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## Federal Regulatory Responses to the Prescription Opioid Crisis: Too Little, Too Late?

Lars Noah  
*University of Florida*

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FEDERAL REGULATORY RESPONSES  
TO THE PRESCRIPTION OPIOID CRISIS:  
TOO LITTLE, TOO LATE?

Lars Noah\*

I first wrote about opioid analgesics more than fifteen years ago.<sup>1</sup> After contrasting the clinical mindset of the U.S. Food and Drug Administration (FDA) with the law enforcement mentality of the Drug Enforcement Administration (DEA), I called for a public health perspective of the sort embodied by the U.S. Centers for Disease Control and Prevention (CDC).<sup>2</sup> Alas, it took a dozen years for the CDC to answer that challenge, issuing guidelines that recommended cautious prescribing by primary care physicians.<sup>3</sup> Separately, my 2003 article had urged the FDA to consider more aggressive distribution controls,<sup>4</sup> but that agency's subsequent efforts to further restrict access to powerful narcotics strike me as entirely too feeble.<sup>5</sup> Watching this crisis continue to deepen—while various government actors engaged in little more than posturing—has convinced me that we needed stronger medicine from the outset.

Part I of this Article suggests that the medical establishment shares more blame for the crisis than many commentators seem to appreciate. Part II canvasses a variety of ways in which the federal government has responded to the opioid problem during the last few years before delving more deeply into the FDA's role in the mess,

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\* © 2019 Lars Noah. Chesterfield Smith Eminent Scholar, University Term Professor, and Professor of Law, University of Florida; author, *LAW, MEDICINE, AND MEDICAL TECHNOLOGY* (Foundation Press 4th ed. 2017).

<sup>1</sup> Lars Noah, *Challenges in the Federal Regulation of Pain Management Technologies*, 31 J.L. MED. & ETHICS 55 (2003).

<sup>2</sup> See *id.* at 64 (“A public health perspective, which the Centers for Disease Control and Prevention (CDC) has expressed in connection with antibiotics as well as vaccine programs, might help to mediate between these two potentially incompatible perspectives.” (footnote omitted)); *id.* at 56 (“[R]ecommending a public health approach that attempts to bridge the FDA’s predominantly clinical focus and the DEA’s preoccupation with the potential adverse consequences for third parties.”).

<sup>3</sup> The CDC proposed guidelines in 2015, which it finalized the following year. See Sabrina Tavernise, *New Standards for Painkillers Aim to Stem Overdose Deaths*, N.Y. TIMES, Mar. 16, 2016, at A1 (summarizing some of the controversy surrounding the issuance of these technically nonbinding guidelines). The CDC recommended, among other things, that physicians first try nonopioid therapies—and then prescribe only a three- to seven-day course of opioids—when treating patients with acute pain. See Deborah Dowell et al., *CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016*, 315 JAMA 1624, 1638 box 5 (2016); Thomas R. Frieden & Debra Houry, *Reducing the Risks of Relief—The CDC Opioid-Prescribing Guideline*, 374 NEW ENG. J. MED. 1501, 1503 (2016) (“When prescribing opioids, the rule of thumb is to ‘start low and go slow.’”).

<sup>4</sup> See Noah, *supra* note 1, at 64.

<sup>5</sup> See *infra* Part II.D.

assessing the different tools that it has tried to use as well as some that it failed to employ. This Article concludes that the agency should have allowed only a narrowly defined subset of physicians to prescribe opioid analgesics, even though the medical community would have pitched a fit about any such intrusion on its prerogatives, to say nothing of the drug manufacturers aghast at the prospect of far more modest sales. Greater use of such restrictions on distribution might have worked to nip this disaster in the bud, and it needs more serious consideration by the FDA before the next one comes down the pike.

### I. SEARCHING HIGH AND LOW FOR CULPRITS

The prescribing of opioids peaked almost a decade ago,<sup>6</sup> but the consequences of the resulting addiction and abuse will linger for many years to come, with few good solutions in sight. Although there is plenty of blame to go around,<sup>7</sup> and the latest wave of tort litigation has identified some handy targets in the industry,<sup>8</sup> it remains useful to try to understand how this happened—and might have been avoided—before a different category of overused pharmaceutical products ushers in the next public health crisis.<sup>9</sup>

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<sup>6</sup> See Anne Schuchat et al., *New Data on Opioid Use and Prescribing in the United States*, 318 JAMA 425, 425 (2017); Abby Goodnough, *Report Finds a Decline in Opioid Prescriptions After a 2010 Peak*, N.Y. TIMES, July 6, 2017, at A13.

<sup>7</sup> See Robert J. Blendon & John M. Benson, *The Public and the Opioid-Abuse Epidemic*, 378 NEW ENG. J. MED. 407, 410 (2018) (reporting that one recent opinion poll found that “the public placed the most blame on doctors who inappropriately prescribe painkillers (33%)”); *id.* at 408 (presenting results from the same poll which showed that 13% blamed pharmaceutical companies and 7% blamed the FDA).

<sup>8</sup> As I have explained in commenting to the press, however, this strikes me as unproductive scapegoating. See Harriet Ryan, *Washington City Sues OxyContin Drugmaker; Everett, Hit Hard by Opioid Addiction, Alleges That Purdue Pharma Ignored Criminal Trafficking*, L.A. TIMES, Jan. 20, 2017, at A1; Mitch Smith & Monica Davey, *With Overdoses on Rise, Cities and Counties Look for Someone to Blame*, N.Y. TIMES, Dec. 22, 2017, at A18 (“Critics say the litigation is a sideshow in the opioid debate—a chance for lawyers to make money and politicians to make headlines—rather than a lasting solution in the overwhelming crisis . . .”).

<sup>9</sup> See, e.g., ALAN SCHWARZ, *ADHD NATION: CHILDREN, DOCTORS, BIG PHARMA, AND THE MAKING OF AN AMERICAN EPIDEMIC* (2016) (discussing the burgeoning use of Schedule II stimulants approved to treat attention deficit hyperactivity disorder); Kirk E. Evoy et al., *Abuse and Misuse of Pregabalin and Gabapentin*, 77 DRUGS 403, 404 (2017) (observing that “less publicized is the increasing abuse of prescription drugs once considered to have little or no abuse potential, among them gabapentin and pregabalin”); *id.* at 424 (concluding a systematic review of the available literature with a call for greater attention to the possibility of abuse but not yet restrictions on the use of gabapentinoids); Anna Lembke et al., *Our Other Prescription Drug Problem*, 378 NEW ENG. J. MED. 693, 694 (2018) (“Despite the many parallels to the opioid epidemic, there has been little discussion in the media or among clinicians, policymakers, and educators about the problem of overprescribing and overuse of benzodiazepines . . .”); *cf.* Stephen Mihm, *Opinion, This Isn’t the First U.S. Opiate-Addiction Crisis*, CHI. TRIB., July 17, 2017, at A11 (“The first great U.S. opiate-addiction

After some time away from the narrower subject of narcotic analgesics, I have now come to believe that the medical community deserves a fair dose of the blame for what has happened. I do not mean venal operators of pill mills or other bad apples among health care professionals;<sup>10</sup> instead, I have in mind the far larger number of well-intentioned physicians who have allowed themselves to get duped too easily and then found themselves far out of their depths.<sup>11</sup> The drumbeat about the undertreatment of pain began in earnest in the late 1980s,<sup>12</sup> and not long thereafter medical experts began urging their colleagues to rethink the well-entrenched resistance to using opioids, relying on only the barest of evidence to make their point.<sup>13</sup> Rather than celebrate caution in the use of narcotic analgesics, these

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epidemic [i.e., the use of morphine after the Civil War] began much the same way, with medications handed out by well-meaning doctors who embraced a wondrous new class of drugs as the answer to a wide range of aches and pains.”)

<sup>10</sup> See Carrie Teegardin, *Years into the Opioid Crisis, the Nation Still Struggles to Rein in Doctors*, ATLANTA J.-CONST., Dec. 3, 2017, at A1 (“[S]ince 2016, more than 1,000 doctors have been brought before medical boards for improperly prescribing opioids to patients. In that same time, nearly 150 have been in federal court on opioid drug charges. Every month, authorities bust another round of doctors gone rogue.”).

<sup>11</sup> See Carrie Teegardin, *The Opioid Crisis; Doctors Rethink Pain Treatment*, ATLANTA J.-CONST., Dec. 7, 2017, at A1 (“[W]ell-meaning physicians who were trained to aggressively treat pain are also a big part of the problem.”); Editorial, *Doctors Fueled Opioid Crisis. Can They Help Cure It?*, USA TODAY, Mar. 20, 2018, at A5 (“Physicians, many of them well-meaning, helped fuel the crisis by handing out opioids like candy.”); *id.* (“Far too many physicians haven’t changed their prescribing habits, even in the face of government guidance, state restrictions, heavy news coverage and studies showing the advantages of other painkillers.”); see also Jonathan H. Chen et al., *Distribution of Opioids by Different Types of Medicare Prescribers*, 176 JAMA INTERNAL MED. 259, 260–61 (2016) (“High-volume prescribers are not alone responsible for the high national volume of opioid prescriptions. Efforts to curtail national opioid overprescribing must address a broad swath of prescribers to be effective.”).

<sup>12</sup> See, e.g., Julie A. Steele, *Cancer Pain: Its Management Emerges as Public Health Issue*, 82 J. NAT’L CANCER INST. 646 (1990); Daniel Goleman, *Patient Care; Physicians Said to Persist in Undertreating Pain and Ignoring the Evidence*, N.Y. TIMES, Dec. 31, 1987, at B5.

<sup>13</sup> See, e.g., Pamela T.M. Leung et al., Letter, *A 1980 Letter on the Risk of Opioid Addiction*, 376 NEW ENG. J. MED. 2194, 2194 (2017) (finding that a “five-sentence letter . . . was heavily and uncritically cited as evidence that addiction was rare with long-term opioid therapy”); Marcia L. Meldrum, *The Ongoing Opioid Prescription Epidemic: Historical Context*, 106 AM. J. PUB. HEALTH 1365, 1365 (2016) (describing the handful of publications from the 1980s that “became the rather fragile foundation of a 20-year campaign for the long-term use of opioids in chronic noncancer pain”); see also Roger Chou et al., *The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop*, 162 ANNALS INTERNAL MED. 276, 283 (2015) (“[R]eliable conclusions about the effectiveness of long-term opioid therapy for chronic pain are not possible due to the paucity of research to date.”); *id.* at 282 (“[T]he lack of scientific evidence on effectiveness and harms of long-term opioid therapy

popularizers condemned “opiophobia” as unenlightened, even barbaric.<sup>14</sup> Drug manufacturers, of course, saw this as an emerging business opportunity, and an ineffectual FDA quickly lost control of the situation. In short, this country had the conditions for a perfect storm that has left lasting damage.<sup>15</sup>

Almost a quarter of a century has passed since the FDA approved an extended-release (ER) version of the Schedule II drug oxycodone (OxyContin®).<sup>16</sup> As a consequence of an aggressive promotional campaign for this controlled substance,<sup>17</sup> OxyContin quickly became an unexpected blockbuster for its manufacturer, Purdue Pharma.<sup>18</sup> This product hardly represented the first opioid analgesic licensed by the

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for chronic pain is clear and is in striking contrast to its widespread use for this condition . . .”).

<sup>14</sup> See Thomas Catan & Evan Perez, *A Pain-Drug Champion Has Second Thoughts*, WALL ST. J., Dec. 15, 2012, at A1; Peter Whoriskey, *The Prescription Painkiller Binge*, WASH. POST, Dec. 31, 2012, at A1 (“[D]rug manufacturers and some pain specialists helped create a body of scientific research assuaging the long-standing worries about opioids and pushed to expand the use of the drugs . . . [One prominent academic funded by the industry] has since expressed regret for his evangelism on behalf of opioids.”).

<sup>15</sup> See William C. Becker & David A. Fiellin, Editorial, *Limited Evidence, Faulty Reasoning, and Potential for a Global Opioid Crisis: Other Countries Must Learn from the Public Health Devastation in the US*, 358 BMJ j3115 (2017); see also Darlena Cunha, *Chronic Pain Meets Worries About Opioid Addiction*, WASH. POST, Feb. 2, 2016, at E1 (“The United States uses 80 percent of the world’s opioids, . . . yet it makes up less than 5 percent of the world’s population.”). See generally ANNA LEMBKE, *DRUG DEALER, MD: HOW DOCTORS WERE DUPED, PATIENTS GOT HOOKED, AND WHY IT’S SO HARD TO STOP* ch. 4 (2016).

<sup>16</sup> See Paul Tough, *The Alchemy of OxyContin*, N.Y. TIMES MAG., July 29, 2001, at 32.

<sup>17</sup> See Art Van Zee, *The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy*, 99 AM. J. PUB. HEALTH 221, 221–23, 225 (2009).

