV. 689, 698 (2015).

²³⁰ 21 U.S.C. § 321(g).

²³¹ 21 U.S.C. §§ 321(p), 355(a); Depak 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 et al., *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 that “substantial evidence” supports the use

synthetic THC and THC analogue drugs, which suggests that the FDA understands marijuana to be a “new drug.”²³² 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),²³³ 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, twenty-seven states enacted laws that permitted the *intrastate* production and sale of laetrile.²³⁴ Laetrile is a compound derived from apricot pits that was marketed as a cancer cure.²³⁵ Despite a lack of evidence supporting this use, healthcare providers and patients challenged the FDA’s restrictions on the sale of the unapproved drug.²³⁶ This challenge led to an unsuccessful lawsuit against the FDA, Congressional hearings, and ultimately the state laws that permitted the intrastate sale of laetrile.²³⁷ 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.²³⁸ 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 Zohdro ban and restrictions. First, a court is unlikely to conclude that state medical marijuana laws are preempted by the FDCA on an impossibility theory.²³⁹ Marketing medical marijuana pursuant to a state

of marijuana for “chronic cancer and neuropathic pain and certain symptoms of multiple sclerosis”).

²³² See Marinol Label, http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018651s025s0261bl.pdf; Cesamet Label, http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677s0111bl.pdf.

²³³ 21 U.S.C. §§ 321(g), 331.

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

²³⁵ See, e.g., *United States v. Rutherford*, 99 S. Ct. 2470 (1979).

²³⁶ See *id.*; Irving J. Lerner, *Laetrile: A Lesson in Cancer Quackery*, 31 CA CANCER CLIN. J. 91 (1981).

²³⁷ See, e.g., Lerner, *supra* note 236, at 94.

²³⁸ And 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 NEJM 989 (2015) (explaining edible marijuana products).

²³⁹ Cf. Mikos, *supra* note 223, at 8 (making the same point with respect to the CSA).

law but without the approval of the FDA would violate federal law (assuming that the drug travels in interstate commerce),²⁴⁰ but nothing in the state medical marijuana laws *compels* a person to violate federal law by selling marijuana without FDA approval.²⁴¹ A person could comply with both state and federal law by obtaining FDA approval to market marijuana before doing so.²⁴² Moreover, to the extent state marijuana laws involve prescriber and dispenser licensing, or prescribing decisions, the laws would apply to parties—*i.e.*, medical practitioners—to whom FDA requirements generally do not directly apply.²⁴³

A challenge to medical marijuana laws under an obstacle preemption theory would be a stronger case, but still may be unlikely to succeed.²⁴⁴ Some courts have been convinced by obstacle preemption arguments with respect to the CSA, 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.²⁴⁵ By permitting the sale of drugs for which there is little evidence of safety and effectiveness at least for some uses,²⁴⁶ 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.²⁴⁷ 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 law²⁴⁸—and outside the preemption

²⁴⁰ 21 U.S.C. §§ 331, 355.

²⁴¹ *See, e.g.*, Sabet, *supra* note 229, at 101.

²⁴² Obtaining FDA approval for marijuana admittedly may be somewhat complicated because it is a “botanical,” *i.e.*, plant-based, drug. As the FDA has explained in draft 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 Draft Guidance on Botanical Drug Development (Aug. 2015), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm458484.pdf>

²⁴³ *See* the discussion of REMS in Part II.2.B, *supra*.

²⁴⁴ 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* Part II.B.2, *supra*.

²⁴⁵ *See, e.g.*, Washburn v. Columbia Forest Products, Inc., 340 Or. 469, 472 (2006).

²⁴⁶ *See* note 230, *supra*.

²⁴⁷ Hines v. Davidowitz, 61 S. Ct. 399, 404 (1941).

²⁴⁸ *See* Ouellette v. Mills, No. 1:13-CV-00347-NT, 2015 WL 751760, at *1 (D. Me.

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.”²⁴⁹ 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 1 million patients obtain medical marijuana under state laws.²⁵⁰

This theory, however, has significant weaknesses, even if courts are increasingly inclined to rely on obstacle preemption to strike down state laws that disrupt careful balancing that the federal government has stuck with a particular policy.²⁵¹ 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.²⁵² 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.²⁵³ 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,²⁵⁴ there is no publicly available documentation that the FDA has considered the use of marijuana for the full range of indications for which states have authorized its use, and rejected those uses.²⁵⁵ In sum, while there are colorable arguments that the FDCA

Feb. 23, 2015).

²⁴⁹ 643 F.2d 1043, 1048 (5th Cir. 1981).

²⁵⁰ ProCon.org, Numer of Legal Medical Marijuana Patients, <http://medicalmarijuana.procon.org/view.resource.php?resourceID=005889>. Moreover, if the FDA were to approve a marijuana product for condition for which state law prohibited it, a court could conclude that state law were preempted under an obstacle preemption theory, just as Judge Zobel did in the Zohydro litigation.

