

COMMENTS

FROM PRESCRIPTION TO ADDICTION: TREATING THE CAUSE OF THE OPIOID EPIDEMIC AND IMPROVING THE FDA’S RISK EVALUATION AND MITIGATION STRATEGIES (REMS) PROGRAM

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INTRODUCTION

In October 2017, President Trump declared the opioid epidemic a public

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health emergency.¹ The following year, 10.3 million people in America misused opioid prescriptions.² By 2018, the U.S. Department of Health and Human Services (HHS) estimated that over 130 people died and will die each day from opioid-related drug overdoses.³ Forty percent of those deaths involved a prescription opioid.⁴ Since 2017, the Food and Drug Administration (FDA) rebuffed some of its own recommended regulations regarding opioid prescriptions and patients with Opioid Use Disorder (OUD).⁵ The Centers for Disease Control and Prevention (CDC) reported that the leading factor in the increase of opioid abuse, addiction, and related deaths is the uptick in prescribing opioids as a pain management method.⁶ Most federal drug regulation focuses on the safety of pharmaceuticals.⁷ However, the FDA will approve pharmaceuticals with a risk of addiction if the effectiveness outweighs the safety risk.⁸ Once the FDA approves a drug—aside from

1. Michael Tackett & Eileen Sullivan, *Trump Declares Commitment to Ending Opioid Crisis 'Once & For All,'* N.Y. TIMES (Apr. 24, 2019), <https://www.nytimes.com/2019/04/24/us/politics/trump-opioid-crisis.html>.

2. *The Opioid Epidemic by the Numbers*, U.S. DEP'T OF HEALTH & HUMAN SERVS., https://www.hhs.gov/opioids/sites/default/files/2019-11/Opioids%20Infographic_letter-SizePDF_10-02-19.pdf (last updated Oct. 2019).

3. *What Is the U.S. Opioid Epidemic?*, U.S. DEP'T OF HEALTH & HUMAN SERVS., <https://www.hhs.gov/opioids/about-the-epidemic/index.html> (last reviewed Sept. 4, 2019).

4. *Id.*

5. *See, e.g., Opioid Medications*, U.S. FOOD & DRUG ADMIN. (July 1, 2019), <https://www.fda.gov/drugs/information-drug-class/opioid-medications> (recommending decreased exposure and prevention of new addiction, support treatments for those with Opioid Use Disorder (OUD), fostering the development of novel pain treatment therapies, and improving enforcement and assessing benefit and risk information).

6. *See U.S. Prescribing Rate Map*, CTRS. FOR DISEASE CONTROL & PREVENTION, <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html> (last reviewed Oct. 3, 2018) [hereinafter *Prescribing Rate Map*] (noting prescriptions peaked in 2012 at a prescribing rate of 81.3 prescriptions per 100 persons); Teresa A. Rummans et al., *How Good Intentions Contributed to Bad Outcomes: The Opioid Crisis*, 93 MAYO CLINIC FOUND. FOR MED. EDUC. & RES. 344, 345–46 (2018) (discussing the historical trend of opioid prescription and how opioid prescriptions became the solution for any form of pain).

7. *See generally Laws, Regulations, Policies and Procedures for Drug Application*, U.S. FOOD & DRUG ADMIN. (Dec. 4, 2014), <https://www.fda.gov/drugs/development-approval-process-drugs/laws-regulations-policies-and-procedures-drug-applications> (stating that the purpose of the Food & Drug Administration (FDA) is to protect the consumer through the application of the Federal Food, Drug, and Cosmetic Act and the promulgation of regulations for Investigational New Drugs (INDs), New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), and Biologics License Application (BLAs)).

8. *See* Donald W. Light, *Risky Drugs: Why the FDA Cannot be Trusted*, HARV. UNIV. BLOG

criminal statutes and drug treatment programs—federal regulation does little to control how doctors prescribe the drug or what to do with a patient who develops an addiction.⁹

In 2007, Congress extended the FDA's authority to create the Risk Evaluation and Mitigation Strategies (REMS) Program.¹⁰ The REMS Program requires drug manufacturers to provide information about any opioid or drug it produces to fully inform prescribers about that drug. This ensures that prescribing the opioid outweighs the risk of abuse, addiction, or any other side effects.¹¹ The program is funded by the drug manufacturers, who provide unrestricted grants to accredited continuing education providers—for the development of educational courses for prescribers based on content outlined by the FDA.¹²

The CDC's data on opioid prescriptions show that, while the overall number of prescriptions began decreasing recently, there are still hotspots that

(July 17, 2013), <https://ethics.harvard.edu/blog/risky-drugs-why-fda-cannot-be-trusted> (“The bar for ‘safe’ is equally low, and over the past 30 years, approved drugs have caused an epidemic of harmful side effects, even when properly prescribed.”); see, e.g., *Approved Risk Evaluation and Mitigation Strategies (REMS)*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cder/remis/index.cfm?event=RemisDetails.page&REMS=17> (last updated Nov. 14, 2019) [hereinafter *Approved REMS*] (containing at least seventy unique opioids, including methadone hydrochloride, morphine sulphate, and oxycodone hydrochloride). See generally 21 C.F.R. § 314.105(c) (2019) (stating that for the FDA to approve a new drug, it only needs to meet “the statutory standards for safety and effectiveness”).

9. Cf. Elinore F. McCance-Katz, *Foreword to Facing Addiction in America: The Surgeon General's Spotlight on Opioids*, U.S. DEP'T HEALTH & HUMAN SERVS. 2 (Sept. 2018), https://addiction.surgeongeneral.gov/sites/default/files/Spotlight-on-Opioids_09192018.pdf (reporting that the U.S. Department of Health & Human Services (HHS) is currently “promoting early intervention and treatment as healthy alternatives to detaining people with opioid addictions in our criminal justice systems . . .”).

10. Food & Drug Administration Amendments Act of 2007, 21 U.S.C. § 355-1(a)(1) (2012).

11. *Risk Evaluation & Mitigation Strategies (REMS)*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems> (last updated Aug. 8, 2019) [hereinafter *REMS*]. In addition to the REMS material, which includes letters to participants, education programs, enrollment forms, program overviews, implementation systems, and other materials, each REMS includes a product list if there are multiple manufacturers, a list of the risks that the REMS seeks to mitigate, a summary of the information included, and an update history that tracks changes made by the contributing manufacturers. See *id.* (providing an example with Zyprexa Relprevv).

12. *Roles of Different Participants in REMS*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/drugs/risk-evaluation-and-mitigation-strategies-rems/roles-different-participants-rems> (last updated Jan. 26, 2018) [hereinafter *REMS*].

have high rates of overdoses.¹³ Additionally, the total number of opioid overdose related deaths have fallen, but this does not provide insight as to whether paramedics and health care providers are better equipped to respond to overdoses or if there are fewer overdoses that are not fatal.¹⁴ Moreover, some hotspots have prescription rates seven times higher than the national average.¹⁵ There is no indication as to what is causing differing rates among the hotspots throughout the country.¹⁶

Former executives of Rochester Drug Co-Operative—a large pharmaceutical company—were recently indicted on charges that several executives' actions contributed to the opioid epidemic.¹⁷ The company received over 2,000 orders from pharmacies that qualified as suspicious under Drug Enforcement Agency (DEA) regulations, but the company only reported four orders as suspicious to the DEA for further investigation.¹⁸ These and other charges against pharmaceutical companies and executives¹⁹ indicate that

13. See *Emergency Department Data Show Rapid Increases in Opioid Overdoses*, CTNS FOR DISEASE CONTROL & PREVENTION (Mar. 6, 2018, 1:00 PM), <https://www.cdc.gov/media/releases/2018/p0306-vs-opioids-overdoses.html> (“All five U.S. regions experienced rate increases; the largest was in the Midwest (70 percent), followed by the West (40 percent), Northeast (21 percent), Southwest (20 percent), and Southeast (14 percent).”).