<sup>18</sup> See Chris Adams, *Painkiller’s Sales Far Exceeded Maker’s Plans—Purdue Pharma Scrambled to Expand Its Production of OxyContin Medication*, WALL ST. J., May 16, 2002, at D2. For more about the history of this drug, though focusing on Purdue’s success in blocking generic competition, see Lars Noah, *Product Hopping 2.0: Getting the FDA to Yank Your Original License Beats Stacking Patents*, 19 MARQ. INTELL. PROP. L. REV. 161, 172–79 (2015); Ameet Sarpatwari et al., *The Opioid Epidemic: Fixing a Broken Pharmaceutical Market*, 11 HARV. L. & POL’Y REV. 463, 466–74 (2017) (contrasting the experience with Purdue’s older ER morphine product MS Contin®). The recommendations offered by the latter set of commentators had little, however, to do with the particular hazards of opioid analgesics; indeed, their ideas for challenging weak patents and responding to anticompetitive behaviors, see *id.* at 477–84, would, on balance, only make the problem worse by driving down prices and increasing supply, see Barrett Devlin et al., *U.S. on Alert for Canadian Drugs*, WALL ST. J., Dec. 5, 2012, at A2 (“Generic medications are usually welcomed in the marketplace as less-expensive alternatives to popular drugs. But in the case of painkillers, many health advocates are wary they will undo years of effort to make it harder for addicts to abuse the pills.”); Anna Wilde Mathews & Leila Abboud, *FDA Approves Generic OxyContin; Teva, Endo Get Clearance After Agreeing to Implement Abuse-Reduction Programs*, WALL ST. J., Mar. 24, 2004, at A3 (“Law-enforcement officials have long been concerned about the potential for a bigger, cheaper, less well-controlled supply once versions of OxyContin are marketed by multiple companies.”).

FDA,<sup>19</sup> but the decision to approve it has left a painful legacy for this country.<sup>20</sup> Nonetheless, the agency continued to approve other long-acting (LA) opioids,<sup>21</sup> including Opana ER<sup>®</sup> (oxymorphone) in 2006,<sup>22</sup> the novel Schedule II analgesic Nucynta<sup>®</sup> (tapentadol) in 2008,<sup>23</sup> the transdermal patch Butrans<sup>®</sup> (buprenorphine) in 2010,<sup>24</sup> and Zohydro ER<sup>®</sup> (hydrocodone) in 2013,<sup>25</sup> as well as novel dosage formulations of the even more powerful narcotic fentanyl such as Onsolis<sup>®</sup> (buccal soluble

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<sup>19</sup> See Jerry Mitchell & Laura Ungar, *How Painkillers Became Killers*, MILWAUKEE J. SENTINEL, Jan. 29, 2018, at A9 (“In 1950, the FDA approved Percodan, which combined oxycodone with aspirin. Nearly a quarter-century later, Percocet—a combination of oxycodone and acetaminophen—followed.”). The agency also previously had authorized the sale of combination drugs using hydrocodone (e.g., Vicodin<sup>®</sup> and Lortab<sup>®</sup>). See Noah, *supra* note 1, at 62; see also *id.* at 58 (referencing the FDA-approved Schedule II drugs hydromorphone (e.g., Dilaudid<sup>®</sup>) and meperidine (e.g., Demerol<sup>®</sup>)). Nonetheless, in this era the FDA appeared to share some of the medical community’s opiophobia. See *id.* at 57 (In approving Zomax<sup>®</sup> (zomepirac) in 1980, “agency reviewers thought that it could substitute for narcotics used in the treatment of severe pain. This excessive concern about patient use of any controlled substances—so much so that it would displace the FDA’s normal resistance to approving nonessential products that create a risk of cancer—appears repeatedly in other contexts.” (endnote omitted)).

<sup>20</sup> See Susan Okie, *How One Painkiller Led to Nationwide Heartbreak*, WASH. POST, Sept. 30, 2018, at B6 (reviewing BETH MACY, *DOPESICK: DEALERS, DOCTORS, AND THE DRUG COMPANY THAT ADDICTED AMERICA* (2018)); see also Betsy McKay, *U.S. Life Expectancy Declines Further*, WALL ST. J., Nov. 29, 2018, at A1 (“Drug-overdose deaths skyrocketed between 2015 and 2017, particularly for adults between ages 25 and 54. The main culprit was fentanyl and other synthetic opioids that became pervasive in illicit drug supplies in the U.S. around that time. Deaths from synthetic opioids rose 45% in 2017, while the death rate from heroin, which had risen sharply after 2010, was flat.”).

<sup>21</sup> See Sabrina Tavernise, *Pressured on Opioids, F.D.A. Takes Steps to Toughen Stance*, N.Y. TIMES, Feb. 5, 2016, at A12 (“The F.D.A. has come under fire for continuing to approve opioids.”).

<sup>22</sup> See Linda Loyd, *Endo Gets Painkiller Approval*, PHILA. INQUIRER, June 24, 2006, at E1; cf. *infra* note 82 and accompanying text (explaining that the manufacturer withdrew a follow-on version of this drug in 2017).

<sup>23</sup> See Final Rule, Schedules of Controlled Substances: Placement of Tapentadol into Schedule II, 74 Fed. Reg. 23,790, 23,791 (May 21, 2009) (codified at 21 C.F.R. pt 1308); see also Sheridan M. Hoy, *Tapentadol Extended Release: In Adults with Chronic Pain*, 72 DRUGS 375, 389–90 (2012) (discussing the long-acting version approved by the FDA three years later).

<sup>24</sup> See Victoria Colliver, *Controlling Chronic Pain Without Dangerous Drugs*, S.F. CHRON., June 5, 2013, at C1. Because it carries a lower risk of abuse, buprenorphine falls into Schedule III. See 21 C.F.R. § 1308.13(e)(2)(i) (2018). At higher doses, this long-acting opioid has become a popular medication for treating opiate addiction. See *infra* note 77 and accompanying text.

<sup>25</sup> See Lars Noah, *State Affronts to Federal Primacy in the Licensure of Pharmaceutical Products*, 2016 MICH. ST. L. REV. 1, 3–7, 13–16 (discussing this controversial approval and the efforts of a few states to prohibit use of the drug); *id.* at 4 (explaining that the approval “drew howls of protest from public health experts and law enforcement officials”); *id.* at 12 (“[M]any observers had misgivings about the wisdom of the FDA’s risk-benefit judgment

film) and Subsys<sup>®</sup> (sublingual spray).<sup>26</sup> Most recently, the FDA approved a sublingual tablet containing the still stronger opioid sufentanil (Dsuvia<sup>®</sup>).<sup>27</sup>

After previously shunning opioids, physicians came to embrace these drugs as a quick fix for a complex problem.<sup>28</sup> Entirely apart from pressures to keep customers satisfied,<sup>29</sup> the well-known role of the placebo response makes it imperative that physicians have something to offer their patients when complaining of pain.<sup>30</sup> As nonnarcotic analgesics increasingly moved to over-the-counter (OTC) status, which

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on Zohydro, and public health officials in Massachusetts had decided to take more seriously concerns about abuse and diversion, especially in light of doubts about the need for yet another powerful opioid analgesic.”).

<sup>26</sup> See Alan M. Wolf, *Local Cancer Drug Gets FDA OK*, NEWS & OBSERVER (Raleigh, NC), July 17, 2009, at B4 (Onsolis); *FDA Backs Pain Reliever from Phoenix Company*, ARIZ. REPUBLIC, Jan. 7, 2012, at D2 (Subsys); see also Linda Loyd, *Fast-Acting Pain Lozenge Is Approved*, PHILA. INQUIRER, Sept. 26, 2006, at D1. There was also a nasal spray version (Lazanda<sup>®</sup>). Previously approved fentanyl products included transdermal patches (Duragesic<sup>®</sup>) and lollipops (Actiq<sup>®</sup>). See Noah, *supra* note 1, at 61–62; Harrison Smith, *Professor’s Fentanyl Lollipop Helped Cancer Patients Alleviate Severe Pain*, WASH. POST, Aug. 8, 2017, at B5 (discussing the development of Actiq, which the FDA approved in 1998).

<sup>27</sup> See Lenny Bernstein, *Stronger Than Fentanyl, Opioid Gets FDA Approval*, WASH. POST, Nov. 3, 2018, at A3 (“The drug approved Friday is a 30-microgram pill form of sufentanil, a powerful, 34-year-old opioid commonly used after surgery and in emergency rooms. Each pill, placed under the tongue for quick absorption, would have the same impact as five milligrams of intravenous morphine. Each would come in a plastic applicator that looks like a syringe.”).

<sup>28</sup> See David W. Baker, *History of The Joint Commission’s Pain Standards: Lessons for Today’s Prescription Opioid Epidemic*, 317 JAMA 1117, 1117 (2017) (“The Joint Commission standards raised concerns that . . . raising pain treatment to a patients’ rights issue could lead to overreliance on opioids. . . . Signals appeared suggesting that some clinicians had become overzealous in treating pain.”).

<sup>29</sup> See Anna Lembke, *Why Doctors Prescribe Opioids to Known Opioid Abusers*, 367 NEW ENG. J. MED. 1580, 1581 (2012); Aleksandra Zgierska et al., *Patient Satisfaction, Prescription Drug Abuse, and Potential Unintended Consequences*, 307 JAMA 1377, 1377–78 (2012); Celine Gounder, *Who Is Responsible for the Pain-Pill Epidemic?*, NEW YORKER (Nov. 8, 2013), <https://www.newyorker.com/business/currency/who-is-responsible-for-the-pain-pill-epidemic> [<https://perma.cc/N4DM-3556>] (“The rise in prescription narcotics may have been driven partly by the pharmaceutical industry, but many patients also welcomed—and encouraged—it. . . . [W]ith a customer-is-always-right mentality having pervaded the doctor’s office, patients were able to pressure physicians to satisfy their requests . . .”); Richard Gunderman, *When Physicians’ Careers Suffer Because They Refuse to Prescribe Narcotics*, ATLANTIC (Oct. 30, 2013), <https://www.theatlantic.com/health/archive/2013/10/when-physicians-careers-suffer-because-they-refuse-to-prescribe-narcotics/280995/> [<https://perma.cc/FV57-VR6N>].

<sup>30</sup> See Adam J. Kolber, *A Limited Defense of Clinical Placebo Deception*, 26 YALE L. & POL’Y REV. 75, 76, 89–90 (2007); Noah, *supra* note 1, at 56 (referring to “the pronounced placebo effect that researchers encounter in this context”); see also Gardiner Harris, *Study Finds Many Doctors Often Give Placebos*, N.Y. TIMES, Oct. 24, 2008, at A12.

itself has spawned cavalier use that endangered consumers,<sup>31</sup> physicians would need something else to prescribe, and insurers preferred picking up the tab for opioids over pricier and more time-consuming approaches to pain management.<sup>32</sup>

With the growing normalization of the medical use of such powerful narcotics, patterns of inexplicable prescribing became commonplace. For instance, one recent study found that a quarter of patients seen in hospital emergency departments with a sprained ankle received opioid analgesics.<sup>33</sup> More importantly, primary care physicians have accounted for almost half of opioid prescriptions,<sup>34</sup> even though

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<sup>31</sup> See Lars Noah, *Reversal of Fortune: Moving Pharmaceuticals from Over-the-Counter to Prescription Status?*, 63 VILL. L. REV. 355, 356–57, 367–71 (2018). In recent research comparing treatments for chronic pain, nonsteroidal anti-inflammatory drugs (NSAIDs) performed as well as narcotic analgesics. See Erin E. Krebs et al., *Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients with Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial*, 319 JAMA 872, 880–81 (2018); cf. Yngvild Olsen et al., *Opioid Prescriptions by U.S. Primary Care Physicians from 1992 to 2001*, 7 J. PAIN 225, 231 (2006) (wondering what would happen after the “market withdrawal of many of the popular COX-2 inhibitor medications [e.g., Vioxx<sup>®</sup> (rofecoxib)] that may previously have been used in lieu of opioids and traditional NSAIDs”).

<sup>32</sup> See Barry Meier & Abby Goodnough, *Treating Pain Without Drugs*, N.Y. TIMES, June 23, 2016, at B1; Katie Thomas & Charles Ornstein, *Insurers Putting Cost over Safety with Painkillers*, N.Y. TIMES, Sept. 18, 2017, at A1. On the range of methods for managing pain, see Lars Noah, *Comfortably Numb: Medicalizing (and Mitigating) Pain-and-Suffering Damages*, 42 U. MICH. J.L. REFORM 431, 461–63 (2009).

<sup>33</sup> See M. Kit Delgado et al., *National Variation in Opioid Prescribing and Risk of Prolonged Use for Opioid-Naïve Patients Treated in the Emergency Department for Ankle Sprains*, 72 ANNALS EMERGENCY MED. 389, 392 (2018); Rita Rubin, *FDA Dispenses Opioid Concern; Pills, Patches “Extensively Used,”* USA TODAY, Feb. 10, 2009, at D7 (reporting that an agency official had identified sprained ankles as an inappropriate use of long-acting opioids); see also Maureen V. Hill et al., *Wide Variation and Excessive Dosage of Opioid Prescriptions for Common General Surgical Procedures*, 265 ANNALS SURGERY 709, 711 (2017) (“[O]pioid pills are greatly over-prescribed for the treatment of acute postoperative pain in general surgery patients: over 70% of the prescribed pills were never taken.”); Tisamarie B. Sherry et al., Letter, *Documented Pain Diagnoses in Adults Prescribed Opioids: Results from the National Ambulatory Medical Care Survey, 2006–2015*, 169 ANNALS INTERNAL MED. 892, 892–93 (2018) (finding that a pain-related diagnosis did not accompany almost 30% of opioid prescriptions, while back pain, arthritis, and other non-cancer pains accounted for two-thirds of prescriptions). Three-quarters of patients presenting with dental pain receive such a prescription. See Catherine Saint Louis, *E.R. Doctors Face Dilemma on Painkillers*, N.Y. TIMES, May 1, 2012, at D1.