²⁵¹ *Brown & Tomar*, *supra* note 20, at *14.

²⁵² *See, e.g.*, *Gade v. Nat’l Solid Wastes Mgmt. Ass’n*, 112 S. Ct. 2374, 2386 (1992); *Lefavre v. KV Pharm. Co.*, 630 F.3d 733, 739 (8th Cir.); *Chemerinsky et al.*, *supra* note 226, at 101.

²⁵³ *See, e.g.*, S. 954, 114th Cong. (2015).

²⁵⁴ *See, e.g.*, U.S. Food & Drug Admin., Summary Minutes of Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee (Dec. 7, 2012), <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/UCM336475.pdf>.

²⁵⁵ The two FDA-approved THC products are approved for various nausea and vomiting-related indications. *See* Marinol Label,

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.²⁵⁶ The term for such treatment use in the FDA’s regulations is “expanded access.”²⁵⁷ FDA regulations specify a process for requesting expanded access, and the agency authorizes approximately ninety-nine percent of patients’ requests.²⁵⁸ But advocacy groups and patients have criticized the FDA process for being slow and burdensome.²⁵⁹ Although there is good reason to think such criticisms of the FDA are not deserved,²⁶⁰ since 2014 twenty-eight states have enacted “right to try” laws, and another sixteen are considering proposed legislation.²⁶¹

“Right to try” laws are based on model legislation drafted by the Goldwater Institute, an organization that advocates for a “constitutionally

http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018651s025s0261bl.pdf;

Cesamet

Label,

http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677s0111bl.pdf.

²⁵⁶ 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, *State Affronts*, *supra* note 7, 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. 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 INTERN. MED. 1885 (2014).

²⁵⁷ 21 C.F.R. pt. 312, subpt. I.

²⁵⁸ See *id.*; U.S. Food & Drug Admin., IND Activity Reports, Expanded Access INDs and Protocols, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/ucm373560.htm>.

²⁵⁹ See e.g., Dennis & Cha, *supra* note 256; Goldwater Inst., Everyone Deserves the Right to Try: Empowering the Terminally Ill to Take Control of Their Treatment (Feb. 11, 2014), <http://goldwaterinstitute.org/en/work/topics/healthcare/right-to-try/everyone-deserves-right-try-empowering-terminally-/>.

²⁶⁰ See Part III., *infra*; cf. Dresser, *supra* note 253, at 1648-53 (describing positive and negative patient experiences with access).

²⁶¹ See Silverman, *supra* note 15.

limited government.”²⁶² 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.²⁶³ 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.²⁶⁴ 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.²⁶⁵

These “right to try” law provide significantly fewer safeguards for patients than the FDA’s expanded access regulations do.²⁶⁶ 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.²⁶⁷ 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 expanded access program before the patient receives the experimental drug.²⁶⁸ 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.²⁶⁹

“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

²⁶² See Goldwater Inst., About, <http://goldwaterinstitute.org/en/about/>.

²⁶³ See 21 C.F.R. § 312.21(a).

²⁶⁴ See, e.g., Right To Try Act, 2015 North Carolina Laws S.L. 2015-137 (H.B. 652); see also Goldwater Institute, 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.

²⁶⁵ See Right to Try Model Legislation, *supra* note 264.

²⁶⁶ See, e.g., Alison Bateman-House et al., *Right-to-Try Laws: Hope, Hype, and Unintended Consequences*, 163 ANNALS INTERN. MED. 796, 796 (2015).

²⁶⁷ 21 C.F.R. § 312.305(a)(1).

²⁶⁷ See 21 C.F.R. §§ 312.305(a)(2), 312.310(a), 312.315(b), 312.320(a).

²⁶⁷ See, e.g., Michele Munz, *Missouri’s ‘right to try’ law no guarantee patients 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.

²⁶⁷ 21 C.F.R. § 312.305(a)(1).

²⁶⁸ *Id.* at § 312.305(d)(4).

²⁶⁹ See 21 C.F.R. §§ 312.305(a)(2), 312.310(a), 312.315(b), 312.320(a).

because, under the Tenth Amendment, “federal regulations that violate constitutional liberties can never trump state law.”²⁷⁰ They argue that “right to try” laws “preserve constitutionally protected rights, such as a person’s right to life and medical self-preservation.”²⁷¹ Although patients often have very sympathetic claims for access to unapproved therapies (and understandable reasons for wanting access),²⁷² courts have declined to recognize such access as a constitutionally protected right.²⁷³ Accordingly, “right to try” laws are not likely to survive preemption challenges on the ground that they protection a constitutional right.²⁷⁴

Yet “right to try” advocates may not be wrong that preemption challenges to “right to try” 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.²⁷⁵ As long as the FDA has authorized the treatment use of the unapproved drug under its regulations, a drug manufacturer would comply 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.²⁷⁶

And as in the medical marijuana context, an obstacle preemption

²⁷⁰ Kurt Altman and Christina Sandefur, *Right-To-Try Laws Fulfill The Constitution’s Promise of Individual Liberty*, HEALTH AFFAIRS BLOG (July 14, 2015), <http://healthaffairs.org/blog/2015/07/14/right-to-try-laws-fulfill-the-constitutions-promise-of-individual-liberty/>; Clint Bolick, *The End of FDA Paternalism?*, DEFINING IDEAS (Aug. 14, 2014), <http://www.hoover.org/research/end-fda-paternalism>; 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.”)

