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Could State Regulations be the Next Frontier for Preemption Jurisprudence?

Drug Compounding as a Case Study

NATHAN A. BROWN^{*}
ELI TOMAR^{**}

The industries regulated by the Food and Drug Administration (FDA) make products that are integral to our lives—medicines upon which we depend and literally the food that we eat. Moreover, these products account for a significant portion of our overall economy.¹ It is not surprising then, that FDA-regulated industries are a frequent target of tort claims and government enforcement actions when people believe they have been harmed by these products. Given the many such actions brought under state law, there is extensive (yet unsettled) jurisprudence concerning the scope of federal preemption for such actions.

Less frequently considered, however, is the appropriate role of state regulation over FDA-regulated industries outside of the civil and criminal enforcement context—in other words, the prophylactic oversight that typically takes the form of licensing and reporting, quality standards, and sales and marketing restrictions. Such questions are likely to become more prominent as Congress continues to expand FDA’s jurisdiction, including into areas in which states have traditionally played a more prominent, and often predominant, oversight role. Moreover, as advancements

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¹ In 2011, the Food and Drug Administration (FDA) estimated that “nearly 25 cents of every dollar spent by Americans are on products regulated by the agency.” FDA, SPECIAL REPORT, PATHWAY TO GLOBAL PRODUCT SAFETY AND QUALITY at 2 (July 2011), available at <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/GlobalProductPathway/UCM262528.pdf>.

in data management and technology have led to greater sophistication in surveillance of product quality, there has also been greater recognition of the value of an integrated and unified approach to quality management. This recognition calls for a reconsideration of the potential for multiple oversight regimes to interfere with federal oversight and undermine—rather than enhance—quality management. In other words, what is often referred to as “conflict” preemption should acknowledge the benefits of uniformity.

The Drug Quality and Security Act (DQSA), which became law in November of 2013,² expanded and clarified FDA’s responsibilities over drug compounding. Among other things, the DQSA created a new statutory entity permitted to compound drugs subject to certain federal standards and federal registration—referred to as an “outsourcing facility.” The law, which is still being implemented, presents a potential test case for considering the optimal roles for state and federal oversight for protecting public health. Congress did not explicitly address the extent to which the DQSA supplants state oversight.³ Moreover, because compounding was previously conducted only under the auspices of a state pharmacy license, states have long been actively engaged in compounding oversight. As FDA has steadily implemented the new law, questions have arisen as to whether new or existing state regulations governing compounding should apply to outsourcing facilities, particularly those regulations that overlap with new FDA oversight.

This paper begins, in Part I, by reviewing the historical expansion of federal regulation of economic activity and analyzes the history of state regulation of FDA-regulated industries and the steady, if episodic, expansion of FDA’s jurisdiction, which has often been driven by public health tragedies. In Part II, we briefly explain federal preemption in the context of FDA law and suggest a lens for understanding the overlap between federal and state authorities. Part III then analyzes the potential preemptive effect of the compounding provisions in the DQSA, providing several examples of existing or proposed state requirements that would potentially interfere with the federal regulatory regime for outsourcing facilities. Part IV concludes by offering preliminary suggestions for properly balancing federal and state oversight in order best to protect the public health.

I. HISTORICAL EXPANSION OF FDA AUTHORITY

As has been widely observed, national tragedies have often served as the precursor to the expansion of federal authority vis-à-vis FDA.⁴ In some cases, FDA lacked the tools to prevent a public health crisis, and in others, the agency deferred to state authorities that were unable to intervene effectively. Regardless, these circumstances provided the impetus for Congress to pass legislation that in some cases had been pending for some time, even decades. Each of these landmark laws sought to achieve one or more of the following objectives:

² Drug Quality and Security Act, Pub. L. No. 113-54, 127 Stat. 587 (codified in scattered sections of 21 U.S.C.).

³ The DQSA also established a new national “track and trace” system to prevent the distribution of counterfeit drugs, expanding FDA’s role in overseeing the various participants in the drug supply chain. Title II of the law, the Drug Supply Chain Security Act, expressly displaced alternative state systems for tracing drug products through channels of distribution. *See infra* note 114..

⁴ *See generally* FDA, THE HISTORY OF DRUG REGULATION IN THE UNITED STATES (2006) [hereinafter “FDA History”].

- Clarify that FDA is responsible for specific activities;
- Shift traditional state responsibilities to FDA; or
- Establish a uniform framework for federal oversight.

These expansions provided greater federal authority to regulate products proactively as well as reactively—for medical products, premarket as well as postmarket. In many cases, however, this federal expansion into proactive regulation did not meaningfully intrude on active state regimes, which generally focused on enforcement.

A. *A Brief History of Food and Drug Law*

FDA's regulatory authority began with medicines, and to a lesser extent foods. It expanded gradually—over the course of more than one hundred years and one hundred statutes—to include medical devices, cosmetics, and eventually tobacco.⁵

Food and drugs were historically overseen by state and local authorities. At the time of the passage of the Pure Food and Drugs Act of 1906,⁶ most states had adulteration statutes on their books but rarely much more.⁷ In the late 1800s, states and municipalities slowly began to take a more active role in ensuring the basic safety of food and drug products, establishing boards of health and hiring epidemiologists. These efforts remained largely reactive, focusing on penalties for harms stemming from adulterated and misbranded goods, but also established objective standards for specific products.⁸

States largely deferred oversight of the therapeutic benefit of drugs to the medical profession generally, and to the American Medical Association (AMA) in particular. The AMA's Council on Pharmacy and Chemistry was established in 1905, one year prior to the 1906 Act, but relied on voluntary cooperation from the makers of "patent medicines" to keep unsafe drugs off the market.⁹ Although the AMA also used the threat of withholding advertisement in the *Journal of the American Medical Association* to police medicinal quality, the association relied heavily on these ads for its revenue.¹⁰ This limited scrutiny was further compromised by states' inability to investigate the source of adulterated drugs, the majority of which were manufactured outside their respective borders.¹¹

⁵ PETER BARTON HUTT ET AL., *FOOD AND DRUG LAW* 5 (4th ed. 2014).

⁶ Pure Food and Drugs Act of 1906, Pub. L. No. 59-384, 34 Stat. 768 (1906) (amended 1938).

⁷ Peter Barton Hutt & Peter Barton Hutt II, *A History of Government Regulation of Adulteration and Misbranding of Food*, 39 *FOOD DRUG COSM. L.J.* 2, 40 (1984).

⁸ Numerous state laws included specific definitions of food products. For example, an 1890 Virginia law stated "the term 'cider vinegar' shall be understood to mean vinegar made exclusively of pure apple juice." Act of 1890, ch. 44, 1889-1890 Va. Acts 34.

⁹ DANIEL CARPENTER, *REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA* 76-77 (Princeton, 2010).

¹⁰ *Id.*

¹¹ See David D. McKinney, *The Mexican-American War Brings Regulation on Drug Importation*, in *U.S. CUSTOMS AND BORDER PROTECTION HISTORY*, Summer 2010, at 50. In contrast, states had been more active in the regulation of food. States had long been viewed as appropriate arbiters of food policy and empowered to exert jurisdiction over food grown, processed, or consumed within their borders. Melvin Hinich & Richard Staelin, *Regulation of the U.S. Food Industry*, *STUDY ON FEDERAL REGULATION*, S. Doc. No. 96-14 at 391 (1978) (describing how states differ in regulating foods based on uniqueness of their locales and, probably more significantly, the influence of special interest groups in the state).

Over the course of the Nineteenth Century, there were numerous instances of tainted or unsafe products harming large numbers of individuals. As a prominent example, investigations into the high mortality rate of soldiers wounded during the Mexican-American War of 1848 concluded that adulterated drugs caused a substantial number of the 1,773 deaths.¹² Support for a greater federal role increased after a tetanus-contaminated vaccine claimed the lives of thirteen children in St. Louis, Missouri.¹³ This tragedy most directly resulted in the passage of the Biologics Control Act of 1902, but also provided momentum for the establishment of the FDA in 1906. While historians popularly credit publication of Upton Sinclair's *The Jungle*, with its vivid descriptions of the squalor that characterized Chicago's meatpacking industry, as the catalyst for the Pure Food and Drug Act,¹⁴ the inability of the states to effectively police unsafe foods and drugs may have played an even greater role.

At its core, the 1906 Act began to consolidate state enforcement efforts with the federal government by prohibiting the interstate movement of adulterated or misbranded drugs and foods. It established the first national program to address the quality of food and drugs, but featured a reactive regulatory framework, authorizing the government to seize products and impose fines and criminal penalties.¹⁵ For drugs, the definition of adulteration relied on the U.S. Pharmacopeia (USP) and the National Formulary for established quality standards. Misbranding was limited to false advertisements.¹⁶

Beginning with these first federal acts at the dawn of the Twentieth Century, state officials largely embraced these developments. New York's regulators had lamented the patchwork of state standards and confusion that it caused. State officials were at the forefront in calling for federal leadership and federal resources to meet the growing need for greater scrutiny of consumer goods. Anticipated enhancements to public health from uniform national standards were widely viewed as outweighing any inherent limitation placed on state autonomy.¹⁷

It was not until another major crisis that the limitations of the 1906 Act became widely acknowledged. In 1937, more than 100 Americans died after taking an anti-infective elixir found to contain diethylene glycol, a toxic chemical used in antifreeze.¹⁸ In the aftermath, FDA was only able to remove the product, Sulfanilamide, from the market on the basis that it was misbranded, as an "elixir" must contain alcohol to be marketed as such.¹⁹ The tragedy broadened consensus that FDA needed a "gatekeeper" function to keep unsafe drugs from getting to the

¹² McKinney, *supra* note 11, at 50-51.

¹³ FDA History, *supra* note 4, at 4.

¹⁴ See HUTT ET AL., *supra* note 5, at 8.

¹⁵ Pure Food and Drugs Act of 1906, Pub. L. No. 59-384, Ch. 3915 § 2, 34 Stat. 768 (1906) (amended 1938).

¹⁶ FDA History, *supra* note 4.

¹⁷ See HUTT ET AL., *supra* note 5, at 7. Notably, neither the 1906 Act nor the FDCA three decades later contained any express preemption provisions.

¹⁸ CARPENTER, *supra* note 9, at 85-89.

¹⁹ *Id.* at 92.

market. In 1938, Congress passed the Food, Drug, and Cosmetic Act foremost to require drugs to be preapproved on the basis of safety.²⁰

The next major expansion of FDA's authority came in 1962, following reports of severe congenital defects in newborns whose mothers had taken the sedative thalidomide. Although FDA had not approved the drug, there were a significant number of cases in the United States because more than 20,000 Americans had participated in premarket "studies."²¹ The centerpiece of the Drug Amendments of 1962 was a strengthening of the premarket approval process to require the demonstration of effectiveness as well as safety.²² The 1962 Act also broadened FDA's oversight of drug marketing, and required production based on good manufacturing practices (GMPs).²³ These amendments specified that state inspections of drugmaking plants could continue so long as they did not directly conflict with the federal inspection programs.²⁴

Although FDA had jurisdiction over medical devices since the FDCA was first enacted in 1938, the core framework that governs premarket review, postmarket surveillance, and other core standards for device manufacturing was enacted in the Medical Device Amendments of 1976 (MDA).²⁵ Congress was at least partially motivated to act by an aggressive new regulatory scheme devised in California to regulate medical devices.²⁶ Unlike earlier laws, the MDA included an express preemption clause that prohibits states from imposing any additional requirements on an FDA-approved medical device.²⁷

Since the 1970s, FDA's role has continued to expand. Sometimes these expansions have been accompanied by express preemptions and other times not. Nevertheless the expansions have favored uniform federal standard as a means of improving public health protections. Food nutrition labels had historically been regulated by states. A series of laws, culminating with the Nutrition Labeling and Education Act (NLEA) of 1990, shifted control to the FDA, leaving only limited

²⁰ Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, § 505, 52 Stat. 1040, 1052-53 (1938) (codified at 21 U.S.C. § 355).