<sup>34</sup> See Benjamin Levy et al., *Trends in Opioid Analgesic-Prescribing Rates by Specialty, U.S., 2007–2012*, 49 AM. J. PREVENTIVE MED. 409, 411 (2015) (concluding that “primary care physicians and non-physician prescribers . . . together comprise the source of more than half of all opioid analgesic prescriptions”); Jan Hoffman, *His Patients in Pain, a Doctor Must Limit Their Use of Opioids*, N.Y. TIMES, Mar. 17, 2016, at A1; see also Katie Thomas, *Doubts Raised About Off-Label Use of a Painkiller*, N.Y. TIMES, May 14, 2014, at B1 (“The F.D.A. approved Subsys only for cancer patients who are already using round-the-clock painkillers, and warned that it should be prescribed only by oncologists and pain



they seem particularly ill-equipped to prescribe them in a careful fashion,<sup>35</sup> and almost one-third of prescriptions issued to adolescents came from dentists.<sup>36</sup> As the next Part concludes, general practitioners should never have enjoyed such easy access to these dangerous controlled substances.

## II. THE FDA'S CENTRAL ROLE AND MISSED OPPORTUNITIES

Different federal entities have turned their attention to the problems associated with the overuse of prescription opioids. Congress has thrown money at the problem,<sup>37</sup> and it also has enacted various measures,<sup>38</sup> most recently the sprawling (and clumsily titled) Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act.<sup>39</sup>

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specialists. But just 1 percent of prescriptions are written by oncologists . . . . About half of the prescriptions were written by pain specialists, and a wide range of doctors prescribed the rest, including general practice physicians, neurologists and even dentists and podiatrists.”)

<sup>35</sup> See Joseph R. Schottenfeld et al., *Pain and Addiction in Specialty and Primary Care: The Bookends of a Crisis*, 46 J.L. MED. & ETHICS 220, 220 (2018) (“[O]pioids quickly became the treatment of choice to manage chronic pain in the overburdened and underresourced context of primary care.”); *id.* at 223–27 (elaborating); Joanna L. Starrels et al., *Low Use of Opioid Risk Reduction Strategies in Primary Care Even for High Risk Patients with Chronic Pain*, 26 J. GEN. INTERNAL MED. 958, 962–63 (2011); Jan Hoffman, *A Dire Need in Addiction Medicine*, N.Y. TIMES, Sept. 11, 2018, at D1 (“[P]rimary care providers . . . routinely encounter these patients but often lack the expertise to prevent, diagnose and treat addiction. . . . [C]omprehensive addiction training is rare in American medical education.”).

<sup>36</sup> See David Armstrong, *Prescribing Opioids Ingrained in Dentistry; One Practitioner's Stance Hurts Business*, BOS. GLOBE, Feb. 21, 2017, at A1 (“Dentists have become a significant source of opioid prescribing—especially for younger patients undergoing wisdom tooth extractions. . . . In many cases, dentists prescribe 20 to 30 tablets of a narcotic painkiller, when a patient in all likelihood will only require a handful of pills.”); *id.* (discussing “the pressures dentists face to prescribe potent pain pills, even as research shows most of their patients would do just fine with over-the-counter medications such as ibuprofen”); see also Alan R. Schroeder et al., *Association of Opioid Prescriptions from Dental Clinicians for US Adolescents and Young Adults with Subsequent Opioid Use and Abuse*, 179 JAMA INTERNAL MED. 145 (2019).

<sup>37</sup> See Abby Goodnough, *\$45 Billion to Fight Opioid Abuse Is Nowhere Near Enough, Experts Say*, N.Y. TIMES, July 1, 2017, at A15 (reporting that Congress had appropriated \$1 billion in 2016 for state treatment programs); *Trump Signs Sweeping Opioid Bill*, SAN DIEGO UNION TRIB., Oct. 25, 2018, at A2 (“Congress has appropriated \$8.5 billion for opioid-related programs this year, but there is no guarantee of additional funding in later years.”).

<sup>38</sup> See, e.g., Comprehensive Addiction and Recovery Act of 2016, Pub. L. No. 114-198, 130 Stat. 695; cf. Scott Higham & Lenny Bernstein, *The Drug Industry's Triumph over the DEA*, WASH. POST, Oct. 15, 2017, at A1 (reporting that Congress had enacted legislation weakening the DEA's enforcement powers).

<sup>39</sup> See Pub. L. No. 115-271, 132 Stat. 3894 (2018). Although a striking feat given low expectations about this deliberative body's ability to accomplish much of anything, some public health experts expressed disappointment. See Abby Goodnough, *What a Bipartisan*

Although the White House acted slowly in the face of calls for an emergency declaration,<sup>40</sup> it has now staked out a fairly hard line in responding to the opioid epidemic.<sup>41</sup> For its part, the DEA has taken some important steps, including the long-delayed rescheduling of combination hydrocodone products into Schedule II,<sup>42</sup> and the reduction of aggregate production quotas,<sup>43</sup> while the Centers for Medicare and Medicaid Services proposed coverage limitations based on the CDC's prescribing guidelines.<sup>44</sup> Commentators have suggested a number of other steps that the federal government should take, though normally emphasizing the need to coordinate with state and local officials.<sup>45</sup>

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*Opioid Bill Includes (and Omits)*, N.Y. TIMES, Sept. 27, 2018, at A15 (“The 653-page bill contains a mix of law enforcement and public health measures . . . . But addiction experts say that while many of the measures will help incrementally, the investment remains meager and scattershot compared with what is needed . . . .”); Katie Zezima & Seung Min Kim, *Trump Signs Bipartisan Opioids Bill*, WASH. POST, Oct. 25, 2018, at A6 (“[E]ven on an issue that has prompted an overwhelming desire for action, political considerations soon took over. . . . Public health officials say the new law is an important first step toward fighting the opioid crisis, but they say it mostly tinkers with the problem rather than addressing it directly.”).

<sup>40</sup> See John Wagner et al., *Trump Targets Opioid Scourge*, WASH. POST, Oct. 27, 2017, at A1.

<sup>41</sup> See Katie Benner, *Justice Dept. Intensifies Global War on Opioids*, N.Y. TIMES, Aug. 23, 2018, at A11; Maggie Haberman et al., *Tough Talk, Few Details in President's Opioid Plan*, N.Y. TIMES, Mar. 20, 2018, at A19.

<sup>42</sup> See Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II, 79 Fed. Reg. 49,661, 49,682 (Aug. 22, 2014) (codified at 21 C.F.R. § 1308.13(e)(1)); see also David Sell, *DEA to Tighten Control of a Type of Pain Pill*, PHILA. INQUIRER, Aug. 22, 2014, at A17 (“Hydrocodone alone had been a Schedule II drug since 1970, when Congress passed the Controlled Substances Act.”).

<sup>43</sup> See Lev Facher, *Pressure Builds on the DEA to Stem the Supply of Controlled Substances, but at What Cost?*, BOS. GLOBE, Dec. 25, 2017, at B9 (reporting that, after many years of dramatically increasing the aggregate production quotas for opioids, the agency has reduced them the last two years); see also Final Adjusted Aggregate Production Quotas for Schedule I and II Controlled Substances and Assessment of Annual Needs for the List I Chemicals Ephedrine, Pseudoephedrine, and Phenylpropanolamine for 2018, 83 Fed. Reg. 63,533 (Dec. 10, 2018); Noah, *supra* note 1, at 63 & n.160 (explaining that, in order to pressure Purdue into taking steps to guard against the overuse of OxyContin, the DEA once had “threatened to slash the company’s annual production quota by approximately 95 percent”). The DEA also recently tightened rules that govern how it sets and annually adjusts these levels. See Controlled Substances Quotas, 83 Fed. Reg. 32,784, 32,789 (July 16, 2018) (to be codified at 21 C.F.R. pt. 1303).

<sup>44</sup> See Jan Hoffman, *Greater Pain If Medicare Pulls Back on Opioids*, N.Y. TIMES, Mar. 28, 2018, at A1.

<sup>45</sup> See, e.g., NAT’L ACADS. OF SCI., ENG’G & MED., PAIN MANAGEMENT AND THE OPIOID EPIDEMIC: BALANCING SOCIETAL AND INDIVIDUAL BENEFITS AND RISKS OF PRESCRIPTION OPIOID USE chs. 5–6 (Jonathan K. Phillips et al. eds., 2017); Hilary Homenko, Note, *Rehabilitating Opioid Regulation: A Prescription for the FDA’s Next Proposal of an Opioid Risk Evaluation and Mitigation Strategy (REMS)*, 22 HEALTH MATRIX 273, 303–13 (2012).

This Part will focus on the FDA's role. In the last few years, that agency has solicited public input for how best to address the problems associated with the misuse of prescription opioid products,<sup>46</sup> though without candidly accepting any real responsibility for having unleashed them. The Sections that follow will consider the use of labeling and other mechanisms for communicating risk information to prescribers and patients, the introduction of abuse-resistant formulations, greater reluctance in approving or allowing the continued marketing of these drugs, and opportunities for imposing various restrictions on their distribution. If the FDA only had the courage to make full use of its power to take that latter course of action (or if Congress did so in even more draconian ways), then we might stand some chance of ending this country's addiction to prescription opioids as well as guarding against the next scourge of this type.

### A. *Misguided Reliance on Messaging*

OxyContin created problems primarily because of what Purdue Pharma said about its drug. Older oxycodone drugs long predated it, and the extended-release formulation initially did not appear to make it particularly hazardous (though the higher dose of the active ingredient in each tablet made it marginally more attractive for diversion). Instead, Purdue's ability to pitch their version as nonaddictive—as well as less prone to abuse and diversion—helped make otherwise cautious physicians more willing to prescribe it.<sup>47</sup>

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<sup>46</sup> See, e.g., Request for Comments, Opioid Policy Steering Committee, 82 Fed. Reg. 45,597, 45,599–600 (Sept. 29, 2017); Notice of Public Workshop and Request for Comments, Data and Methods for Evaluating the Impact of Opioid Formulations with Properties Designed to Deter Abuse in the Postmarket Setting: A Scientific Discussion of Present and Future Capabilities, 82 Fed. Reg. 27,271, 27,272 (June 14, 2017); see also Robert M. Califf et al., *A Proactive Response to Prescription Opioid Abuse*, 374 NEW ENG. J. MED. 1480 (2016) (discussing the FDA's planned initiatives); *id.* at 1483 (“Until clinicians stop prescribing opioids far in excess of clinical need, this crisis will continue unabated.”); cf. Chris McGreal, *FDA's Opioids Adviser Accuses Agency of Having “Direct” Link to Crisis*, GUARDIAN (Jan. 24, 2019), <https://www.theguardian.com/us-news/2019/jan/24/fda-opioids-big-pharma-prescriptions> [<https://perma.cc/Y9N2-N3VP>] (“[Raeford] Brown, an anesthesiologist who chairs the FDA committee of specialists advising the agency on whether to approve new opioid painkillers, said he no longer had confidence in repeated assurances by the FDA leadership that it was taking the epidemic seriously and prepared to put public health above the commercial interests of drug makers.”).

<sup>47</sup> See Barry Meier, *Owners Tied to Plan to Hide OxyContin Risk*, N.Y. TIMES, Jan. 16, 2019, at B1 (“Company sales representatives told doctors that OxyContin couldn't be abused and were trained to say that the drug had an addiction risk for patients of ‘less than one percent,’ a claim that had no scientific backing.”). More recently, Insys Therapeutics, the manufacturer of the fentanyl product Subsys, got caught bribing physicians. See Lars Noah, *Doctors on the Take: Aligning Tort Law to Address Drug Company Payments to Prescribers*, 66 BUFF. L. REV. 855, 867–68 & nn.36–37 (2018); Nishant Mohan, *Insys Therapeutics to Settle with U.S.*, WALL ST. J., Aug. 9, 2018, at B3; see also Scott E. Hadland et al., *Industry Payments to Physicians for Opioid Products, 2013–2015*, 107 AM. J. PUB. HEALTH 1493,

Initially, the FDA authorized Purdue to make such claims in the labeling for OxyContin and, by extension, in the company's advertising to health care professionals. Only belatedly did the agency come to appreciate that the assertions about a lower propensity for addictiveness or diversion lacked any real foundation.<sup>48</sup> In 2001, responding to emerging patterns of irresponsible prescribing, the FDA demanded that OxyContin's professional labeling add a black-box warning.<sup>49</sup> This represented part of a risk-management plan that also included a mechanism for tracking suspected sources of diversion, educating physicians, and supplying special prescription pads.<sup>50</sup> In 2016, the agency demanded that immediate-release opioids add black-box warnings that it had ordered for all extended-release versions three years earlier.<sup>51</sup>

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1494 (2017) (finding that one out of twelve physicians had received payments from sellers of opioids during the study period, totaling over \$46 million); Abby Goodnough, *Study Links Opioid Makers' Gifts for Doctors to Higher Overdose Death Rates*, N.Y. TIMES, Jan. 19, 2019, at B3.