²⁷¹ Altman and Sandefur, *supra* note 270.

²⁷² Cf. Arthur Caplan and 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.”).

²⁷³ Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach, 495 F.3d 695, 697 (D.C. Cir. 2007); Shah & Zettler, *supra* note 33, at 140-52.

²⁷⁴ 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*, 117 S. Ct. 2365 (1997); Chemerinsky et al., *supra* note 213, at 101.

²⁷⁵ Compare 21 C.F.R. pt. 312, subpt. I with Goldwater Institute, *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; but see Caitlyn Martin, *Question the “Right in State Right to Try Laws: Assessing the Legality and Effectiveness of These Laws*, 77 OHIO STATE L.J. 159, 178 (2016) (arguing that “right to try” laws are preempted on impossibility grounds).

²⁷⁶ 21 U.S.C. § 360bbb.

challenge to “right to try” laws is a closer call but may face some difficulties.²⁷⁷ 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.²⁷⁸ And there is evidence—in the form of detailed regulations—that 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.²⁷⁹ 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.²⁸⁰

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 actually thwart the FDA’s expanded access policy. 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

²⁷⁷ *But see* David Farber et. al, *How State Right-To-Try Laws Create False Expectations*, HEALTH AFFAIRS BLOG (May 22, 2015), <http://healthaffairs.org/blog/2015/05/22/how-state-right-to-try-laws-create-false-expectations> (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* Part II.B.2, *supra*.

²⁷⁸ 21 U.S.C. § 360bbb.

²⁷⁹ *See* 21 C.F.R. pt. 312, subpt. I.

²⁸⁰ *See* Part II.2.D., *supra*.

²⁸¹ *See* Munz, *supra* note 267. In recent 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 US, FDA Issues*, RAPS.org (Feb. 25, 2016), <http://raps.org/Regulatory-Focus/News/2016/02/25/24410/Congressional-Hearings-Focus-on-Compassionate-Use-FDA-Issues/>; *see also* Julie Turkewitz, *Patients Seek “Right to Try” New Drugs*, N.Y. TIMES (Jan. 11, 2015), <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 . . .”).

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 Torreson did not disagree.²⁸⁶

²⁸² FDA, Guidance for Industry, Expanded Access to Investigational Drugs for Treatment Use—Questions and Answers (June 2016), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf>; FDA, Guidance for Industry, Charging for Investigational Drugs Under an IND—Questions and Answers (June 2016), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351264.pdf>; Goldwater Institute, 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.

²⁸³ See, e.g., Evans, *Practice and Products Regulation*, *supra* note 17, at 288; Noah, *Ambivalent Commitments*, *supra* note 18, at 154-71; Zettler, *supra* note 18, at 430-31.

²⁸⁴ See *id.*

²⁸⁵ 37 Fed. Reg. 16503 (Aug. 15, 1972).

²⁸⁶ *Ouellette v. Mills*, No. 1:13-CV-00347-NT, 2015 WL 751760, at *5 (D. Me. Feb. 23, 2015); cf. *McCuskey*, *supra* note 90 (questioning whether a tradition of state regulation is “compelling evidence” with respect to Congressional intent to preempt).

The history of drug and medical practice regulation explained in Park 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 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 porous. 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 Torreson and Zobel concluded that FDA oversight preempted both state efforts, implicitly collapsing the distinction between regulating medical

²⁸⁷ See *Lambert v. Yellowly*, 272 U.S. 581, 596-97 (1926); Zettler, *supra* note 18, at 339-441; 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 18, at 442-46. This persistence may be 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, *States vs. FDA*, *supra* note 20 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) (repealed 2015).

²⁹⁰ See Me. Rev. Stat. tit. 32, § 13731.

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

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 Torreson 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 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 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

²⁹² *Id.*; *Ouellette v. Mills*, No. 1:13-CV-00347-NT, 2015 WL 751760, at *1, 5 (D. Me. Feb. 23, 2015).

²⁹³ *See id.*; *cf. McCuskey*, *supra* note 90 (questioning whether a tradition of state regulation is "compelling evidence" with respect to Congressional intent to preempt).

