

**PAINKILLERS AND POMEGRANATES:  
TODAY'S FIERCEST PREEMPTION BATTLEFIELDS**

**Catherine M. Sharkey**  
**Crystal Eastman Professor of Law**  
**NYU School of Law**

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**Excerpts: Catherine M. Sharkey, *States v. FDA*, 83 GEO. WASH. L. REV. (forthcoming 2015).**

Food and drugs are essential goods. But they pose serious health and safety risks to all people. In the United States, to manage these risks, there is a stringent ex ante, centralized regulatory regime led by the public Food and Drug Administration (FDA) and a robust ex post, decentralized system enforced primarily by private litigants. The FDA regulates at the national level, while private litigants enforce (or attempt to enforce) state tort law protections. The health and safety risks posed by food and drugs are thus simultaneously regulated by federal and state law. This federalist structure, operating on dual regulatory levels, sets the stage for both synergy and conflict. Moreover, while the FDA (and Congress) clearly exists to vindicate the relevant national interests, it is less clear who speaks for the relevant state regulatory interests, given the decentralized, private enforcement of state tort law.

The FDA and other federal regulatory agencies have promulgated regulations that expressly claim to preempt—that is, to oust—conflicting state tort law. Since these agency pronouncements of preemption have such substantial effect on state interests, agencies are supposed to consult directly with the states before enacting preemptive regulations.<sup>1</sup> The Administrative Conference of the United States (ACUS) has urged federal agencies to take this state consultation mandate seriously. More specifically, ACUS in 2010 issued an official recommendation titled “Agency Procedures for Considering Preemption of State Law” (for which I served as Academic Consultant), aimed at facilitating state representatives’ participation in the preemptive rulemaking process.<sup>2</sup> And, several federal agencies have taken the recommendations to heart.<sup>3</sup>

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<sup>1</sup> Exec. Order No. 13,132, 64 Fed. Reg. 43,255 (Aug. 4, 1999) (directing federal agencies to avoid infringing on states’ policymaking authority and to consult state-level authorities in developing policies that could restrict such authority). Such consultation is likewise consistent with the Obama Administration’s official position “that preemption of State law by executive departments and agencies should be undertaken only with full consideration of the legitimate prerogatives of the States and with a sufficient legal basis for preemption.” Preemption: Memorandum for the Heads of Executive Departments and Agencies, 74 Fed. Reg. 24,693, 24,693 (May 20, 2009).

<sup>2</sup> See Adoption of Recommendation, 76 Fed. Reg. 81, 82 (Jan. 3, 2011) (explaining the Conference’s decision to adopt recommendations designed to facilitate participation by state representatives in federal agencies’ preemptive rulemakings); see also Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521, 582-90 (2012) (setting forth specific measures that would improve consultation between states and federal agencies with regard to potentially preemptive rulemakings).

<sup>3</sup> The Department of Transportation (DOT), for example, has issued a “Federalism” statement as follows:

The DOT has internal procedures to ensure compliance with the preemption provisions of Executive Order 13132. Many of our procedures are modeled after Administrative Conference of the United States (ACUS) recommendations found in a December 9, 2010, Recommendation 2010-1 on “Agency Procedures for Considering Preemption of State Law.” For example, DOT encourages relationship building with State and local officials and reaching out to those officials when we consider rules that may have a preemptive effect. When done in the course of rulemaking proceedings, we disclose to the public when meetings take place by placing a memorandum in the rulemaking docket in accordance with our policies on ex parte communications.

*Federalism*, U.S. Dep’t of Transp., <http://www.dot.gov/regulations/federalism> (last updated Sept. 25, 2012). <http://www.dot.gov/regulations/federalism>.

The Consumer Financial Protection Bureau entered into a memorandum of understanding with state banking officials, pursuant to which the regulators would adhere to an agreed-upon framework intended to help

Two recent high-profile preemption lawsuits address the role of states vis-à-vis the FDA in regulating food and drug safety head on. In *Zogenix, Inc. v. Patrick*, a federal district court enjoined the Massachusetts government from enacting a statewide ban on Zohydro, an FDA-approved opioid drug,<sup>4</sup> but upheld the state's subsequent restrictions on how the drug is prescribed and dispensed.<sup>5</sup> In *Grocery Mfrs. Ass'n v. Sorrell*, food industry representatives have mounted a challenge to a recently enacted Vermont law mandating labeling of genetically engineered food, which the FDA, at least thus far, does not require.<sup>6</sup>

Both cases explore the extent to which states can regulate drug and food safety without treading impermissibly upon the FDA's turf. They further raise the issue of who should decide if the state regulatory efforts are in synch—or at odds—with the federal regulatory scheme. In turn, these cases implicate such interesting questions as: To what degree must administrative agencies consider state interests in promulgating and enforcing federal regulations? Should they have to do so only during the rulemaking process or in the related drug-application approval context, or should agencies also be required to consider states' views after the regulatory actions in question have been finalized? And, in the absence of agencies' due consideration to state interests and concerns, when and to what extent are states free to take matters into their own hands by passing more stringent regulations of their own?

## I. Drug Regulation in a Federalism Framework

Pharmaceutical companies face dual levels of regulation at numerous junctures during the process of bringing a product to market. When the FDA approves a prescription drug, it approves not only the safety and efficacy of the drug, but also the drug's labeling. State tort law regulates health and safety of products, including pharmaceutical drugs and devices, via design defect claims for unreasonably dangerous products as well as failure to warn claims for labeling deficiencies.<sup>7</sup> Several of the U.S. Supreme Court's high-profile preemption cases over the last decade have given rise to the questions of whether and to what extent states can continue to enforce their own standards in defective design and/or failure to warn actions against pharmaceutical companies, when such standards are inconsistent with FDA's approval of a drug

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these regulatory bodies coordinate and cooperate. See Miriam Seifter, *States as Interest Groups in the Administrative Process*, 100 VA. L. REV. 953 (2014).

<sup>4</sup> 2014 WL 1454696, at \*3 (D. Mass. Apr. 15, 2014).

<sup>5</sup> 2014 WL 4273251, at \*1 (D. Mass. Aug. 28, 2014).

<sup>6</sup> See Complaint for Declaratory and Injunctive Relief, *Grocery Mfrs. Ass'n v. Sorrell*, No. 5:14-cv-00117 (D. Vt. June 12, 2014). Connecticut and Maine have recently enacted GMO labeling bills with an intriguing additional feature—they are contingent on other states enacting similar measures primarily to keep their states from being “outliers,” and also out of concern that, absent broader state participation, one state would face increased litigation risk. See 56 H.R. Proc., Pt. 19, 2013 Sess., at 9044 (Conn. 2013) (addressing the possibility that the Connecticut bill could present “legal and market obstacles” absent this feature); S. 126-1160, 1st Sess., at 1174 (Me. 2013) (explaining that the measure helped guard against the danger that the Maine legislation would effectively turn the state into “an outlier”).

<sup>7</sup> See, e.g., *Wyeth v. Levine*, 555 U.S. 555, 573–81 (2009) (holding that defendant brand-name drug manufacturer was liable under state tort law for failure to warn, despite the drug label's compliance with applicable FDA regulations); *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 492–97 (1996) (ruling that defendant medical device manufacturer could be held liable for negligent design under state law).

or device.<sup>8</sup> But there is another layer of potential overlap. While the FDA regulates the safety and efficacy of prescription drugs, states regulate medical practice, including the licensing of doctors and pharmacists.<sup>9</sup>

The *Zogenix* case confronted both dimensions of this regulatory overlap. The state's ban of the sale of Zohydro in Massachusetts implicates the issue of whether the state can take a different position from that of the FDA on the safety and efficacy of Zohydro. The state's subsequent restrictions on how the drug was to be prescribed and dispensed fall squarely within the state's domain of regulating the practice of medicine; still, the question remained: in enforcing those regulations, did Massachusetts obstruct the FDA's regulatory goals?<sup>10</sup>

While I agree with the court's ultimate conclusions—that the statewide ban is preempted, but the state's subsequent restrictions are not—in this Part I highlight two fundamental considerations on which the court's preemption holdings should turn: the FDA's position on the tension between state and federal regulatory goals and state participation in the deliberative process. The court missed an opportunity to resolve the preemption dispute regarding the state-level restrictions on prescribing and dispensing Zohydro by deferring to the FDA's publicly stated position that such state law regulatory efforts were not only consistent with, but facilitated, federal regulatory goals. With respect to Massachusetts' enactment of the ban, given that the state had an opportunity to participate in the regulatory process and evidence that the federal agency gave due consideration to the precise risks that gave rise to the state's objection, I argue that states should be less entitled to escape federal preemption and enact regulatory schemes of their own.