<sup>48</sup> See Carrie Johnson, *OxyContin Makers Admit Deception; Addiction Danger from Painkiller Was Understated*, WASH. POST, May 11, 2007, at A1 ("From 1996 to 2001, Purdue claimed that the 'miracle drug' was safer than rival medications despite repeated studies that suggested patients had developed a risk of abuse and had serious trouble withdrawing from OxyContin."). Indeed, precisely the opposite seems to have happened. See Harriet Ryan et al., *OxyContin's 12-Hour Problem; It Fades Hours Early in Many Patients, Increasing Their Risk of Addiction*, L.A. TIMES, May 8, 2016, at A1.

<sup>49</sup> See Josh White, *More Warnings About OxyContin; FDA, Drugmaker Advise Caution in Prescribing Addictive Painkiller*, WASH. POST, July 26, 2001, at B2 (explaining that this also entailed having Purdue mail out 800,000 letters to physicians in order to draw attention to this labeling revision); see also Lars Noah, *The Imperative to Warn: Disentangling the "Right to Know" from the "Need to Know" About Consumer Product Hazards*, 11 YALE J. ON REG. 293, 360 (1994) (discussing the FDA's use of "Dear Doctor" letters designed to draw attention to such new risk information). Such efforts do not, however, seem to do much good. See, e.g., Walter Smalley et al., *Contraindicated Use of Cisapride: Impact of Food and Drug Administration Regulatory Action*, 284 JAMA 3036, 3039 (2000). An entirely different type of "Dear Doctor" letter, issued by the local medical examiner's office, appears to have more of an impact. See Jason N. Doctor et al., *Opioid Prescribing Decreases After Learning of a Patient's Fatal Overdose*, 361 SCIENCE 588, 588-89 (2018); cf. Carolyn Y. Johnson, *Sales Pitch Has Doses of Evidence and Caution*, WASH. POST, Feb. 2, 2019, at A1 (discussing counterdetailing efforts).

<sup>50</sup> See Mathews & Abboud, *supra* note 18, at A3; see also U.S. CONG., GEN. ACCOUNTING OFFICE, *PRESCRIPTION DRUGS: OXYCONTIN ABUSE AND DIVERSION AND EFFORTS TO ADDRESS THE PROBLEM*, No. GAO-04-110 (2003). Although Purdue became increasingly suspicious of diversion by particular physicians, clinics, and pharmacies, the company apparently failed to share this information with the DEA in a timely fashion. See Harriet Ryan et al., *More Than 1 Million OxyContin Pills Ended up in the Hands of Criminals and Addicts. What the Drugmaker Knew*, L.A. TIMES, July 10, 2016, at A1.

<sup>51</sup> See Lenny Bernstein, *New Labels on Opioids Will Warn of Risks of Addiction, Overdose, Death*, WASH. POST, Mar. 23, 2016, at A19; see also Laurie McGinley, *FDA Requires New Warnings on Dangers of Mixing Drugs*, WASH. POST, Sept. 1, 2016, at A12

Apart from communicating enhanced risk information, the government took further steps to limit the favorable pitches that Purdue could make.<sup>52</sup> By 2008, the FDA directed the company to cease claiming that OxyContin posed only a small risk of addiction in patients.<sup>53</sup> Meanwhile, the Justice Department brought misbranding prosecutions, and Purdue paid \$600 million to settle lawsuits brought by numerous parties after pleading guilty to felony charges for fraudulently asserting that OxyContin was less prone to abuse.<sup>54</sup> In 2018, belatedly attempting to counteract decades of criticism about its promotional practices, the company announced that it would cease all marketing campaigns directed to physicians.<sup>55</sup> In fact, some commentators have suggested imposing a blanket prohibition on the advertising of opioids,<sup>56</sup> but any such move would surely run afoul of the First Amendment.<sup>57</sup>

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(reporting that soon thereafter the agency mandated black-box warnings to emphasize the serious risks associated with using opioids in combination with benzodiazepines).

<sup>52</sup> See, e.g., Chris Adams, *FDA Asks Maker of OxyContin to Pull “Misleading” Print Ads*, WALL ST. J., Jan. 23, 2003, at D3 (reporting that the agency sent Purdue “an unusually harsh letter” objecting to advertisements that the company had run in *JAMA* because they “underplayed the most serious risks”).

<sup>53</sup> See Whoriskey, *supra* note 14, at A1 (“The FDA did not say what evidence led the agency to allow the previous claims or what new findings led it to ask for the removal of those claims.”). In contrast, the FDA’s decision in 2015 to approve pediatric labeling for the drug, which promised an additional period of market exclusivity, triggered howls of protest. See Brady Dennis, *OxyContin for Kids Evokes Fierce Feelings*, WASH. POST, Sept. 10, 2015, at A3; Catherine Saint Louis, *F.D.A. Approval of OxyContin Use for Children Continues to Draw Scrutiny*, N.Y. TIMES, Oct. 9, 2015, at A20.

<sup>54</sup> See *United States v. Purdue Frederick Co.*, 495 F. Supp. 2d 569, 572–73, 576 (W.D. Va. 2007) (accepting plea agreements by the company as well as three high-ranking corporate officers each of whom received sentences of three years of probation and together paid \$34.5 million in fines); see also *Friedman v. Sebelius*, 686 F.3d 813, 828 (D.C. Cir. 2012) (reversing orders that excluded these officers from participating in federal health care programs).

<sup>55</sup> See Ben Poston, *Opioid Maker Limits Sales Efforts; Under Pressure over Addiction Crisis, Purdue Pharma Will No Longer Promote Its Painkillers to Doctors*, L.A. TIMES, Feb. 11, 2018, at A1.

<sup>56</sup> See Andrew Kolodny & Thomas R. Frieden, *Ten Steps the Federal Government Should Take Now to Reverse the Opioid Addiction Epidemic*, 318 JAMA 1537, 1537 (2017) (recommending that the FDA narrow the “labeling for chronic pain and greatly restrict or eliminate marketing of opioids for this indication”); see also Bruce Psaty & Joseph O. Merrill, *Addressing the Opioid Epidemic—Opportunities in the Postmarketing Setting*, 376 NEW ENG. J. MED. 1502, 1503 (2017) (“If it’s not clear that the FDA has the authority to limit the off-label marketing of controlled substances, Congress could expand the agency’s authority to modify what has been one of the main drivers of the opioid epidemic.”).

<sup>57</sup> See Lars Noah, *Truth or Consequences?: Commercial Free Speech vs. Public Health Promotion (at the FDA)*, 21 HEALTH MATRIX 31, 67–68, 72–84 (2011); see also *id.* at 87 (explaining that, until 2001, the agency followed a policy of disallowing direct-to-consumer advertising for Schedule II drugs).

*B. The False Promise of Technological Fixes*

In recently enacting the SUPPORT for Patients and Communities Act, Congress made essentially no changes to the FDA's statutory authority, preferring instead to call on the agency to hold public meetings and issue guidance documents on particular issues related to opioids in the hopes that it would take a hint.<sup>58</sup> The one modification related to the FDA's delegated powers would allow it to dictate special packaging for narcotic analgesics as well as other hazardous drugs.<sup>59</sup> Entirely apart from the fact it had managed to impose such restrictions under the enabling statute before this minor amendment,<sup>60</sup> and already had planned to do so for opioids,<sup>61</sup> requiring that such products get dispensed in blister packs containing only a few doses hardly seems like the silver bullet needed to combat this problem. Nonetheless, it aligns quite nicely with the growing search for technological solutions to prescription opioid abuse.<sup>62</sup>

Within five years of OxyContin's introduction, Purdue began work on an abuse-resistant formulation.<sup>63</sup> Originally, the company considered adding a

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<sup>58</sup> See Pub. L. No. 115-271, §§ 3001–3002, 132 Stat. 3894, 3932–34 (2018); *id.* § 3041(c), 132 Stat. at 3943. A couple of years earlier, members of the Senate used a confirmation process in an effort to get the agency's attention. See Sabrina Tavernise, *F.D.A. Chief Is Confirmed After Debate on Painkillers*, N.Y. TIMES, Feb. 25, 2016, at A11.

<sup>59</sup> See Pub. L. No. 115-271, § 3031, 132 Stat. at 3940–41 (to be codified at 21 U.S.C. § 355-1(e)(4)). Separately, the grant of recall authority specific to these drugs, *see id.* § 3012, 132 Stat. at 3935–36 (to be codified at 21 U.S.C. § 360bbb–8d), seems like an odd way of responding to their well understood (as opposed to newly emergent) hazards, though it might well increase the agency's leverage in securing concessions from opioid manufacturers.

<sup>60</sup> See, e.g., Noah, *supra* note 31, at 375 (explaining that the FDA recently “asked manufacturers [of loperamide] to adopt more cumbersome blister packs for each dose and include only enough doses for short-term use” to address the newly discovered abuse potential of this nonprescription antidiarrheal drug); *see also* Andrew Schneider, *Banned Pesticide Allowed as Medicine; U.S. Bars Lindane, Except to Treat Lice*, BALT. SUN, Aug. 14, 2006, at 1A (reporting that the agency ordered the manufacturer of this pediculocide to warn physicians against prescribing more than enough for a single application); *cf.* Nutritional Health Alliance v. FDA, 318 F.3d 92, 100–04 (2d Cir. 2003) (invalidating an FDA requirement that higher dose iron supplements use blister packs to guard against accidental poisoning in children because the authority to impose packaging restrictions for such purposes resided with a different agency).

<sup>61</sup> See David Crow, *FDA Eyes Cut in Prescriptions to Help Contain Opioids Crisis; US Regulator Seeks to Limit Exposure; Doctors to Face “Additional Hoops,”* FIN. TIMES, Dec. 12, 2017, at 11.

<sup>62</sup> *Cf.* Tamara Mathias, *U.S. Regulators Snip Red Tape for Medical Devices to Curb Opioid Crisis*, REUTERS (Nov. 9, 2018), <https://www.reuters.com/article/usa-opioids/rpt-focus-us-regulators-snip-red-tape-for-medical-devices-to-curb-opioid-crisis-idUSL2N1XJ1NE> [tps://perma.cc/6N3Q-VUFL] (“Although the FDA contest is limited to devices and app-based solutions for pain and addiction, the current regulatory climate is also conducive to companies developing opioid-alternative pharmaceuticals.”).

<sup>63</sup> See Barry Meier, *U.S. Asks Painkiller Maker to Help Curb Wide Abuse*, N.Y. TIMES, May 1, 2001, at A16; *see also* Linda Loyd, *Against Opioid Abuse*, PHILA. INQUIRER, Apr. 3,

sequestered opioid antagonist (such as naltrexone) that could counteract the oxycodone when crushed.<sup>64</sup> Ultimately, Purdue decided to harden the tablets by infusing them with a polymer.<sup>65</sup> In 2010, more than two years after submitting an application for this reformulation to the FDA, the sponsor secured approval for OxyContin OP<sup>®</sup>.<sup>66</sup> Then, on the very day that Purdue's initial patents expired, the agency announced that the company had withdrawn its original formulation of OxyContin on safety grounds.<sup>67</sup>

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2016, at E1 (explaining that the FDA has encouraged the development of abuse-resistant formulations of other opioids).

<sup>64</sup> See Barry Meier, *Maker Chose Not to Use a Drug Abuse Safeguard: Company Says It Didn't Anticipate Problems*, N.Y. TIMES, Aug. 13, 2001, at A11 (adding that other manufacturers previously had done so for opioid analgesics with a lower abuse potential, including the addition of naloxone to Talwin<sup>®</sup> (pentazocine) in 1983). Along similar lines, some had suggested including a chemical irritant such as capsaicin that would make a crushed tablet unpleasant to snort or otherwise consume. See Sandra Blakeslee, *Drug Makers Hope to Kill the Kick in Pain Relief*, N.Y. TIMES, Apr. 20, 2004, at F1 (adding that manufacturers of paregoric, an old liquid opiate formulation, had responded to its abuse by adding camphor to trigger a gag reflex, which led abusers simply to boil off that ingredient).

<sup>65</sup> See Timothy W. Martin, *OxyContin Maker Guards Exclusivity*, WALL ST. J., June 28, 2012, at A1 ("The new version of the pill is infused with polyethylene oxide, a polymer that makes the pill tough to crush for snorting or to heat for intravenous injection. The company also altered the formula so that the pill's powdery contents turn into a jellylike substance if water is added to make a solution for an injection."); *id.* ("Users can still get high from the pills if they are willing to swallow enough of them or engage in more elaborate processing.").