²⁹⁴ *Zogenix*, 2014 WL 1454696, at *2; *Ouellette*, 2015 WL 751760, at *5

²⁹⁵ *Ouellette*, 2015 WL 751760, at *5.

²⁹⁶ *See Noah, Ambivalent Commitments*, *supra* note 18, at 154-71; *Zettler*, *supra* note 18, at 467-74; *cf. INST. OF MED., LEADERSHIP COMMITMENTS TO IMPROVE VALUE IN HEALTHCARE* 242-43 (2009), <http://www.ncbi.nlm.nih.gov/books/NBK52854> ("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. *7-9 (forthcoming 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), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2712711.

²⁹⁷ *See Part II.A., supra.*

²⁹⁸ *Food & Drug Admin. v. Brown & Williamson Tobacco Corp.*, 120 S. Ct. 1291, 1301 (U.S. 2000).

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 prescribers and dispensers—and FDA requirements do not directly apply to practitioners—it, arguably, 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) 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 nebulousness 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 begins to consider the relationship between the FDA and the states, by considering 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.

²⁹⁹ *Zogenix, Inc. v. Patrick*, No. CIV.A. 14-11689-RWZ, 2014 WL 1454696, at *1 (D. Mass. Apr. 15, 2014). 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 pre-approval. *See* Noah, *State Affronts*, *supra* note 7, at 8-12; *cf. Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2478 n.5 (2013) (“the mere fact that a manufacturer may avoid liability by leaving the market does not defeat a claim of impossibility”).

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. The term “regenerative medicine” generally refers to therapies involving stem cell transplantation, and is 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

³⁰⁰ See, e.g., Evans, *Product and Practice Regulation*, *supra* note 17, at 288; CLEMENT & TRIBE, *supra* note 23, at 11.

³⁰¹ The FDA’s attempts to assert authority over new technologies are not the only context in which the argument that 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. 58942, 58951–52 (Dec. 11, 1992) (codified at 21 C.F.R. pts. 314 & 601).

³⁰² See, e.g., PAUL KNOEPFLER, *STEM CELLS: AN INSIDER’S PERSPECTIVE* 10 (2013); Kalina Kamenova and Timothy Caulfield, *Stem Cell Hype: Media Portrayal of Therapy Translation*, 7 *SCI. TRANSLATIONAL MED.* 278 (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 and Caulfield, *supra*; Aaron D. Levine and 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).

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 providing 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 stems cells from that bone marrow, processing those stems cells, and then re-implanting 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 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 it concluded that the stem cell therapy was a product, rather than a procedure.³⁰⁸ The court also expressed skepticism about the practice-

³⁰³ See e.g., R. Alta Charo, *On the Road (to a Cure?)—Stem-Cell Tourism and Lessons for Gene Editing*, 374 NEJM 901, 902 (2016); Leigh Turner and Paul Knoepfler, *Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry*, 19 Cell Stem Cell 1 (2016); McFarling, *supra* note 2323; Cell Surgical Network, <http://stemcellrevolution.com/>; cf. Levine and Wolf, *supra* note 302 (describing stem cell clinics in other countries).

³⁰⁴ See, e.g., Margaret Foster Riley, *Twenty-First-Century Technology with Twentieth-Century Baggage*, in *FDA IN THE TWENTY-FIRST CENTURY* 455, 460 (Holly Fernandez Lynch & I. Glenn Cohen, eds., 2015); Charo, *supra* note 303, at 902; Richard Epstein, *The FDA’s Misguided Regulation of Stem-Cell Procedures: How Administrative Overreach Blocks Medical Innovation*, Legal Policy Report, Sept. 2013, at 1, available at http://www.manhattan-institute.org/pdf/lpr_17.pdf; Cell Surgical Network, FDA, <http://stemcellrevolution.com/fda/>; see also 21 C.F.R. § 1271.3 (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 pre-market review. See generally *United States v. Regenerative Sciences, LLC*, 741 F.3d 1314 (D.C. Cir. 2014); 21 C.F.R. § 1271.10(a); *supra* notes 232-237 and accompanying text

³⁰⁵ *United States v. Regenerative Sciences, LLC*, 878 F. Supp. 2d 248, 251-52 (D.D.C. 2012).

³⁰⁶ See *id.*

³⁰⁷ *United States v. Regenerative Sciences, LLC*, 741 F.3d 1314, 1319 (D.C. Cir. 2014).

³⁰⁸ See *id.*

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 And this argument is likely to resurface while the FDA is actively considering finalizing draft guidance documents regarding its 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) genetic tests fall within a category known as

³⁰⁹ *See id.*

³¹⁰ *Id.*

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 23 (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”); Cell Surgical Network, FDA, *supra* note 303 (“the 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. 23661 (Apr. 22, 2016).