²¹ FDA History, *supra* note 4, at 8. FDA widely discredits the claim that all of this thalidomide utilization is attributable to legitimate investigative studies as more than 1,000 physicians prescribed the drug to patients.

²² Drug Amendments of 1962, Pub. L. No. 87-781, § 104, 76 Stat. 780, 781 (1962).

²³ *Id.* § 104, 76 Stat. at 784.

²⁴ *Id.* § 202, 76 Stat. at 793.

²⁵ These amendments were also a long time coming, and many commentators believe they were helped across the finish line by high-profile failures of pacemakers and severe injuries, miscarriages, and infertility caused by the Dalkon Shield intrauterine device, all of which received public attention in the early 1970s. See *In re N. D. of Cal., Dalkon Shield IUD Prods. Liab. Litig.*, 693 F.2d 847, 848-49 (9th Cir. 1982).

²⁶ As Justice Ginsburg explained in her lone dissent in *Riegel*, "Congress' reason for enacting §360k(a) is evident. Until 1976, the Federal Government did not engage in premarket regulation of medical devices. Some States acted to fill the void by adopting their own regulatory systems for medical devices. Section 360k(a) responded to that state regulation, and particularly to California's system of premarket approval for medical devices, by preempting State initiatives absent FDA permission." *Riegel v. Medtronic Inc.*, 552 U.S. 312, 333 (2008) (Ginsburg, J., dissenting).

²⁷ Medical Device Amendments of 1976, Pub. L. No. 94-295 § 521(a), 90 Stat 574 (1976) (codified as amended at 21 U.S.C. § 360(k)) (prohibiting states from imposing "any requirement . . . in addition to, any requirement applicable under this Act").

aspects of labeling for dual state-federal regulation.²⁸ Congress expressly prohibited states from imposing virtually any regulation on nonprescription (“over-the-counter”) drugs with the passage of Food and Drug Administration Modernization Act of 1997 (FDAMA).²⁹ In 2009, Congress passed the Family Smoking Prevention and Tobacco Control Act, effectuating federal uniformity in tobacco product standards.³⁰ These are not the only examples and will not be the last. More recently, proposals for uniform federal oversight of cosmetics have gained traction as well.³¹

B. DQSA in Historical Context

The expansion of FDA authority over pharmacy compounding in 2013³² fits the historical pattern of Congress responding to a high-profile public health crisis by expanding FDA’s oversight role.³³ Unlike some of the medical products previously subjected to expanded FDA oversight, however, compounded drugs had long fallen under state oversight. Notably, compounded drugs are characterized by how they are produced. The act of compounding is defined as the preparation, mixing, assembling, or altering of a drug substance.³⁴ The quintessential example is reformulating a drug to remove an additive that a patient is allergic to, or adding a flavor to a serum so that a child will take it. Its primary distinction from manufacturing is that it was traditionally performed by a pharmacist, in small volumes, for individual patients. In 1997, Congress amended the FDCA to exempt from the new drug requirements of the Act certain drug compounding activities that reflected the traditional practice of pharmacy under a state license.³⁵ Under a new section 503A, drugs compounded within the limitations of the exemption were not subject to new drug approval, or to the requirements to have adequate directions for use and to be made in accordance with GMPs.³⁶

²⁸ Nutrition Labeling and Education Act of 1990, Pub. L. No. 101-535, 104 Stat. 2353 (1990) (codified at 21 U.S.C. § 343-1(a)).

²⁹ Food and Drug Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2353, 2373 (1997).

³⁰ Pub. L. No. 111-31, 123 Stat. 1776 (2009) (codified at 21 U.S.C. § 387p(a)). Although states are preempted from issuing alternative or additional regulations relating to any of these requirements, Congress expressly reserved a continued role for states to regulate the sale, advertising, distribution, possession, and usage of tobacco products. 21 U.S.C. § 387p(a)(2)(B).

³¹ In 2012 and 2013, FDA and the cosmetics industry engaged in ongoing discussions about adopting a more robust federal regulatory scheme for cosmetics, in exchange for stronger preemption of state and local requirements. Similar proposals are now part of a bill sponsored by Senators Diane Feinstein (D-CA) and Susan Collins (R-ME). *See* Personal Care Products Safety Act, S. 1014, 114th Cong. (2015).

³² Under the legal framework that preceded DQSA, all compounded drugs are “new drugs,” as defined at 21 U.S.C. § 355(a), and thus subject to the entire regulatory framework governed by the FDCA. Federal law contains explicit, but discrete exemptions for compounded drugs, such as an exemption from the premarket review requirements.

³³ As discussed *infra*, many scholars maintain that all major expansions of FDA’s authority have followed national tragedies that either provided Congress cover to pass desired legislation or compelled Congress to “do something” in response to the loss of American lives. *See, e.g.,* DANIEL CARPENTER, *supra* note 9, at 73-78. The Agency itself has recognized this trend in FDA History, *supra* note 4.

³⁴ U.S. Pharmacopeia, *Chapter (795) Pharmaceutical Compounding, in* USP COMPOUNDING COMPENDIUM, 1 (Jan. 2014).

³⁵ *See generally* 21 U.S.C. § 353a.

³⁶ Food and Drug Administration Modernization Act, Pub. L. No. 105-115, § 127, 111 Stat. 2296, 2328 (1997). The newly added section 503A exempted qualifying compounded drugs from sections 505,

In 2012, several lots of contaminated steroidal injections were shipped by the Massachusetts-based New England Compounding Center (NECC) to health care providers and administered to more than 14,000 patients in twenty-three states.³⁷ The Centers for Disease Control and Prevention (CDC) identified a total of 751 cases of fungal infections, including sixty-four deaths related to fungal meningitis.³⁸ By 2012, there was legitimate need for hospital outsourcing of compounded drugs, as discussed in Part III.A, which could not be served within the patient-specific confines of section 503A. As evidenced by NECC, however, there were also illegitimate practices operating in the void created by legal uncertainty.³⁹ Not unlike the frightening state of the so-called patent medicines in the Nineteenth Century, mass-produced compounded drugs have killed far more than sixty-four people in recent years.⁴⁰

In early 2013, the Energy and Commerce Committee in the House of Representatives launched an investigation of FDA's response to the outbreak and held several hearings on the topic.⁴¹ The Health, Education, Labor and Pensions (HELP) Committee in the Senate simultaneously began working on a compounding reform bill. Both committees ultimately acknowledged the need to modernize federal laws relating to the agency's oversight of compounding. The most pressing legal issue that Congress had to address through legislation was a constitutional defect in section 503A of the FDCA. As enacted in FDAMA in 1997, section 503A regulates "pharmacy compounding" by exempting these products from the core premarket approval requirements for new drugs so long as they satisfy certain conditions, including that they are prepared after receiving an individual patient prescription or in limited amounts in anticipation of such prescription.⁴² The original section 503A also prohibited compounding pharmacies from "promot[ing] the compounding of any particular drug, class of drug, or type of drug."⁴³ The Supreme Court found this provision to be an unconstitutional burden on the pharmacies' First Amendment right

502(f)(1), and 501(a)(2)(B) of the FDCA pertaining to new drug applications, adequate directions for use, and GMPs, respectively.

³⁷ Centers for Disease Control and Prevention, *Multistate Outbreak of Fungal Meningitis and Other Infections* (Oct. 23, 2013), <http://www.cdc.gov/hai/outbreaks/meningitis.html>.

³⁸ *Id.*

³⁹ See notes 45-46, *infra*.

⁴⁰ A compilation of pharmacy compounding errors by the Pew Charitable Trusts identified over 25 separate errors since 2001, responsible for more than 1,000 adverse events, including 89 deaths. PEW CHARITABLE TRUSTS, U.S. ILLNESSES AND DEATHS ASSOCIATED WITH COMPOUNDED OR REPACKAGED MEDICATIONS, 2001-PRESENT (Sept. 6, 2014), http://www.pewtrusts.org/~media/Assets/2014/09/CompoundingOutbreaks_ChartSept2014_v3.pdf?la=en.

⁴¹ See generally H. COMM. ON ENERGY & COMMERCE, 113th Cong., FDA'S OVERSIGHT OF NECC AND AMERIDOSE: A HISTORY OF MISSED OPPORTUNITIES?, PRELIMINARY MAJORITY STAFF REPORT (Apr. 16, 2013). The Commonwealth of Massachusetts acknowledged many failings in the lead up to the NECC outbreak, but there were also indications that FDA should have done more with its existing authorities to prevent the outbreak. The Agency had received numerous warnings from both state regulators and private entities that NECC was operating outside the scope of traditional pharmacy compounding. FDA had also investigated several of these complaints and pursued a series of actions against the company. *Id.* at 7-16.

⁴² 21 U.S.C. §353a(a). In the latter case, the compounded drug may only be dispensed once the prescription is received.

⁴³ Food and Drug Administration Modernization Act, Pub. L. No. 105-115, § 127(c), 111 Stat. 2296, 2330 (1997).

to free speech,⁴⁴ and two federal circuits diverged on the severability of the unconstitutional provision from the remainder of section 503A.⁴⁵ As a result of this circuit split, it was uncertain whether section 503A had legal effect, and FDA instead sought to regulate compounding pharmacies through the exercise of conditional enforcement discretion according to a nonbinding Compliance Policy Guide.⁴⁶

In 2013, the DQSA struck the unconstitutional provision, otherwise keeping the preexisting section 503A intact, but also added a new section 503B to regulate and facilitate the larger scale operations more akin to manufacturing that would not need to compound on an individual prescription basis. The DQSA established a fairly comprehensive framework for these “outsourcing facilities,” establishing federal requirements relating to annual registration, inspection schedules and standards, the types of compounds and materials that can be utilized, semiannual product reporting, drug labeling, adverse event reporting, fees, and other aspects of operation.⁴⁷

II. OVERLAPPING CONSTITUTIONAL POWERS

Our constitutional structure is clear that the states’ police powers to regulate are quite broad, checked primarily by the competing liberty interests of individual citizens. Federal powers, by contrast, are narrow and discrete. As Chief Justice Roberts recently explained, “In our federal system, the National Government possesses only limited powers; the States and the people retain the remainder.”⁴⁸

The Twentieth Century saw a vast expansion of federal powers, particularly over the regulation of interstate commerce.⁴⁹ In the post-New Deal era, any subject deemed to have a substantial effect on the modes, channels, or instrumentalities of interstate commerce became eligible for federal regulation.⁵⁰ Commentators began to question whether there remained any practical limit on the scope and breadth of the commerce power, or whether virtually anything the federal government aspired to regulate, in the aggregate, had a “substantial effect” on interstate commerce.⁵¹ In the last several decades, the Supreme Court has scaled back that expansive interpretation

⁴⁴ *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 360-61 (2002).