<sup>66</sup> See Abby Goodnough & Katie Zezima, *Drug Is Harder to Abuse, but Users Persevere*, N.Y. TIMES, June 16, 2011, at A21; see also Lisa Girion, *FDA Approves Recast Painkiller; Experts Are Wary of a Drug Called a Less-Addictive Form of OxyContin*, L.A. TIMES, July 24, 2014, at AA1 ("Purdue Pharma's Targiniq ER combines a long-acting form of the opioid analgesic oxycodone with the medication naloxone, which is commonly used to reverse the effects of an opioid overdose. . . . The naloxone becomes active when the pills are crushed."); *id.* ("Dr. Andrew Kolodny, president of Physicians for Responsible Opioid Prescribing, said the FDA's approval of Targiniq could 'exacerbate this crisis.' If doctors believe Targiniq is safe, they may be more inclined to prescribe it instead of seeking alternatives. . . . 'Coming up with new gimmicks isn't going to help.'").

<sup>67</sup> See Notice, Determination That the OXYCONTIN (Oxycodone Hydrochloride) Drug Products Covered by New Drug Application 20-553 Were Withdrawn from Sale for Reasons of Safety or Effectiveness, 78 Fed. Reg. 23,273 (Apr. 18, 2013); see also Noah, *supra* note 18, at 175-79 (discussing anticompetitive concerns with this maneuver). Shortly thereafter, the FDA rejected a similar request from Endo Pharmaceuticals after that company introduced a reformulated version of its ER oxymorphone product Opana because the agency found the new drug no better at deterring abuse. See *id.* at 176 n.52; see also *infra* note 82 and accompanying text (discussing its subsequent withdrawal).

Other opioid analgesics now incorporate abuse-resistant features.<sup>68</sup> Some observers have questioned the utility of such reformulations.<sup>69</sup> In the case of OxyContin, however, the effort seemed to work, but researchers found that this simply drove abusers to substitute heroin and resulted in no net reduction in overdose deaths.<sup>70</sup> Indeed, before OxyContin came along, few companies marketed single-ingredient oxycodone or other opioid products;<sup>71</sup> instead, they previously had included aspirin, acetaminophen, or ibuprofen, which amounted to nonnarcotic “impurities” from the perspective of abusers.<sup>72</sup> In a sense, then, the agency’s willingness to approve a variety of single-ingredient opioids over the last two decades unwittingly removed an abuse-resistant feature of the older formulations.

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<sup>68</sup> See, e.g., Bradley J. Fikes, *Painkiller Unit Sold for \$100M Upfront; San Diego-Based Zogenix to Use Proceeds for Other Drug Trials*, SAN DIEGO UNION-TRIB., Mar. 11, 2015, at C1 (noting the reformulation of Zohydro to resist abuse); Lisa Girion, *Powerful Painkiller Approved*, L.A. TIMES, Nov. 21, 2014, at A8 (reporting that the FDA approved Purdue’s third abuse-resistant opioid, the once-a-day hydrocodone drug Hysingla ER<sup>®</sup> containing more than twice the dosage of Zohydro); see also Notice of Availability, Guidance for Industry, Abuse-Deterrent Opioids—Evaluation and Labeling, 80 Fed. Reg. 17,765 (Apr. 2, 2015); Timothy W. Martin & Jonathan D. Rockoff, *Race Accelerates for Safer Painkiller*, WALL ST. J., May 6, 2013, at B1 (explaining that the push for abuse-resistant formulations offered brand-name manufacturers a lucrative new business opportunity).

<sup>69</sup> See William C. Becker & David A. Fiellin, *Abuse-Deterrent Opioid Formulations—Putting the Potential Benefits into Perspective*, 376 NEW ENG. J. MED. 2103 (2017); Pamela Leece et al., *Tamper-Resistant Drugs Cannot Solve the Opioid Crisis*, 187 CAN. MED. ASS’N J. 717 (2015).

<sup>70</sup> See Theodore J. Cicero et al., Letter, *Effect of Abuse-Deterrent Formulation of OxyContin*, 367 NEW ENG. J. MED. 187, 189 (2012); Harriet Ryan, *OxyContin Shift Tied to Heroin Deaths; “Abuse-Deterrent” Pain Pills Inadvertently Helped Fuel a Rise in Fatal Overdoses of the Street Drug, Study Says*, L.A. TIMES, Jan. 12, 2017, at A7.

<sup>71</sup> See Noah, *supra* note 25, at 4–5 (“Hydrocodone when used as the sole active ingredient had always faced Schedule II controls, which may help to explain why no company had ever before [Zohydro’s approval in 2013] commercialized such a product.” (footnote omitted)); Klaus T. Olkkola & Nora M. Hagelberg, *Oxycodone: New “Old” Drug*, 22 CURRENT OPINION ANESTHESIOLOGY 459, 459 (2009) (“Before the 1990s, for instance in the United States of America and Canada, oxycodone was mainly consumed in combination preparations combined with antipyretic analgesics.”); see also Single-Ingredient, Immediate-Release Drug Products Containing Oxycodone for Oral Administration and Labeled for Human Use; Enforcement Action Dates, 77 Fed. Reg. 40,069, 40,070 (July 6, 2012) (mentioning a couple of more recently approved single-ingredient oxycodone products).

<sup>72</sup> See Blakeslee, *supra* note 64, at F1 (reporting that OxyContin abusers “liked the fact that the drugs were pure”); see also John Fauber & Ellen Gabler, *FDA to Weigh Tighter Restrictions on Vicodin: Addiction, Overdose Deaths Rising in U.S.*, MILWAUKEE J. SENTINEL, Jan. 23, 2013, at A1 (“FDA researchers concluded that one of the reasons hydrocodone products were less likely to be abused than drugs such as oxycodone was because all hydrocodone products are combined with over-the-counter pain relievers . . . [which] reduces the amount of hydrocodone needed . . .”).



Whether or not they deter abuse, the latest reformulations do absolutely nothing to reduce the risk of addiction.<sup>73</sup>

Similarly, various countermeasures now exist to manage opioid overuse, which some critics have assailed for serving to facilitate continued misuse.<sup>74</sup> For instance, in the last two decades, the FDA approved Movantik<sup>®</sup> (naloxegol) to treat opioid-induced constipation,<sup>75</sup> a nasal spray formulation of the opiate antagonist Narcan<sup>®</sup> (naloxone) as an antidote for overdose,<sup>76</sup> and Suboxone<sup>®</sup> (high-dose buprenorphine combined with naloxone to deter abuse) for maintenance treatment of addicts.<sup>77</sup>

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<sup>73</sup> See Alan Schwarz, *Painkillers Resist Abuse, but Experts Still Worry: Inventive Addicts Thwart Safeguards*, N.Y. TIMES, June 7, 2015, at A16 (“[T]he active ingredients in abuse-deterrent drugs provide the same high and remain just as addictive as in regular formulations.”); *id.* (“[M]any misunderstand the persistent risks, said Dr. G. Caleb Alexander, a co-director of the Center for Drug Safety and Effectiveness at the Johns Hopkins Bloomberg School of Public Health. A national survey of internists, family physicians and general practitioners that [he] led last year found that . . . almost half of those doctors thought that abuse-deterrent pills were inherently less addictive.”); see also Lewis S. Nelson et al., Editorial, *Addressing the Opioid Epidemic*, 314 JAMA 1453, 1453 (2015) (“New opioid medications, many of them with tamper-resistant formulations, continue to be marketed despite the lack of evidence that these preparations reduce the risk of addiction.”).

<sup>74</sup> See Ariana Eunjung Cha, *An Industry’s Answer to Deadly Opioid Addiction: More Pills*, WASH. POST, Oct. 16, 2016, at A1 (“[E]ach of these submarkets—addiction, overdose and side effects—is worth at least \$1 billion a year in sales. These economics, experts say, work against efforts to end the epidemic.”); *id.* (“By promoting opioid-induced constipation as a condition in need of more targeted treatment, critics say the drug industry is creating incentives to maintain the painkillers at full strength and add another pill instead.”); Katharine Q. Seelye, *A Lifesaver for Heroin Users, but No Cure for an Epidemic*, N.Y. TIMES, July 31, 2016, at A14 (“Critics say that [Narcan] gives drug users a safety net, allowing them to take more risks as they seek higher highs.”).

<sup>75</sup> See Cha, *supra* note 74, at A1 (reporting that the FDA approved the drug in 2014 and a competing product (Relistor<sup>®</sup>) two years later); see also Matt Pearce, *What a Super Bowl Ad Didn’t Say: Pharmaceutical Firms That Funded the Spot on Opioid-Induced Constipation Are Criticized for Not Mentioning Addiction*, L.A. TIMES, Feb. 11, 2016, at A6 (discussing controversy related to consumer ads for this drug to treat a common side effect of opioid use).

<sup>76</sup> See Sabrina Tavernise, *F.D.A. Approves a Nasal Spray to Combat Opioid Overdose*, N.Y. TIMES, Nov. 18, 2015, at A20; see also Bridget M. Kuehn, *Easy-to-Use Overdose Antidote Earns Fast-Track Approval*, 311 JAMA 1600, 1600 (2014) (discussing Evzio<sup>®</sup>, an autoinjector that represented “the first FDA-approved naloxone product designed for use by nonclinicians”); Max Blau, *The Next Naloxone?: Companies, Academics Search for Better Overdose-Reversal Drugs*, BOS. GLOBE, Apr. 16, 2018, at B8 (reporting that, given the challenges posed by far more powerful synthetic opioids, Opiant Pharmaceuticals is developing a nasal spray formulation of nalmefene, which the FDA had approved in 1995 as an injectable drug (Revex<sup>®</sup>) but the manufacturer discontinued in 2008 because of insufficient demand).

<sup>77</sup> See Brian Mund & Kate Stith, *Buprenorphine MAT as an Imperfect Fix*, 46 J.L. MED. & ETHICS 279, 281 (2018); see also *id.* at 279–86 (explaining the downsides of buprenorphine as a treatment for addiction, and concluding that physician training requirements and other existing limitations on its prescribing remain necessary). Other

Even though it seems unlikely that the availability of such products would make physicians and patients more willing to take greater chances with incautious opioid use,<sup>78</sup> their approval may work to salve the FDA's conscience about allowing continued easy access to a variety of opioid analgesics.<sup>79</sup>

### C. *Just Say No: Nonapproval or License Withdrawal*

As cataloged earlier, the FDA's profligacy in approving new opioids has hardly abated,<sup>80</sup> though perhaps its willingness to do so has finally plateaued. For instance, the agency recently rejected an application for an immediate-release oxycodone product, though primarily because it found inadequate evidence that the inclusion of a dye would justify labeling the proposed product as abuse-deterrent.<sup>81</sup> In 2017, at the FDA's urging, Endo withdrew its reformulated version of Opana from the market, though primarily because abusers no longer able to snort it would liquefy the drug for injection, which the added inactive ingredients may have made more hazardous,<sup>82</sup> and the sharing of hypodermic needles had caused localized outbreaks

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formulations that dispense with naloxone (and do not come as a sublingual strip) include Subutex<sup>®</sup> (sublingual tablet), Probuphine<sup>®</sup> (subdermal implant that lasts six months), and Sublocade<sup>®</sup> (monthly injection). *See id.* at 281, 286, 289 n.101; Laurie McGinley, *FDA Approves First Implantable Drug for the Treatment of Opioid Addiction*, WASH. POST, May 27, 2016, at A3; *see also* Brendan Saloner et al., *Moving Addiction Care to the Mainstream—Improving the Quality of Buprenorphine Treatment*, 379 NEW ENG. J. MED. 4 (2018).

<sup>78</sup> *See* Nick Werle & Ernesto Zedillo, *We Can't Go Cold Turkey: Why Suppressing Drug Markets Endangers Society*, 46 J.L. MED. & ETHICS 325, 333 (2018) (“Opponents claimed that reducing overdose risk through naloxone access would encourage injection drug use and would discourage entry to abstinence-based treatments. However, numerous studies have disproven these assertions applying deterrence theory to naloxone access.”); *cf.* Lars Noah, *Assisted Reproductive Technologies and the Pitfalls of Unregulated Biomedical Innovation*, 55 FLA. L. REV. 603, 654–55 (2003) (“[T]he introduction of selective [embryo] reduction offers an apparent fix for high-order multifetal pregnancies, which in turn may encourage [fertility] patients and providers to gamble with more aggressive and risky interventions.”).

<sup>79</sup> Recently, a pair of FDA advisory committees recommended revisions in the labeling of narcotic analgesics to encourage routine co-prescribing of naloxone. *See* Lenny Bernstein, *Panels: Prescribe Opioid Antidote with Painkillers*, WASH. POST, Dec. 19, 2018, at A11.

<sup>80</sup> *See supra* notes 21–27 and accompanying text.

<sup>81</sup> *See* Denial of Hearing Request Regarding Proposal to Refuse to Approve a New Drug Application for Oxycodone Hydrochloride Immediate-Release Abuse-Deterrent Formulation, Oral Capsules, 5 Milligrams, 15 Milligrams, and 30 Milligrams; Order Refusing Approval, 83 Fed. Reg. 54,598, 54,600–03 (Oct. 30, 2018); *id.* at 54,600 n.9 (calling this deficiency “the primary focus of this order”); *id.* at 54,602–03 (declining to address broader policy questions); *see also id.* at 54,599 (summarizing other deficiencies in the application).