## **A. *Zogenix*: Opioid Drug Preemption Case**

### **1. FDA's Controversial Approval of Zohydro**

In October, 2013, the FDA approved Zohydro ER, a powerful, extended-release formulation of hydrocodone, an opioid prescription drug.<sup>11</sup> The agency's action was

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<sup>8</sup> See, e.g., *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2478–2480 (2013) (holding that FDA regulations preempted the plaintiff's state-law products liability claims against defendant generic drug manufacturer); *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2577–78 (2011) (deferring to FDA's interpretation of its regulations in determining that such laws foreclosed the plaintiff's state law failure-to-warn claim against a generic drug manufacturer).

<sup>9</sup> See, e.g., INST. OF MED. (U.S.) ROUNDTABLE ON EVIDENCE-BASED MED., LEADERSHIP COMMITMENTS TO IMPROVE VALUE IN HEALTHCARE: FINDING COMMON GROUND: WORKSHOP SUMMARY (2009), available at <http://www.ncbi.nlm.nih.gov/books/NBK52854/> (“The states directly regulate the practice of medicine and the healthcare workforce. . . . Because these duties are not assigned to the federal government by the Constitution, [the Tenth Amendment] provides the states the right to enact laws and regulations to protect the health and general welfare of their residents.”).

<sup>10</sup> See Verified Second Amended Complaint at 21–22, *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 3339610 (D. Mass. July 8, 2014) (No. 14-11689-RWZ) (arguing that the states are bound to use their authority to regulate the practice of medicine in ways that do not undermine FDA's power to approve prescription drugs, and that the Massachusetts regulations do not adhere to this requirement).

<sup>11</sup> See Press Release, U.S. Food & Drug Admin., FDA Approves Extended-Release, Single-Entity Hydrocodone Product (Oct. 25, 2013), <http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm372287.htm>. Typically, the FDA reviews new drug applications using a review team, the members of which analyze the drug's clinical trials in order to determine whether the drug is effective for its proposed use, as well as whether the drug's benefits outweigh the apparent risks. See *The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective*,

controversial, as the decision overrode the recommendation of its own Anesthetic and Analgesic Drug Products Advisory Committee,<sup>12</sup> which voted 11-2 against approving the drug.<sup>13</sup> The committee took the position that opioids like Zohydro should not be approved without abuse-deterrent or similar risk-mitigation properties.<sup>14</sup> The committee's vote occurred in the wake of a public meeting regarding the risks and benefits of Zohydro, attended by citizens who urged the committee to vote against the drug's approval in light of public health considerations.<sup>15</sup> In approving the drug, the FDA stated that it had thoroughly assessed the underlying science of the proposed drug and concluded that, on balance, the potential benefits outweighed the risks.<sup>16</sup> Moreover, in approving the drug, the FDA chose not to require that the drug manufacturer incorporate abuse-deterrent features to protect against potential misuse and addiction, citing factors such as the imperfect and underdeveloped nature of abuse-deterrent technology.<sup>17</sup>

## 2. State Law Ban Preempted; State Law Restrictions Upheld

Five months later, in March, 2014, Massachusetts Governor Deval Patrick issued an emergency order banning "the prescribing and dispensing" of Zohydro within the state.<sup>18</sup> Zogenix, the manufacturer of Zohydro, filed a motion for a temporary restraining order and

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U.S. FOOD & DRUG ADMINISTRATION, <http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm> (last updated Nov. 6, 2014).

<sup>12</sup> FDA advisory committees are composed of outside experts, and may be called upon to weigh in on uncertainties that the FDA review team has identified or to provide input on broader policy-related issues. *FDA 101: Advisory Committees*, U.S. FOOD & DRUG ADMINISTRATION, <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048040.htm> (last updated Oct. 14, 2014). According to the FDA, "For specific products, advisory committees consider the available evidence and provide scientific and medical advice on safety, effectiveness, and appropriate use. Committees might also advise the agency on broader regulatory and scientific issues." *Id.*

<sup>13</sup> See, e.g., Cathryn Jakobson Ramin, *Why Did the F.D.A. Approve a New Pain Drug?*, THE NEW YORKER (Dec. 2, 2013), available at <http://www.newyorker.com/business/currency/why-did-the-f-d-a-approve-a-new-pain-drug> (discussing the FDA's decision to approve Zohydro against the committee's recommendation).

<sup>14</sup> U.S. FOOD & DRUG ADMIN., CTR. FOR DRUG EVAL. & RESEARCH, REF. NO. 3396196, SUMMARY REVIEW FOR REGULATORY ACTION: NDA# 202880 25 (2013), available at [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/202880Orig1s000SumR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202880Orig1s000SumR.pdf) (summarizing the committee's position that prescription opioids such as Zohydro should not be approved unless they have features to discourage or prevent abuse).

<sup>15</sup> The agency publishes notices of advisory committee meetings in the Federal Register at least 15 calendar days in advance of a meeting. An advisory committee calendar is also posted on the FDA's website. 41 CFR § 102-3.150 (2014). See generally PHILIP MA ET AL., MCKINSEY CTR. FOR GOV'T, FDA ADVISORY COMMITTEE OUTCOMES (Oct. 2013), available at [http://www.mckinsey.com/~media/McKinsey/dotcom/client\\_service/Public%20Sector/Regulatory%20excellence/FDA\\_advisory\\_committee\\_outcomes.ashx](http://www.mckinsey.com/~media/McKinsey/dotcom/client_service/Public%20Sector/Regulatory%20excellence/FDA_advisory_committee_outcomes.ashx) (analyzing FDA advisory committee meetings and their apparent influence on the agency's decisions).

<sup>16</sup> U.S. FOOD & DRUG ADMIN., CTR. FOR DRUG EVAL. & RESEARCH, *supra* note 14, at 29.

<sup>17</sup> *Id.* at 32 ("[T]he technology used to produce abuse-deterrent opioid formulations is still in the nascent stages . . . . [E]ven the currently available abuse-deterrent technologies only limit abuse by routes other than oral administration.").

<sup>18</sup> Press Release, Mass. Exec. Office of Health & Human Servs., Governor Patrick Announces Immediate Restrictions on Powerful New Painkiller in Response to Public Health Emergency (Apr. 22, 2014), <http://www.mass.gov/eohhs/gov/newsroom/press-releases/dph/new-painkiller-restriction.html>.



preliminary injunction against the ban on the ground that it was preempted by federal law.<sup>19</sup> Zogenix argued that the FDA’s determination that Zohydro was safe and effective preempted state laws based on contrary findings, such as the Massachusetts ban.

In April, 2014, a Massachusetts federal district court granted Zohydro’s motion and enjoined the Commonwealth from enforcing the prohibition.<sup>20</sup> The court based its holding on obstacle preemption, reasoning that the state “obstruct[ed] the FDA’s Congressionally-given charge”—the “charge” in question being the responsibility to protect and promote public health by ensuring that “drugs are safe and effective”—when the state had “interposed its own conclusion about Zohydro ER’s safety and effectiveness by virtue of [the] emergency order.”<sup>21</sup>

In response, the state changed tactics and instead targeted the practices of prescribing and dispensing medications—areas traditionally within the purview of state law. The Commonwealth’s Board of Registration in Medicine issued an emergency regulation restricting the prescription and dispensation of the drug.<sup>22</sup> Two additional state regulatory bodies—the Board of Registration of Physician Assistants and Board of Registration in Pharmacy—promulgated additional restrictions on the prescription and dispensation, respectively, of Zohydro.<sup>23</sup>

Anticipating the argument that the regulations were within an area traditionally left to state control, Zogenix amended its complaint.<sup>24</sup> Massachusetts’ motion to dismiss emphasized that “state governments have not only concurrent, but primary, authority to regulate matters of

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<sup>19</sup> Complaint at 14–15, *Zogenix, Inc. v. Patrick*, 2014 WL 1454696 (D. Mass. Apr. 15, 2014) (No. 14-11689-RWZ). The complaint also alleged that the order violated the dormant Commerce Clause and the Contracts Clause. *Id.* at 16–18.