14. See Selena Simmons-Duffins, *U.S. Overdose Deaths Dipped in 2018, But Some States Saw ‘Devastating’ Increases*, SHOTS HEALTH NEWS FROM NPR (July 18, 2019, 4:56 PM), <https://www.npr.org/sections/health-shots/2019/07/18/743161724/u-s-overdose-deaths-dipped-in-2018-but-some-states-saw-devastating-increases> (reporting that nationwide, opioid overdose deaths decreased nationwide by 4.2 percent in 2018). *But see Naloxone: The Opioid Reversal Drug that Saves Lives*, U.S. DEP’T OF HEALTH & HUMAN SERVS. 1 (Dec. 2018), <https://www.hhs.gov/opioids/sites/default/files/2018-12/naloxone-coprescribing-guidance.pdf> (encouraging an “all hands on deck” approach to the opioid epidemic by increasing the availability of Naloxone—the opioid overdose reversing drug).

15. Simmons-Duffins, *supra* note 14 (reporting that the overall rate of OUD-related deaths fell 4.2 percent, but eighteen states saw an increase, including Missouri with a seventeen percent increase).

16. *Id.*

17. Richard Gonzales, *Drug Distributor & Former Execs Face First Time Criminal Charges in Opioid Crisis*, NPR (Apr. 23, 2019, 9:43 PM), <https://www.npr.org/2019/04/23/716571375/drug-distributor-and-former-execs-face-first-criminal-charges-in-opioid-crisis>.

18. Gonzales, *supra* note 17.

19. Gonzales, *supra* note 17; Ashley Turner, *Insys Therapeutics Founder, Former Executives Found Guilty in Criminal Fentanyl Bribery Case*, CNBC (May 2, 2019), <https://www.cnbc.com/2019/05/02/insys-therapeutics-former-executives-found-guilty-in-criminal-opioid-case.html> (stating that these charges range from drug trafficking to racketeering); see also *Prescribing Rate Map*, *supra* note 6 (showing the Center for Disease Control and Prevention’s (CDC’s) data regarding the correlation between the number of opioid prescriptions and the rate of an OUD).

there are factors outside the hands of doctors and patients that are contributing to the opioid epidemic.

With opioids as the recommended treatment for conditions like cancer and chronic pain, prescribers must balance the benefit to the patient with the risk of OUD when opioid refills are no longer available.²⁰ The FDA is tasked with making prescription opioids as safe for the public as possible, which implies that the public should be kept safe when their prescription ends.²¹ One strategy of achieving this goal is to inform the prescribers of the risks associated with the particular opioid. There are existing resources and procedures that doctors can utilize when they suspect that a patient is abusing opioids.²² However, these strategies do not prevent patients from developing an OUD. Pushback on stricter opioid regulation is typically rooted in the need for doctors to have discretion when making a professional judgement between writing a prescription for patients to have access to the pharmaceuticals that they need to manage legitimate health problems and avoiding the risk of addiction altogether.²³

Most states have enacted legislation to limit the availability of opioids by restricting the supply that the patient can pick up from a pharmacy each

has been available since 2006).

20. Cf. Kylie Urban, *Prescribing Opioids for a Sprained Ankle?*, UNIV. OF MICH. HEALTH LAB (July 11, 2019), <https://labblog.uofmhealth.org/body-work/prescribing-opioids-for-a-sprained-ankle> (reporting that doctors do not typically prescribe opioids to patients with minor or temporary conditions like a sprained ankle but that 11.9 percent of sprained ankle patients receive an opioid prescription); *Prescription Opioid Use is a Risk Factor for Heroin Use*, NAT'L INST. ON DRUG ABUSE 6, <https://www.drugabuse.gov/node/pdf/19774/prescription-opioids-and-heroin> (last updated Jan. 2018) (reporting that almost 80 percent of heroin users reported first abusing prescription opioids before using heroin).

21. 21 U.S.C. § 393(b)(1) (2012) (stating that the FDA's mission is to "promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner . . .").

22. *Federal Resources*, U.S. DEP'T OF HEALTH & HUMAN SERVS. (Dec. 26, 2018), <https://www.hhs.gov/about/agencies/iea/partnerships/opioid-toolkit/federal-resources/index.html> (including "Prevention & Treatment Resources" and "Youth & Family Resources").

23. See Elizabeth Llorente, *As Doctors Taper or End Opioid Prescriptions, Many Patients Driven to Despair, Suicide*, FOX NEWS (Dec. 10, 2018), <https://www.foxnews.com/health/as-opioids-become-taboo-doctors-taper-down-or-abandon-pain-patients-driving-many-to-suicide> (noting how individuals legitimately prescribed opioids suffer from the current dosage regulations and lead them to commit suicide). Forcibly reducing dosage of prescription opioids causes some pain patients to consider or attempt suicide as an alternative to dealing with chronic pain. Cf. *Conant v. Walters*, 309 F.3d 629, 644–45 (9th Cir. 2002) (Kozinski, J., concurring) (cautioning that heavy government regulation limiting patients' access to drugs they need—here marijuana—will likely lead them to use find and use the drug on their own).

visit.²⁴ These regulations vary by state and have exceptions and means to work around the regulations.²⁵ For example, in Florida, the statute restricts patients to a three-day supply of opioids, but a doctor can prescribe a seven-day supply using his or her professional judgment.²⁶ Due to the recency of these regulations, there is a lack of reliable research showing whether the states' laws have impacted rates of OUD.²⁷

While the REMS Program is comprised of helpful information, the available information does not combat the risk of malicious drug manufacturers acting fraudulently and engaging in conduct that increases the number of unnecessary prescriptions.²⁸ Accordingly, the FDA should expand the REMS Program to include information on the drug manufacturers, including criminal charges and convictions of current and previous executives. This information will encourage doctors to be more sensitive to and cognizant of manufacturers' behavior. Ideally, before writing an opioid prescription, doctors will review this information about manufacturers, and exercise professional judgment to not write a prescription from one of these manufacturers when avoidable. The REMS Program statute already gives the FDA the authority to expand the information included in all of the drugs' REMS.²⁹ Under *Chevron v. National Resources Defense Council*,³⁰ the FDA's interpretation is the controlling interpretation.³¹

Moreover, Congress should act to strengthen the FDA's authority over opioid prescription by giving the FDA the power to enforce mandatory

24. See *Prescribing Policies: States Confront Opioid Overdose Epidemic*, NAT'L CONF. OF STATE LEGISLATORS (June 30, 2019), <http://www.ncsl.org/research/health/prescribing-policies-states-confront-opioid-overdose-epidemic.aspx> [hereinafter NAT'L CONF. OF STATE LEGISLATORS] (stating that thirty-three states have enacted opioid restricting legislation); Llorente, *supra* note 23 (same).

25. NAT'L CONF. OF STATE LEGISLATORS, *supra* note 24.

26. NAT'L CONF. OF STATE LEGISLATORS, *supra* note 24. Opioid restrictive laws limiting the supply of opioids to a patient range from three to fourteen days among states. Some states have included limits on Morphine Milligram Equivalents (MME), and others have given statutory direction or authorization to other entities to set limits or guidelines.

27. C. S. Davis et al., *Laws Limiting the Prescribing or Dispensing of Opioids for Acute Pain in the United States: A National Systematic Legal Review*, ELSEVIER (Nov. 3, 2018), <https://doi.org/10.1016/j.drugalcdep.2018.09.022>.

28. *Cf. REMS*, *supra* note 12 (omitting any information on the conduct of drug manufacturers).

29. 21 U.S.C. § 355-1 (2012) (stating that the Secretary of HHS will consider the "seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug").

30. 467 U.S. 837 (1984).

31. *Id.* at 865.

REMS Program training. Congress should take the authority and duty to monitor opioid orders from pharmacies. The FDA and the DEA are better suited for this task than the pharmaceutical companies, which have breached their duty to report.³²

Part I of this Comment examines the FDA's efforts to reduce the prevalence and risk associated with opioid prescriptions, particularly focusing on the REMS Program. Part II looks at the efforts made by other agencies—individually and cooperatively—including the CDC, HHS, and the DEA, to provide information to health care professionals on opioid prescriptions. Part III reviews how drug manufacturers have influenced doctors and consumers and the effects of their influence. Finally, Part IV provides recommendations for changes to the REMS Program and the communication and interaction between the agencies as a way to improve the efforts to quell the opioid crisis and limit the harsh effect that drug manufacturers have had on opioid prescriptions.