<sup>82</sup> *See id.* at 54,601 n.14 (“[P]ostmarket data showed a significant shift in the route of abuse from nasal to injection following the product’s reformulation . . . [ , which has] been associated with serious adverse events, including numerous cases of thrombotic

of HIV and hepatitis C.<sup>83</sup> In 2005, Purdue's extended-release hydromorphone product (Palladone<sup>®</sup>) spent less than a year on the market before its withdrawal, but that happened because it posed potentially fatal risks to users if consumed with alcohol.<sup>84</sup> The agency still seems hesitant, however, to consider collateral effects such as propensity for misuse in making licensing judgments.

Commentators have urged the FDA to take such a broader view when assessing the safety of opioids and other drugs prone to abuse.<sup>85</sup> The agency had tried doing so several decades ago with methadone, only to have the federal courts invalidate its effort.<sup>86</sup> Although subsequent statutory amendments appear to grant the FDA greater authority to consider factors other than a product's intrinsic safety when prescribed to patients for an intended use, the agency seemingly remains cautious about doing

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microangiopathy which are thought to have been related to injection of the excipients included to deter abuse.”).

<sup>83</sup> See Scott Gottlieb & Janet Woodcock, *Marshaling FDA Benefit-Risk Expertise to Address the Current Opioid Abuse Epidemic*, 318 JAMA 421, 421–22 (2017); Jeanne Whalen, *Painkiller Is Pulled from U.S. Market*, WALL ST. J., July 7, 2017, at A3 (“[T]he agency called [this] its first effort to remove an opioid pain drug from the market over abuse concerns.”).

<sup>84</sup> See Marc Kaufman, *Painkiller Palladone Pulled over Alcohol Risk*, WASH. POST, July 14, 2005, at A14. In 2010, the FDA finally ordered the withdrawal of propoxyphene (e.g., Darvon<sup>®</sup>), which it first approved in 1957, because of its association with heart rhythm abnormalities. See *In re Darvocet, Darvon & Propoxyphene Prod. Liab. Litig.*, 756 F.3d 917, 923–24 (6th Cir. 2014); Duff Wilson, *Painkiller to Be Pulled off Market*, N.Y. TIMES, Nov. 20, 2010, at B1. In contrast, the agency previously had tried to address longstanding concerns about addiction to this weaker (Schedule IV) opioid with the addition of ineffectual warnings. See Thomas J. Moore et al., *Time to Act on Drug Safety*, 279 JAMA 1571, 1572 (1998) (“[N]ew warnings about the addictive properties of propoxyphene had no effect on either prescription volume or the number of overdose deaths.”).

<sup>85</sup> See Patricia J. Zettler et al., *Implementing a Public Health Perspective in FDA Drug Regulation*, 73 FOOD & DRUG L.J. 221, 223–24, 235–41, 255–56 (2018); cf. Noah, *supra* note 1, at 56 (“[S]uch regulatory actions—whether expressed as a refusal to allow an analgesic product to enter the market initially or the withdrawal of such a product in the face of rampant abuse—would have to grapple with the classic difficulty of choosing between the medical needs of individual patients and the broader societal hazards associated with the availability of such products.”); *id.* at 64 (“[L]icensing decisions should not reflect an excessive preoccupation with the potential for abuse unless the products genuinely have no value as therapeutic interventions.”).

<sup>86</sup> See *Am. Pharm. Ass’n v. Weinberger*, 377 F. Supp. 824, 828–31 (D.D.C. 1974) (invalidating the FDA’s effort to limit the dispensing of methadone because the standard for drug approval relates only to a drug’s intrinsic safety when used as directed and also because Congress had assigned responsibility to restrict the distribution of controlled substances to the DEA), *aff’d per curiam sub nom.* *Am. Pharm. Ass’n v. Mathews*, 530 F.2d 1054 (D.C. Cir. 1976); see also *Mathews*, 530 F.2d at 1055 (McGowan, J., concurring) (“[M]ethadone is safe for its intended use notwithstanding the possibility that it will be employed in unintended fashions.”); *Ass’n Am. Physicians & Surgeons, Inc. v. FDA*, 226 F. Supp. 2d 204, 216–18 (D.D.C. 2002) (interpreting the methadone decision as limiting the agency’s ability to evaluate the safety of unintended uses of drugs even when not subject to DEA controls).

so given the all-or-nothing judgment involved in licensure.<sup>87</sup> As the next Section explains, risk-management tools more aggressive than stern directions in the approved labeling but less draconian than nonapproval offer an intermediate option for addressing concerns about irresponsible prescribing practices and misuse by patients.<sup>88</sup>

#### *D. Failures to Impose Radical Distribution Controls*

In previous work, I have called for restrictions on the types of health care professionals entitled to prescribe drugs prone to inappropriate use,<sup>89</sup> including

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<sup>87</sup> See Bernstein, *supra* note 27, at A3 (“FDA Commissioner Scott Gottlieb issued an unusual statement saying he would seek more authority for the agency to consider whether there are too many similar drugs on the market, which might allow the agency to turn down future applications for new opioid approvals. . . . [A]gency critics and some public officials have clamored for a holistic approach to narcotic painkillers, instead of the FDA’s practice of evaluating each opioid application on its own.”); see also *id.* (adding that, “[i]ncluding brand name and generic drugs, there are nearly 400 opioids on the market”).

<sup>88</sup> See Noah, *supra* note 1, at 56 (“Providing more refined regulatory options may allow for a more sensible resolution of the perennial tension between patient access and drug diversion.”); *id.* at 64 (“[T]he [FDA] may have placed excessive faith in the good sense of physicians and the power of labeling to encourage proper use and to limit the occasions for inappropriate prescribing.”); cf. Lars Noah, *Medicine’s Epistemology: Mapping the Haphazard Diffusion of Knowledge in the Biomedical Community*, 44 ARIZ. L. REV. 373, 437–40 & n.290 (2002) (explaining that the agency has lost some of its confidence in the willingness of health care professionals to pay attention to important labeling information); *id.* at 440 (“FDA officials openly chastised physicians for disregarding instructions in the labeling for newly approved drugs, and they warned that the agency might have to become more cautious in approving medical technologies because physicians seemed incapable of following directions.”); *id.* at 462 (concluding that “it makes little sense for the courts to disregard what may be the most evidence-based of all practice guidelines just because doctors habitually ignore them”).

<sup>89</sup> See Lars Noah, *Ambivalent Commitments to Federalism in Controlling the Practice of Medicine*, 53 U. KAN. L. REV. 149, 188–89 (2004).

One particularly controversial risk management strategy would allow only a limited group of medical specialists to prescribe certain especially hazardous drugs. After all, with the ever-expanding number and complexity of pharmaceutical treatments, general practitioners find it difficult to stay informed of appropriate interventions for different conditions, and they may find it even more difficult to resist the demands made by patients who have seen a product advertised for what ails them. The result may be indiscriminate prescribing of powerful therapeutic agents. Moreover, if states increasingly allow non-physicians to prescribe drugs, the FDA may have to rethink its broad deference to state licensing judgments and respond by imposing such special restrictions more frequently or even by creating different classes of prescription drugs.

opioid analgesics.<sup>90</sup> Although the FDA enjoyed no statutory authority to impose such controls at the time, it had successfully persuaded manufacturers of particularly hazardous nonnarcotic drugs to accept restrictions on distribution as a condition of continued licensure.<sup>91</sup> As elaborated below, Congress delegated explicit power to impose such restrictions more than a decade ago, but the agency has made only feeble attempts to use these tools to crack down on the inappropriate prescribing of opioid analgesics.

Approved treatments for persons addicted to opioids face additional restrictions on access by virtue of special federal legislation. In 1974, Congress mandated that physicians would have to secure a separate registration from the DEA before dispensing any controlled substance for the purposes of detoxification (short-term) or maintenance (long-term) treatment of opiate-dependent individuals.<sup>92</sup> At the time, only the Schedule II drug methadone served this purpose, and only clinics accredited as opioid treatment programs by the Substance Abuse and Mental Health Services Administration (SAMHSA) could dispense the drug. Physicians could, however,

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*Id.* at 190–91 (footnotes omitted); *see also id.* at 189–90 (identifying several prescription drugs already subject to special distribution restrictions). As I explained at length in that article, the Constitution would not stand in the way of doing so. *See id.* at 158–71; *see also id.* at 168 (“Congress has chosen to leave matters of medicine to the states, which in turn have chosen to leave these matters largely to professional self-regulation. Nothing in the Constitution requires that doctors be given such a wide berth.”); *id.* at 193 (“[E]fforts to protect patients by limiting the distribution of hazardous prescription drugs should not founder on an exaggerated preoccupation with the rights of either states or physicians.”).

<sup>90</sup> *See* Noah, *supra* note 1, at 64 (“[T]he government might limit access to those medical specialists who usually encounter persons suffering severe or chronic pain—including, for instance, oncologists and orthopedic surgeons along with pain specialists—in the hopes that such specialists would better resist the tendency to prescribe Schedule II analgesics for patients for whom milder agents would work equally well.”); *cf. id.* (conceding, however, that “this would risk creating serious access problems for legitimate patients, at least if the range of specialists was defined too narrowly”); *id.* at 63 (elaborating on this concern).

<sup>91</sup> *See* Lars Noah, *Governance by the Backdoor: Administrative Law(lessness?) at the FDA*, 93 NEB. L. REV. 89, 132–36 (2014); Scott Gottlieb, Opinion, *Prescription for Trouble*, WALL ST. J., Mar. 6, 2007, at A19 (explaining that risk-management plans “already guide the use of about 30 marketed drugs as part of ‘voluntary’ arrangements with drug companies”); *cf. Anna Wilde Mathews & Gary Fields, Federal Agencies Seek to Curb Abuse of Potent Painkillers*, WALL ST. J., Dec. 3, 2003, at B1 (“The FDA has never limited any opioid to certain pharmacies, and agency officials say they don’t have the authority to block certain physicians from prescribing a drug.”).

<sup>92</sup> *See* Narcotic Addict Treatment Act of 1974 (NATA), Pub. L. No. 93-281, § 3, 88 Stat. 124, 124–25 (codified as amended at 21 U.S.C. § 823(g)); *see also* Stephen P. Molinari et al., *Federal Regulation of Clinical Practice in Narcotic Addiction Treatment: Purpose, Status, and Alternatives*, 22 J.L. MED. & ETHICS 231, 238 (1994) (“The NATA has created a closed distribution system unique to pharmacotherapy and the practice of medicine.”). *See generally* INST. OF MED., FEDERAL REGULATION OF METHADONE TREATMENT (Richard A. Rettig & Adam Yarmolinsky eds., 1995).

continue to freely prescribe methadone for pain relief.<sup>93</sup> In 2000, Congress authorized waivers of these registration and dispensing requirements for drugs residing in a lower schedule.<sup>94</sup> A couple of years later, the FDA approved the Schedule III drug buprenorphine (e.g., Suboxone) for use in treating opioid use disorder.<sup>95</sup>

In order to qualify for a waiver, physicians interested in prescribing buprenorphine could complete eight hours of special training (unless they already had certain specialty certifications or experience), secure a certificate from SAMHSA subject to annual renewal, and, after a limit of thirty patients during their first (probationary) year, they could treat no more than one hundred patients at a time with buprenorphine.<sup>96</sup> Such obstacles have discouraged physicians from offering medication-assisted treatment for addiction.<sup>97</sup> In 2016, SAMHSA raised the cap on the number of patients to 275 (after a physician had spent one year at the one-hundred-patient cap),<sup>98</sup> and in 2018 the SUPPORT for Patients and Communities Act included a provision that could loosen the prerequisites for a waiver even

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<sup>93</sup> See Schottenfeld et al., *supra* note 35, at 228 (“Primary care providers may legally prescribe methadone for pain with little to no training on how to do so safely, but they cannot prescribe it to treat addiction in primary care, since it can only be dispensed for that purpose from specially licensed clinical settings.”); see also Erik Eckholm & Olga Pierce, *Methadone Rises as a Painkiller with Big Risks*, N.Y. TIMES, Aug. 17, 2008, at A1 (“Methadone, once used mainly in addiction treatment centers to replace heroin, is today being given out by family doctors, osteopaths and nurse practitioners for throbbing backs, joint injuries and a host of other severe pains.”); Catherine Larkin, *Advisory Issued on Methadone; The Drug Could Kill or Seriously Hurt New Patients Taking It for Pain, the FDA Says*, PHILA. INQUIRER, Nov. 28, 2006, at A6.

<sup>94</sup> See Drug Addiction Treatment Act of 2000, Pub. L. No. 106-310, tit. XXXV, § 3502(a)(5), 114 Stat. 1101, 1222 (codified as amended at 21 U.S.C. § 823(g)(2)).

<sup>95</sup> See Christine Vestal, *Few Doctors Sign up to Treat Opioid Addiction*, WASH. POST, Mar. 15, 2016, at E1. In 2010, the FDA approved naltrexone (e.g., Vivitrol®) to treat addiction, though unlike the other two it operates as an opioid antagonist and therefore has no use as an analgesic. See *id.* (adding that “it is expensive and not widely used for opioid addiction in much of the country”).