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 and Knoepfler, *supra* note 303; Andrew Joseph, *Drive To Get More Patients Experimental Stem Cell Treatments Stirs Concern*, STAT NEWS (June 30, 2016), <https://www.statnews.com/2016/06/30/stem-cell-political-fight/>.

³¹⁴ *See, e.g.,* James P. Evans & Michael S. Watson, *Genetic Testing and FDA Regulation: Overregulation Threatens the Emergence of Genomic Medicine*, 313 JAMA 667, 667 (2015). Although genetic tests within the scope of FDA’s jurisdiction are devices rather than drugs, *see* 21 U.S.C. § 321 (g), (h), 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 and Elizabeth Pike, *Consuming Genomics: Regulating Direct-to-Consumer Genetic and Genomic Information*, 92 NEB. L. REV. 677, 728-31 (2014).

“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 But because of changes to the LDT industry and testing technology, in 2014 the FDA proposed to phase in enforcement of applicable regulatory requirements for “high and moderate risk” LDTs, including many genetic tests.³¹⁹ Various stakeholders and commentators have criticized this proposal on numerous legal and policy grounds.³²⁰

One argument that some laboratory stakeholders have advanced is 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.³²¹ A challenge to the FDA’s authority over LDTs based on solely

³¹⁵ See, e.g., Barbara J. Evans et al., *The FDA and Genomic Tests—Getting Regulation Right* 372 NEJM 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, Draft Guidance, Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs) 5 n.4 (Oct. 2014), <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm416685.pdf>.

³¹⁶ See, e.g., LDT Draft Guidance, *supra* note 315.

³¹⁷ See U.S. Food & Drug Admin., Laboratory Developed Tests, <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm407296.htm>.

³¹⁸ See *id.*

³¹⁹ LDT Draft Guidance, *supra* note 315.

³²⁰ See generally Evans & Watson, *supra* note 314, at 667; CLEMENT & TRIBE, *supra* note 23; Gail Javitt, *FDA’s Legally-Suspect Shift of Clinical Lab Test Regulation Through Guidance Documents*, Washington Legal Foundation (Aug. 20, 2014), <https://wfllegalpulse.com/2014/08/20/fdas-legally-suspect-shift-of-clinical-lab-test-regulation-through-guidance-documents/>; see also Evans et al., *The FDA and Genomic Tests*, *supra* note 315 (arguing for “a relatively modest set of statutory reforms” to improve FDA oversight); Bradley Merrill Thompson, *LDT Debate: Understanding FDA’s Jurisdiction Over IVDs Made at a Clinical Lab* Health Law Advisors (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> (analyzing several legal questions raised by the FDA’s proposal).

³²¹ See Evans & Watson, *supra* note 314, at 667; CLEMENT & TRIBE, *supra* note 23; Merrill Thompson, *supra* note 320; cf. Evans, *Product and Practice Regulation*, *supra* note 17, at 288-92 (discussing the practice-products distinction in the context of personalized medicine).

on this argument, however, seems unlikely to succeed.³²² 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 statutes³²³—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 explores one the 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.

1. The Mixed Practical Effect of State Regulation

Preemption is not the only reason that state drug regulation be without significant effect. State regulation that establishes a scheme more

³²² See Merrill Thompson, *supra* note 320; cf. Evans et al., *The FDA and Genomic Tests*, *supra* note 315, at 2258 (“there is little doubt that the FDA has ample power to impose at least some new regulatory requirements on genomic testing”).

³²³ See, e.g., *United States v. Regenerative Sciences, LLC*, 741 F.3d 1314 (D.C. Cir. 2014).

permissive than the FDA's does not exempt drug manufacturers from federal requirements.³²⁴ For example, marketing marijuana for conditions for which state governments have given their approval does not confer approval of such drugs under federal law.³²⁵ 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.³²⁶ That is, the very argument 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.³²⁷ 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 dollars of medical marijuana (and another 313 million dollars of recreational marijuana) in Colorado alone.³³¹

³²⁴ Other reasons might also include dormant commerce clause and substantive due process challenges. See Noah, *State Affronts*, *supra* note 7, at 35-54.

³²⁵ See 21 U.S.C. §§ 321(g), 355(a); FDA Draft Guidance on Botanical Drug Development, *supra* note 219.

³²⁶ See 21 C.F.R. pt. 312, subpt. I.

³²⁷ See, e.g., World Health Organization, Pharmaceutical Industry, <http://www.who.int/trade/glossary/story073/en/>.

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 Part II.B.4, *supra*.

³³⁰ See Number of Legal Medical Marijuana Patients, *supra* note 233.