⁴⁵ The Supreme Court’s decision in *Western States* in 2002 did not address the severability of the advertising and promotion provision from the remainder of section 503A, and the resulting circuit split caused ambiguity as to the effect of section 503A. Compare *W. States Med. Ctr. v. Shalala*, 238 F.3d 1090, 1096-98 (9th Cir. 2001) with *Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 401 (5th Cir. 2008).

⁴⁶ FDA, Compliance Policy Guide Section 460.200 Pharmacy Compounding (June 7, 2002), withdrawn in 2013, see 78 Fed. Reg. 72841, 72902 (Dec. 4, 2013). For a more complete description of this saga, see ANDREW NOLAN, CONG. RESEARCH SERV., No. R43038, FEDERAL AUTHORITY TO REGULATE THE COMPOUNDING OF HUMAN DRUGS (Apr. 2013).

⁴⁷ See generally 21 U.S.C. § 353b.

⁴⁸ *Nat’l Fed’n of Indep. Bus. v. Sebelius*, 132 S. Ct. 2566, 2577 (2012).

⁴⁹ Renee M. Landers, *Reporter’s Draft for the Working Group on the Mission of the Federal Courts, Roundtable on State and Federal Jurisdiction*, 46 HASTINGS L.J. 1255, 1258-59 (1995).

⁵⁰ *Wickard v. Filburn*, 317 U.S. 111 (1942) (expanding the reach of the Commerce Clause to touch private agricultural consumption activities that, in the aggregate, has a substantial impact on the interstate market for crops).

⁵¹ E.g., Stephen Gardbaum, *New Deal Constitutionalism and the Unshackling of the States*, 64 U. CHI. L. REV. 483, 505 (1997).

somewhat.^{52,53} The reach of the federal commerce power generally to include food and drug regulation, however, has not been seriously questioned in recent years.

A. *The Supremacy Clause*

“From the existence of two sovereigns follows the possibility that laws can be in conflict or at cross-purposes.”⁵⁴ Although state power is inherently broad, and federal power constitutionally narrow, where the two clash, the state must give way. The Supremacy Clause of Article VI of the Constitution has been interpreted to allow Congress to override existing state laws (and foreclose future state laws) that conflict or otherwise interfere with the operation of the federal law. It states: “This Constitution, and the Laws of the United States . . . shall be the supreme Law of the Land[.]”⁵⁵ Courts describe preemption analysis as beginning with the words of the federal statute and then inquiring whether Congress intended to displace state law.⁵⁶ Whether or not Congress declares its intent to preempt a particular area of state regulation, however, state action that interferes with the application of a valid federal law is often deemed preempted.⁵⁷ Thus, it is often federal courts, rather than the Congress directly, that decide whether a state law or regulation can coexist with federal law.

B. *Types of Preemption*

Federal law preempts state efforts to regulate in different circumstances according to various tests applied by the Supreme Court. The clearest case is express preemption, which exists whenever Congress has explicitly stated that it has limited the application of other law. The federal Food, Drug, and Cosmetic Act (FDCA) contains numerous instances of express preemption. Congress has expressly prohibited states or other political subdivisions from establishing or continuing in effect any requirement relating to sunscreen and nonprescription drugs,⁵⁸ nutrient

⁵² See, e.g., *United States v. Morrison*, 529 U.S. 598, 617-19 (2000) (invalidating a provision of the Violence Against Women Act granting victims of gender violence standing to sue in federal court for having no reasonable relationship to interstate commerce). See also *United States v. Lopez*, 514 U.S. 549, 560-61 (1995) (striking down the Gun-Free School Zones Act as unconstitutional because gun violence in schools is beyond the scope of the federal commerce power).

⁵³ Most recently, in 2012, the Supreme Court ruled that although the Affordable Care Act’s so-called “individual mandate” is a permissible tax, individual decisions whether or not to purchase health insurance “cannot be sustained under a clause authorizing Congress to ‘regulate Commerce.’” *Sebelius*, 132 S. Ct. at 2591.

⁵⁴ *Arizona v. United States*, 132 S. Ct. 2492, 2500 (2012).

⁵⁵ U.S. Const. art. VI, § 2.

⁵⁶ *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 484-86 (1996) (“our analysis of the scope of the preemption statute must begin with its text . . .”). See also *Jones v. Rath Packing Co.*, 430 U.S. 519, 525 (1977) (quoting *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947)) (“we start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress”) (internal quotations omitted).

⁵⁷ As Justice Harlan II put it, preemption questions “are designed with a common end in view: to avoid conflicting regulation of conduct by various official bodies which might have some authority over the subject matter.” *Amalgamated Ass’n of St., Elec. Ry. & Motor Coach Emps. of America v. Lockridge*, 403 U.S. 274, 285-86 (1971).

⁵⁸ 21 U.S.C. § 379(r) (2012).

content in food labeling,⁵⁹ the safety and effectiveness of class III medical devices,⁶⁰ and product tracking and tracing requirements,⁶¹ among others.

In the absence of express preemption language, courts have found preemption to be *implied* using several doctrinal tests that often overlap.⁶² “Conflict” preemption is the most straightforward of these tests, and as the name suggests, exists when state and federal regulations conflict. A common manifestation of conflict preemption arises when a regulated entity is unable to comply simultaneously with both a state and federal requirement.⁶³

Conflict preemption does not actually require a physical impossibility, however. Even where it is possible for a regulated entity to comply with both directives, if compliance with state law would undermine the federal purpose, it is preempted.⁶⁴ This is sometimes referred to as “obstacle” preemption. Courts have often struck down state standards that go beyond the related federal requirement, reasoning that stricter state standards disturb a deliberate balance struck by Congress.⁶⁵ For example, state-mandated warnings on nationally-distributed products subject to FDA-directed labeling have been rejected on these grounds. Although judges frame the question as whether Congress intended to foreclose state action, in practice, courts have generally considered whether the laws can productively coexist, regardless of specific intent.⁶⁶

In turn, “field” preemption exists where the federal scheme is “so pervasive” that it can be inferred that Congress left no room for the states to supplement it with their own regulations.⁶⁷ Courts do not require an explicit statement of such intent, either in statutory language or legislative history, but instead may infer it based on the breadth of the regulatory scheme. A related but distinguishable test for field preemption exists where the federal government’s interest in regulating an area is so dominant that the state cannot also regulate.⁶⁸ Even if the federal scheme is not necessarily comprehensive, and thus a state could reasonably complement it with additional requirements, the federal interest in regulating the area is “so dominant” that states may not act.⁶⁹ State laws pertaining to national security, civil rights, and other collective priorities have been struck down on these grounds.⁷⁰ Confusing the matter

⁵⁹ 21 U.S.C. § 343(r)(1) (2012).

⁶⁰ 21 U.S.C. § 360k (2012).

⁶¹ 21 U.S.C. § 360eee(4) (2012).

⁶² The Supreme Court has acknowledged that “pre-emption categories are not rigidly distinct.” *Gade v. Nat’l Solid Wastes Mgmt. Ass’n*, 505 U.S. 88, 104 n.2 (1992) (internal quotations omitted).

⁶³ *Cal. Fed. Sav. & Loan Ass’n v. Guerra*, 479 U.S. 272, 281-82 (1987); see also *Com. of Pa. v. Nelson*, 350 U.S. 497, 509 (1956).

⁶⁴ *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941). Legislative purpose, in this context, is different from legislative intent. Whether or not Congress specifically *intended* to foreclose state regulation in an area, Congress had a substantive *purpose* to regulate that area in a manner that diverges from the state regulation.

⁶⁵ See, e.g., *id.* at 69-70; see also *Cosmetic, Toiletry & Fragrance Ass’n v. Minnesota*, 440 F. Supp. 1216, 1224-25 (D. Minn. 1977), *aff’d per curiam* 575 F.2d 1256 (8th Cir. 1978).

⁶⁶ See *Fla. Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 143-144 (1963).

⁶⁷ *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230.

⁶⁸ *Id.*

⁶⁹ *Id.*

somewhat, the Supreme Court explained that “field pre-emption may be understood as a species of conflict pre-emption.”⁷¹

It is often said that field preemption has never been successfully pleaded by a litigant in the realm of food and drug law.⁷² However, a U.S. district court in Maine recently struck down the State’s law allowing its residents to import pharmaceutical products not approved by FDA on field preemption grounds.⁷³ In the purely domestic context, at least one court has found that “consumer product labeling requires exclusive federal regulation in order to achieve uniformity vital to national interests,”⁷⁴ although there is not a well-established consensus on this point.

C. *Competing presumptions about preemption*

When Congress does not expressly preclude state regulation, there is a judicial presumption against implied preemption. In general, courts are disinclined to strike down acts of the legislative branch, federal or state, when they can avoid doing so.⁷⁵ If a court strikes down a state law that Congress did not intend to preempt, it has intruded upon the State’s prerogatives under the Tenth Amendment to exercise all powers not delegated to the federal government.⁷⁶ Some scholars lament this presumption, which they argue is based on the fiction that Congress necessarily acted with a specific intent not to preempt and would correct any erroneous ruling by the court. Moreover, they view this presumption as a distortion of the founding principles of federalism.⁷⁷

As federal powers have expanded, the preemption doctrine has evolved from what some scholars have called “dual federalism”⁷⁸—where courts referee the constitutional boundaries between state and federal jurisdiction—to a paradigm of concurrent authority. Rather than draw bright lines based on exclusive subject matters, courts began to construe state regulations as complementary to federal ones. This paradigm has been described various ways in the context of food and drugs,

⁷⁰ *E.g.*, *Hines*, 312 U.S. at 69-70.

⁷¹ *Crosby v. Nat’l Foreign Trade Council*, 530 U.S. 363, 372 n.6. (2000) (quoting *English v. Gen. Elec. Co.*, 496 U.S. 72, 79 n.5 (1990)).

⁷² HUTT ET AL., *supra* note 5, at 298 (“In view of the states’ traditional role in regulating food and drugs, and the strong presumption against inferring that Congress intended to displace state laws . . . courts have uniformly resisted finding field preemption in areas covered by the FD&C Act.”); *see also id.* at 294 (“the contention that Congress has impliedly ‘occupied the field’ of food and drug regulation-has apparently failed in every case in which it has been advanced.”).

⁷³ *Ouellette v. Mills*, 91 F. Supp. 3d 1, 12 and n.11 (D. Me. 2015) (“Because they are contrary to clear Congressional intent to occupy the field of pharmaceutical importation, [Maine’s laws] violate the Supremacy Clause and are therefore preempted The Court does not reach the Plaintiffs’ additional theories of preemption because the MPA Amendments are unconstitutional under the theory of field preemption.”)

⁷⁴ *See Cosmetic, Toiletry & Fragrance Ass’n*, 440 F. Supp. at 1223.

⁷⁵ *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449 (2005).

⁷⁶ U.S. Const. amend. X.