<sup>96</sup> See 21 U.S.C. § 823(g)(2)(B), (G)(ii) (2018).

<sup>97</sup> See Goodnough, *supra* note 39, at A15 (“Only about 5 percent of the nation’s doctors are licensed to prescribe [buprenorphine], and shortages are especially acute in rural regions.”); see also C. Holly A. Andrilla et al., *Barriers Rural Physicians Face Prescribing Buprenorphine for Opioid Use Disorder*, 15 ANNALS FAM. MED. 359, 359 (2017). In 2016, Congress provided that nurse practitioners and physician assistants could also qualify after completing 24 hours of training. See Comprehensive Addiction and Recovery Act of 2016, Pub. L. No. 114-198, § 303(a)(1)(C)(v), 130 Stat. 695, 721 (codified at 21 U.S.C. § 823(g)(2)(G)(iv)).

<sup>98</sup> See Medication Assisted Treatment for Opioid Use Disorders, 81 Fed. Reg. 44,712, 44,738–39 (July 8, 2016) (codified at 42 C.F.R. pt. 8(F)); Juliet Eilperin, *HHS Allows More Patients to Obtain Medication to Treat Opioid Addiction*, WASH. POST, July 7, 2016, at A15.

further.<sup>99</sup> Nonetheless, physicians can more easily prescribe narcotic analgesics than the controlled substances used to treat those addicted to such opioids.<sup>100</sup> This arrangement strikes me as precisely backwards.

In 2007, Congress granted the FDA authority to adopt various distribution controls—called “risk evaluation and mitigation strategy” (REMS) requirements, particularly the so-called “elements to assure safe use” (ETASU).<sup>101</sup> These may include requirements that:

- (A) health care providers who prescribe the drug have particular training or experience, or are specially certified . . . ;
- (B) pharmacies, practitioners, or health care settings that dispense the drug are specially certified . . . ;
- (C) the drug be dispensed to patients only in certain health care settings, such as hospitals;
- (D) the drug be dispensed to patients with evidence or other documentation of safe-use conditions, such as laboratory test results;
- (E) each patient using the drug be subject to certain monitoring; or
- (F) each patient using the drug be enrolled in a registry.<sup>102</sup>

More than a decade later, however, the FDA has not tested the full reach of these new powers.

Each of the clauses in the statutory provision offers an opportunity for guarding against the irresponsible use of opioids.<sup>103</sup> Indeed, the FDA could use its REMS/ETASU powers to impose on a nationally uniform basis many of the state-

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<sup>99</sup> See Pub. L. No. 115-271, § 3202(a), 132 Stat. 3894, 3945 (2018) (to be codified at 21 U.S.C. § 823(g)(2)(G)(ii)(VIII)) (allowing waivers for recent graduates based on proof of a certain amount of coverage of these issues in medical school).

<sup>100</sup> See Schottenfeld et al., *supra* note 35, at 228 (“[O]nce opioid use disorder develops, it is far more difficult for the same primary care providers to offer treatment than it was for them to contribute to the development of that disorder in the first place.”); *id.* at 232 (favoring the reduction of restrictions on the prescribing of buprenorphine in treating addicts); see also Melissa M. Ferrara, Comment, *The Disparate Treatment of Addiction-Assistance Medications and Opiate Pain Medications Under the Law: Permitting the Proliferation of Opiates and Limiting Access to Treatment*, 42 SETON HALL L. REV. 741, 744, 756–61, 766–67 (2012).

<sup>101</sup> See Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(b), 121 Stat. 823, 926, 930–37 (codified at 21 U.S.C. § 355-1(f)–(h)); see also Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 SAN DIEGO L. REV. 427, 463 (2015) (“The drug manufacturer is the entity ultimately responsible for ensuring that REMS requirements are met—meaning that the drug manufacturer, and not medical practitioners, will be the subject of any FDA enforcement actions that result from REMS violations . . . [, though] practitioners are responsible for carrying out many of the elements to assure safe use.”).

<sup>102</sup> 21 U.S.C. § 355-1(f)(3) (2018).

<sup>103</sup> See Lewis S. Nelson & Jeanmarie Perrone, *Curbing the Opioid Epidemic in the United States: The Risk Evaluation and Mitigation Strategy (REMS)*, 308 JAMA 457 (2012).

level opioid initiatives that have drawn praise.<sup>104</sup> For instance, clause (D) could support regular urine testing of patients to confirm appropriate use before issuing a new prescription (as the CDC guidelines recommended), much like the pregnancy tests required for drugs known to cause birth defects.<sup>105</sup> Similarly, the agency might use clause (E) to insist that prescribers enter into “opioid agreements” with their patients as a few state legislatures have mandated.<sup>106</sup> Although the clause (F) registry

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<sup>104</sup> In recent years, the states have taken the lead in addressing this crisis. See Barry Meier & Sabrina Tavernise, *States Push to Curb Painkiller Overuse*, N.Y. TIMES, Mar. 12, 2016, at B1 (“[T]he pace of activity in states has grown so intense that experts are having difficulty keeping track. Currently, there are about 375 proposals in state legislatures that would regulate pain clinics and several aspects of prescribing painkillers . . .”). See generally Andrew M. Parker et al., *State Responses to the Opioid Crisis*, 46 J.L. MED. & ETHICS 367, 368–76 (2018). Limitations on the number of doses to prescribe initially represent one popular response. See *id.* at 368 (“Half the states have limited the number of opioid pills that can be written in an initial prescription.”); *id.* at 369 (“Massachusetts . . . set a seven-day policy for new prescriptions, which has become the most common benchmark nationwide, though some states set limits as low as three days while others go up to 14 days.”).

<sup>105</sup> See Lars Noah, *The Little Agency That Could (Act with Indifference to Constitutional and Statutory Strictures)*, 93 CORNELL L. REV. 901, 915 (2008) (“For instance, when it approved Thalomid<sup>®</sup> (thalidomide) for the treatment of leprosy patients, the FDA conditioned approval on extremely strict marketing controls because of the serious risk of birth defects: distribution only through specially registered physicians and pharmacists, and tracking of patients, who must agree to use two forms of contraception and undergo frequent pregnancy tests.”); Lars Noah, *Too High a Price for Some Drugs?: The FDA Burdens Reproductive Choice*, 44 SAN DIEGO L. REV. 231, 234–35 (2007) (explaining that, in 2001, the FDA approved Hoffmann-La Roche’s program for Accutane<sup>®</sup> (isotretinoin), which “attempted to require (through physician registration with the manufacturer and use of special qualification stickers as a prerequisite for dispensing by pharmacists) a negative pregnancy test before prescribing a nonrefillable one month supply in addition to an agreement by patients to use two methods of contraception or abstain from sexual activity”); *id.* at 233–39 (elaborating on these and other efforts to restrict access to teratogenic drugs); *id.* at 245 (explaining the nominally voluntary nature of these programs given the agency’s lack of delegated authority to mandate them at the time); see also *id.* at 245–46 (“In the event of widespread noncompliance by physicians, pharmacists, or patients, the FDA could threaten to withdraw the manufacturer’s license to sell the drug, but it could take no action against noncompliant providers or users.”); *id.* at 248–58 (questioning the constitutionality of the indirectly imposed requirement for the concomitant use of contraceptives).

<sup>106</sup> See, e.g., ARK. CODE ANN. § 20-7-707(a)(2) (2018); MASS. GEN. LAWS ANN. 94C § 18A(b) (2018); N.J. STAT. ANN. § 24:21-15.2(e), (g) (2018); see also Michelle Andrews, *When Patients Have to Sign “Pain Contracts,”* WASH. POST, Apr. 5, 2011, at E4. These laws seek to reduce rates of abuse either because the added burden created by such mandates make health professionals hesitate or because the agreements usefully engage patients in minimizing risks. See Joanna L. Starrels et al., *Systematic Review: Treatment Agreements and Urine Drug Testing to Reduce Opioid Misuse in Patients with Chronic Pain*, 152 ANNALS INTERNAL MED. 712, 717–18 (2010). In 2009, the FDA suggested including such a requirement in its opioid REMS but then dropped the idea in the face of objections. See



contemplates more of an epidemiological undertaking, it could allow for the creation of a federal version of the prescription drug monitoring databases (PDMPs) now used in various ways in every state.<sup>107</sup> More broadly, the agency might cap the duration of use more stringently than the DEA's current ninety-day limit on a single prescription for Schedule II drugs.<sup>108</sup>

The first three clauses of the statutory provision quoted above would allow even more onerous restrictions on access. In fact, the FDA imposed a hospital-only limitation under clause (C) when it recently approved a sublingual tablet form of sufentanil (Dsuvia),<sup>109</sup> and perhaps other narcotic analgesics belong only in skilled nursing facilities or hospice centers. The FDA could demand more careful scrutiny by pharmacists, as some states have done, pursuant to clause (B). Potentially the most powerful REMS/ETASU authority, clause (A), adds parenthetically that “the opportunity to obtain such [prescriber] training or certification with respect to the drug shall be available to any willing provider from a frontier area in a widely available training or certification method (including an on-line course or via mail) as approved by the Secretary.”<sup>110</sup> Interestingly, however, no such caveat applies (nor

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Richard Payne et al., *A Rose by Any Other Name: Pain Contracts/Agreements*, AM. J. BIOETHICS, Nov. 2010, at 5, 7.

<sup>107</sup> See Notice of Public Hearing, Opioid Policy Steering Committee: Prescribing Intervention—Exploring a Strategy for Implementation, 82 Fed. Reg. 58,572, 58,574 (Dec. 13, 2017); see also Rebecca L. Haffajee, *Preventing Opioid Misuse with Prescription Drug Monitoring Programs: A Framework for Evaluating the Success of State Public Health Laws*, 67 HASTINGS L.J. 1621, 1632 (2016) (“PDMPs are a popular, state-level, legal mechanism that have gained the reputation of having incredible promise for addressing opioid misuse.”); *id.* at 1634–37, 1685–86 (elaborating); *id.* at 1672–76 (reviewing the literature on their effectiveness); Joanna Shepherd, *Combating the Prescription Painkiller Epidemic: A National Prescription Drug Reporting Program*, 40 AM. J.L. & MED. 85, 110–12 (2014) (advocating the creation of a federal PDMP).

<sup>108</sup> *Cf. supra* note 60 (discussing FDA efforts to limit the number of dosage units dispensed). A rule adopted by the DEA allowed a limited circumvention of the statutory prohibition on refills for Schedule II drugs by letting patients receive three 30-day prescriptions at a single visit. See Issuance of Multiple Prescriptions for Schedule II Controlled Substances, 72 Fed. Reg. 64,921, 64,930 (Nov. 19, 2007) (codified at 21 C.F.R. § 1306.12(b)).

<sup>109</sup> See Abby Goodnough, *F.D.A. Clears Potent Opioid Despite Worry Abuse Is Likely*, N.Y. TIMES, Nov. 3, 2018, at A12 (“[I]ts only permitted use will be in hospitals, surgical centers and other medically supervised settings. . . . Dsuvia will not be dispensed to patients for home use or available at retail pharmacies, and . . . it should only be administered by health care providers with the single-dose applicators.”); see also *id.* (adding that the REMS also required “monitoring distribution of the drug and auditing wholesalers’ data; evaluating whether hospitals and other health care providers are using the drug properly; and monitoring for any diversion or abuse”); *cf. Swayze v. McNeil Labs., Inc.*, 807 F.2d 464, 465–66, 471–72 (5th Cir. 1987) (discussing allegations about poorly supervised surgical use of Sublimaze® (fentanyl) by certified registered nurse anesthetists in Mississippi hospitals).

<sup>110</sup> 21 U.S.C. § 355-1(f)(3)(A) (2018). A similar caveat appears in the second clause, which relates to dispensers. Congress more generally specified that ETASU requirements must “not be unduly burdensome on patient access to the drug.” *Id.* § 355-1(f)(2)(C). In

could it) to the option of demanding that a prescriber have “particular . . . experience,” which would seem to allow requiring expertise not attainable through a quickie distance training session.

In one of its first attempts to use this power on a class-wide basis, the agency initiated a REMS process for extended-release (long-acting) opioids that would have allowed prescribing only after a physician had completed an educational program.<sup>111</sup> Physicians evidently resisted this idea, with one survey reporting that more than 13 percent of primary care doctors would stop prescribing opioids if first forced to take 4–8 hours of training.<sup>112</sup> To me that means the proposed training requirement was not nearly onerous enough, but the FDA took precisely the opposite lesson away from such feedback and opted for a voluntary approach.<sup>113</sup> More recently, however, it has expressed renewed interest in mandatory training for prescribers.<sup>114</sup>

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construing this caveat, however, the FDA should reference its approved labeling as defining the narrow class of appropriate patients.

<sup>111</sup> See Notice of Public Meeting, Risk Evaluation and Mitigation Strategies for Certain Opioid Drugs, 74 Fed. Reg. 17,967, 17,969 (Apr. 20, 2009); Gardiner Harris, *F.D.A. to Place New Limits on Prescriptions of Narcotics*, N.Y. TIMES, Feb. 10, 2009, at A13; see also Notice of Availability, Draft Blueprint for Prescriber Education for Long-Acting/Extended-Release Opioid Class-Wide Risk Evaluation and Mitigation Strategy, 76 Fed. Reg. 68,766 (Nov. 7, 2011). A few states subsequently imposed such a requirement. See, e.g., N.Y. PUB. HEALTH LAW § 3309-a(3) (2018) (requiring three hours of specialized training every three years).