<sup>20</sup> *Zogenix, Inc. v. Patrick*, 2014 WL 1454696, at \*3 (D. Mass. Apr. 15, 2014).

<sup>21</sup> *Id.* at \*2. The court rejected the state’s reliance on *Wyeth v. Levine*:

*Wyeth* assumed the availability of the drug at issue and analyzed whether stronger state labeling requirements obstructed the FDA’s objectives. Here, the obstruction is clearer because the drug Massachusetts wants Zogenix to adopt—Zohydro ER with an “abuse-resistant formulation”—has not been approved by the FDA. To satisfy the Commonwealth, Zogenix would be required to return to the FDA and seek approval of a drug different from the one the FDA has already deemed safe.

*Id.*

<sup>22</sup> 243 MASS. CODE REGS. 2.07(25) (2014). Zogenix amended its complaint to include a claim that the Board’s regulations amounted to “an effective ban” and were unconstitutional. Verified Amended Complaint at 26, *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 3339610 (D. Mass. July 8, 2014) (No. 14-11689-RWZ). Zogenix alleged that the regulatory action “represent[ed] an impermissible effort by Massachusetts to establish its own drug approval policy,” and “specifically undermine[d] the FDA’s assessment that Zohydro ER is a safe and effective product that may be distributed in all fifty states.” *Id.* at 26–27. The regulation, Zogenix argued, also posed an obstacle to “the FDA’s comprehensive regulatory scheme for nationally-effective drug approvals.” *Id.* at 26. The amended complaint also maintained that the restrictions, like the initial ban, contravened the Contract Clause and Commerce Clause, and also violated the Equal Protection Clause. *Id.* at 8.

<sup>23</sup> 263 MASS. CODE REGS. 5.07(12) (2014) (Board of Registration of Physician Assistants regulation); 247 MASS. CODE REGS. 8.05(3) (2014) (Board of Registration in Pharmacy regulation); 247 MASS. CODE REGS. 9.04(8) (2014) (additional Board of Registration in Pharmacy regulation). Prior to issuing their regulations, the Boards held hearings and public comment periods. Memorandum in Support of Defendants’ Motion to Dismiss Plaintiff’s Verified Second Amended Complaint at 13 n.13, *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 3339610 (D. Mass. July 8, 2014) (No. 14-11689-RWZ).

<sup>24</sup> Verified Second Amended Complaint at 19–29, *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 3339610 (D. Mass. July 8, 2014) (No. 14-11689-RWZ).

health and safety, including the practices of health professionals.”<sup>25</sup> Zogenix’s revised complaint conceded that states *did* have the power to regulate the practices of prescribing and dispensing medications, but argued that they were bound to do so in a way that did not “interfere[] with FDA’s authority to approve drugs as safe and effective.”<sup>26</sup> After requiring the state to go back to the drawing board and refine its restrictions,<sup>27</sup> the court granted the state’s motion to vacate the preliminary injunction, and upheld the new regulations as valid and constitutional.<sup>28</sup> The court rejected Zogenix’s preemption argument on the ground that the state law restrictions were now consistent with federal law and thus not in conflict.<sup>29</sup>

## **B. Deference to the FDA’s Position: A Missed Opportunity to Resolve the Preemption Dispute**

With respect to the FDA’s drug approval process, the agency contemplates the states assuming an ongoing, active role in ensuring the safe, legal, and effective use of prescription drugs. Moreover, the FDA’s Zohydro approval process indisputably aired—if not resolved—the issues that the states considered critical. This situation thus is one in which deference to the agency’s position effectively respects state interests and autonomy.

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<sup>25</sup> Memorandum in Support of Defendants’ Motion to Dismiss Plaintiff’s Verified Second Amended Complaint at 6, *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 3339610 (D. Mass. July 8, 2014) (No. 14-11689-RWZ).

<sup>26</sup> Verified Amended Complaint, *supra* note 24, at 23. By this theory, state restrictions that “require indications for the drug that are inconsistent with the indication for which the drug was approved by FDA,” are preempted by federal law. *Id.* Zogenix also advanced the same obstacle preemption arguments it had previously articulated, again asserting that the regulations posed an obstacle to the regulatory scheme created by the FDA. *Id.* at 34 (arguing that the regulations “specifically undermine the FDA’s assessment that Zohydro ER is a safe and effective product that may be distributed in all fifty states,” and thus “impede the FDA’s Congressional mandate to approve a range of safe treatments to promote the public health”).

<sup>27</sup> On July 8, 2014, the district court allowed in part Zogenix’s motion for a preliminary injunction against enforcement of the Massachusetts regulations. *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 3339610 (D. Mass. July 8, 2014). The court concluded that one of the restrictions—which required doctors to certify that other pain-management treatments had failed when prescribing Zohydro—was ambiguous, and reasoned that, as a result, the regulation could be enforced in a way that would “severely frustrate the drug’s availability” and thus “pose significant constitutional concerns.” *Id.* at \*4. The court advised the state defendants that if they “provide adequate and constitutional guidance to physicians regarding the prerequisites for prescribing Zohydro in compliance with the regulation, then they may thereafter move to lift the injunction.” *Id.* at \*5.

Taking up the district court’s direction, Massachusetts amended the regulations. First, the regulations no longer required that alternative pain management treatment options have “failed,” but rather that such treatment options have been “inadequate.” *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 4273251, at \*2 (D. Mass. Aug. 28, 2014). Second, doctors no longer had to reference failed treatments in the letters of medical necessity that they were required to send when prescribing the drug. *Id.* at \*3.

<sup>28</sup> *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 4273251, at \*3 (D. Mass. Aug. 28, 2014). In response to the district court’s decision, Zogenix filed a third amended complaint, maintaining that the revised regulations still constituted an “effective ban” that was “inconsistent with the federal regulatory scheme governing the approval of prescription drugs.” Verified Third Amended Complaint at 7, *Zogenix, Inc. v. Patrick*, No. 14-11689-RWZ (D. Mass. Sept. 9, 2014). Zogenix launched the familiar assault on the Boards’ regulations, arguing that the restrictions were obstacle preempted because the Commonwealth’s power to regulate pharmaceutical practices “must not be exercised in a manner that interferes with FDA’s authority to approve drugs as safe and effective.” *Id.* at 26. Zogenix also relied heavily on the argument that the intent of the government had been to impose an effective ban on the drug. *Id.* at 34–37. The company also maintained its Equal Protection Contract Clause, and Commerce Clause claims, which had not been substantively addressed in any of the district court decisions. *Id.* at 11.

<sup>29</sup> *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 4273251, at \*3 (D. Mass. Aug. 28, 2014).

## 1. FDA's Position

### a) FDA Commissioner Supports State Restrictions

While the FDA has primary authority to oversee and monitor risks associated with opioid drugs, the agency also contemplates a significant role for state regulation.