³³¹ Christopher Ingraham, *Colorado's Legal Weed Market: \$700 million in sales last year, \$1 billion by 2016*, WASH. POST (Feb. 12, 2015),

One reason for this vigorous, but federally illegal, marijuana market is almost certainly that the federal government announced that it would not pursue prosecution in many circumstances in which marijuana is sold in compliance with state law.³³² But medical marijuana laws were also utilized before this enforcement discretion policy was in place.³³³ 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.³³⁴ 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,³³⁵ mainstream drug companies might nevertheless wish to seek approval for any marijuana products because insurers often consider FDA approval when making coverage decisions.³³⁶

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).³³⁷ “Right to try” laws may have limited impact because the laws are new compared with medical marijuana laws, they do not require drug companies to provide unapproved drugs to terminally ill patients, and the laws do not address many valid industry concerns regarding the practical and ethical questions that expanded access raises.³³⁸

<http://www.washingtonpost.com/news/wonkblog/wp/2015/02/12/colorados-legal-weed-market-700-million-in-sales-last-year-1-billion-by-2016/>.

³³² See DOJ Memo, *supra* note 227.

³³³ See, e.g., *United States v. Oakland Cannabis Buyers' Co-op.*, 121 S. Ct. 1711 (2001).

³³⁴ Cf. Alex Halperin, *How to Brand, Market, and Sell Marijuana Without Breaking the Law*, FASTCOMPANY.COM (Apr. 23, 2015), <http://www.fastcompany.com/3045240/rebranding-pot/how-to-brand-market-and-sell-weed-without-breaking-the-law> (describing the “best-known” cannabis brands in Colorado); Mike Adams, *First Ever Marijuana Superstore*, HIGH TIMES (Jan. 24, 2014) (explaining that the first largescale marijuana retail establishment is slated to be built in Colorado), <http://www.hightimes.com/read/first-ever-marijuana-superstore>.

³³⁵ See DOJ Memo, *supra* note 227.

³³⁶ See, e.g., U.S. Food & Drug Admin., *Why won’t my insurance company pay for certain drugs?*, <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDE/ucm082690.htm#6>.

³³⁷ See, e.g., Munz, *supra* note 267.

³³⁸ See, e.g., Right To Try Act, 2015 North Carolina Laws S.L. 2015-137 (H.B. 652); Goldwater Institute, *Right to Try Model Legislation*, https://goldwater-media.s3.amazonaws.com/cms_page_media/2015/1/28/RIGHT%20TO%20TRY%20MOD

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.³³⁹ For example, the primary trade organizations for brand-name drug manufacturers, the Pharmaceutical Research and Manufacturers Associate (PhRMA) and the Biotechnology Industry Organization (BIO), have publicly expressed reservations about right-to-try laws.³⁴⁰ Only one company, Neuralstem, Inc. has indicated any interest in providing unapproved drugs under these state laws.³⁴¹

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. Driving 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

[EL%20LEGISLATION%20%282%29_1.pdf](#); *see also* Shah & Zettler, *supra* note 33, 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.*, Right To Try Act, 2015 North Carolina Laws S.L. 2015-137 (H.B. 652).

³³⁹ *See, e.g.*, Zettler & Greely, *supra* note 256; Dennis & Cha, *supra* note 256.

³⁴⁰ *See, e.g.*, Zettler & Greely, *supra* note 256.

³⁴¹ 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), <http://www.fiercebiotech.com/story/neuralstem-wades-murky-water-plan-offer-unapproved-therapy/2014-06-06>. 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* Part III.A.1, *supra*; Kamenova & Caulfield, *supra* note 301.

states use their limited resources to enact and defend drug laws. One possibility is that states find regulation to be useful tool for influencing federal policy.³⁴²

The federal government itself, as well as commentators, have recognized that states ought to have a voice in federal policy.³⁴³ Indeed, administrative agencies have been directed to provide states the opportunity to participate in agency decision-making.³⁴⁴ The FDA’s own policy is that “[f]ederal, state, and local cooperation shall be fostered whenever possible,”³⁴⁵ and it established an “Office of Partnerships” to facilitate that goal.³⁴⁶

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.³⁴⁷ Although no state officials spoke at the meeting, they could have chosen to voice their concerns then.³⁴⁸

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.³⁴⁹ Accordingly, state

³⁴² Cf. Gerken and Holzblatt, *supra* note 28, at 91 (“‘defensive preemption’ [is] used to describe how state spillovers reverse industry opposition to broadly popular legislation and thus break up congressional gridlock”).

³⁴³ See, e.g., Exec. Order No. 13,132, 64 Fed. Reg. 43,255, 43,255 (Aug. 4, 1999); Miriam Seifter, *States as Interest Groups in the Administrative Process*, 100 VA. L. REV. 953, 959 (2014).

³⁴⁴ See 64 Fed. Reg. at 43,255.

³⁴⁵ U.S. Food & Drug Admin., Investigations Operations Manual § 3.1.1, <http://www.fda.gov/ICECI/Inspections/IOM/ucm122518.htm>.