I. THE FDA'S RESPONSE TO THE OPIOID EPIDEMIC

The REMS Program includes a list of all of the medications included in the program and all certified manufacturers of the drug.³³ The information in the REMS Program pertains to the protocol the prescriber must follow, including certifications, pharmacies to use, forms to complete, and the specific events the program is attempting to avoid, such as prescribing and dispensing to patients who are abusing opioids.³⁴

32. William C. Becker & David A. Fiellin, *Federal Plan for Prescriber Education on Opioids Misses Opportunities*, ANNALS OF INTERNAL MED. (Aug. 7, 2012), <https://annals.org/aim/fullarticle/1305526>. See generally Brien T. O'Connor et al., *DOJ Settlement Looks to Set New Benchmark for Suspicious Order Monitoring*, ROPES & GRAY (July 14, 2017), <https://www.ropesgray.com/en/newsroom/alerts/2017/07/DOJ-Settlement-Looks-to-Set-New-Benchmarks-for-Suspicious-Order-Monitoring> (stating that a recent settlement should cause drug manufacturers to change how they monitor their customers' orders and how seriously the DEA is taking the manufacturers' duty).

33. See, e.g., *Approved Risk Evaluation & Mitigation Strategies (REMS)*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm> (last visited Dec. 1, 2019) (listing the fifty-eight approved entries); see also *Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation & Mitigation Strategy (REMS)*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=60> (last updated Sept. 7, 2017) (listing the nine manufacturers of a particular opioid, transmucosal immediate release fentanyl (TIRF), along with the information each manufacturer has provided to the REMS, which includes instructions on how to prescribe and track patients' use).

34. *REMS*, supra note 12.

In September 2018, the FDA expanded the REMS Program and created the Opioid Analgesic REMS.³⁵ Under this updated program, doctors, patients, pharmacies, and nurses have training available on pain management, including alternatives to opioids and safer ways to administer opioids.³⁶ The program is geared toward outpatient opioid prescriptions and is meant to communicate information about the risk of OUD directly to patients and doctors alike.³⁷ Since the expansion of the REMS Program into the Opioid Analgesic REMS Program, the rate of OUD has either remained constant or decreased, but the changes cannot be solely attributed to the REMS Program.³⁸ However, the Opioid Analgesic REMS Program does not require that doctors or health care professionals take the training.³⁹ Because the program is not mandatory for health care providers, its effect is limited to the prescribers who use the REMS Program.⁴⁰ The purpose of the program is to provide information on opioids with the intent that prescribers will write only educated and necessary prescriptions after considering this information.⁴¹

To illustrate the importance of education as it relates to opioid prescribing, HHS provided a five-point strategy for combating the opioid epidemic with the second point as improving data.⁴² The REMS and Opioid Analgesic

35. *FDA Takes Important Steps to Encourage Appropriate & Rational Prescribing of Opioids Through Final Approval of New Safety Measures Governing the Use of Immediate-Release Opioid Analgesic Medication*, U.S. FOOD & DRUG ADMIN. (Sept. 18, 2018), <https://www.fda.gov/news-events/press-announcements/fda-takes-important-steps-encourage-appropriate-and-rational-prescribing-opioids-through-final>.

36. *Id.*

37. *Id.*

38. M. Soledad Cepeda et al., *ER/LA Opioid Analgesics REMS: Overview of Ongoing Assessments of Its Progress & Its Impact on Health Outcomes*, 18 PAIN MED. 78, 84 (2017) (explaining that data shows that “complimentary initiatives as a whole have been associated with decreases in abuse of ER/LA opioids, but cannot be causally attributed to the REMS”).

39. *See* Cepeda, *supra* note 38.

40. Cepeda, *supra* note 38; *see Risk Evaluation & Mitigation Strategies (REMS)*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rem>s (last updated Aug. 8, 2019).

41. *REMS*, *supra* note 12.

42. Alex M. Azar II, *Strategy to Combat Opioid Abuse, Misuse, & Overdose*, U.S. DEP’T OF HEALTH & HUMAN SERVS. 3, 5–6, <https://www.hhs.gov/opioids/sites/default/files/2018-09/opioid-fivepoint-strategy-20180917-508compliant.pdf> (last visited Sept. 19, 2019) (outlining HHS’s strategy to respond to the opioid epidemic, which includes better information and better communication of the implications of that information); *Opioid Abuse in the U.S. & HHS Actions to Address Opioid-Drug Related Overdoses & Deaths*, U.S. DEP’T OF HEALTH & HUMAN SERVS. 1, 5 (Mar. 26, 2015), <https://aspe.hhs.gov/basic-report/opioid-abuse-us-and-hhs-actions-address-opioid-drug-related-overdoses-and-deaths> (identifying the goal of reducing the

REMS Programs provide useful information about opioid use and risks; however, without any enforcement, the information is not as effective in achieving its goals.⁴³ The effectiveness of FDA regulations relies heavily on communication, which includes the communication between the FDA and prescribers regarding what the FDA and other relevant agencies have identified as the risks of opioids.⁴⁴ There is currently no reliable data on the effectiveness of current FDA regulations, nor is there a clear idea of what “best practices” are for carrying out regulations.⁴⁵ Focusing on reliable information and a means of disseminating that information to the relevant parties would benefit the FDA in its efforts to fight the epidemic.

The FDA has made other efforts to address the opioid epidemic, including efforts to decrease access to illegitimately-obtained opioids by targeting illegal marketing practices and online sales of unapproved and unregulated opioids.⁴⁶ The FDA is also concerned with the packaging and disposal of current opioids and the approval of new opioids,⁴⁷ but the reality is that the

prevalence of OUD and stating that voluntary prescribing guidelines from the 2007 REMS Program are associated with a decline in opioid use).

43. Stephen Porada, *REMS: Red Tape or Remedy for Opioid Abuse?*, 60 J. FAM. PRAC. S55, S61 (Sept. 2011), <https://mdedge-files-live.s3.us-east-2.amazonaws.com/files/s3fs-public/Document/September-2017/CHPP001090S55.pdf> (criticizing the REMS Program’s reliance on doctors to utilize the program based only on their own initiative). See Cepeda *supra* note 38, at 78 (reporting that the REMS Program is distinct from continuing education (CE) training courses, and prescribers who completed REMS Program training had more knowledge of opioid tolerance, conversion between different opioid products, and product-specific information regarding indications and usage).

44. Cf. Becky A. Briesacher et al., *A Critical Review of Methods to Evaluate the Impact of FDA Regulatory Actions* 22, PHARMACOEPIDEMOLOGY & DRUG SAFETY 986 (2013) (“Among those studies finding significant intended effects of FDA actions, all cited the importance of intensive communication efforts.”).

45. See *id.* (identifying a “best practice” would mean finding the most accurate way to evaluate risk and consider how to reliably address the risk).

46. Deborah Kotz, *FDA Takes New Enforcement Actions as Part of the Agency’s Ongoing Effort to Combat the Illegal Online Sales of Opioids*, U.S. FOOD & DRUG ADMIN. (Apr. 2, 2019), <https://www.fda.gov/news-events/press-announcements/fda-takes-new-enforcement-actions-part-agencys-ongoing-effort-combat-illegal-online-sales-opioids>.

47. Douglas Throckmorton, *Statement by Douglas Throckmorton MD Deputy Center Director for Regulatory Programs in FDA’s Center for Drug Evaluation & Research on New Opioid Analgesic Labeling Changes to Give Providers Better Information for How to Properly Taper Patients Who Are Physically Dependent on Opioids*, U.S. FOOD & DRUG ADMIN. (Apr. 9, 2019), <https://www.fda.gov/news-events/press-announcements/statement-douglas-throckmorton-md-deputy-center-director-regulatory-programs-fdas-center-drug-0> (stating the FDA’s plans to begin requiring fixed-quantity packaging and to approve opioids that pose less risk than current options).