On April 29, 2014—after the district court enjoined Massachusetts from enforcing the total ban on Zohydro, and after the state's Board of Registration in Medicine issued its regulations on the prescribing and dispensing of the drug—Dr. Margaret Hamburg, FDA Commissioner, published a post on the FDA's official blog, responding in part to the steps that Massachusetts had taken to regulate the drug within the state.<sup>30</sup> Commissioner Hamburg took the position that the prescribing and dispensing restrictions represented an appropriate exercise of state regulatory authority: "As the entities with responsibility for overseeing the practice of medicine, the states have an important role to play in addressing a critical driver of opioid abuse—inappropriate prescribing practice."<sup>31</sup> She argued further that the Massachusetts restrictions—and similar measures that had been adopted in Vermont—were "consistent with the essential tenets of numerous medical society guidelines on appropriate pain management," and were "precisely what responsible physicians should be doing."<sup>32</sup>

Commissioner Hamburg even encouraged ongoing state participation in the drug regulation process. "We urge those states with active prescription drug monitoring programs, as well as insurers and pharmacy benefit managers, to help identify and halt inappropriate prescribing. And we urge all states to consider requiring common sense, responsible pain management prescribing practices for all opioids."<sup>33</sup>

The district court nonetheless found that the state restrictions had the potential to "severely frustrate [Zohydro's] availability," which would "pose significant constitutional concerns."<sup>34</sup> Although Commissioner Hamburg had referred approvingly to the regulation requiring doctors to certify that other pain-management treatments had failed before prescribing Zohydro,<sup>35</sup> the district court, despite having the most concern about that particular requirement, did not squarely address Commissioner Hamburg's statements. Instead, the court, while

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<sup>30</sup> Margaret A. Hamburg, M.D., *The Way Forward on Opioid Abuse: A Call to Action for Science-Based, Comprehensive Strategies*, FDA VOICE (Apr. 29, 2014), <http://goo.gl/WFSdZ2>.

<sup>31</sup> *Id.*

<sup>32</sup> *Id.* Indeed, Commissioner Hamburg advocated extending the restrictions beyond Zohydro to apply to the entire class of opioid drugs. *Id.*

<sup>33</sup> *Id.* The Massachusetts government, in its motion to dismiss Zohydro's second amended complaint, brought the FDA Commissioner's statements to the court's attention by asserting that the FDA "has long acknowledged state authority to regulate how medical practitioners prescribe and pharmacists dispense prescription drugs." Memorandum in Support of Defendants' Motion to Dismiss Plaintiff's Verified Second Amended Complaint, *supra* note 25, at 7-8.

<sup>34</sup> *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 3339610, at \*4 (D. Mass. July 8, 2014).

<sup>35</sup> Commissioner Hamburg specifically mentioned that the regulations would obligate physicians to "take certain steps such as screening for abuse risk and documenting medical need before prescribing the opioid Zohydro ER." Hamburg, *supra* note 30.

acknowledging states' authority to regulate in this area, held that states must do so in a way that was not "inconsistent with the federal law," such that they "prevent[ed] the accomplishment of the FDCA's objective that safe and effective drugs be available to the public."<sup>36</sup> Nor did the court address the FDA's position when it subsequently ruled, after the state's further revisions to the regulations, to lift the injunction.<sup>37</sup>

Massachusetts raised what I see as the key point: "Clearly, the FDA does not regard the Boards' emergency regulations as an obstacle to its new-drug-approval process."<sup>38</sup> Moreover, in this instance, I argue, the FDA's views were entitled to deference.<sup>39</sup>

## **2. Ensuring State Participation: Carrots and Sticks**

Where deference is to be accorded to the position of the FDA, however, some form of accountability to state interests must be demanded. The ACUS project was sensitive to the oft-overlooked issue of who represents the relevant state interests. While recognizing that major economic regulations, or those with federalism implications, should be developed in consultation with generalist groups within the "Big Seven" such as the National Conference of State Legislatures or the Council of State Governments, the ACUS project aimed to facilitate additional direct channels of communication between federal and state agencies—both what Miriam Seifter has aptly termed "generalist" collections of state-level elected officials and "specialist" bodies composed of "subject-focused" state administrators.<sup>40</sup>

### **a) Cooperation: Federal-State Collaboration in the Regulatory Process**

The ACUS project was designed to enhance and encourage cooperation between federal and state officials. Ensuring that federal agencies have adequate mechanisms in place to facilitate state participation, however, was only a partial solution. Even if the FDA, for example, invited feedback from state health administrators or Attorney General office staff on a particular drug application, a mechanism is required to ensure that such an invitation is accepted. ACUS left largely unexplored how to motivate states to participate in the regulatory process. States could establish roles or divisions within their AG offices to handle relationships with federal regulators. States could play an enhanced role, too, in the post-market risk surveillance phase of the drug regulatory process. States might be particularly well suited to observe at close range the efficacy and safety of a particular drug and to collect relevant data and report back to the FDA.<sup>41</sup>

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<sup>36</sup> *Id.* at \*4.

<sup>37</sup> *Zogenix, Inc. v. Patrick*, 2014 U.S. Dist. WL 4273251 (D. Mass. Aug. 28, 2014).

<sup>38</sup> Memorandum in Support of Defendants' Motion to Dismiss Plaintiff's Verified Second Amended Complaint, *supra* note 25, at 8.

<sup>39</sup> Indeed, Massachusetts so argued. *Id.* ("[O]f course, the agency's own views should make a difference.") (citing *Williamson v. Mazda Motor of Am., Inc.*, 131 S. Ct. 1131, 1139 (2011) and *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 883 (2000)).

<sup>40</sup> Miriam Seifter, *States as Interest Groups in the Administrative Process*, 100 VA. L. REV. 953 (2014).

<sup>41</sup> Consider in this regard the recent letter five New England governors sent to the Department of Health and Human Services (HHS). The Governors, while asking HHS to overrule the FDA's Zohydro approval decision, also highlighted states' responsibility in responding to the opioid abuse crisis and outlined specific steps they were prepared to take:

We know that this crisis is about more than one drug and that a multifaceted action plan is necessary. That is why we have agreed to jointly explore a number of potential tools to address this epidemic. These

With respect to the FDA’s approval of Zohydro, to what extent did state representatives participate in the regulatory process? Although state officials can attend (or send representatives to) public drug advisory committee meetings and may register ahead of time to make comments at these events,<sup>42</sup> no state officials or other purported representatives of the states attended or spoke at the advisory committee’s public meeting about Zohydro.<sup>43</sup>

To what extent should courts facing preemption challenges—and more specifically, considering the level of deference to accord to any agency’s view regarding a regulation’s preemptive effect—consider whether the states could have participated but did not participate in the regulatory process? And how meaningful would such state participation in the drug approval process be? While the advisory committee holds public hearings and entertains comments, the committee typically votes immediately after public comments are made. Moreover, drug advisory committee members are typically scientists and statisticians, namely professionals within technical fields who might not fully appreciate the political or policy-driven nuances of state officials’ positions.<sup>44</sup>

### **b) Conflict: States Taking Matters into Their Own Hands?**

State officials unleashed a firestorm of criticism after the FDA announced it had approved Zohydro.<sup>45</sup> More than two dozen state attorneys general urged the agency to reconsider its approval, or at least to implement abuse-deterrent technology.<sup>46</sup> Other state

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include: regional data sharing among our prescription monitoring programs, regional prevention campaigns directed to the public, regional prescribing guidelines and educational campaigns to ensure safe opioid prescribing, expansion of treatment options across the region including medication assisted therapy, and increased and better coordinated law enforcement efforts.

Letter from Dannel P. Malloy, Gov., Conn., et al., to Hon. Sylvia Mathews Burwell, Sec., U.S. Dept. of Health & Human Servs. at 1 (Aug. 28, 2014), *available at* [http://www.governor.ri.gov/documents/press-attachments/NEng%20Letter-%20HHS%20Burwell\\_Opioid\\_signed\\_8-28-14.pdf](http://www.governor.ri.gov/documents/press-attachments/NEng%20Letter-%20HHS%20Burwell_Opioid_signed_8-28-14.pdf)

<sup>42</sup> Given that the media reported on FDA’s early consideration of the drug, it seems as though states could have contacted the agency at that time to express their concerns. See Anna Edney, *Zogenix Painkiller Fails to Win Support of U.S. Advisers*, BLOOMBERG NEWS (Dec. 7, 2012), <http://goo.gl/7Bu28j>. State representatives were subject to notice of the proceedings through the Federal Register, in which advisory committee meetings are announced; moreover, the fact that the story made immediate news indicates that at least some information about the drug application had been made available to the public at large. See, e.g., *id.*

<sup>43</sup> U.S. FOOD & DRUG ADMIN., ANESTHETIC & ANALGESIC DRUG PRODUCTS ADVISORY COMMITTEE MEETING TRANSCRIPT, at 214-70 (Dec. 7, 2012), *available at* <http://goo.gl/66aJLn>.