<sup>112</sup> See Kieran A. Slevin & Michael A. Ashburn, *Primary Care Physician Opinion Survey on FDA Opioid Risk Evaluation and Mitigation Strategies*, 7 J. OPIOID MGMT. 109 (2011). Other researchers noted that some health care providers had expressed concerns that ETASU may cause improper substitutions, including “non-REMS pain drugs, such as Tylenol III, for Onsolis in order to avoid having to comply with the REMS requirements.” Andrew Wilson & Christopher-Paul Milne, *FDA’s Risk Evaluation and Mitigation Strategies (REMS): Effective and Efficient Safety Tools or Process Poltergeist*, 66 FOOD & DRUG L.J. 569, 579 (2011); see also *id.* at 580 (noting a similar comment from surveyed pharmacists). Encouraging the substitution of a Schedule II (fentanyl) drug with a Schedule III (acetaminophen with codeine) drug strikes me, however, as a generally favorable consequence.

<sup>113</sup> See Notice of Public Workshop, Training Health Care Providers on Pain Management and Safe Use of Opioid Analgesics—Exploring the Path Forward, 82 Fed. Reg. 18,300, 18,302 (Apr. 18, 2017) (“The ER/LA Opioid Analgesics REMS [approved in July 2012] requires that prescriber training in the form of accredited continuing education be made available to health care providers who prescribe ER/LA opioid analgesics.”); John F. Peppin et al., *Issues and Critiques of the Forthcoming Risk Evaluation and Mitigation Strategy (REMS) for Opioids in Pain Management*, 27 ISSUES L. & MED. 91, 98–109, 114–16, 118–19 (2012); Barry Meier, *F.D.A. Won’t Order Doctors to Get Pain-Drug Training*, N.Y. TIMES, July 10, 2012, at B2. In 2016, a pair of advisory committees recommended, among other changes, extending this REMS to cover immediate-release (IR) opioids and making the prescriber training mandatory. See Notice of Availability, Draft Revisions to the Food and Drug Administration Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioids, 82 Fed. Reg. 21,818, 21,819 (May 10, 2017).

<sup>114</sup> See Laurie McGinley, *FDA Plans New Rules for Opioid Makers*, WASH. POST, July 11, 2017, at A6; Barry Meier, *Training Is Weighed for Opioid Prescribers*, N.Y. TIMES, May

Educational outreach of this type has not, however, worked particularly well in promoting adherence to clinical practice guidelines.<sup>115</sup>

Separately, to guard against the dangerous off-label use of transmucosal immediate-release fentanyl (TIRF) products, which it approved to treat breakthrough pain in cancer patients already taking (and tolerant to) other opioids, the FDA exercised its ETASU authority in 2011 to create a special distribution oversight program that imposed far greater restrictions than the REMS for other opioids.<sup>116</sup> As later summarized by the agency, this program “requires that healthcare providers who prescribe TIRF medicines for outpatient use are specially certified, that pharmacies that dispense TIRF medicines for inpatient and outpatient use are specially certified, and that completion of the prescriber-patient agreement form occurs prior to dispensing TIRF medicines for outpatient use.”<sup>117</sup> Because, however, the FDA left implementation up to the industry, the effort reportedly has failed to accomplish its goals.<sup>118</sup> The agency needs to show its willingness to enforce

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3, 2016, at B1. In discussing steps that the agency might now take, FDA officials noted that sodium oxybate, a non-opioid controlled substance derivative approved for narcolepsy (Xyrem<sup>®</sup>), faces a number of distribution restrictions including prescriber certification, patient enrollment, and dispensing from only a single mail-order pharmacy. *See* Gottlieb & Woodcock, *supra* note 83, at 422.

<sup>115</sup> *See* Noah, *supra* note 88, at 396 & n.94, 421–22 & n.210; *see also* Elizabeth A. McGlynn et al., *The Quality of Health Care Delivered to Adults in the United States*, 348 NEW ENG. J. MED. 2635, 2641–44 (2003) (finding widespread failures by physicians to follow patient care guidelines); Aaron E. Carroll, *It’s Hard for Doctors to Unlearn Things. That’s Costly for All of Us*, N.Y. TIMES, Sept. 11, 2018, at B5 (“The public shares some culpability. Americans often seem to prefer more care than less. But a lot of it still comes from physicians, and from our inability to stop when the evidence tells us to. Professional organizations and others that issue such guidelines also seem better at telling physicians about new practices than about abandoning old ones.”).

<sup>116</sup> *See Approved Risk Evaluation and Mitigation Strategies (REMS): Transmucosal Immediate-Release Fentanyl (TIRF) Products*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cder/remis/index.cfm?event=RemsDetails.page&REMS=60> [<https://perma.cc/GDB4-F9G8>]; *see also* Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for Purposes of the Food and Drug Administration Amendments Act of 2007, 73 Fed. Reg. 16,313, 16,314 (Mar. 27, 2008) (converting sixteen voluntary undertakings into REMS, including one for the fentanyl lollipop Actiq).

<sup>117</sup> Notice of Meeting, Joint Meeting of the Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee, 83 Fed. Reg. 32,134, 32,135 (July 11, 2018).

<sup>118</sup> *See* Emily Baumgaertner, *F.D.A. Documents Show It Failed to Stop Misuse of a Fast-Acting Opioid*, N.Y. TIMES, Aug. 3, 2018, at A13 (“About 5,000 pages of documents, obtained by researchers at Johns Hopkins University through the Freedom of Information Act . . . , show that the F.D.A. had data showing that so-called off-label prescribing was widespread. But officials did little to intervene.”). *See generally* Jeffrey Eric Rollman et al., *Assessment of the FDA Risk Evaluation and Mitigation Strategy for Transmucosal Immediate-Release Fentanyl Products*, 321 JAMA 676 (2019).

such requirements by visiting meaningful sanctions on noncompliant manufacturers of these products.

To my mind, the time has come for the FDA to take opioid analgesics out of the hands of primary care physicians, dentists, and other health care professionals apt to prescribe these drugs inappropriately.<sup>119</sup> Instead, chronic pain patients would have to get referred to specialists with the expertise to assess a patient's need for powerful relief and consider alternative treatments—in other words, reserve long-acting opioids as a last resort.<sup>120</sup> After it received express authority in 2007 to impose distribution controls, the agency could limit the power to prescribe certain particularly hazardous drugs to only a subset of health care professionals, along the same lines that Congress has restricted the Schedule III drug buprenorphine when used in treating addiction.<sup>121</sup>

Alternatively, Congress could decide to prohibit any and all off-label usage of Schedule II drugs. It did so once before with a narrow class of controlled substances,<sup>122</sup> and the DEA attempted to do so as well in connection with another

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<sup>119</sup> Unlike the DEA, which may revoke federal licenses to prescribe controlled substances on an individual basis (and only for cause), *see* 21 U.S.C. § 824(a) (2018), the FDA could use its REMS/ETASU authority to exclude large swaths of state-licensed prescribers without having to surmount the same procedural hurdles imposed on the DEA.

<sup>120</sup> *See* Noah, *supra* note 1, at 63 (“[T]he DEA urged Purdue Pharma to consider restricting distribution [of OxyContin] to pain management specialists on the theory that these physicians would know to use the drug only as a last resort, if other pharmaceutical options did not help a patient.”); Schottenfeld et al., *supra* note 35, at 226–27; *cf. id.* at 232 (“[S]ome states (such as Rhode Island) require primary care providers to consult with a pain medicine specialist or justify not doing so when opioids above a certain dose are prescribed.”); *id.* at 234 (disagreeing with this approach). Specialists can, of course, fall prey to the same fads and marketing pitches as general practitioners. *See, e.g.,* Catan & Perez, *supra* note 14, at A1 (focusing on Dr. Russell Portenoy and his subsequent change of heart); Barry Meier, *Tightening the Lid on Pain Prescriptions: Doctors Shift Amid Alarm on Overuse*, N.Y. TIMES, Apr. 9, 2012, at A1 (focusing on Dr. Jane Ballantyne and her revised views); *see also* Noah, *supra* note 88, at 405 & n.139 (warning of some of the dangers associated with medical specialization).

<sup>121</sup> *See supra* notes 94–99; *see also* Ferrara, *supra* note 100, at 763 (“OxyContin prescribers should be required to meet similar training standards. The OxyContin REMS is insufficient to ensure that practitioners are properly trained. Although information that the manufacturer provides to practitioners contains useful guidelines, there is no requirement that practitioners follow the guidelines, or even read the materials before prescribing the medication.”); *id.* (“Perhaps a DEA registration-and-waiver structure similar to that applicable to buprenorphine should also apply to OxyContin. This would allow practitioners with particularized training in pain management to prescribe OxyContin, and encourage . . . patients to pursue care with a practitioner with expertise in relieving pain.”).

<sup>122</sup> *See* 21 U.S.C. § 333(e)(1) (2018) (prohibiting the distribution of human growth hormone (HGH) for off-label use); *see also* United States v. Bader, 678 F.3d 858, 874–75 (10th Cir. 2012); Thomas T. Perls et al., *Provision or Distribution of Growth Hormone for “Antiaging”*: *Clinical and Legal Issues*, 294 JAMA 2086, 2087–88 (2005); Zettler, *supra* note 101, at 457–59 (concluding that Congress sought primarily to prohibit off-label uses that lacked any therapeutic purpose, including by athletes); *cf. id.* at 488 (“[S]ome

Schedule II drug.<sup>123</sup> However accomplished, such a move would no doubt infuriate many physicians and the powerful associations that represent their interests,<sup>124</sup> but so far they have largely managed to avoid taking responsibility for getting so easily duped by the pharmaceutical industry. In turn, drug manufacturers, who in the past may have preferred seeking approval only for the narrowest use while counting on widespread off-label prescribing,<sup>125</sup> would now have incentives to try to convince the FDA that their products deserve approval for “broad spectrum” usage; if they failed to do so, then only a narrow class of patients would receive such treatments.

At least with respect to the provisions addressing the FDA, the SUPPORT for Patients and Communities Act grants the agency little in the way of new authority; instead, this recently enacted legislation seems more preoccupied with nudging regulatory officials to make fuller use of their existing powers. It should not take yet another act of Congress to prod the FDA into taking serious—even if unpopular—steps that might come to grips with a problem that it had helped to unleash. Obviously, an urgent need exists for other efforts to address those individuals already harmed by past prescribing practices, but we can still take measures to guard against creating even more addicts as well as learn a lesson before another prescription drug epidemic emerges.

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commentators estimate that thirty percent of prescriptions for HGH are off-label, despite the prohibition on such prescription.”); *id.* at 498 n.410 (“The FDA has not exercised its REMS authority to prohibit off-label prescribing of drugs . . . .”); Jeff Swiatek, *FDA OKs Lilly Growth Drug*, INDIANAPOLIS STAR, July 26, 2003, at 1C (reporting that, in approving expanded use of Humatrope® to treat very short children, the FDA persuaded the manufacturer to market this new use only to pediatric endocrinologists).

<sup>123</sup> See Noah, *supra* note 89, at 179 & n.130 (discussing the DEA’s threat when it downscheduled the marijuana derivative dronabinol (Marinol®) to revoke the registration of any practitioner dispensing this anti-emetic beyond the FDA’s approved use in cancer patients). Insofar as a few states have specifically authorized certain off-label uses of Schedule II drugs, Congress might want to exempt these from such a prohibition.

<sup>124</sup> See Noah, *supra* note 57, at 74–75 (conceding that “any such initiative would trigger howls of protest from physician groups”); Meier, *supra* note 114, at B1 (reporting that the AMA strenuously objected when the FDA first proposed mandatory prescriber training for opioids); see also Lars Noah, *The Whole “Truthiness,”* 162 U. PA. L. REV. ONLINE 261, 263 (2014) (“Although it surely would offend the American Medical Association, which makes the idea politically unrealistic, such a conduct-focused solution to this supposedly intractable problem [of off-label prescription drug use] would not offend the Constitution, and . . . plainly would allow a ban on any affiliated advertising.”); Parker et al., *supra* note 104, at 369 (“Leaders of organizations including the American Medical Association . . . argue that [opioid] prescription limits undermine patient care because they are too rigid and interfere with doctors’ ability to create appropriate, individualized treatment plans.”); Zettler, *supra* note 101, at 441–46 (discussing the AMA’s political clout).

<sup>125</sup> See, e.g., Katie Thomas, *Drug Company Enlists Doctors Under Scrutiny: Big Payments for Top Painkiller Prescribers*, N.Y. TIMES, Nov. 28, 2014, at A1 (“The aggressive marketing of Subsys [by Insys], the company’s only brand-name product, is especially remarkable, given that its use is highly restricted; it is approved only for cancer patients who are already taking opioid painkillers around the clock. Previous analyses have shown that only 1 percent of prescriptions for the product are written by cancer specialists.”).