REMS Program may not be working as intended.⁴⁸ Additionally, the FDA is putting many of its resources toward border security to reduce the prevalence of illegal opioids, such as heroin, in the United States by partnering with the Customs and Border Protection (CBP).⁴⁹

Under current drug approval regulations, the FDA treats all pharmaceuticals nearly the same: it either approves or denies the drug and then moves on and reviews the next drug for approval.⁵⁰ To receive FDA approval for sale, the manufacturer must conduct its own research and submit it to the FDA. In this new drug application (NDA), evidence must demonstrate that the drug is safe and effective.⁵¹ The FDA's Center for Drug Evaluation and Research (CDER) has a team of physicians, statisticians, chemists, pharmacologists, and other scientists who will evaluate the manufacturer's evidence.⁵² The CDER team will not test the drug, but will conduct its own limited research.⁵³ If the CDER team verifies the information provided by the manufacturer, then the drug is approved and the manufacturer can market it, doctors may begin prescribing it, or drugstores may sell it as an over-the-counter drug.⁵⁴

The REMS Program and its opioid-focused expansions are additions to the FDA's usual practice that come after the FDA has approved the opioid.⁵⁵

48. Andrew Wilson & Christopher-Paul, *FDA's Risk Evaluation & Mitigation Strategies (REMS): Effective & Efficient Safety Tool or Process Poltergeist?*, 66 FOOD & DRUG L.J. 569, 585 (2011); see also Aaron Toleos, *It's Time to Wake Up from the REMS Cycle*, LOWN INST. (July 1, 2019), <https://lowninstitute.org/news/blog/its-time-to-wake-up-from-the-rems-cycle/> (reporting that there are fears that the REMS Program justifies the approval of drugs with adverse side-effects).

49. Scott Gottlieb, *Statement from FDA Commissioner Scott Gottlieb, M.D. on the Agency's 2019 Policy & Regulatory Agenda for Continued Action to Forcefully Address the Tragic Epidemic of Opioid Abuse*, FOOD & DRUG ADMIN. (Feb. 26, 2019), <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-agencys-2019-policy-and-regulatory-agenda-continued>.

50. Dov Fox, *Safety, Efficacy, & Authenticity: The Gap Between Ethics & Law in FDA Decision Making*, 2005 MICH. ST. L. REV. 1135, 1161–62 (2005).

51. *How Drugs Are Developed & Approved*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/drugs/development-approval-process-drugs/how-drugs-are-developed-and-approved> (last updated Jan. 7, 2019) (stating that the Center for Drug Evaluation and Research does not test drugs and that it only reviews the data provided by the company and limited data that it does collect).

52. *Id.*

53. *Id.*

54. *Id.*

55. See Fox, *supra* note 50, at 1161–62 (detailing the various steps of the approval process for new products).

However, the REMS Program currently does not go far enough. It should include regular updates on ways to prevent addiction, abuse, and most importantly, unnecessary prescriptions.

A. *The REMS Program*

Without mandatory training, the success of the Opioid Analgesic REMS Program depends on doctors making the choice to participate in the training or to review the information provided by the drug manufacturers.⁵⁶ When the program first began in 2007, commentary predicted that the FDA could not expect hope to be sufficient to induce wide-spread participation and that changing the program to make REMS training mandatory was inevitable.⁵⁷ However, Congress has yet to authorize mandatory REMS training twelve years later.

Since its implementation and even without compulsory training, the rates of OUD have either stabilized or begun shrinking.⁵⁸ However, there are many anti-opioid prescription and anti-OUD factors that could have contributed to this, so it would be inappropriate to assert that the REMS Program is the sole cause of the decrease in OUD.⁵⁹

The REMS Program is important because it provides information on each drug provided by the manufacturers.⁶⁰ By having the manufacturers participate, the REMS Program “misses opportunities to construct a system that avoids pharmaceutical industry influence, reaches an adequate number of prescribers, and includes competency-based prescribing.”⁶¹ As discussed in

56. Porada, *supra* note 43, at S61.

57. See Porada, *supra* note 43, at S61; Cepeda et al., *supra* note 38, at 84 (stating that the decrease in opioid abuse, overdose, and death that occurred after the REMS was implemented suggests that these complimentary initiatives as a whole have been associated with decreases in abuse of extended release long acting opioids, “but cannot be causally attributed to the REMS”).

58. Cepeda, *supra* note 38, at 81.

59. See 21 U.S.C. § 355-1 (2012) (including Prevention & Treatment Resources and Youth & Family Resources); Simmons-Duffins, *supra* note 14 (reporting that thirteen states saw a decrease between ten-to-thirty percent and eighteen states saw an increase of up to seventeen percent and stating that, with federal focus and funding, states have “focused on expanding access to medication-assisted treatment, and saturating communities with naloxone—the opiate overdose antidote”).

60. See Porada, *supra* note 43, at S59.

61. Becker & Fiellin, *supra* note 32; see David J. Rothman et al., *Professional Medical Associations and Their Relationships with Industry: A Proposal for Controlling Conflict of Interest*, AM. MED. ASS'N 1367, 1367–68 (Apr. 1, 2009) (stating that physician leaders and public officials fear that the drug industry’s influence over regulation will negatively affect prescriber’s ability to deliver effective health care while also “undermining the reputation” of the medical profession).

Part IV, there are legitimate reasons as to why we should be hesitant to trust pharmaceutical companies.⁶²

II. OTHER AGENCIES' RESPONSES TO THE OPIOID EPIDEMIC

Both the CDC and HHS have guidelines covering how prescribers ought to write prescriptions for opioids, and both agencies created these guidelines to prevent abuse and addiction.⁶³ Both agencies focus on prescribing as small of a dosage as necessary for as short of a time as possible, while heavily monitoring the patient for potential abuse.⁶⁴ However, these guidelines are not binding. The Health Insurance Portability and Accountability Act of 1996 (HIPAA), and a few other regulations, like the Affordable Care Act (ACA),⁶⁵ are the only controlling regulations that doctors must follow. The scope of HIPAA includes prevention of fraud and abuse; it does not include a method to specifically prevent opioid abuse and addiction.⁶⁶

The CDC and HHS collaborated on the Rx Awareness Campaign, a large and extensively-tested multimedia campaign to increase awareness and knowledge about the risks associated with prescription opioids and to prevent their misuse.⁶⁷ The Campaign is a platform for people who struggle with addiction to share their stories to warn against the dangers of prescription

62. See generally Beth Mole, *DEA Tracked Every Opioid Pill Sold in the U.S. The Data is Out—And It's Horrific*, ARS TECHNICA (July 17, 2019, 3:21 PM), <https://arstechnica.com/science/2010/07/76-billion-opioid-pills-in-7-years-how-pharma-companies-drowned-us-in-drugs> (stating that nearly 100,000 people were killed by overdoses from opioid drugs between the years of 2006 and 2012).

63. See *Safe Opioid Prescribing*, U.S. DEP'T OF HEALTH & HUMAN SERVS., <https://www.hhs.gov/opioids/prevention/safe-opioid-prescribing/index.html> (last updated Aug. 14, 2019); Deborah Dowell et al., *CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016*, 65 MORBIDITY & MORTALITY WKLY. REP. 1, 2 (Mar. 18, 2016).

64. See Dowell, *supra* note 63 (describing CDC's recommended guidelines for prescribing opioids; HHS also recommends these guidelines).

65. *Affordable Care Act Issues Physicians Need to Know*, AM. COLL. OF PHYSICIANS (2019), <https://www.acponline.org/advocacy/state-health-policy/help-your-patients-enroll-in-health-insurance/affordable-care-act-issues-physicians-need-to-know> (listing the requirements created by the ACA for doctors is limited to accepting patients with particular insurance plans and coverage).

66. *HIPAA: An Overview*, AM. COLL. OF PHYSICIANS (Sept. 2013), https://www.acponline.org/system/files/documents/running_practice/practice_management/regulatory_compliance/hipaa/hipaa_overview2013.pdf.