<sup>44</sup> *FDA 101: Advisory Committees*, U.S. FOOD & DRUG ADMINISTRATION, <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048040.htm> (last updated Oct. 14, 2014).

<sup>45</sup> See, e.g., Bill Trott, *State AGs Urge FDA to Rethink Approval of Painkiller Zohydro*, REUTERS (Dec. 12, 2013 5:33 PM), <http://goo.gl/KpvdeX> (reporting on a letter sent by 28 states’ attorneys general to the FDA, asking the agency to reconsider its decision to approve the drug); Ed Silverman, *Governors to HHS: Rescind FDA Approval of the Zohydro Painkiller*, WALL ST. J. (Sept. 4, 2014, 9:02 AM), <http://goo.gl/A5jhIC> (describing a letter sent by the governors of five New England states urging HHS to overturn FDA’s approval of Zohydro).

<sup>46</sup> Letter from Pamela Jo Bondi, Fla. Att’y General, et al., to Margaret Hamburg, M.D., Comm’r, U.S. Food & Drug Admin. (Dec. 10, 2013), *available at* <http://www.oag.state.md.us/Press/Zohydro.pdf>. According to the state AGs, allowing onto the market painkiller drugs without abuse-deterrent properties “created an environment whereby our nation witnessed a vicious cycle of overzealous pharmaceutical sales, doctors over-prescribing the narcotics, and patients tampering with these drugs, ultimately resulting in a nationwide prescription drug epidemic claiming thousands of lives.” *Id.* at 1.

officials raised similar concerns about the national epidemic of opioid abuse and addiction in urging the FDA to reconsider its position.<sup>47</sup> The FDA declined to do so, and instead met the criticism by defending its decision to approve the drug.<sup>48</sup>

At that point, Massachusetts took matters into its own hands and enacted its state-wide ban. It cited health and safety concerns as grounds for the ban—the very reasons rejected by the FDA in approving Zohydro, pursuant to a process that Massachusetts officials chose not to attend.<sup>49</sup> The state would thus be hard-pressed to make a claim that it had been precluded from

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Patient advocacy groups have advanced similar arguments. *See, e.g.*, Letter from The FED Up! Coalition Steering Committee to Margaret A. Hamburg, M.D., Comm’r, U.S. Food & Drug Admin. (Feb. 26, 2014), *available at* <http://www.citizen.org/documents/2185.pdf> (“In the midst of a severe drug addiction epidemic fueled by overprescribing of opioids, the very last thing the country needs is a new, dangerous, high-dose opioid.”); Laura Sullivan, *Critics Question FDA’s Approval of Zohydro*, NPR (Feb. 26, 2014, 5:00 AM), <http://www.npr.org/2014/02/26/282836473/critics-question-fdas-approval-of-zohydro> (covering an interview with representatives from patient advocacy groups, law enforcement officers, and the chief medical officer of Zogenix). *See generally* Roni Carin Rabin, *New Painkiller Rekindles Addiction Concerns*, N.Y. TIMES, Apr. 22, 2014, at D1, *available at* [http://well.blogs.nytimes.com/2014/04/21/new-painkiller-rekindles-addiction-concerns/?\\_php=true&\\_type=blogs&\\_r=0](http://well.blogs.nytimes.com/2014/04/21/new-painkiller-rekindles-addiction-concerns/?_php=true&_type=blogs&_r=0) (providing an overview of the positions taken by the FDA and its critics with respect to the agency’s decision to approve Zohydro).

<sup>47</sup> *See, e.g.*, Letter from Kirsten E. Gillibrand, U.S. Senator, et al., to Margaret Hamburg, M.D., Comm’r, U.S. Food & Drug Admin. (Dec. 6, 2013), *available at* [http://www.manchin.senate.gov/public/index.cfm/files/serve?File\\_id=a4ba49fd-9bde-4ff7-a834-2dcf0a470c38&SK=5622C75FC16231198083213DE70C2C3F](http://www.manchin.senate.gov/public/index.cfm/files/serve?File_id=a4ba49fd-9bde-4ff7-a834-2dcf0a470c38&SK=5622C75FC16231198083213DE70C2C3F) (citing statistics on opioid abuse and overdose rates); Letter from Greg Zoeller, Ind. Att’y General, et al., to Hon. Kathleen Sebelius, Sec., U.S. Dept. of Health & Human Servs. (Mar. 25, 2014), *available at* [http://ag.ky.gov/pdf\\_news/zohydro-letter.pdf](http://ag.ky.gov/pdf_news/zohydro-letter.pdf). The Governors of Massachusetts, Vermont, Connecticut, Rhode Island, and New Hampshire have also written to the HHS Secretary Burwell, urging HHS to overturn the FDA’s approval of Zohydro. Letter from Dannel P. Malloy, Gov., Conn., et al., to Hon. Sylvia Mathews Burwell, Sec., U.S. Dept. of Health & Human Servs. (Aug. 28, 2014), *available at* <http://votesmart.org/public-statement/916887/letter-to-sylvia-matthews-burwell-secretary-of-health-and-human-services-rejecting-zohydro-extended-release#.VMsK1WTF8mV..> The Governors appealed to the “public health and safety crisis” of opioid abuse in New England. *Id.*

<sup>48</sup> FDA officials most recently responded to critics by publishing an essay defending the agency’s decision in the *Journal of the American Medical Association*. Christopher M. Jones, et al., *Addressing Prescription Opioid Overdose: Data Suggest a Comprehensive Policy Approach*, 312 J. AM. MED. ASS’N 1733, 1733 (Nov. 2014). The officials suggested that policies like Massachusetts’—which in practice would affect only Zohydro, rather than the broader class of opiate drugs to which it belonged—were misguided, and provided justifications for the agency’s decision to ignore the advisory committee’s recommendation. *Id.* (describing steps that the FDA took subsequent to its approval of Zohydro to increase the safety of opiate drugs as a class).

In the months following Zohydro’s approval, Commissioner Hamburg also unequivocally defended the FDA’s position and publicly made substantive counterarguments regarding the safety of the drug. *See* Margaret Hamburg, M.D., Comm’r, U.S. Food & Drug Admin., Address to the National Rx Drug Abuse Summit: Regulating in an Era of Increasingly Sophisticated Medicines (Apr. 22, 2014), *available at* <http://www.fda.gov/newsevents/speeches/ucm394400.htm>. Moreover, in a move that could be seen as “doubling down” on its decision to green-light Zohydro, the FDA has recently approved Hysingla ER, an alternative to Zohydro that will ostensibly be in direct competition with the drug. Press Release, U.S. Food & Drug Admin., *FDA Approves Extended-Release, Single-Entity Hydrocodone Product With Abuse-Deterrent Properties* (Nov. 20, 2014), *available at* <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm423977.htm>.

<sup>49</sup> *See* Brian MacQuarrie, *Governor Declares an Emergency on Opiate Abuse*, BOSTON GLOBE (Mar. 27, 2014), <http://www.bostonglobe.com/metro/2014/03/27/with-heroin-overdoses-rise-gov-patrick-declares-public-health-emergency-mass/hOajTIJKNnSHKAnWjZ6wYL/story.html>.



presenting its case to the FDA. Moreover, the FDA—having taken a look at the state’s contrary position and the evidence it cited on its behalf—came to a different conclusion.<sup>50</sup>

The case for preemption is strong in such a situation such as this, in which the state’s contrary decision was grounded in health and safety concerns—the very same basis for the FDA’s approval decision.<sup>51</sup> The FDA considered the exact same health considerations that the state did, and its decision to nonetheless approve the drug reflected (at least as a formal matter) the outcome of a deliberate weighing of these risks against the benefits that the drug would yield. Where the states had an opportunity to participate in the agency’s decision-making process, where the agency has clearly assessed the problem underlying the states’ objection, and where the state clearly retain the authority to address the problem by other means—here, through regulating the practice of medicine—preemption of state action is, as a matter of policy, defensible.