³⁴⁶ U.S. Food & Drug Admin., Federal-State Relations Activities, <http://www.fda.gov/ForFederalStateandLocalOfficials/StateActionInformationNewsletterSAIL/default.htm>

³⁴⁷ See U.S. Food & Drug Admin., Summary Minutes of Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee (Dec. 7, 2012), <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/UCM336475.pdf>.

³⁴⁸ See *id.*; Sharkey, *States vs. FDA*, *supra* note 20.

³⁴⁹ See, e.g., Yuhua Bao et al., *Prescription Drug Monitoring Programs Are Associated With Sustained Reductions in Opioid Prescribing by Physicians*, 35 HEALTH AFFAIRS 1045 (2016); Dennis Thompson, *The States with the Worst Prescription Painkiller Problem*, CBSNEWS.COM (July 1, 2014), <http://www.cbsnews.com/news/the-states-with->

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,³⁵⁰ 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.³⁵¹ 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, combined with gridlock at the federal level, may also lead advocacy organizations lobby for legal change at the state, rather than federal, level.³⁵²

Moreover, federal agencies have a “dismal track record” in considering states' input.³⁵³ Commentators have expressed concern that federal agencies—which, today, are the federal entities that often make “critical decisions about the actual scope of state powers and autonomy”³⁵⁴—are not adequately protecting state regulatory interests.³⁵⁵ 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.³⁵⁶

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-worst-prescription-painkiller-problem/](#).

³⁵⁰ See Pew Research Center, *State Governments Viewed Favorably as Federal Rating Hits New Low* (Apr. 15, 2013), <http://www.people-press.org/2013/04/15/state-governments-viewed-favorably-as-federal-rating-hits-new-low/>.

³⁵¹ 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); Huberfeld, *supra* note 286, 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.”); J.R. DeShazo & Freeman, *supra* note 28, at 1509 (describing a similar wave of state and local efforts in environmental regulation); Justin Weinstein-Tull, *Election Law Federalism*, 114 MICH. L. REV. 747, 789 (2016) (describing state resistance to federal election statutes)

³⁵² See, e.g., Gerken and Holzblatt, *supra* note 28, at 91.

³⁵³ See Sharkey, *supra* note 27, at 2125.

³⁵⁴ See Gillian E. Metzger, *Federalism Under Obama*, 53 WM. & MARY L. REV. 567, 570 (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) (“federal statutes may now be the primary way in which state power is created and protected”)

³⁵⁵ See, e.g., Sharkey, *supra* note 27, at 2172; Miriam Seifter, *States, Agencies, and Legitimacy*, 67 VAND. L. REV. 443, 445 (2014); Seifter, *supra* note 27, at 956.

³⁵⁶ See *id.*

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.³⁵⁷

And the Zohydro ban may have achieved Massachusetts's desired policy outcome—even though the ban was enjoined.³⁵⁸ 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.³⁵⁹ Additionally, 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.³⁶⁰ As a final example, in March 2016, the Centers for Disease Control and Prevention released new guidelines on opioid prescribing intended to combat opioid misuses and overdoses.³⁶¹

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, Congress considered bills in 2013

³⁵⁷ A search for "Zohydro" in ProQuest's News and Newspapers Database, which includes over 2,000 publications, indicates that in the two months after the state attorneys general letter, there were 11 articles about Zohydro. In the two months after Massachusetts banned Zohydro and Vermont restricted its use (which were enacted within the span of one week), there were 171 articles about Zohydro.

³⁵⁸ See Part II.B.2., *supra*.

³⁵⁹ See Letter from the U.S. Food & Drug Admin. To Zogenix, Inc. (Jan. 30, 2015), <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.LabelApprovalHistory#labelinfo>; cf. *Zogenix, Inc. v. Patrick*, No. CIV.A. 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 *Zogenix, Inc., Zogenix Receives FDA Approval for Zohydro* (Oct. 28, 2013), <http://ir.zogenix.com/phoenix.zhtml?c=220862&p=irol-newsArticle&ID=1868848>.

³⁶⁰ See, e.g., S. 954, 114th Cong. (2015); Alexander Gaffney, *Tougher FDA Approval Process for Opioids Sought by Congress*, Raps.org (Apr. 16, 2015), <http://www.raps.org/Regulatory-Focus/News/2015/04/16/21987/Tougher-FDA-Approval-Process-for-Opioids-Sought-by-Congress/>.