67. *Rx Awareness*, CTRS. FOR DISEASE CONTROL & PREVENTION (Mar. 12, 2019), <https://www.cdc.gov/rxawareness/about/index.html>.

opioid abuse.⁶⁸ The Rx Awareness Campaign focuses solely on the user, rather than on the role the prescriber plays in influencing over-prescription of opioids, while avoiding any consequences for the resulting OUD.⁶⁹

HHS launched its five-point response strategy to the opioid crisis in 2017.⁷⁰ The five points are: (1) access to better prevention, treatment, and recovery; (2) better data; (3) better pain management; (4) better training of overdose-reversing drugs; and (5) better research on pain and addiction.⁷¹ Most of HHS's actions focus on identifying persons with opioid abuse and offering treatment, recovery, and overdose support.⁷² The strategy offers guidance around which the FDA could structure its REMS Program for a more unified and cohesive effort against the opioid epidemic that focuses on the same risks; however, the REMS Program still leaves room for potential bad actors to escape liability.⁷³

There is potential for the FDA and the DEA to work together to ensure ethical reporting of suspicious opioid orders.⁷⁴ The DEA created the Automation of Reports and Consolidated Orders System (ARCOS) to help manufacturers and distributors identify suspicious opioid orders.⁷⁵ However,

68. *Id.*

69. *Cf. id.* (indicating that the prescription can lead to an overdose death, but not indicating that the prescriber has any role in preventing an addiction or death).

70. Azar, *supra* note 42.

71. Azar, *supra* note 42.

72. *See, e.g., Better Treatment, Prevention, & Recovery Services*, U.S. DEP'T OF HEALTH & HUMAN SERVS., <https://www.hhs.gov/opioids/about-the-epidemic/hhs-response/better-access/index.html> (last updated May 15, 2018).

73. *See* Alana Semuels, *Are Pharmaceutical Companies to Blame for the Opioid Epidemic?*, THE ATL. (June 2, 2017), <https://www.theatlantic.com/business/archive/2017/06/lawsuit-pharmaceutical-companies-opioids/529020/> (reporting that consumer attempts to sue pharmaceutical companies for the effects of the company's marketing fraud are unsuccessful because courts typically view individual consumers as responsible for their own addiction). *But see* Lenny Bernstein, *Johnson & Johnson Ordered to Pay \$572 Million for Its Role in Oklahoma's Opioid Crisis*, WASH. POST (Aug. 26, 2019), https://www.washingtonpost.com/health/johnson-and-johnson-is-responsible-for-fueling-oklahomas-opioid-crisis-judge-rules-in-landmark-case/2019/08/26/ed7bc6dc-c7fe-11e9-a4f3-c081a126de70_story.html.

74. *See Suspicious Order Reporting and Prescription Medications*, HEALTHCARE DISTRIBUTION ALL. (May 22, 2019), <https://hda.org/news/2019-05-22-suspicious-order-reporting> (reporting that, while the DEA's guidelines for suspicious orders is sparse, suspicious orders include unusual sizes, deviations, or frequencies).

75. *See* Jason Hedges et al., *DEA Launches New ARCOS Enhancement to Help Manufacturers & Distributors "Know Your Customer" & Detect Suspicious Orders*, HOGAN LOVELLS (Mar. 4, 2019), <https://www.hoganlovells.com/en/publications/dea-launches-new-arcos-enhancement-to-help-manufacturers-and-distributors-know-your-customer-and-detect-suspicious-orders>

manufacturers and distributors left the majority of suspicious opioid orders unreported,⁷⁶ contributing to the continuance of the epidemic. The FDA and DEA could address this problem through improved communication. If the DEA made the FDA aware of the risk posed by unreported orders, the FDA could respond appropriately.

III. DRUG MANUFACTURERS' CONTRIBUTION TO THE EPIDEMIC

In July 2019, a three-judge panel in the Northern District of Ohio ordered the release of the ARCOS database that detailed drug manufacturers' distribution of opioid pills.⁷⁷ The Department of Justice (DOJ) uses the ARCOS to bring federal charges against malicious manufacturers.⁷⁸ Under the current enforceable regulations, doctors have discretion in prescribing medication.⁷⁹ However, because of the lack of enforceable regulations, pharmaceutical companies have been able to use racketeering and corporate-level drug trafficking to take advantage of doctors' ability to prescribe.⁸⁰

Some courts have ruled against drug manufacturers and have imposed fines for criminal conduct.⁸¹ These sanctioned companies have responded

(describing how the ARCOS flags the sale of unusual quantities of opioids).

76. See, e.g., Madelein Thompson et al., *Drug Companies Shipped Hundreds of Millions of Suspicious Opioid Orders to Ohio*, *Court Documents Say*, CNN (July 22, 2019, 4:15 PM), <https://www.cnn.com/2019/07/22/us/opioid-crisis-violations-controlled-substances-act/index.html> (stating that Mallinckrodt Pharmaceuticals shipped 1,200 bottles of a oxycodone to one distributor in one night and failed to report it); Meredith Cohn, *Pharmaceutical Distributor Settles Claims It Failed to Report Suspicious Orders from Maryland, Elsewhere*, THE BALT. SUN (Dec. 23, 2016, 8:09 PM), <https://www.baltimoresun.com/health/bs-hs-cardinal-drug-settlement-20161223-story.html> (reporting that Cardinal Health, Inc. failed to report suspicious orders in Maryland, Florida, and New York).

77. Mole, *supra* note 62 (“[J]ust three companies made 88% of the opioid pills: SpecGx, Actavis Pharma, and Par Pharmaceutical, a subsidiary of Endo Pharmaceuticals.”).

78. See Mole, *supra* note 62.

79. Judith G. Edersheim & Theodore A. Stern, *Liability Associated with Prescribing Medications*, 11 PRIMARY CARE COMPANION J. CLINICAL PSYCHIATRY 115, 116 (2009) (stating that as long as the physician can demonstrate that the choice of prescription is within the standard of care, there is no liability for the occurrence of an adverse side-effect).

80. See Turner, *supra* note 19 (summarizing that the founder and four executives of Insys Therapeutics found guilty of racketeering).

81. See Gonzales, *supra* note 17 (reporting that the U.S. Attorney for the Southern District of New York charged Rochester Drug Co-Operative and two former executives with conspiracy to distribute controlled narcotics for non-medical reasons and conspiracy to defraud the United States).

by paying the fines.⁸² If the punishment is not deterring the behavior, then the punishment needs to change.

A. *Illegal Conduct*

It is well-documented that pharmaceutical companies were aware of the growing opioid epidemic as early as the late 1990s.⁸³ Given the severe consequences of the companies' conduct, companies and their executives are often analogized to drug cartels and street drug dealers.⁸⁴ This information would be particularly useful to doctors, since they—and the prescriptions they write—are the link between patients and companies.⁸⁵ Under this indirect drug distribution system, pharmaceutical companies focus on profit and use illicit payments and misleading information to persuade prescribers that their opioids are safer and more effective than the drugs actually are.⁸⁶ Moreover, the government has been aware of the problem, but has been slow to act against these companies.⁸⁷

82. See David Evans, *Pfizer Broke the Law by Promoting Drugs for Unapproved Uses*, HEAL (Nov. 9, 2009), <http://www.heal-online.org/pfizer110909.pdf> (“At Pfizer’s Pharmacia sentencing on Oct. 16, U.S. District Court Judge Douglas Woodlock said companies don’t appear to take the law seriously. ‘It has become something of a cost of doing business for some of these corporations, to shed their skin like certain animals and leave the skin and move on,’ he said.”).

83. See Barry Meier, *Origins of an Epidemic: Purdue Pharma Knew Its Opioids Were Widely Abused*, N.Y. TIMES (May 28, 2018, 4:37 PM), <https://www.nytimes.com/2018/05/29/health/purdue-opioids-oxycotin.html> (highlighting examples of the companies’ awareness of opioid abuse as early as 1997, such as emails from Purdue Pharma’s general counsel referring to remarks of abuse of opioids on the Internet in early 1999).