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## 1. Regulatory Inaction; States Filling the Void

Plaintiffs point to FDA statements, policy statements, and guidance documents to make the case that the FDA has explicitly taken a position antithetical to mandatory GMO labeling. Specifically, the plaintiffs reference Commissioner Hamburg’s statements at the House subcommittee hearings, the FDA’s 1992 policy statement and the FDA’s 2001 draft guidance document.<sup>52</sup>

Vermont has countered with a legal argument that neither the FDA’s policy statement nor draft guidance is entitled to preemptive effect.<sup>53</sup> Moreover, the state argued, the FDA’s inaction with respect to GMO labeling, though deliberate, did not support a finding of preemption.<sup>54</sup>

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<sup>50</sup> See U.S. FOOD & DRUG ADMIN., CTR. FOR DRUG EVAL. & RESEARCH, REF. NO. 3396196, SUMMARY REVIEW FOR REGULATORY ACTION: NDA# 202880 30–33 (2013), *available at* [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/202880Orig1s000SumR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202880Orig1s000SumR.pdf) (recognizing the potential health and safety risks posed by opioid drugs like Zohydro, but finding these to be outweighed by the drug’s benefits).

<sup>51</sup> A more difficult case would arise whereby the state asserted a different type of purpose or interest—one that was not directly contrary to the FDA’s health and safety determination. To take an admittedly extreme example, suppose that the state enacted a ban on a painkiller drug not due to health and safety concerns, but instead because it wanted to recognize and encourage its citizens’ puritan-minded, buck-up in the face of pain streak. The U.S. Supreme Court seemed to embrace just such a “purpose-based” test in the *Pom Wonderful* case (discussed *infra*). Such an approach, however, raises difficult issues with respect to whether a court should accept a state’s rationale at face value, how to handle cases where the effects, if not the purpose, are antithetical to the federal purpose, etc. Here, too, I would encourage courts to solicit the view of the relevant federal agency—and then interrogate that position based upon the existing evidence.

<sup>52</sup> Complaint for Declaratory and Injunctive Relief at 8-9, *Grocery Mfrs. Ass’n v. Sorrell*, No. 5:14-cv-00117 (D. Vt. June 12, 2014).

<sup>53</sup> Defendants’ Motion to Dismiss Plaintiffs’ Complaint at 35, *Grocery Mfrs. Ass’n v. Sorrell*, No. 5:14-cv-00117 (D. Vt. Aug. 8, 2014).

<sup>54</sup> *Id.* at 35-36.

While the U.S. Supreme Court has not weighed in on this specific preemption issue, its decision in *Pom Wonderful LLC v. Coca-Cola Co.*, which addresses displacement of federal law by another federal law, is nonetheless enlightening.<sup>55</sup> In *Pom Wonderful*, the Ninth Circuit Court of Appeals held that FDA regulations barred the plaintiff’s federal Lanham Act (trademark) claim for an allegedly misleading label on a juice beverage.<sup>56</sup> In so ruling, the Ninth Circuit remarked that the FDA “comprehensively regulate[d] food and beverage labeling.”<sup>57</sup> Moreover, the court reasoned “for a court to act when the FDA has not—despite regulating extensively in this area—would risk undercutting the FDA’s expert judgments and authority.”<sup>58</sup> In essence, the Ninth Circuit embraced a “field preemption” view, such that even no action on the part of the FDA would preclude states taking any action to fill the void.

The Court emphatically rejected the position that the FDA had sole regulatory authority over the field of juice beverage labeling. Before the Court, the Solicitor General (representing the U.S. and the FDA) argued that “nothing in the FDCA, the NLEA, FDA’s regulations, or the preambles to those regulations suggests that FDA has marked the metes and bounds of all possible misleading material on juice labels, or that its authority must be deemed exclusive even as to matters the agency has never specifically addressed.”<sup>59</sup> Moreover, the Solicitor General highlighted “the many foods that FDA’s regulations do not specifically address at all.”<sup>60</sup> In the face of this incomplete federal regulatory scheme, the Court rejected Coca-Cola’s counter-argument that allowing Lanham Act claims would “undermine the pre-emption provision’s goal of ensuring that food and beverage manufacturers can market nationally without the burden of complying with a patchwork of requirements.”<sup>61</sup> Since Coca-Cola’s arguments parallel those made by the food industry in *Sorrell*, there is every reason to believe that the Court would extend its reasoning in *Pom Wonderful* to find that state-based labeling does not impermissibly conflict with the FDA’s failure to mandate such labeling in the context of genetically engineered foods.

## 2. Deference to the FDA

At the same time, *Pom Wonderful* also casts a cloud of doubt on deference to the FDA’s position. While the Solicitor General rejected the field preemption view of the Ninth Circuit, he did embrace a more narrow conflict preemption view—and one that would distinguish between

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<sup>55</sup> “Although the Court’s pre-emption precedent does not govern preclusion analysis in this case, its principles are instructive insofar as they are designed to assess the interaction of laws that bear on the same subject.” *POM Wonderful LLC v. Coca-Cola Co.*, 134 S. Ct. 2228, 2236 (2014).

<sup>56</sup> The plaintiff’s Lanham Act claim involved several aspects of the product’s label. The label bore the phrases “Pomegranate Blueberry” and “Flavored Blend of 5 Juices,” with the former presented above and in “larger, more conspicuous type” than the latter. *Pom Wonderful LLC v. Coca-Cola Co.*, 679 F.3d 1170, 1177 (9<sup>th</sup> Cir. 2012). The plaintiff contended that the name of the product was misleading (since it contained only a tiny percentage of pomegranate juice) and that the font size/display of the labeling was likewise misleading. *Id.*

<sup>57</sup> *Id.* at 1175.

<sup>58</sup> *Id.* at 1177.

<sup>59</sup> Brief for the United States as Amicus Curiae at 11–12, *POM Wonderful LLC v. The Coca-Cola Co.*, 134 S. Ct. 2228 (2014) (No. 12-761).

<sup>60</sup> *Id.* at 12.

<sup>61</sup> 134 S. Ct. at 2239.



the different Lanham Act claims on the basis of whether the FDA had enacted a specific regulation on point that should take priority.<sup>62</sup> The Solicitor General argued that the FDA regulations did clearly authorize defendant to name its product “Pomegranate Blueberry Flavored Blend of 5 Juices,” and that the portion of the Lanham Act claim challenging the name should thus be precluded. According to the Solicitor General, the FDA’s regulation reflected the agency’s “considered determination that complaint names would not be misleading,” based on a “weigh[ing of] the competing interests relevant to the particular requirement in question.”<sup>63</sup> Thus, according to the SG, a Lanham Act claim based on the product’s name “would directly contravene FDA’s judgment by declaring misleading what FDA determined to be nonmisleading.”<sup>64</sup> The Supreme Court rejected this analysis:

Even if agency regulations with the force of law that purport to bar other legal remedies may do so, it is a bridge too far to accept an agency’s after-the-fact statement to justify that result here. An agency may not reorder federal statutory rights without congressional authorization.<sup>65</sup>

## II. Conclusion

In this article, I advance two primary claims. First, courts, when facing preemption challenges, should consider what the FDA’s view on the matter is—namely whether the agency itself considers the state-level regulation in tension with its national regulatory agenda. In *Zogenix*, it is striking that the court paid no attention to the FDA Commissioner’s overt support of Massachusetts’ proposed restrictions on the prescribing and dispensing of Zohydro. In *Sorrell*, the court has before it informal policy guidance from the FDA that suggests that the agency has not taken a definitive position against state mandatory labeling. Deference to the FDA’s position in each case provides resolution to the preemption challenge.

Second, these cases reiterate and reinforce an argument I have previously articulated and that was at the heart of the ACUS Recommendation: if we are ever to achieve a coherent body of case law and regulatory policy in the realm of food and drug laws, courts should take heed of the degree to which the federal agency gave due regard to relevant state interests before acting.<sup>66</sup> Rather than blindly defer to the federal agency’s view, they should evaluate whether that view was adopted in a context that warrants deference—and this evaluation should consider the extent to which states had a meaningful opportunity to put forth their view of how the state regulation fits with the federal regulatory scheme.

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<sup>62</sup> Brief for the United States as Amicus Curiae, *supra* note 82, at 29.