³⁶¹ Centers for Disease Control and Prevention, CDC Releases Guideline for Prescribing Opioids for Chronic Pain, <http://www.cdc.gov/media/releases/2016/p0315-prescribing-opioids-guidelines.html>. Massachusetts also continues to consider how best to address prescription drug abuse at the state level. See, e.g., H.D. 4309 (filed Oct. 15, 2015), <http://www.mass.gov/governor/legislationexecorder/legislation/substance-use-treatment-education-and-prevention.html>.

and 2015 that would allow U.S. patients to purchase cheaper, foreign drugs from certain countries.³⁶² And following Judge Torreson’s decision invalidating Maine’s law, a spokesperson for the bill’s sponsor, Senator John McCain, said “[t]his decision highlights the importance that Congress act to change federal law.”³⁶³

Likewise, although “right to try” laws have had no practical effect on the drug market, they have received significant media attention, and Congress has taken note.³⁶⁴ In July 2015 and May 2016 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.³⁶⁵ Additionally, the FDA recently has taken steps to clarify and streamline its expanded access process.³⁶⁶ 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.³⁶⁷ The agency is also now developing an “expanded access navigator,” to serve as a resource for interested patients and medical practitioners.³⁶⁸

State marijuana laws also appear to have instigated change to federal

³⁶² Personal Drug Importation Fairness Act of 2013, H.R. 3715, 113th Cong. (2013); Safe and Affordable Drugs from Canada Act of 2015, S. 122, 114th Cong. (2015); Ed Silverman, *Senators Re-Introduce Bill to Allow Imported Medicines from Canada*, Wall St. J. (Jan. 9, 2015), <http://blogs.wsj.com/pharmalot/2015/01/09/senators-re-introduce-bill-to-allow-imported-medicines-from-canada/>.

³⁶³ Ed Silverman, *Judge Strikes Down Maine Law for Importing Prescription Medicines*, Wall St. J. (Feb. 25, 2015), <http://blogs.wsj.com/pharmalot/2015/02/25/judge-strikes-down-maine-law-for-importing-prescription-medicines/>.

³⁶⁴ See, e.g., Farber et al. *supra* note 277.

³⁶⁵ Right to Try Act of 2015, H.R. 3012, 114th Cong. (2015); Trickett Wendler Right to Try Act of 2016, S. 2912, 114th Cong. (2016).

³⁶⁶ 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.

³⁶⁷ Guidance on Expanded Access, *supra* note 282; U.S. Food & Drug Admin., Statement from FDA Commissioner Robert Califf, MD, on the Release of the Final Individual Patient Expanded Access Form, <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm504579.htm>. The FDA implemented the new application for “individual patient” expanded access, the program that accounts for approximately 96% of all expanded access requests. FDA, Expanded Access Submission Receipts Reports Oct. 1, 2013 – Sept. 30, 2014, <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/UCM430188.pdf>.

³⁶⁸ Public Workshop: Expanded Access Navigator—May 16, 2016, <http://www.reaganudall.org/news-and-events/events-2/public-workshop-expanded-access-navigator/>.

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.³⁶⁹ 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.³⁷⁰ 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 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.³⁷¹

While the previous examples all 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 law.³⁷² 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.³⁷³ But California, which is a large market for drugs, has been credited with motivating industry to support for a federal system.³⁷⁴ When California enacted its own track and trace requirements, it created the

³⁶⁹ DOJ Memo, *supra* note 227.

³⁷⁰ See, e.g., Zachary S. Price, *Enforcement Discretion and Executive Duty*, 67 VAND. L. REV. 671, 681 (2014).

³⁷¹ See, e.g., Consolidated Appropriations Act, 2016, Pub. L. No. 114-113, § 542, 129 Stat. 2242, 2332–33 (2015); *United States v. McIntosh*, No. 15-10117, 2016 WL 4363168, at *2 (9th Cir. Aug. 16, 2016); S. 683, 114th Cong. (2015); Drug Policy Alliance, *Senators Cory Booker (D-NJ), Rand Paul (R-KY), and Kirsten Gillibrand (D-NY) Introduce Historical Medical Marijuana Legislation*, <http://www.drugpolicy.org/news/2015/03/senators-cory-booker-d-nj-rand-paul-r-ky-and-kirsten-gillibrand-d-ny-introduce-historic>.

³⁷² Drug Quality and Security Act, Pub. L. No. 113-54 (2013).

³⁷³ See, e.g., Pharmaceutical Commerce, *Drug Quality and Security Act Becomes Law*, (Jan. 20, 2014), http://pharmaceuticalcommerce.com/index.php?pg=legal_regulatory&articleid=27095&keyword=Drug%20Quality%20and%20Security%20Act-supply%20chain-monitoring; U.S. Food & Drug Admin, *FDA Track and Trace Public Workshop Summary*, <http://www.fda.gov/downloads/Drugs/NewsEvents/ucm249331.pdf>.

³⁷⁴ See, e.g., David Pittman, *House Passes ‘Track and Trace’ Drug Bill*, MEDPAGETODAY.COM (June 4, 2013), <http://www.medpagetoday.com/Washington-Watch/Washington-Watch/39616>.

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 demonstrate that state regulation appears to be an effective strategy for affecting federal law and policy. And even those state laws and regulations that are preempted, or have little practical impact on the pharmaceutical market, may be influential in certain circumstances.

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.