⁷⁷ *See, e.g.*, Roger Pilon, *Into the Pre-emption Thicket: Wyeth v. Levine*, 2008-2009 CATO SUP. CT. REV. 85, 105-06 (2009).

⁷⁸ Ernest A. Young, “*The Ordinary Diet of the Law*”: *The Presumption Against Preemption in the Roberts Court*, 2011 SUP. CT. REV. 253, 254-55 (Spring 2011).

which are squarely within the states' longstanding police power to protect the public health.⁷⁹

Nevertheless, in recent years the presumption against preemption appears to have receded from its ostensible high-water mark embodied *Wyeth v. Levine* in 2009. Several subsequent decisions have avoided following *Wyeth* and narrowed its holding,⁸⁰ and the presumption has never garnered more than a plurality of the Supreme Court since.⁸¹ This doctrinal preference has been counterbalanced somewhat by an emerging appreciation for the value of comprehensive and uniform federal regulation of complex products like drugs, biologics, and medical devices. Although Congress has shown varying degrees of willingness expressly to foreclose the possibility of additional state regulation, some courts have demonstrated a proclivity towards uniform, and exclusive, federal oversight. In short, while courts still begin with the presumption that new federal schemes supplement existing state law, they have shown a decreasing tolerance for disharmony between the respective laws.⁸²

D. A Civil Tort Exception?

A partial exception to the broader trend of federalizing food and drug oversight is the doctrine that has emerged through three Supreme Court decisions since 2009 regarding civil tort suits against drug manufacturers arising under state law causes of action. FDA retains a monopoly on approving warning labels for branded and generic prescription drugs, but *Wyeth* determined that state civil law—and lay juries—can decide that warnings on branded prescription drugs fail to provide adequate warning to people harmed by the drug's side effects.⁸³ According to the Supreme Court, the same is not true for generic drugs, which are currently required to maintain the same labeling as their branded reference counterpart.⁸⁴ It may also not apply to other strict product liability theories brought against branded drugs.⁸⁵ Although branded drugs are not entirely immune from all civil products liability, states do not share in FDA's responsibility to assess safety and efficacy data and make determinations about the drugs' approved uses or approved labeling. These recent Supreme Court decisions therefore provide only limited insights as to the

⁷⁹ Within public health, the presumption has perpetuated in fields with a history of state law regulation, even if there is also a history of federal involvement. See *In re Pharm. Indus. Average Wholesale Price Litig.*, 582 F.3d 156, 178 (1st Cir. 2009) (citing *Wyeth v. Levine*, 555 U.S. 555, 565 n.3 (2009)).

⁸⁰ See *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2589-90 (2011) (Sotomayor, J., dissenting).

⁸¹ See *id.* at 2590-92.

⁸² See *infra* Part II.E.

⁸³ *Wyeth v. Levine*, 555 U.S. 555, 574-75 (2009).

⁸⁴ *PLIVA*, 131 S. Ct. at 2580-81 (holding that state law claims requiring generic drug manufacturers to modify their warning labels directly conflict with, and thus are preempted by, the federal FDCA, which requires their labels be identical to their branded reference drug). See also *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2479-80 (2013) (following *PLIVA* in rejecting the argument that a generic manufacturer could stop selling a drug to avoid liability and preempting state law that would require it to modify its design in direct violation of the federal FDCA requirement that generic drugs be identical to branded reference drugs).

⁸⁵ See *Yates v. Ortho-McNeil-Janssen Pharms., Inc.*, 808 F.3d 281 (6th Cir. 2015).

extent to which state governmental entities may proactively impose separate requirements on FDA-regulated products.⁸⁶

A central teaching of the tort preemption doctrine relates to the role of federal agencies in assessing federal law's preemptive force. In *Wyeth*, Justice Stevens' majority opinion reaffirmed longstanding precedent that federal agencies' regulations can preempt conflicting state requirements to the same degree as federal statutes.⁸⁷ The opinion further acknowledged that the Court has at times given "some weight" to an agency's views about the impact of state law on achieving federal objectives, but underscored that the Court has "not deferred to an agency's conclusion that state law is pre-empted."⁸⁸ Other cases and scholars have proffered explanations for why such agency interpretations are not entitled to conventional *Chevron* deference,⁸⁹ but the key point is that it is ultimately for a court—and not the agency—to assess potential conflicts between state and federal law.⁹⁰

E. FDA Law and Federalism

The dominant strain of FDA-related preemption cases arise in the context of civil tort and other state enforcement actions. What cases there are relating to state regulatory requirements have generally arisen in the context of food or cosmetics—areas in which states have traditionally been more active. As noted, the Supreme Court has often defaulted to the view that industry may be subject to concurrent state and federal oversight, particularly for products affecting public health.⁹¹ In earlier preemption cases, even seemingly conflicting state requirements were upheld unless there was an "irreconcilable conflict" with federal law.⁹² In *Florida Lime & Avocado Growers, Inc. v. Paul*, California's standard for "mature" avocados was based on oil weight and differed from the minimum federal standard, which was based on picking date, but was upheld as applied to out-of-state growers. The Court singled out "foodstuffs" as a matter particularly within states' interest.⁹³

Over time, courts began to expand the boundaries of what constituted a conflict.⁹⁴ Facts similar to those in *Florida Lime* led to a different outcome in *Jones v. Rath*

⁸⁶ These civil cases are distinct from positive rule-making by states in several respects, but courts importantly distinguish that although tort lawsuits may second guess decisions made under a federal regulatory system, they only require a correction within that regulatory context (i.e., stronger warnings submitted to FDA for review), and not unique state-specific requirements, as the industry defendants asserted. *Wyeth*, 555 U.S. at 574-76.

⁸⁷ *Wyeth*, 555 U.S. at 576.

⁸⁸ *Id.* (emphasis in the original).

⁸⁹ *PLIVA*, 131 S. Ct. at 2575 n.3 ("[a]lthough we defer to the agency's interpretation of its regulations, we do not defer to an agency's ultimate conclusion about whether state law should be pre-empted").

⁹⁰ *Wyeth*, 555 U.S. at 576 (citing *Geier v. Am. Honda Motor Co.*, 529 U.S. 861 (2000)).

⁹¹ *E.g.*, *Wyeth*, 555 U.S. at 578 ("... it appears that the FDA traditionally regarded state law as a complementary form of drug regulation."). *But see PLIVA*, 131 S. Ct. at 2591 (Sotomayor, J., dissenting).

⁹² *Florida Lime*, 373 U.S. 132, 146 (1963).

⁹³ *Id.* As the *Florida Lime* Court explained, "The maturity of avocados seems to be an inherently unlikely candidate for exclusive federal regulation . . . [it] is a subject matter of the kind this Court has traditionally regarded as properly within the scope of state superintendence. Specifically, the supervision of the readying of foodstuffs for market has always been deemed a matter of peculiarly local concern." 373 U.S. at 143-44.

⁹⁴ *See, e.g.*, *Rath Packing Co.*, 430 U.S. at 519.

Packing Co., in which the Court rejected California's alternative standard establishing parameters for weight variance in bagged flour.⁹⁵ The Court asserted that, as a result of the application of California's different standard, consumers across the country attempting to make value comparisons would be stymied by the discordant state-specific weight standards, a problem the federal law sought to correct.⁹⁶ Some observers saw this decision as stealthily overruling *Florida Lime*, including Justice Rehnquist in his lone dissent.⁹⁷

Courts began to question whether consumer goods in commerce were appropriately overseen by the states, even in a supplemental capacity.⁹⁸ In *Cosmetic, Toiletry & Fragrance Association (CTFA) v. Minnesota*, a federal court struck down a Minnesota statute that required a chlorofluorocarbon warning to appear on containers of aerosol cosmetic products because FDA required the warning to appear only on the outermost packaging.⁹⁹ There was no physical impossibility here, as cosmetic manufacturers could have satisfied both warning requirements; nor was there express preemption language in the statute or regulations. The court nevertheless found that FDA's decision to require only the warning visible at the time of purchase reflected an incompatible policy goal,¹⁰⁰ the very theory rejected in *Florida Lime*.

Some courts began to coalesce around the idea that Congress or the agency would have already considered a range of possible requirements, and ultimately settled on an optimal position based on the public health benefits, costs to industry and ultimately consumers, and other considerations. As the *CTFA* court put it, "this benefit - cost imbalance increases as other subordinate governmental entities enact their own species of regulation . . .," undermining the "dual national goal of the most effective warning at the least possible cost."¹⁰¹ In this case and others, federal courts viewed stricter state regulations as disrupting a delicate balance struck by a federal cost-benefit determination.¹⁰² The courts sometimes further relied on a slippery slope rationale, suggesting that even if it would be feasible to comply with one state's additional requirements, complying with fifty different standards would obliterate efficiencies achieved by a uniform national standard.¹⁰³ The Supreme

⁹⁵ *Id.* at 543.

⁹⁶ *Id.*

⁹⁷ *Id.* at 549 (Rehnquist, J., dissenting) (criticizing the Court's "approach to the question of preemption [as] wholly at odds with that enunciated in *Florida Lime* This Court rejected a test which looked to the similarity of purposes, and noted instead that a manufacturer could have complied with both statutes by modifying procedures somewhat, which demonstrated that there was "no inevitable collision between the two schemes of regulation, despite the dissimilarity of the standards . . ." (citations omitted).

⁹⁸ *E.g.*, *Cosmetic, Toiletry & Fragrance Ass'n.*, 440 F. Supp. at 1223 (articulating "the common sense notion that in an economy where goods are distributed on a national level, a subordinate unit of government should not be able to require that an interstate producer create special packaging or manufacture a special product for a limited distribution area once the federal government has acted . . .").

⁹⁹ *Id.* at 1225-26.

¹⁰⁰ *Id.* at 1224.

¹⁰¹ *Id.* *But see*, *Wyeth*, 555 U.S. at 575-76 (expressing doubt that Congress settled on a "Goldilocks" position in the context of drug warning labels).

¹⁰² *E.g.*, *Abbott v. American Cyanamid Co.*, No. 86-857-A, 1987 U.S. Dist. LEXIS 14355, at *9-10 (E.D. Va. Mar. 9, 1987).

¹⁰³ *E.g.*, *Rath Packing Co.*, 430 U.S. at 519-20.

Court pushed back somewhat in the *Wyeth* decision, refuting the defendant pharmaceutical company's assertion that federal law established both a floor and a ceiling for regulating drug warnings.¹⁰⁴ Although the Court rebuffed this theory, it grounded its view in contrary statements throughout the FDCA's decades of legislative history asserting the lack of preemptive intent and the value of state participation in monitoring drug safety.¹⁰⁵ Historically, states have played a more prominent role in enforcement of safety issues.