84. See Ryan Hampton, *Trump’s Border Wall Won’t Solve Addiction Crisis — but Finally Targeting Big Pharma Can*, USA TODAY (Feb. 5, 2019, 5:00 AM), <https://www.usatoday.com/story/opinion/voices/2019/02/05/trump-state-union-address-sackler-purdue-pharma-opioids-column/2766865002/> (commenting that the drug dealer Americans should worried about is big pharma, not “a drug lord from Mexico”); Aashish Hermranjani, *Opioids for the Masses—Is Big Pharma America’s Biggest Drug Dealer?*, THE FULLEST (Sept. 23, 2018), <https://thefullest.com/2018/09/23/opioids-for-the-masses-is-big-pharma-americas-biggest-drug-dealer/> (hypothesizing that big pharma is “America’s biggest drug dealer”).

85. See Michael L. Barnett et al., *Opioid Prescribing Patterns of Emergency Physicians and Risk of Long-Term Use*, 376 NEW ENG. J. MED. 663, 669–70 (Feb. 16, 2017), https://www.nejm.org/doi/full/10.1056/NEJMsa1610524?query=featured_home#t=abstract (analyzing data that suggests that receiving just one legal prescription for an opioid greatly increases the patient’s risk of long-term use and adverse outcomes).

86. See Ty McCoy, *The Need for Higher Punishment: Lock up the Real Drug Dealers*, 54 GONZ. L. REV. 48, 57 (2018).

87. See McCoy, *supra* note 86, at 57; cf. Geoff Mulvihill & Mark Gillispie, *Email: Opioid*

While our criminal system does not overlook the liability of corporate executives who enact illegal policies that have illegal repercussions,⁸⁸ the focus of law enforcement has been on the individual with OUD.⁸⁹ If the goal is to shrink the opioid epidemic and to use the authority of the CDC and HHS as guideposts, then the focus of OUD response and prevention should be on the pharmaceutical companies.⁹⁰

B. Pharmaceutical Marketing

One of the leading ways that pharmaceutical companies contribute to overprescribing is by aggressive, and occasionally misleading, marketing directly to doctors and consumers.⁹¹ Some countries have addressed this problem by banning marketing by pharmaceutical companies altogether.⁹²

Talks Fail, Purdue Bankruptcy Filing Expected, ASSOCIATED PRESS (Sept. 8, 2019), <https://apnews.com/7ab815a1ad1843f085a4137699b88631> (reporting on current litigation between Purdue Pharma and every state and 2,000 local governments).

88. *Cf.* *United States v. Park*, 421 U.S. 658, 670 (1975) (ruling that a criminal conviction based on strict liability was not unconstitutional). Thus, as the law stands, being ignorant of a corporation's criminal acts will not save an executive from the very real possibility of facing punishment, including incarceration.

89. *See* Kathryn F. Hawk et al., *Reducing Fatal Opioid Overdose: Prevention, Treatment and Harm Reduction Strategies*, 88 *YALE J. BIOLOGY & MED.* 235, 237–39 (2015) (highlighting that efforts to curtail the opioid epidemic have focused on (1) primary prevention, which focuses on individuals who are more likely to abuse opioids based on factors such as age and sex, (2) access to effective treatment, which means to increase access to methadone and buprenorphine to treat an OUD, and (3) harm reduction strategies, which includes increased access to Nalaxone and legislation addressing overdose response).

90. Bernstein, *supra* note 73 (describing a court verdict where a judge ruled that Johnson & Johnson was liable in part for the opioid epidemic in Oklahoma and ordered the company to pay damages for the cost of treatment, emergency care, law enforcement, social services, and other addiction-related needs for one year). *See also* Mulvihill & Gillispie, *supra* note 87 (reporting that the Pennsylvania Attorney General believes the Sackler family, the owner of Purdue, have “blood on their hands” for their role in the opioid epidemic).

91. *See* Charles Ornstein & Ryann Grochowski Jones, *Opioid Makers, Blamed for Overdose Epidemic, Cut Back on Marketing Payment to Doctors*, *PROPUBLICA* (June 28, 2018, 5:00 AM), <https://www.propublica.org/article/opioid-makers-blamed-for-overdose-epidemic-cut-back-on-marketing-payments-to-doctors%C2%A0>. Boston University School of Medicine “reported in May [2019] that for every meal a physician received related to an opioid product in 2014, there was an increase in opioid claims by that doctor for Medicare patients the following year. And a report from the New York State Health Foundation published this month found that physicians who received payments from opioid makers prescribed more opioids to Medicare patients than doctors who didn’t receive the payments.” *Id.*

92. *See* Susan Kelly, *U.S. Doctor Group Calls for Ban on Drug Advertising to Consumers*, *REUTERS*

Corporate greed has caused pharmaceutical companies to push ads onto both doctors and consumers alike with harmful results.⁹³ Pharmaceutical companies marketed their opioids to doctors as being more effective and less addictive than they actually are.⁹⁴ As a result of this deceptive marketing, there are ongoing lawsuits.⁹⁵ In a suit involving 2,300 local governments from twenty-three states that is nearing a settlement that would include future revenue from opioid sales going into a trust to help communities hit by the opioid epidemic and shift the leadership of Purdue Pharma from the Sackler family to a board of trustees, Attorney Generals are attempting to hold pharmaceutical companies and their leaders responsible for the epidemic.⁹⁶

(Nov. 17, 2015, 6:41 PM), <https://www.reuters.com/article/us-pharmaceuticals-advertising/u-s-doctor-group-calls-for-ban-on-drug-advertising-to-consumers-idUSKCN0T62WT20151117> (“The United States and New Zealand are the only two countries that allow direct-to-consumer advertising of prescription drugs.”); cf. *BREAKING: McCaskill Report Shows 1.6 Billion Opioid Doses Entered Missouri from 2012–2017*, U.S. S. COMM. ON HOMELAND SECURITY & GOVERNMENTAL AFFAIRS (July 12, 2018) (reporting that U.S. Senator Claire McCaskill began investigating the drug manufacturers Mallinckrodt, Endo, Teva, and Allergan for possible improper marketing, among other violations).

93. See Amanda L. Connors, Comment, *Big Bad Pharma: An Ethical Analysis of Physician-Directed & Consumer-Directed Marketing Tactics*, 73 ALB. L. REV. 243, 244 (2009) (asserting that brand name pharmaceutical company’s marketing toward doctors and patients compromises the fiduciary duty to the patient). See also Connors, *supra*, at 271 (showing that increased pharmaceutical advertisements are correlated to an increase in prescription drug sales while not sufficiently educating consumers on the drugs).

94. See Chris McGreal, *Johnson & Johnson Ran ‘Cunning’ Opioid Scheme to Market Opioids, Attorney Says*, THE GUARDIAN (July 19, 2019, 4:29 PM), <https://www.theguardian.com/us-news/2019/jul/15/johnson-johnson-trial-opioids-crisis-oklahoma-attorney-general> (elaborating that drug companies pressured doctors with false claims of the opioid’s increased effectiveness and decreased addictiveness).

95. McGreal, *supra* note 94. It “[i]s the conduct of these [defendant drug manufacturers] in embarking on a cunning, cynical and deceitful scheme to create and feed the need for opioids, engineer a mutant poppy to amplify the need they created, overstate the effectiveness and minimise [sic] the risk of these drugs, and to oversupply the addictive drugs that have devastated Oklahoma communities and wrecked countless Oklahoma families.” *Id. E.g.*, *City of Chicago v. Purdue Pharma*, 211 F. Supp. 3d 1058, 1063 (N.D. Ill. 2016) (stating that the City of Chicago alleged that the pharmaceutical company defendants engaged in deceptive marketing practices that caused doctors to submit claims that were allegedly false because they represented that opioids were medically necessary to treat chronic pain).

96. Brian Mann & Bobby Allyn, *Purdue Pharma Reaches Tentative Deal to Settle Thousands of Opioid Lawsuits*, NPR (Sept. 11, 2019, 8:21 PM), <https://www.npr.org/2019/09/11/759967610/purdue-pharma-reaches-tentative-deal-to-settle-thousands-of-opioid-lawsuits>.