<sup>63</sup> *Id.* at 9.

<sup>64</sup> *Id.*

<sup>65</sup> 134 S. Ct. at 2241.

<sup>66</sup> See Catherine M. Sharkey, *Products Liability Preemption: An Institutional Approach*, 76 GEO. WASH. L. REV. 449 (2008) (proposing a novel “agency reference” model for judicial review in the field of products liability preemption); see also Catherine M. Sharkey, *Federalism Accountability: “Agency-Forcing” Measures*, 58 DUKE L.J. 2125 (2009) (elaborating on the federalism dimension of this judicial model).

UNITED STATES DISTRICT COURT  
DISTRICT OF MASSACHUSETTS

CIVIL ACTION NO. 14-11689-RWZ

ZOGENIX, INC.

v.

DEVAL PATRICK, in his official capacity as  
GOVERNOR OF MASSACHUSETTS, *et al.*

MEMORANDUM OF DECISION

July 8, 2014

ZOBEL, D.J.

The issue is whether two Massachusetts regulations limiting the prescribing and handling of Zohydro™ ER (“Zohydro”), a Food and Drug Administration-approved opioid analgesic, frustrate federal statutory objectives in violation of the Supremacy Clause of the United States Constitution. Plaintiff Zogenix, Inc., believes they do and moves for a preliminary injunction barring their enforcement (Docket # 46).

Defendants, Commonwealth health officials sued in their official capacities, believe they do not and move to dismiss (Docket # 44). Plaintiff’s motion is ALLOWED IN PART and DENIED IN PART. Defendants’ motion is DENIED.

**I. Background<sup>1</sup>**

On October 25, 2013, the Food and Drug Administration (“FDA”) approved

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<sup>1</sup>I take the basic, undisputed facts from the Verified Second Amended Complaint (Docket # 51).

whether the drug is safe. 21 C.F.R. § 314.125(b)(3)-(4). But if a new drug passes the benefit-risk assessment, the FDA “promote[s] the public health” by making it available to the public. 21 U.S.C. § 393(b)(1).

The essence of plaintiff’s preemption argument is that defendants are trying to make scarce or altogether unavailable a drug that the FDA, by approving it, has said should be available. First, they contend the regulations amount to a *de facto* ban on Zohydro. The LMN requirement that “other pain management treatments have failed” requires a physician to cycle a patient through unnecessary and possibly dangerous pain management alternatives before prescribing Zohydro. And the “pharmacist-only” regulation is incompatible with the staffing structure of many pharmacies, making it impracticable for pharmacies to carry Zohydro. If physicians cannot readily prescribe Zohydro and pharmacies will not stock it, then Zohydro is not, as the FDA required, available to the public. Second, it claims that federal law preempts the regulations even if they do not functionally ban Zohydro. The FDA approved Zohydro for “management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.” Docket # 49-1 at 29. The alternative treatment options must only be inadequate; they need not have been tried and failed, as the Commonwealth’s regulation requires. The regulation thus undermines the FDA’s power to approve drugs for specific uses and purposes.

Defendants see it differently. The “LMN regulation” does not refer to any particular treatments that must fail. The regulation does not require physicians to prescribe other opioids or subject patients to medically ill-advised treatments before

prescribing Zohydro. Mem. in Supp. of Mot. to Dismiss, Docket # 45, at 12 n.12. The regulation gives physicians far more flexibility than plaintiff is willing to admit. Zohydro will thus remain available, and the regulations are permissible. Furthermore, state governments have primary authority to regulate health and safety, including the practice of medical professionals. The FDA itself has recognized that it “does not generally regulate the practice of pharmacy or the practice of medicine -- the States traditionally have regulated both the prescribing and dispensing of drugs.” Hearing Before the Subcomm. on Oversight & Investigations of the House Comm. on Commerce, 106th Cong. 99 (1999) (statement of Janet Woodcock, M.D., Director of the FDA Center for Drug Evaluation & Research). Defendants are not treading on federal ground, they say, but are merely regulating within the proper scope of their constitutional authority.

Sure enough, the Commonwealth’s police powers permit it to regulate the administration of drugs by the health professions. Gonzales v. Oregon, 546 U.S. 243, 270-71 (2006); Whalen v. Roe, 429 U.S. 589, 603 (1977). But it may not exercise those powers in a way that is inconsistent with federal law. Preemption principles have no less heft because health is a matter of “special concern” to the states. Fidelity Fed. Sav. & Loan Ass’n v. de la Cuesta, 458 U.S. 141, 153 (1982) (concluding as much with respect to real property law); see Free v. Bland, 369 U.S. 663, 666 (1962) (“The relative importance to the State of its own law is not material when there is a conflict with a valid federal law, for the Framers of our Constitution provided that the federal law must prevail.”); Gibbons v. Ogden, 22 U.S. (9 Wheat.) 1, 210 (1824) (state laws

passed pursuant to police powers must yield if they conflict with federal law). To say, as defendants do, that they are exercising their constitutional authority does not answer the question. I must do as Savage instructs and assess whether the regulations prevent the accomplishment of the FDCA's objective that safe and effective drugs be available to the public.

By any reckoning, the text of the "LMN regulation" is ambiguous. Exactly what "pain management treatments" must fail before a doctor may prescribe Zohydro? Plaintiff believes other opioids must fail. Defendants do not believe a physician must prescribe other opioids before she may prescribe Zohydro. One need look no further than defendants' own affiant to doubt their position. The affidavit of Dr. Jane Liebschutz, Associate Chief of General Internal Medicine at Boston Medical Center, states the following:

- "[B]efore a provider could appropriately prescribe Zohydro™ ER, there would have to be a series of conditions met. First and foremost, the patient would have to have tried multiple non-opioid medications." Docket # 56-5 ¶ 2.
- "I would not prescribe Zohydro™ ER to a patient who had not been on daily short-acting opioids for at least 12 weeks. In my professional opinion, Zohydro™ ER is only suitable for patients who are already opioid tolerant[.]" Id. ¶ 3.
- "In my professional opinion, Zohydro™ ER would be a *last-resort opioid* because there are safer and more effective options for treating pain such as long acting morphine, and long-acting oxycodone with abuse-deterrent formulation (e.g. Oxycontin™). Id. ¶ 7 (emphasis added).

Of course, this may be one doctor's opinion. But if the Commonwealth interprets its regulation to make Zohydro a last-resort opioid, it undeniably makes Zohydro less

available. That presents a constitutional problem.

The “LMN regulation” is unclear in another way. How long ago must the “other pain management treatments” have failed? As a Schedule II drug, Zohydro prescriptions are subject to a thirty-day maximum. Sec. Am. Compl., Docket # 51, ¶ 48. Must a physician try a new treatment—or, because it is plural in the regulation, *treatments*—before writing each new prescription, or may she rely upon a failed treatment in the more distant past? If she may, how distant? For example, if a physician had prescribed a different opioid six months ago with no success, could she write a prescription for Zohydro and still comply with the “LMN regulation?” Could a fellow physician rely on a failed regimen of vitamins and acupuncture two months ago? What, indeed, does “failure” mean in this context? The regulation has no response to these rather obvious contingencies. If the Commonwealth interpreted its regulation to require a fresh failure as a precondition to each 30-day Zohydro prescription, it would severely frustrate Zohydro’s availability and pose significant constitutional concerns.

As for the “pharmacist-only regulation,” the parties rely on competing affidavits. In a sealed declaration, Zogenix co-founder and Chief Executive Officer Roger L. Hawley discloses that unspecified major retail pharmacy chains do not plan to stock Zohydro because the “pharmacist-only regulation” is “fundamentally incompatible with personnel infrastructure and established policies for dispensing ER/LA opioids.” Declaration of Roger L. Hawley ¶ 3. Defendants present the affidavit of Michael Reppucci, R. Ph., owner of and pharmacist at Inman Pharmacy in Cambridge, Massachusetts. Docket # 56-6. Reppucci states that because BORIP already regulates

pharmacy technicians, “prohibiting any pharmacy technicians from transporting and handling Zohydro does not add any substantial administrative burden or present substantial logistical problems.” Id. ¶ 6. Neither party directs the court to any pharmacy’s announcement that it will or will not carry Zohydro.