With the exception of *Wyeth*—the current reach of which is uncertain—courts including the Supreme Court have strayed from a presumption of concurrent authority in the latter part of the Twentieth Century. Courts appear more willing to strike state regulations that are not impossible to abide, but which complicate industry's compliance with an overarching federal program.¹⁰⁶ However, courts typically require some degree of tangible incongruity between the state and federal schemes, refusing to presume that Congress implicitly reserved an entire field for the federal government to oversee.¹⁰⁷ Courts have almost always required Congress to be explicit if it wants to remove an entire domain from the states' jurisdiction.¹⁰⁸ Even the federal regulation of prescription drugs has not been construed to categorically prohibit states from regulating in the field,¹⁰⁹ at least beyond the limited context of importing drugs from abroad.¹¹⁰

III. POTENTIAL PREEMPTION OF STATE COMPOUNDING REGULATIONS

The DQSA defines compounding to include “combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug,”¹¹¹ at least in the context of newly added section 503B of the FDCA. By performing these actions, the compounder is taking an FDA-approved drug or substance and making a new, and unapproved, drug. Many FDA-approved drugs come only in sterile vials rather than ready-to-use formulations and must be prepared (i.e., mixed, diluted, or transferred

¹⁰⁴*Wyeth*, 555 U.S. at 573-74.

¹⁰⁵*Id.* at 573-75.

¹⁰⁶*Abbott*, 1987 U.S. Dist. LEXIS at *9.

¹⁰⁷*E.g., Hillsborough Cty. v. Automated Med. Labs., Inc.*, 471 U.S. 707, 716-17 (1985) (“We reject the argument that an intent to pre-empt may be inferred from the comprehensiveness of the FDA’s regulations To infer pre-emption whenever an agency deals with a problem comprehensively is virtually tantamount to saying that whenever a federal agency decides to step into a field, its regulations will be exclusive.”). *But see Ouellette*, 91 F. Supp.3d at 12.

¹⁰⁸*See, e.g., Holk v. Snapple Beverage Corp.*, 575 F.3d 329, 336 (3rd Cir. 2009) (holding that Congress has not signaled its intent to regulate food or beverages so comprehensively as to displace state-specific requirements). *But see Ouellette*, 91 F. Supp. 3d at 10-12 (inferring that Congress’ creation of a regulatory process to facilitate drug importation was intended to foreclose states from setting up their own processes).

¹⁰⁹*E.g., Lefèvre v. KV Pharm. Co.*, 636 F.3d 935, 941 (8th Cir. 2010) (“The Court’s comments in *Wyeth* regarding drugs and drug labeling strongly imply that field preemption does not apply in the present case. Specifically, in relating the history of federal regulation of drugs . . . the federal statutory or regulatory scheme in the present case is not so pervasive in scope that it occupies the field”) (internal quotations omitted).

¹¹⁰*Ouellette*, 91 F. Supp.3d at 12.

¹¹¹21 U.S.C. § 353b(d)(1) (2013).

to a syringe or IV bag) before they can be administered to a patient. For example, virtually all pain epidurals used during labor and delivery in this country are compounded from one or more approved drugs. Hospitals and other health care settings maintain that they must have ready-to-use dosage forms on hand and cannot rely on pharmacy compounding in the conventional frame of sending a prescription to a pharmacist to fill and send back. In a 2013 survey, more than 90 percent of hospitals reported using compounded sterile preparations.¹¹² The same study found that 85 percent of these hospitals reported outsourcing the preparation of these sterile compounds to third-party vendors.¹¹³

A. Enactment of the DQSA

The DQSA is actually a compilation of two distinct laws: title I, reforming compounding oversight via the Compounding Quality Act (CQA); and title II, establishing a federal “track and trace” system via the Drug Supply Chain Security Act (DSCSA). Although both Acts were motivated by significant public health challenges, a major impetus for the DSCSA was congressional desire to preempt a California law slated to take effect on July 1, 2014. Accordingly, the DSCSA includes express preemption provisions prohibiting states from maintaining track and trace requirements that go beyond the federal requirements.¹¹⁴ The DSCSA also contains a preemption provision relating to licensure standards for wholesale drug distributors and third party logistics providers.

In contrast, the CQA has no express preemption language. A primary motivation for the law was to draw clearer lines of authority since the 2012 outbreak was due in part to the deference state and federal regulators showed to each other and the “finger pointing” that ensued.¹¹⁵ As the HELP Committee Chairman Tom Harkin (D-IA) and Ranking Member Lamar Alexander (R-TN) often explained, the law was intended to create a new regulatory category of compounders under exclusive federal control, called outsourcing facilities, and for which FDA was “on the flagpole.”¹¹⁶

¹¹²OFFICE OF THE INSPECTOR GEN., MEMORANDUM REPORT: HIGH-RISK COMPOUNDED STERILE PREPARATIONS AND OUTSOURCING BY HOSPITALS THAT USE THEM, OEI-01-13-00150, at 1 (Apr. 10, 2013).

¹¹³*Id.* at 1-2. This outsourcing is typically in addition to compounding activities that occur within the hospital pharmacy, generally for drugs that are easier to compound.

¹¹⁴DSCSA section 585(a) (“ . . . no State or political subdivision of a State may establish or continue in effect any requirements for tracing products through the distribution system (including any requirements with respect to statements of distribution history, transaction history, transaction information, or transaction statement of a product as such product changes ownership in the supply chain, or verification, investigation, disposition, notification, or recordkeeping relating to such systems, including paper or electronic pedigree systems or for tracking and tracing drugs throughout the distribution system) which are inconsistent with, more stringent than, or in addition to, any requirements applicable under [the federal law]”).

¹¹⁵See H. COMM. ON ENERGY & COMMERCE PRELIMINARY MAJORITY STAFF REPORT, *supra* note 41; see also Comments of Senator Alexander, *infra* note 116.

¹¹⁶See 159 CONG. REC. S7941 (daily ed. Nov. 12, 2013) (comments of Sen. Tom Harkin). Senator Alexander responded to the Chairman’s remarks on the Senate floor, stating: “[M]y priority was to find a way to clarify who is accountable for large-scale drug compounding facilities, who is on the flagpole for overseeing the safety of drugs made in these facilities. [After providing a metaphor for why ambiguity over who is in charge of regulating a particular entity is dangerous, the Senator continued] . . . There should be no confusion, after this bill is passed and signed by the President, who is on the flagpole for a particular facility that makes sterile drugs This legislation creates a new, voluntary third category which we call an outsourcing facility . . . [that must] follow one nationwide quality standard, and the FDA

Their initial bill, the Pharmaceutical Compounding Quality and Accountability Act, would have conceivably done more to clarify the respective federal and state roles by prohibiting “compounding manufacturers”—the precursor to outsourcing facilities—from holding a pharmacy license in any state.¹¹⁷ The final law provides that outsourcing facilities are not required to, but presumably may, maintain a state pharmacy license.¹¹⁸

In order to qualify for the exemptions in section 503B from premarket approval,¹¹⁹ outsourcing facilities must register with FDA on an annual basis, pay registration and re-inspection fees designed to support periodic risk-based FDA inspections, report all drug production to FDA on a semiannual basis, label compounded drugs as such and in accordance with statutory criteria, and report adverse events to FDA, among other requirements.¹²⁰ In addition, the law establishes certain minimum standards and requirements relating to the types of products that can be compounded, the types of materials that may be used, and so forth.¹²¹ Perhaps most significantly, outsourcing facilities are not exempted from the requirement to make their drugs in accordance with current good manufacturing practices (cGMPs), which apply to drug manufacturing under the FDCA.¹²² It is this latter requirement that significantly distinguishes registered outsourcing facilities from traditional pharmacies compounding under section 503A, which contains an exemption from cGMPs.¹²³ The law thus imposes a high cost bar for any entity wishing to qualify under section 503B, as cGMP compliance necessitates much more significant investment than most traditional pharmacy operations.

The preemption question is not as simple as the admonition that only one regulator will be “on the flagpole.” In addition to leaving the pharmacy licensure question unresolved, section 503B mandates that all compounding must occur under

is responsible for all the drugs made in that facility. FDA is on the flagpole. What is the advantage of this? First, it eliminates the confusion, it eliminates the finger pointing. If, Heaven forbid, this should happen again, it will be clear whose fault it was, who didn't do their job of regulating.” *Id.* at S7942-43.

¹¹⁷S. 959, 113th Cong. § 503A(c)(2)(A)(i) (2013). That bill, and the final law, had the support of the National Association of Boards of Pharmacy, suggesting a state interest in greater clarity, at the very least. In a compromise with the House of Representatives, the proposal was modified to permit state-licensed pharmacies to dually register for the new federal category.

¹¹⁸21 U.S.C. § 353b(d)(4)(B) (2012).

¹¹⁹“Premarket approval,” the default pathway for new innovator and generic drugs to come to market, includes the submission of a new drug application to FDA supported by the presentation of adequate data often based on clinical trials as well as extensive information to include in the product's label. *See generally* 21 U.S.C. § 355. The costs associated with new drug applications vary considerably, but have been estimated to range from tens of millions to several billion dollars. *See* Joseph A. DiMasi et al., *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 46 J. HEALTH ECON. (forthcoming Mar. 2016).

¹²⁰21 U.S.C. §§ 353b(b)(1), 353b(a)(9), 353b(b)(2), 353b(a)(10) & 353b(b)(5).

¹²¹*Id.* §§ 353b(a)(2)–(6).

¹²²Outsourcing facilities are subject to section 501(a)(2)(B) of the FDCA, establishing the cGMP requirement in statute. During negotiations over the DQSA, FDA indicated its intent to tailor those standards to outsourcing, which is conducted at a scale and volume well below traditional drug manufacturing.

¹²³The legal framework generally recognizes the prescription requirement that is at the core of section 503A as an inherent limitation on production volume. Because this limitation is absent under section 503B, production volume could be quite large, necessitating strict controls on environmental conditions.

the direct supervision of a licensed pharmacist.¹²⁴ Despite the progression of new drug oversight from state to federal control, the pharmacy profession has historically been regulated by the states vis-à-vis boards of pharmacy. The prominent role of pharmacists in outsourcing facilities may explain lingering confusion by many state regulators as to their intended role and a desire to continue existing compounding oversight by others.¹²⁵

For its part, FDA has not been forthcoming about its interpretation of the respective state and federal responsibilities under the DQSA. In several 50-state meetings with boards of pharmacy officials, FDA has not formally presented about the boundaries of state and federal oversight of 503A and 503B-regulated entities.¹²⁶ As discussed below, the agency has sometimes indicated that it expects outsourcing facilities to comply with state regulations in addition to federal ones.¹²⁷

B. State Oversight of Outsourcing

At the time of writing this article, the DQSA is less than three years old. The practice of compounding is considered to be hundreds of years old, long preceding the modern manufacture of pharmaceuticals.¹²⁸ Up until, and even since, the passage of the DQSA, states have employed strikingly different approaches to the oversight of compounding practices that are now intended to be undertaken by outsourcing facilities. A number of states have required these facilities to maintain a pharmacy license and to meet certain pharmacy requirements, particularly with regard to personnel, while overlooking more fundamental aspects of pharmacy practice, such as the relationship with patients (or lack thereof).¹²⁹ Other states have treated out-of-state compounding operations as wholesalers and manufacturers. Other states still have created distinct categories for large-scale, anticipatory, or sterile compounding outfits. Since the passage of the DQSA, some states have looked to hand off most or all responsibilities to FDA, while many others continue to maintain their alternative regulatory schemes. Some states have adopted entirely new regulatory frameworks for outsourcing, with varying degrees of alignment with the DQSA.¹³⁰

The remainder of Part III analyzes several pending examples of state laws or proposals that could conflict with federal requirements or otherwise thwart the potential public health benefits of those federal provisions.