Without any notification system, doctors in the remaining states could remain unaware of the litigation, not realizing that the pharmaceutical companies' practices may have influenced them and resulted in harm to their patients.

With the right to advertise pharmaceuticals well-established,⁹⁷ combating the opioid epidemic must be done while still preserving direct-to-consumer marketing because

[M]arketing will always be marketing; whatever restrictions are placed on drug company activities, and whatever efforts drug companies make to inform about the risks of their products, they have to sell, and must promote their product. . . . [R]estrictions can constrain appropriate prescribing, with subsequent harm to patients.⁹⁸

The FDA must balance the competing interests of ensuring that patients have access to drugs they need, pharmaceutical companies maintain their right to market their products, and doctors are able to prescribe opioids based on their medical judgment.⁹⁹ Countering the aggressive and potentially misleading pharmaceutical marketing with facts about the manufacturers' conduct could be an effective response.¹⁰⁰

IV. EXPANDING THE REMS PROGRAM TO ADDRESS RISKS CREATED BY DRUG MANUFACTURERS

Because the risk of writing unnecessary opioid prescriptions has far-reaching consequences,¹⁰¹ doctors must balance their duty to ethically prescribe with their duty to treat pain.¹⁰² To keep society from experiencing

97. See C. Lee Ventola, *Direct-to-Consumer Pharmaceutical Advertising: Therapeutic or Toxic?*, U.S. NAT'L LIBR. OF MED. (Oct. 2011), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278148/> (noting that the Supreme Court has upheld the right of pharmaceutical companies to advertise as protected under the First Amendment).

98. Jane C. Ballantyne, *Opioid Controls: Regulate to Educate*, 11 PAIN MED. 480, 480–81 (2010).

99. See generally Ameet Sarpatwari et al., *The Opioid Epidemic: Fixing a Broken Pharmaceutical Market*, 11 HARV. L. & POL'Y REV. 463, 483–84 (2017) (recommending that the FDA charge fees to pharmaceutical companies for fraudulent marketing and use the fees to fund research not sponsored by the pharmaceutical companies).

100. See Sarpatwari, *supra* note 99, at 484.

101. David L. Robinson, *Bridging the Gaps: Improved Legislation to Prohibit the Abuse of Prescription Drugs in Virginia*, 9 APPALACHIAN J.L. 281, 298 (2010) (showing that doctors' discretion in prescribing medication has led to an increase in addiction, which in turn has led to increased crime).

102. See *AMA Principles of Medical Ethics*, AM. MED. ASSOC., <https://www.ama-assn.org/about/publications-newsletters/ama-principles-medical-ethics> (last visited Jan. 26, 2020) ("A physician shall be dedicated to providing competent medical care, with compassion and respect for human dignity and rights."); Ben A. Rich, *Physicians' Legal Duty to Relieve Suffering*, 175 W.J. MED. 151, 152 (2001) (citing two cases where the courts found the defendant-prescribers

the negative consequences of overprescription, “physicians should remain vigilant when prescribing opioids and should . . . perform risk analysis and stratification . . . to ensure the benefits outweigh these important risks.”¹⁰³ Any regulation regarding prescriptions should be created with respect to this duty.

Even if the FDA is successful with its ongoing efforts to reduce the number of illegal opioids purchased online and in the streets, the market for illegal opioids still exists in the people with OUD whose addiction started with a legal prescription for an FDA-approved drug. To further complicate matters, FDA advisors may be receiving payments from pharmaceutical companies.¹⁰⁴ Since the advent of the REMS Program, there have been positive changes in the rates of opioid abuse, addiction, and overdose that indicate that it is possible to end the epidemic.¹⁰⁵ Currently, the biggest obstacle that remains—and is mostly untouched—is the influence that drug manufacturers have over doctors, consumers, and the REMS Program itself.¹⁰⁶ Congress gave the FDA the power to create the REMS Program with the intent

liable for gross negligence or recklessness for refusing to prescribe opioids to treat pain).

103. Kenneth Kirsh et al., *Characterization of Prescription Opioid Abuse in the United States: Focus on Routes of Administration*, 26 J. PAIN & PALLIATIVE CARE PHARMACOTHERAPY 348 (2012); see also Michael C. Barnes & Gretchen Arndt, *The Best of Both Worlds: Applying Federal Commerce and State Police Powers to Reduce Prescription Drug Abuse*, 16 J. HEALTH CARE L. & POL'Y 271, 273 (2013) (arguing that changes to federal regulation must provide national prescribers education that addresses patient health, safety, and welfare).

104. *Compare Light*, *supra* note 8 (analyzing systematic and qualitative evidence showing that, since pharmaceutical companies have been making large contributions to both the FDA and members of Congress, the FDA has sped up the approval process of drugs with risks that include hospitalization and death), and Alex Keown, *Investigation Examines Big Pharma Payments to FDA Advisers*, BIOSPACE (July 6, 2018), <https://www.biospace.com/article/investigation-examines-big-pharma-payments-to-fda-advisers/> (cautioning that “regulatory agencies failed to identify and disclose conflicts with the companies they are regulating,” including money paid by the pharmaceutical companies for travel and advice), with John LaMattina, *The Biopharmaceutical Industry Provides 75% Of The FDA's Drug Review Budget. Is This A Problem?*, FORBES (June 28, 2018, 7:42 AM), <https://www.forbes.com/sites/johnlamattina/2018/06/28/the-biopharmaceutical-industry-provides-75-of-the-fdas-drug-review-budget-is-this-a-problem/#3b6e088649ec> (affirming that the FDA's high rate of rejection for new drug applications indicates that the FDA is not controlled by the pharmaceutical companies that act as its financial backers).

105. See, e.g., Alice Park, *Doctors Are Writing Half as Many New Opioid Prescriptions as They Used To, Study Says*, TIME (Mar. 13, 2019), <https://time.com/5550686/opioid-prescribing-patterns-drop/>.

106. See Connors, *supra* note 93, at 244; Becker & Fiellin, *supra* note 32, at 205–06; C. Lee Ventola, *Direct-to-Consumer Pharmaceutical Advertising: Therapeutic or Toxic?*, 36 U.S. NAT'L LIBR. OF MED. 669, 673–74 (2011), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278148/>.

that the program could prevent abuse and misuse.¹⁰⁷ The language provided in the REMS Program statute allows the FDA to factor in drug manufacturer misconduct as increasing the risk of OUD.¹⁰⁸

A. Mandate REMS Program Training

There are other potential changes that could be made to the REMS Program to address issues discussed above, such as the influence that manufacturers have over each of the REMS for the drugs they produce, the influence manufacturers have through marketing, and that the REMS Program is not mandatory for any health care provider. To address this, Congress should act to make the Opioid Analgesic REMS Program training mandatory for opioid prescribers.

With the current Congress, statutory amendments are uncommon.¹⁰⁹ However, historically Congress has successfully passed legislation regulating opiates.¹¹⁰ Accordingly, an amendment to the REMS Program statute that addresses the opioid epidemic as a public health crisis is entirely feasible, especially considering the strong research supporting mandatory REMS Program training for prescribers as a means to reduce overprescription.¹¹¹

B. Provide REMS Information from CDER

Further, Congress should authorize an independent committee to compile the REMS for each pharmaceutical using the information gathered during the drug manufacturer's research and development phase and the FDA's approval process. However, these changes would require Congress to enable

107. Food & Drug Administration Amendments Act of 2007, 121 Stat. 823; 21 U.S.C.S. § 355-1(a)(1) (2007).

108. *Id.* § 355-1(b)(1), (3), (6) (referencing “new safety information, . . . an adverse event occurring in the course of the use of the drug in professional practice [and] . . . signal of a serious risk [from] other scientific data deemed appropriate by the Secretary”).

109. See Drew Desilver, *A productivity scorecard for the 115th Congress: More laws than before, but not more substance*, PEW RES. CTR. (Jan. 25, 2019), <https://www.pewresearch.org/fact-tank/2019/01/25/a-productivity-scorecard-for-115th-congress/> ([T]he 115th Congress passed 442 public laws, the most since the 110th Congress. . . . [Sixty-nine percent] were substantive”).