What is the proper remedy given such uncertainty? Defendants may interpret and enforce the challenged regulations in a way that obstructs the FDCA’s objectives. At present, however, given the lack of a record of enforcement, it is unclear whether such an obstacle exists. The Supreme Court has reminded lower courts that they should not find preemption where there is no clearly discernible conflict between state and federal law. See Geier v. Am. Honda Motor Co., 529 U.S. 861, 866 (2000); Huron Portland Cement Co. v. City of Detroit, 362 U.S. 440, 446 (1960). At the same time, plaintiff should not bear the brunt of the defendants’ vague regulations, waiting for an adequate record of enforcement to develop while the clock ticks on its three-year exclusivity period. See 21 U.S.C. §§ 355(c)(3)(E); (j)(5)(F). And of course, defendants may not use vague regulations to sidestep or countermand federal law.

With these principles in mind, I conclude as follows:

- Plaintiff has stated a plausible claim for relief. Defendants’ motion to dismiss is denied without prejudice.<sup>4</sup>
- Plaintiff’s motion to preliminarily enjoin the “LMN regulation,” 243 CMR 2.07(25)(d) and 263 CMR 5.07(12)(d), is allowed. If defendants provide adequate and constitutional guidance to physicians regarding the prerequisites for prescribing Zohydro in compliance with the regulation, then they may thereafter move to lift the injunction.

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<sup>4</sup>Defendants also move to dismiss on standing grounds, but they failed to develop this argument in their memorandum in support of their motion to dismiss. It is therefore waived.

- Because its sealed declaration does not provide sufficient detail that pharmacies will not carry Zohydro, plaintiff has not met its burden of proof on the “pharmacist-only regulation,” 247 CMR 8.05(3). Its motion for a preliminary injunction is denied without prejudice to renewal upon a more detailed submission.

#### **IV. Conclusion**

Plaintiff’s motion for a preliminary injunction (Docket # 46) is ALLOWED IN PART and DENIED IN PART without prejudice. Defendants’ motion to dismiss (Docket # 44) is DENIED without prejudice.

July 8, 2014

DATE

/s/Rya W. Zobel

RYA W. ZOBEL  
UNITED STATES DISTRICT JUDGE



UNITED STATES DISTRICT COURT  
DISTRICT OF MASSACHUSETTS

CIVIL ACTION NO. 14-11689-RWZ

ZOGENIX, INC.

v.

DEVAL PATRICK, in his official capacity as  
GOVERNOR OF MASSACHUSETTS, *et al.*

MEMORANDUM OF DECISION

August 28, 2014

ZOBEL, D.J.

On July 8, 2014, I preliminarily enjoined two Massachusetts regulations which required that a licensed prescriber write a “letter of medical necessity” certifying “that other pain management treatments have failed” before prescribing Zohydro ER<sup>TM</sup> (“Zohydro”). Docket # 66 at 10 (citing 243 CMR § 2.07(25)(d); 263 CMR § 5.07(12)(d)). I invited defendants, Commonwealth health officials sued in their official capacities, to move to lift the injunction if they “provid[ed] adequate and constitutional guidance to physicians regarding the prerequisites for prescribing Zohydro.” *Id.* Defendants have accepted the invitation and so moved, arguing, *inter alia*,<sup>1</sup> that the Commonwealth has promulgated new regulations which no longer offend the Supremacy Clause of the United States Constitution. Docket # 68; see U.S. Const. art. VI cl. 2. I agree and lift

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<sup>1</sup>Defendants also argue that my July 8, 2014 memorandum was moot—at least in part—because the old regulations had expired before it was issued. I need not address that argument given today’s memorandum.

found a sufficiently alleged injury. See Harvey v. Veneman, 396 F.3d 28, 34 (1st Cir. 2005); Mass. Indep. Certification, Inc. v. Johanns, 486 F. Supp. 2d 105, 114-15 (D. Mass. 2007). Plaintiff satisfies the injury prong.

Defendants contest the causation prong on the ground that plaintiff cannot trace its reputational injury to the passage of the regulations, “as opposed to one or more of the multitude of well-publicized critical comments.” Docket # 56 at 17. Plaintiff must show that the injury it alleges is not “overly attenuated” from the challenged action. Donahue v. City of Bos., 304 F.3d 110, 115 (1st Cir. 2002). It doubtless has done so. The economic injury it alleges is directly tied to the regulations; in other words, the burdens the regulations impose on prescribers lead them to write fewer prescriptions, which impacts plaintiff’s bottom line. And although defendants have not been the only parties to criticize Zohydro, the Commonwealth’s ban and subsequent restrictions on the drug have been highly publicized. It is not “overly attenuated” to trace a reputational injury to the regulations and the accompanying publicity. Plaintiff satisfies the causation prong.

Defendants concede redressability, and I agree that a favorable resolution of plaintiff’s claim would likely redress the alleged injury. Katz, 672 F.3d at 72. Having satisfied each part of the “familiar triad,” plaintiff has constitutional standing to sue.

## **B. Merits**

Obstacle preemption, on which plaintiff relies, occurs when, “under the circumstances of [the] particular case, [the challenged state law] stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.”

Hines v. Davidowitz, 312 U.S. 52, 67 (1941). The doctrine requires a conflict between state and federal law. See id.; Savage v. Jones, 225 U.S. 501, 533 (1912). Here, however, the new regulation omits the conflicting, troublesome language. Where formerly other pain management treatments must have “failed,” now they must be “inadequate.” 243 CMR § 2.07(25)(a) (Docket # 65-1); 263 CMR § 5.07(12)(a) (Docket # 68-1).<sup>2</sup> The substitution is significant for two reasons.

First, the words have different meanings. “Fail” means “[t]o prove so deficient as to be totally ineffective” or “[t]o be unsuccessful,” Webster’s II New Riverside University Dictionary 461 (1984), whereas “inadequate” means not “[a]ble to satisfy a requirement.” Id. 616 (referencing id. 78). If a course of action has failed, it has been tried but has proven unsuccessful. But a course of action need not be tried to be “inadequate;” it must simply be unable to satisfy a requirement. The upshot is that the new regulation does not require a licensed prescriber to actually prescribe “other pain management treatments.” Instead, he or she must only consider those treatments unable to satisfy the relevant requirement—here, alleviating the patient’s pain. Taken one step further, the new regulation does not relegate Zohydro to a last-resort opioid, which, as I explained in my prior memorandum, “makes Zohydro less available” and therefore “presents a constitutional problem.” Docket # 66 at 8-9. The obstacle—mandatory preliminary prescribing of other opioids—has now been removed.

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<sup>2</sup>The Board of Registration in Pharmacy (“BORIP”) has also promulgated a new regulation, which provides that pharmacy interns may handle Zohydro, but certified pharmacy technicians, pharmacy technicians, and pharmacy technician trainees may not. 247 CMR § 8.05(3) (Docket # 65-2). This memorandum does not address the BORIP regulation.

Second, the new regulation mimics the language the Food and Drug Administration approved for Zohydro's label. See Docket # 51-8. Plaintiff has conceded that such a regulation passes constitutional muster.

THE COURT: Now, assume for the moment that the doctor's regulations include the letter of medical necessity without any reference to failed treatments. Would there be a problem?

MR. HOLLMAN [Counsel for Plaintiff]: If the medical necessity is only the same as the approved indication, which is to show that other – which is to state that other medications are inadequate, that would be supported by the clinical testing that was performed, supported by the approval that the FDA gave, and it would be consistent with the FDA's approval. So, no, under those circumstances, no objection.

Transcript of June 10, 2014 Oral Argument at 14-15. Plaintiff's statement sums it up neatly: there is no conflict between state and federal law, and thus, no preemption.

**C. Conclusion**

Defendants' motion to vacate the preliminary injunction (Docket # 68) is ALLOWED. The court has set a scheduling conference for September 11, 2014, at 3:00 p.m.

August 28, 2014

DATE

/s/Rya W. Zobel

RYA W. ZOBEL  
UNITED STATES DISTRICT JUDGE