¹²⁴21 U.S.C. § 353b(a) (2012).

¹²⁵See, e.g., Jack W. Campbell IV, *The Drug Quality and Security Act: What Does It Mean for Compounding Pharmacies?*, 43:8 NAT'L ASS'N. OF BOARDS OF PHARMACY NEWSL. 165, 170 n.14 (Sept. 2014) (“[the National Association of Boards of Pharmacy] is drafting a brief memo on this issue, encouraging states whose current statutory definition of a pharmacy does not include an outsourcing facility to find a way to license these facilities either as pharmacies or as a new type of licensee so that patients may still be protected at the state level”).

¹²⁶See, e.g., FOOD & DRUG ADMIN., SUMMARY OF PROCEEDINGS: MARCH 18-19, 2015, INTER-GOVERNMENTAL WORKING MEETING ON COMPOUNDING (Apr. 2015), <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM447435.pdf>.

¹²⁷See *infra* note 161.

¹²⁸Roy Guharoy et al., *Compounding Pharmacy Conundrum: “We Cannot Live Without Them but We Cannot Live With Them” According to the Present Paradigm*, 143 CHEST 896, 896 (Apr. 2013).

¹²⁹See *infra* notes 172 – 174.

¹³⁰See Part III.E, *infra*.

C. *Conflicting or Supplemental Production Standards*

Despite being unapproved, federal law is unambiguous that compounded drugs are “new drugs” and thus are subject to all the requirements of the FDCA, other than those exemptions enumerated in sections 503A (for pharmacies) and 503B (for outsourcing facilities) of the Act. In an acknowledgment that compounding drugs is substantively different and occurs at a different scale from conventional drugmaking, FDA has proposed in draft guidance cGMPs tailored for section 503B.¹³¹ Specifying modified expectations for cGMP compliance within a specific sector is commonplace. At the time of writing, however, FDA had issued only interim guidance and not yet proceeded to rulemaking. One question that has already arisen is whether the manufacturing standards captured in the interim cGMPs should preempt alternative or supplemental standards that a state purports to impose on outsourcing facilities.

New Hampshire has offered an early case study for examining this question. In 2015, the legislature passed SB 202 to regulate outsourcing facilities shipping into the State. The new law includes specific standards for end-product sterility testing and release requirements. Newly added section 318:51-d provides:

Outsourcing facilities shall be required to test all finished drug products compounded from bulk active pharmaceutical ingredients (API) to determine whether they meet final product specifications before their release for distribution. No products shall be released for use until this testing is conducted and the results confirm that the finished drug product meets specifications. Outsourcing facilities compounding drug products from sterile, commercially available raw materials shall confirm sterility through process control validated by testing of at least 20 percent of the lots of each product shipped into New Hampshire.¹³²

These requirements differ from FDA’s draft cGMPs, which use a numerical threshold rather than a percentage of lots that must be tested, and which permit products to be dispensed prior to laboratory confirmation under certain circumstances.¹³³ Although draft guidance admittedly lacks binding effect, once implemented via regulations, as expected, then these federal standards would carry the same preemptive effect as a statutory standard. More broadly, the guidance serves to operationalize the agency’s view as to how an outsourcing facility may operate in compliance with the statute.

Because the DQSA included no express statements of preemption relating to compounding standards, or general preemption language relating to the oversight of outsourcing facilities, a legal challenge on preemption grounds would turn on whether preemption on the specific issue of compounding standards was implied. The broadest inquiry is thus whether the DQSA “filled the field” of compounding standards by requiring outsourcing facilities to operate according to cGMPs, as

¹³¹See generally FOOD & DRUG ADMIN., CURRENT GOOD MANUFACTURING PRACTICE — INTERIM GUIDANCE FOR HUMAN DRUG COMPOUNDING OUTSOURCING FACILITIES UNDER SECTION 503B OF THE FD&C ACT (July 2014) [hereinafter “cGMP GUIDANCE”].

¹³²SB 202 § 318:51-d, 2015 Leg., N.H. Laws 15-0906 (internal punctuation omitted).

¹³³cGMP GUIDANCE, *supra* note 131, at 14-16 (providing that all batches of ten or more units to undergo batch-level laboratory testing to ensure, inter alia, sterility, but permitting outsourcing facilities to distribute product pending final laboratory results).

implemented by FDA.¹³⁴ Volume and complexity of federal regulations are indicia of field preemption, but are not necessarily sufficient to find that Congress intended to displace supplemental state regulation.¹³⁵ cGMP requirements are voluminous and technically complex, even when compared to other aspects of food and drug regulation. For example, the Inspection Technical Guides for making sterile drugs exceed one thousand pages in total.¹³⁶ Regardless, a court would look for additional indicia that Congress intended cGMPs to preempt additional standards for compounding sterile drugs, particularly given that Congress did not legislate the complex standards directly.

Although field preemption has rarely served as the basis for preempting state food and drug regulation, it is also unusual for a state to impose additional manufacturing standards on FDA-regulated medical products.¹³⁷ Case law asserts that the federal government has exclusive jurisdiction over the approval of new drugs, which includes the manufacture, package and label specifications prescribed by FDA.¹³⁸ Because products made by outsourcing facilities are considered to be new drugs—albeit unapproved new drugs—and their manufacturing, packaging and labeling is regulated by FDA, assertions of field preemption could arguably extend to the preparation of these products.

In the absence of field preemption, cGMPs function only as a federal floor (or ceiling) such that state regulation can be enforced to the extent it is compatible with federal regulation. Courts have routinely struck down requirements that would force a manufacturer to choose between complying with the federal requirement or the state one.¹³⁹ On its face, SB 202 appears to conflict directly with federal cGMP requirements. Despite the fact that final cGMP regulations are not yet in place for outsourcing facilities, this provision does not purport to apply federal release testing standards, but rather establishes a state-specific standard. Although cGMP guidance is technically nonbinding on regulated entities, it is generally treated as a safe harbor with flexibility for regulated entities to adopt alternative controls that meet or exceed baseline statutory expectations.¹⁴⁰ Moreover, FDA is already enforcing its interim

¹³⁴Although cGMPs are detailed in non-binding guidance documents, they are grounded in an underlying statutory requirement that outsourcing facilities, like all FDA-regulated manufacturers, must comply with good manufacturing practices. 21 U.S.C. § 351(a)(2)(B) (2012). As noted, outsourcing facilities have faced adverse regulatory actions, including warning letters and recalls, as a result of failing to adequately align practices with cGMP guidance. The alternative to complying with the guidance is to adopt another rigorous approach that satisfies the current regulatory and statutory standards, which would also appear to be out of alignment with the standards set out in SB 202.

¹³⁵*Hillsborough*, 471 U.S. at 718.

¹³⁶FOOD & DRUG ADMIN., *Inspection Technical Guides* (2015), <http://www.fda.gov/ICECI/Inspections/InspectionGuides/InspectionTechnicalGuides/>.

¹³⁷Drug manufacturers, for example, are subject only to federal cGMPs and not additional state manufacturing standards, as far as the authors are aware.

¹³⁸*See Ouellette*, 91 F. Supp.3d at 10 (citing *United States v. 1500 90-Tablet Bottles*, 384 F. Supp.2d 1205, 1218 (N.D. Ill. 2005)).

¹³⁹*E.g., Grocery Mfrs. of Am. v. Gerace*, 755 F.2d 993, 1001 (2d Cir. 1985).

¹⁴⁰FOOD & DRUG ADMIN., FACTS ABOUT THE CURRENT GOOD MANUFACTURING PRACTICES (CGMPs) (Jan. 2015), <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm169105.htm> (“The CGMP requirements were established to be flexible in order to allow each manufacturer to decide individually how to best implement the necessary controls by using scientifically sound design, processing methods, and testing procedures. The flexibility in these regulations allows

cGMP requirements on outsourcing facilities through the issuance of warning letters, product recalls, and other enforcement actions.¹⁴¹ Notably, Congress created outsourcing facilities in part to provide for interstate distribution, given the challenges states faced in attempting to police out of state pharmacies compounding under section 503A.¹⁴²

According to FDA's draft guidance, federal law is satisfied by the testing of *all* lots for sterility, rather than the twenty percent required by New Hampshire. In addition, the cGMPs permit outsourcing facilities to ship products *before* testing results are confirmed under certain circumstances, whereas New Hampshire requires confirmation prior to shipment.¹⁴³ The New Hampshire law simultaneously raises the floor and lowers the ceiling established under the cGMPs. For these provisions of the New Hampshire law to stand, cGMPs could be neither a ceiling nor a floor, because SB 202's standards are simultaneously more and less strict than the federal rules governing release testing.

Setting alternative standards for release testing—among the most core aspects of compounding governance—presents a direct conflict in that it will likely be impossible for facilities to comply with these standards simultaneously with federal law. Even if it were theoretically possible for an outsourcing facility to comply with both sets of rules, it is difficult to argue that state rules that both strengthen and relax the federal requirements do not frustrate Congress' objective to hold large-scale sterile compounding to uniform national production standards.

D. Parallel (but Different) Requirements for Outsourcing

Among other requirements, section 503B includes drug labeling requirements, a semiannual product reporting program, and a system for reporting adverse events. State laws governing compounding have addressed these areas as well, generally as part of a state's pharmacy code.

In the 2015–2016 legislative session, a bill is pending in California's Senate that would overhaul state regulation of entities compounding sterile drugs, including federally registered outsourcing facilities. This bill would supersede pending regulations that would also overhaul sterile compounding requirements within the context of existing statutory law.¹⁴⁴ These proposals contain provisions that cover each of the aforementioned elements of the federal regulatory framework relating to labeling, product reporting, and reporting adverse events. The legislation, SB 619, would establish an adverse event reporting system entirely separate from FDA's MedWatch program for adverse event reporting. SB 619 would require “[a]

companies to use modern technologies and innovative approaches to achieve higher quality through continual improvement”).

¹⁴¹FOOD & DRUG ADMIN., REGISTERED OUTSOURCING FACILITIES (Jan. 1, 2016), <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm378645.htm>

¹⁴²See 21 U.S.C. § 353a(b)(3)(B) (2012) for the somewhat cumbersome restrictions on interstate distribution of compounded drugs by traditional pharmacies regulated under section 503A of the FDCA.

¹⁴³cGMP Guidance, *supra* note 131, at 15.