110. See H.R.3580 – FOOD AND DRUG ADMINISTRATION AMENDMENTS ACT OF 2007, <https://www.congress.gov/bill/110th-congress/house-bill/3580/actions> (last visited Jan. 22, 2020) (showing that the REMS Program statute passed in the 110th Congress with 405 votes); Benjamin Hammer, *The 115th Congress in Review*, GOVTRACK (Dec. 28, 2018), <https://govtrackinsider.com/the-115th-congress-in-review-76efbaadf03d> (reporting that “Congress unanimously passed two bills directly to respond to the opioid crisis”).

111. See Cepeda, *supra* note 38, at 83–84; Porada, *supra* note 43, at S61.

the FDA to make and enforce these changes. An act of Congress regulating the manufacturers would face the process of approval, which includes debates and votes.

After CDER concludes its evaluation, data is available from both the CDER team and the manufacturer.¹¹² Authorizing an independent committee to synthesize these two collections of data into a REMS—similar to the CDER advisory committees that provide the FDA with independent opinions and recommendations¹¹³—would produce a REMS Program with information from the manufacturer, supported by data from the FDA, and reviewed and compiled by an independent committee. This committee could provide doctors with clear and helpful information on the risks and benefits of drugs. Again, a statutory amendment of this nature is feasible.¹¹⁴

C. *Include Information on Manufacturer Misconduct in REMS Program*

The government has previously imposed fines on pharmaceutical companies that have proven themselves to be bad actors, but this has not stopped their misconduct.¹¹⁵ If the punishment is not deterring the manufacturers, then the punishment is ineffective. The FDA should expand the REMS on each opioid to include a notice of both past and current litigation and criminal charges against pharmaceutical companies and executives that relate to the opioid epidemic. The information should be available on the REMS Program website and on the particular REMS webpage for each pharmaceutical so that every prescriber that visits the page will see it at least once during the mandatory training. Currently, drug manufacturers are taking advantage of doctors' discretion. Making this information accessible and available would hold the drug manufacturer accountable and allow doctors to use their professional judgment and consider all relevant information,

112. *How Drugs are Developed and Approved*, U.S. FOOD & DRUG ADMIN. (Jan. 7, 2019), <https://www.fda.gov/drugs/development-approval-process-drugs/how-drugs-are-developed-and-approved>.

113. *Human Drug and Advisory Committees*, U.S. FOOD & DRUG ADMIN. (Oct. 5, 2017), <https://www.fda.gov/advisory-committees/committees-and-meeting-materials/human-drug-advisory-committees> (listing the human drug advisory committees, which include the CDER Advisory Committee and other FDA Advisory Committees).

114. *Cf.* Porada, *supra* note 43, at S59, S61 (stating that the drug manufacturers must make training available to prescribers on proper patient selection, patient counseling, and assessment for addiction and risk and that the training and that this training will likely become mandatory for prescribers).

115. Ken Stier, *Curbing Drug-Company Abuses: Are Fines Enough?*, TIME (May 30, 2010), <http://content.time.com/time/business/article/0,8599,1990910,00.html>.

including ongoing litigation against pharmaceutical companies. Through *Chevron* deference, the FDA has the authority to interpret its own statutes.¹¹⁶

Drug manufacturers' bad practices contribute to a higher rate of opioid prescriptions, which feeds into the epidemic.¹¹⁷ Despite all of the marketing that doctors and consumers are exposed to, doctors can still decline to prescribe an opioid if the prescription is not necessary. Giving doctors relevant information on risk created by the manufacturers would give doctors a more comprehensive picture of the opioid epidemic and the role that they themselves play, as well as the role of the manufacturer. Doctors need all of the relevant information available when deciding whether a prescription is appropriate, especially considering that there are often multiple manufacturers for the same drug,¹¹⁸ and an expanded REMS could give doctors a new perspective.¹¹⁹ Like the CDC and HHS believe, better information has the potential to positively affect the epidemic.¹²⁰ Accordingly, including this information would affect prescribers, patients, and the manufacturers, which makes notice-and-comment rulemaking the best means of implementing this change so that effected parties can provide their own viewpoint before the change takes effect.¹²¹

Currently, profits drive pharmaceutical companies,¹²² but that is not what health care is meant to be about. Considering the current regulatory system that allows for problems that create space for the opioid epidemic,

116. See *Chevron U.S.A. Inc. v. Nat'l Res. Def. Council, Inc.*, 467 U.S. 837, 861–62 (1984) (qualifying the FDA to interpret the language of the REMS Program statute to include risks created by the misconduct of drug manufacturers).

117. Sarpatwari, *supra* note 99, at 474 (stating that state instituted prescription drug monitoring programs that are rigorous are associated with a reduction in opioid related deaths).

118. See, e.g., *Approved REMS*, *supra* note 8 (listing all the manufacturers for each FDA approved drug under the REMS Program).

119. See e-mail from David Reitman, M.D., Medical Director of the Student Health Center at American University to author (Aug. 16, 2019, 1:27 EST) (on file with author) (“In general (except in certain situations) doctors really don’t have any idea who a given drug manufacturer is.”).

120. See Anuj Shah, *Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use—United States, 2006–2015*, 66 MORBIDITY & MORTALITY WKLY. REP. 265, 265–69 (2017), <https://www.cdc.gov/mmwr/volumes/66/wr/mm6610a1.htm>.

121. See generally Administrative Procedure Act, 5 U.S.C. §§ 551–559, 561–570a, 701–706 (2012).

122. See Chris Tomlinson, *Big Pharma makes big profits in opioid crisis*, HOUS. CHRON. (Oct. 17, 2017), <https://www.houstonchronicle.com/business/columnists/tomlinson/article/Big-Pharma-makes-big-profits-in-opioid-crisis-12281529.php> (detailing the lengths pharmaceutical companies have gone to in order to protect their profits).

“stakeholders from every perspective in the system agree that the program is overly burdensome, not very effective, and actually leaves them worse off than before.”¹²³ As people continue to suffer from OUD, the FDA should constantly be adapting to improve the REMS Program to the extent that it has the authority, and Congress should likewise continually endow the FDA with the authority it needs to adjust its programs to better address health risks.

CONCLUSION

With the rate of OUD and death cases by opioid overdose leveling out or shrinking, now is the perfect time for the FDA to act.¹²⁴ The FDA has the authority it needs to include information that would alert doctors to more risk factors than what is available through REMS today.¹²⁵ It has been well established and reported since 2006 that overprescribing is a major factor in the opioid epidemic, and the FDA has an opportunity to address the issue directly.¹²⁶ The CDC and HHS believe that better information and communication could substantially shrink the opioid epidemic, and without acting, the FDA would fail to address a grave risk that is just as dangerous as the side-effects of opioids.¹²⁷

123. Andrew Wilson & Christopher-Paul Milne, *FDA's Risk Evaluation & Mitigation Strategies (REMS): Effective & Efficient Safety Tool or Process Poltergeist?*, 66 FOOD & DRUG L.J. 569, 585 (2011).

124. Cepeda, *supra* note 38, at 83.

125. 21 U.S.C. § 393(b)(1) (2012) (requiring the FDA to promote public health by reviewing clinical research “promptly and efficiently” and undertaking the timely “marketing of regulated products”).

126. *U.S. Opioid Prescribing Rate Maps*, CTRS. FOR DISEASE CONTROL & PREVENTION, <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html> (last reviewed Oct. 3, 2018) (table 1); Teresa A. Rummans et al., *How Good Intentions Contributed to Bad Outcomes: The Opioid Crisis*, 93 MAYO CLINIC FOUND. FOR MED. EDUC. & RES. 344, 348 (2018) (stating that opioid prescription rates rose from 2006 to 2012 and that the FDA is among the groups attempting to better regulate opioids).

127. *See Safe Opioid Prescribing*, U.S. DEP'T OF HEALTH & HUMAN SERVS. (Aug. 14, 2019), <https://www.hhs.gov/opioids/prevention/safe-opioid-prescribing/index.html>; Dowell, *supra* note 63.