¹⁴⁴CALIFORNIA STATE BOARD OF PHARMACY, DRAFT REGULATION TO AMEND § 1735 IN ARTICLE 4.5 OF DIVISION 17 OF TITLE 16 OF THE CALIFORNIA CODE OF REGULATIONS (Sept. 2014). *Note*, both the current and proposed California regulations also include conditions that appear to conflict with requirements of section 503B by requiring alternative items on the drug label, establishing manufacturing standards that differ from cGMP, and other unique requirements.

nonresident outsourcing facility [to] provide to the board notice within twenty-four hours after learning of adverse effects reported or potentially attributable to a nonresident outsourcing facility's products."¹⁴⁵ The California Board would be tasked with implementing this alternative event reporting system.¹⁴⁶

The DQSA subjects outsourcing facilities to section 310.305 of title 21 of the Code of Federal Regulations, the existing program requiring drug manufacturers to report serious and unexpected adverse events.¹⁴⁷ Under section 310.305, entities have fifteen days to submit an initial report of an adverse event. Another notable distinction between the California and federal requirements is the definition of a reportable event. The federal program requires the reporting of only *serious and unexpected* adverse events.¹⁴⁸ The text of SB 619 indicates that it applies to *all* adverse events—serious, unexpected, and otherwise, which substantially broadens the number of events that would have to be investigated and reported to California.¹⁴⁹

It would be difficult for a challenger to argue that it is physically impossible to comply with both the federal and California's adverse event reporting system, as there is nothing to prevent outsourcing facilities from submitting different reports to different regulators. The next doctrinal inquiry, then, is whether the state reporting system stands as an obstacle to the federal regime. As discussed in Part II.E, early case law required an "irreconcilable conflict" between the respective regimes, though later cases frequently required only that the state law frustrate the federal scheme in some tangible way. In *Rath Packing Co.*, the Court found California's alternative food weight standard would undermine a central purpose of the federal uniformity by confusing consumers desiring to draw apples-to-apples comparisons.¹⁵⁰ Other cases rejected states' alternative mechanisms to warn of potential harms because they appeared to be motivated by competing policy goals or were perceived to disturb a deliberate balance adopted by the federal policy.¹⁵¹

In other areas of the law, states sometimes require entities to duplicate reporting obligations to the federal government. For example, the Health Information Portability and Accountability Act (HIPAA) features a federal reporting scheme for breaches of protected health information.¹⁵² Approximately forty-seven states have health privacy breach reporting laws, and several require HIPAA-covered entities to report additional information or apply different timelines relating to the same breaches that trigger federal reporting.¹⁵³ A privacy breach, however, can be defined objectively. Adverse event reports *may* or *may not* be caused by a drug; it is generally the aggregation of many reports that provides epidemiologically meaningful data.

¹⁴⁵SB 619 § 4129.2(f), 2015–16 Leg., 2015–16 Sess. (Cal. 2015).

¹⁴⁶*Id.* § 4129(c).

¹⁴⁷21 U.S.C. § 353b(b)(5) (2012).

¹⁴⁸21 C.F.R. § 310.305(b) (2015).

¹⁴⁹SB 619 at § 4129.2(e)(3), 2015–16 Leg., 2015–16 Sess. (Cal. 2015).

¹⁵⁰*Rath Packing Co.*, 430 U.S. at 543.

¹⁵¹*See Cosmetic, Toiletry & Fragrance Ass'n*, 440 F. Supp. at 1222–23.

¹⁵²*See* 45 C.F.R. § 164.408 (2015).

¹⁵³*E.g.*, CAL HEALTH & SAFETY § 1250 (2015).

The most important question, however, is simply whether the state's alternative program frustrates the federal one. California's proposed adverse event reporting program, with a shorter reporting period and broader definition of reportable events, could be found to be an obstacle to the federal program. Outsourcing facilities challenging this provision might assert that the resources diverted to preparing a hasty report to California would compromise their ability to fully investigate and report to FDA within fifteen days. SB 619's sponsors might argue the opposite—that their program gives outsourcing facilities a head start in responding to FDA, but it is more likely that the requirement to submit forms by a given date to one state (or fifty) would impede the valuable investigation intended to inform the report to FDA. Courts have sometimes combined cost-benefit concerns with a slippery slope argument.¹⁵⁴ While it might be feasible to comply with two different adverse event reporting regimes, with different definitions of reportable events, content and deadlines, it would be impractical to comply with fifty unique programs.

The balance FDA (and Congress) struck in its 15-day reporting requirement may have something to do with costs and benefits, but is more likely driven by the inherent tradeoff between timely information and complete information. There are few actions the California Board of Pharmacy could take with the earlier adverse event information that would not already be undertaken without the Board's involvement. For example, it is FDA's responsibility to determine whether a national recall of distributed product is warranted and to work directly with the outsourcing facility to request and oversee the recall.¹⁵⁵ Notably, Congress established outsourcing facilities in recognition that states have difficulty regulating compounded drugs that are produced out of state.

Perhaps the greater concern with California's proposed 24-hour reporting period is not the inconvenience to outsourcing facilities but that incomplete and inaccurate information would be reported and ultimately make its way into the public domain. As compared to privacy breach information, for example, adverse event reporting feeds into a broader collection of data that, in the aggregate, allows for effective postmarket surveillance. Experts suggest that the information available immediately following adverse events in a hospital—the setting outsourcing facilities predominantly serve—is often unreliable as hospitals typically administer inpatients multiple medications and the majority of errors are related to factors other than the defectiveness of the drug product itself.¹⁵⁶ The CDC and other entities aggregate and analyze adverse event information, and thus there is a potential for this data to be distorted by the proliferation of distinct state-reported adverse events. Commentators have increasingly recognized that current postmarket surveillance efforts for drugs and devices are limited by incomplete reports, and an abundance of reports that do not reflect actual adverse events or problems (“noise”)—and that postmarket surveillance could be enhanced by more aggregation of data via registries or other

¹⁵⁴*Cosmetic, Toiletry & Fragrance Ass'n*, 440 F. Supp. at 1224–25.

¹⁵⁵See FOOD & DRUG ADMIN., ADVERSE EVENT REPORTING FOR OUTSOURCING FACILITIES UNDER SECTION 503B OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT: GUIDANCE FOR INDUSTRY (Oct. 2015).

¹⁵⁶T.M. Atkinson et al., *Reliability of Adverse Symptom Event Reporting by Clinicians*, 21(7) QUAL. LIFE RES. 1159, 1163 (2012).

mechanisms.¹⁵⁷ Moreover, FDA and other stakeholders have pointed out that even the current approach to postmarket reporting for medical products produces large quantities of data at the expense of quality data.¹⁵⁸ It stands to reason that requiring outsourcing facilities to file reports with FDA and one or more states, using different fields and different timelines, will result in less rigorous investigation feeding the federal reports, in order to respond to multiple filing obligations under quicker timelines. It is also worth asking what surveillance value exists in a silo of one state's reporting data.

In addition to the question of congressional intent, courts sometimes consider agency intent.¹⁵⁹ Although FDA has not spoken definitively on this subject, as it often did during the George W. Bush Administration,¹⁶⁰ the agency has signaled that it does not intend to supplant states' reporting programs. In a footnote to its Adverse Event Reporting Guidance, FDA states: "Certain state boards of pharmacy may also require outsourcing facilities licensed in their states to report adverse events. Outsourcing facilities must comply with any applicable state reporting requirements independent of and in addition to reporting adverse events as described in this guidance."¹⁶¹ Although an agency's opinions about whether federal requirements preempt state ones are not controlling, agencies "do have a unique understanding of the statutes they administer and an attendant ability to make informed determinations about how state requirements may pose an obstacle to the accomplishment and execution of the full purposes and objectives of Congress."¹⁶² In any event, FDA's general statement does not address specific reporting requirements and does not reveal the type of careful consideration that generally receives deference. It is also not clear that FDA is aligned with Congressional intent.¹⁶³

E. Licensing Outsourcing Facilities

Perhaps the most complicated preemption questions that may arise under section 503B relate to facility licensure under state law. The DQSA establishes a fairly

¹⁵⁷ENGELBERG CTR. FOR HEALTH CARE REFORM, STRENGTHENING PATIENT CARE: BUILDING AN EFFECTIVE NATIONAL MEDICAL DEVICE SURVEILLANCE SYSTEM 11–12 (2015), <http://www.brookings.edu/~media/research/files/papers/2015/02/23-medical-device-policy-surveillance/med-device-report-web.pdf>.

¹⁵⁸*See id.*

¹⁵⁹For a good review of the relevant case law, see Amanda Frost, *Judicial Review of FDA Preemption Determinations*, 54 FOOD DRUG L. J. 367 (1999).

¹⁶⁰Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521, 546 (2012) (noting that from 2001 to 2008, FDA was the second most active agency in issuing preemption determinations).

¹⁶¹FOOD & DRUG ADMIN., ADVERSE EVENT REPORTING FOR OUTSOURCING FACILITIES UNDER SECTION 503B OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT: GUIDANCE FOR INDUSTRY (Oct. 2015) at 3 n.11.

¹⁶²*Wyeth*, 555 U.S. at 577 (internal quotations omitted).

¹⁶³The lead Senate sponsors appear to have presumed that outsourcing facilities would be able to opt into federal oversight and out of state oversight. At a hearing shortly after the law's passage, Senator Alexander told then-FDA Commissioner Margaret Hamburg, "some states are indicating . . . they may require an outsourcing facility that's chosen to be regulated by the FDA also to be regulated by the state as a pharmacy" despite congressional intent "to permit a facility to choose one or the other." Commissioner Hamburg testified that, to her knowledge, this was not the case. *Protecting the Public Health: Examining FDA's Initiatives and Priorities Before the S. Comm. on Health, Educ., Labor & Pensions*, 113th Cong. 21 (2014).

robust outsourcing facility “licensure” scheme, featuring registration, reporting of products, and an annual fee to support periodic federal inspections. Numerous states, however, have signaled their intent to continue separate licensure of outsourcing facilities.

It is unlikely that Congress specifically intended to prohibit states from licensing outsourcing facilities. Ultimately, the question regarding state licensure likely is not whether states may impose any licensure requirement on FDA-registered outsourcing facilities. States have conventionally retained the right to license FDA-regulated manufacturers under state law and hold them to applicable *federal* standards (as well as narrowly tailored state requirements).¹⁶⁴ Rather, the question is how states may license these facilities and subject to what requirements.

Historically, compounding operations were governed under state law as pharmacies. With the passage of FDAMA in 1997, Congress clarified that compounded drugs are subject to certain federal requirements for new drugs, but designed the framework so that states were responsible for the day-to-day oversight of these operations. Even prior to the DQSA’s passage, however, many states licensed large-scale compounding operations as something other than a pharmacy, such as a wholesaler, manufacturer, or other regulatory category.¹⁶⁵ The DQSA presumed a continuation of this trend away from pharmacy with definitional provisions specifying that an outsourcing facility is not required to hold a pharmacy license¹⁶⁶ and not required to obtain prescriptions,¹⁶⁷ the centerpiece of the exemptions under section 503A.¹⁶⁸

Presuming Congress did not want to strip states entirely of their ability to license in-state facilities, the preemption issue arises when one considers what additional rules come along with the licensure requirements. Virtually all state pharmacy codes require that a pharmacy dispense drug products pursuant to a prescription and assume some degree of responsibility for the individual to whom it dispenses.¹⁶⁹ This presents a conundrum for outsourcing facilities, many of which do not prepare patient-specific compounds, do not obtain prescriptions for the products they ship, and may not know anything about the ultimate end users, including their names. In fact, they are not the pharmacy of record for these patients, who only obtain a compounded drug once it has been prescribed and dispensed by another pharmacy, typically in a health care setting. Congress recognized the need for an advanced supply of non-patient-specific stock for hospitals and physicians, sometimes referred to as “office use,” when establishing the new regulatory category.¹⁷⁰ That is why

¹⁶⁴As of April 22, 2016, 45 of the 50 states had adopted the Uniform FDCA, permitting them to enforce state obligations that mirror the federal law. See FOOD & DRUG ADMIN., INVESTIGATIONS OPERATIONS MANUAL § 3.3.3 (2015).

¹⁶⁵*States Pass New Legislation for Oversight of Compounding Facilities*, 43(8) NABP NEWSLETTER (Nat’l Ass’n of Bds. of Pharmacy, Mount Prospect, IL), Sept. 2014, at 173.

¹⁶⁶21 U.S.C. § 353b(d)(4)(B).

¹⁶⁷*Id.* § 353b(d)(4)(C).

¹⁶⁸*Id.* § 353a(a) (specifying that under the exemption drugs must be “compounded for an identified individual patient based on the receipt of a valid prescription order . . .”).

¹⁶⁹See NAT’L ASS’N. OF BDS. OF PHARMACY, MODEL STATE PHARMACY ACT § 102 (Aug. 2015).

¹⁷⁰*Hearing on the Meningitis Outbreak Investigation Before the H. Energy & Commerce Subcomm. on Oversight & Investigations*, 113th Cong. 4 (2013).

Congress explicitly exempted outsourcing facilities from the federal requirement to obtain prescriptions for compounded drugs.¹⁷¹

A wide range of other requirements accompanies pharmacy licensure requirements, including pharmacist licensure, pharmacy-to-technician staffing ratios, and inspectional requirements. For example, New York is among nearly a dozen states requiring out-of-state outsourcing facilities to employ a pharmacist licensed in the State.¹⁷² California requires an out-of-state outsourcing facility to also maintain a pharmacy license from its resident state.¹⁷³ Florida law requires an outsourcing facility to pass a cGMP inspection every six months.¹⁷⁴ These types of requirements impose some degree of impracticality on outsourcing facilities, but it is not clear that any make it impossible for the facility to comply with both state and federal law.

In some instances, state regulators acknowledge that certain of these requirements would be impossible for outsourcing facilities to comply with, but maintain they are bound by their state laws. For example, a California law requiring a nonresident outsourcing facility to hold a pharmacy license in its home state is impossible for facilities located in many states, which no longer recognize, or license, outsourcing facilities as pharmacies. This is because most outsourcing facilities are not engaged in the “practice of pharmacy” as it is traditionally understood—they don’t receive or interpret prescriptions, they don’t consult patients regarding uses, risks, or contraindications, and they don’t have knowledge of who will be receiving their drugs. Illustratively, the California legislature is considering a bill that would join these states by prohibiting an outsourcing facility from holding a pharmacy license.¹⁷⁵

Longstanding Supreme Court precedent dictates that state laws may not “hinder or obstruct the free use of a license granted under an act of Congress,”¹⁷⁶ or impose additional licensing requirements that impede activity sanctioned by a federal license.¹⁷⁷ Congress intended outsourcing facilities to be able to prepare and ship interstate non-patient-specific compounded drugs. However, it is not clear that registration with FDA under section 503B constitutes a “license” to engage in outsourcing beyond the scope of practice permitted under state law. The statutory language could be read to suggest only that compliance with section 503B provides a license, or exemption, from more onerous requirements of *federal* law, such as premarket approval for new drugs.

The *Wheeling & Belmont Bridge* precedent was first adapted to FDA law four decades ago. In *State v. Interstate Blood Bank, Inc.*, a Wisconsin statute prohibited for-profit blood banks from operating within the state’s borders despite the fact that

¹⁷¹ See 21 U.S.C. § 353a(a).

¹⁷² E.g., N.Y. EDUC. LAW § 6808(5)(f) (2015).

¹⁷³ CAL. BUS. & PROF. CODE § 4112(d) (2015).

¹⁷⁴ FLA. STAT § 465.0158(3)(e) (2015).

¹⁷⁵ SB 619 § 4129(b), 2015–16 Leg., 2015–16 Sess. (Cal. 2015).

¹⁷⁶ *Pennsylvania v. Wheeling & Belmont Bridge Co.*, 54 U.S. 518, 566 (1851).

¹⁷⁷ E.g., *Sperry v. Florida*, 373 U.S. 379, 385 (1963) (“A State may not enforce licensing requirements which, though valid in the absence of federal regulation, give ‘the State’s licensing board a virtual power of review over the federal determination’ that a person or agency is qualified and entitled to perform certain functions, or which impose upon the performance of activity sanctioned by federal license additional conditions not contemplated by Congress . . .”).

the FDCA both permitted commercial blood banks to compensate donors and otherwise regulated their other practices.¹⁷⁸ In striking down the Wisconsin law as preempted, the court explained:

[W]hen the federal government has undertaken a comprehensive regulatory and licensing system of an occupation engaged in interstate commerce for a particular purpose, i.e., to insure the safety, potency, and purity of a particular product, the states are pre-empted from prohibiting the same occupation as a means of accomplishing the same purposes.¹⁷⁹

The court further reasoned that whether Congress intended to replace state regulations of blood banks was irrelevant because the federal regulatory scheme revealed a desire for uniform policy favoring the continuation of commercial blood banks.¹⁸⁰ More recently, in 2013, the Supreme Court employed similar reasoning when it rejected the notion that an actor can comply with both state and federal law by simply ceasing to act within the state's borders.¹⁸¹ Writing for the majority, Justice Alito explained that "if the option of ceasing to act defeated a claim of impossibility, impossibility pre-emption would be all but meaningless."¹⁸²

If this line of reasoning were followed in the outsourcing facility context, states would be prohibited from imposing additional licensure requirements that made it impossible for outsourcing facilities to operate within a state. However, the *Interstate Blood Bank* court acknowledged that states have a greater interest in preventing their residents from consuming certain products than they do in regulating interstate business.¹⁸³ This view would suggest that even if states could potentially limit in-state hospitals from using outsourcing facilities, a state could not prohibit an outsourcing facility from shipping into or out of the state without frustrating the federal purpose of section 503B.¹⁸⁴ Ultimately, the inquiry leads back to the fundamental question of whether the DQSA sought to establish a uniform federal outsourcing program or simply created accommodations in the law to ensure "office use" compounding was not prohibited by federal law. As noted, there are indications that Congress believed it was exempting outsourcing facilities from state regulation as a pharmacy.¹⁸⁵

New York is among the states seeking to require every outsourcing facility in the country wishing to serve customers within its borders to employ a pharmacist licensed by the State.¹⁸⁶ This standard differs from the federal requirement, which

¹⁷⁸*State v. Interstate Blood Bank, Inc.*, 65 Wis. 2d 482 (Wis. 1974).

¹⁷⁹*Id.* at 496–97.

¹⁸⁰*Id.* at 496–97.

¹⁸¹*Bartlett*, 133 S. Ct. at 2470–71.

¹⁸²*Id.* at 2477 (internal quotations omitted).

¹⁸³*See Interstate Blood Bank*, 65 Wis. 2d at 498–99.

¹⁸⁴Prohibiting in-state hospitals from outsourcing production to registrants of the federal category would impede their ability to heed the advice of FDA, however. *See* Letter from Margaret Hamburg, FDA Commissioner, to Hospital/Purchasers (Jan. 8, 2014), <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM380599.pdf> (encouraging hospitals to exclusively contract with registered outsourcing facilities).

¹⁸⁵*See supra* note 163. The authors are not aware of any legislative history to the contrary.

¹⁸⁶N.Y. EDUC. LAW § 6808.

requires only that compounding occur “under the direct supervision of a licensed pharmacist.”¹⁸⁷ Unless challengers could demonstrate an insufficient supply of New York-licensed pharmacists, this requirement would not be impossible for outsourcing facilities to comply with. In some parts of the country, it may be challenging to recruit and retain such a pharmacist. The question is therefore whether the requirement is so impractical that it serves as an obstacle to operation of the federal program. Applying the slippery slope test sometimes adopted by courts, having pharmacists licensed by each of the fifty states in every outsourcing facility in the nation would immensely complicate the federal purpose and probably eliminate the existence of outsourcing facilities altogether. This outcome could begin to approach the “stop-selling solution” that was rejected in *Bartlett* and subsequent cases.¹⁸⁸ Although courts analyzing state-specific requirements do not always jump to a slippery slope test, nor should they.

The in-state pharmacist licensure requirement, which was on the books in approximately a dozen states in 2015, would seem to disrupt the position settled on by Congress in requiring only that compounding occur under the supervision of a pharmacist. For example, Congress could have gone further and required that each drug product be compounded by the pharmacist himself, which would have arguably enhanced safety and quality, but at considerable cost. It is unclear how employing a pharmacist licensed by New York would protect the State’s residents or otherwise further the broad safety objectives of the federal law. For example, New York does not require that each drug shipped into the State be compounded by that New York pharmacist. However, the preemption doctrine does not directly consider the state’s rational basis. If it would be reasonable for outsourcing facilities to have pharmacists on staff obtain licenses in each state with this requirement, then it may also not frustrate the federal purpose. But as more states adopt—and enforce—this requirement, the cost-benefit analysis weighs heavily against the imposition, and a case could be made that an in-state pharmacist requirement needlessly impedes the operation of federal law.

IV. CONCLUSION

The DQSA is still in its relative infancy, and the potential federal-state conflicts identified above may ultimately be resolved as stakeholders become more familiar with the new law and FDA continues its implementation. However, for the moment states have incentives to continue exercising their own oversight over outsourcing facilities, including lingering distrust that FDA will exercise sufficiently robust scrutiny, possible desires to protect in-state compounding pharmacies, FDA’s own suggestion of non-preemption, and states’ historical role in regulating drug compounding. It is this historical factor that makes the (at least partial) federalization of compounding oversight different from the path to federalizing regulation of other drugs as well as devices and biologics.

Any consideration of preemption in this context should not lose sight of Congress’ awareness that it is both laws *and* resources that dictate the success of governmental oversight and enforcement. Under the DQSA, outsourcing facilities are designed to

¹⁸⁷21 U.S.C. § 353b(a) (2012).

¹⁸⁸*E.g.*, *Yates*, 808 F.3d at 300.

handle the higher risk compounding needs; section 503B provides for sterile compounding, at a higher volume (not prescription-by-prescription), with unfettered interstate sales. They pay fees to support FDA inspections. Congress simultaneously assigned responsibility for these actors to FDA, while reserving oversight of pharmacies performing the less risky types of compounding to the states (i.e., prescription-by-prescription, with limitations on interstate sales and greater role of non-sterile compounding).

In an era in which government resources are spread thin, the federal government's own strategy for enhancing public safety has been to embrace "smart" regulation—by placing greater onus on manufacturers to adopt best practices across facilities and using data to hone postmarket surveillance. On a global level, there is an inexorable trend towards information sharing and convergence rather than duplication. These trends hold great promise to improve public health. With the checkered history of drug compounding, the federal government and the states cannot afford to ignore these trends, and do not appear to have the resources to duplicate, rather than complement, their oversight efforts.

If forced to resolve these issues, courts should keep in mind the salutary effects of uniform policies in the areas of product quality and postmarket vigilance. In the interim, the objectives of the DQSA in improving public health will be advanced by greater federal and state education and coordination.